Foreword

Tuberculosis (TB) is a significant public health problem in Zimbabwe with high morbidity and mortality rates. Zimbabwe is one of the eight countries in Africa that appear in all of the three World Health Organization (WHO) lists of top 30 countries with high absolute numbers and or per capita incidence of TB, TB/HIV and Multi – Drug Resistant TB (MDR-TB). These countries contribute 80% of the world's burden of TB. The country conducted a TB prevalence survey in 2014 which led to a more accurate estimate of the burden of this disease. The estimated TB incidence rate in 2015 was 242 (95% CI 179-314) cases per 100 000 population per year and in the same year about 8 000 deaths were attributed to TB alone.

The focus of TB prevention, care and control is to detect all TB cases early, particularly the bacteriologically positive cases, and provide them with effective treatment in a patient centred approach so as to reduce individual short and long term TB morbidity and mortality, stop TB transmission and reduce or eliminate the risk of development of drug resistance. In 2015, TB treatment coverage, defined as the number of new and relapse cases that were notified and treated, divided by the estimated number of all incident TB cases that occurred in that year, expressed as a percentage, was estimated at 72% while the treatment success rate (the percentage of all notified TB patients who were successfully treated) was 81%. This performance is below the global benchmark target for effective TB care and prevention of at least 90% treatment coverage and 90% treatment success rate.

The TB epidemic in Zimbabwe is being fuelled by the parallel HIV epidemic, as in other countries in the Southern African Development Community (SADC) region. In 2015, 70% of notified TB cases were co-infected with HIV. HIV is known to make the diagnosis of TB more difficult, and of note is the fact that TB is the leading cause of death among people living with HIV (PLHIV). By 2016 the prevalence of HIV among adults aged 15-64yrs in Zimbabwe had declined to 14.6% from a peak of 29.3% in 1990 while coverage with anti-retroviral treatment (ART) among PLHIV had increased from 31.3% in 2007 to 86.8% in 2016. Of the adults on ART, 85.6% are virally suppressed. The declining HIV incidence and the increasing ART coverage may partly explain the continuing decline in TB case notification that begun in 2007.

The estimated burden of DR-TB in Zimbabwe are based on the 2015- 2016 National Drug Resistance Survey. The estimates among new and previously treated cases of MDRTB were 1.8% (95%CI 1.0 – 2.5)

and 4.6% (95%CI 3.0- 6.2) respectively. In 2016, 510 cases of MDR-TB cases were detected of whom 484 (95%) were initiated on treatment.

Zimbabwe is committed to ending TB and has adopted the End TB Strategy with its targets of reducing TB incidence by 90% and TB mortality by 95% by 2035 compared with the situation in 2015. Additionally, Zimbabwe has committed to the African regional framework to implement this strategy. The End TB Strategy also commits to ending catastrophic costs due to TB with a target of 0% by 2020. These targets are in line with the global Sustainable Development Goals (SDGs) which have also been adopted by the country. Achieving these targets will be the focus of national efforts over the era of the SDGs. This document serves to provide a guide to all health care workers, at all levels, in both the public and private health sectors including those directly responsible for clinical care and public health practitioners and planners, to increase the scope and quality of case finding and case holding practices in order to attain the targets of the End TB Strategy. The implementation of the practice recommendations outlined in this document will be carried out under the leadership of the National TB and Leprosy Control Programme (NTLP).

This document has been revised based on new evidence and best practices in line with the current international standards. Pursuant to its commitment to end TB, The Government of Zimbabwe (GoZ) through the Ministry of Health and Child Care (MoHCC) pledges to provide and mobilize the required human, material and financial resources for the full implementation of the recommended approaches outlined in this document until the epidemic of TB is ended in Zimbabwe, preferably sooner than 2035.

Brigadier General (Dr.) G. Gwinji

SECRETARY FOR HEALTH & CHILD CARE

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Glossary and Abbreviations

ACSM	Advocacy, communication and social mobilisation
ADR	Adverse Drug Reaction
aDSM	active Drug Safety Monitoring
AE	Adverse Event
AFB	Acid Fast Bacilli
ART	Anti- Retroviral Therapy
ATZ/r	Atazanavir/ritonavir
BB	Borderline – Borderline (for leprosy)
BCG	Bacillus Calmette-Guerine
BDQ	Bedaquiline
BL	Borderline -lepromatous
BMI	Body Mass Index
BT	Borderline Tuberculoid (for leprosy)
CBOs	Community Based Organisation
CFR	Case Fatality Ratio
CFZ	Clofazimine
CI	Contact Investigation
CKD	Chronic Kidney Disease
CP	Continuation Phase (of anti –TB treatment)
CPT	Cotrimoxazole Preventive Therapy
COPD	Chronic Obstructive Pulmonary Disease
CTBC	Community TB care
CSOs	Civil Society Organisations
CXR	Chest X- ray
DDI	Didanosine
DHE	District Health Executive
DHIS.2	District Health Information System.2
DMO	District Medical Officer
DOT	Directly observed treatment

DR-TB	Drug Resistant Tuberculosis
DST	Drug Susceptibility Testing
DTLC	District TB and Leprosy Coordinator
DTG	Dolutegravir
E	Ethambutol
EHF	Eye –Hand – Foot (score for leprosy)
EFV	Efavirenz
ENL	Erythema Nodosum Leprosum
EPTB	Extra –Pulmonary Tuberculosis
FAO	Food and Agricultural Organization
FBOs	Faith based organisation
FDC	Fixed Dose Combination
FLDs	Fine Line Drugs
FNA	Fine Needle Aspirate
GoZ	Government of Zimbabwe
H	Isoniazid
HCWs	Health Care Workers
HIV	Human Immuno-deficiency Virus
IGRA	Interferon Gamma Release Assay
INH	Isoniazid
INR	International Normalized Ratio
IP	Intensive Phase (of anti-TB treatment)
IPC	Infection, Prevention and Control
IPT	Isoniazid Preventive Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
ISTC	International Standards for Tuberculosis care
IUATLD	International Union Against Tuberculosis and Lung Disease (The UNION)
LF-LAM	Lateral Flow – Urinary Lipoarabinomannan assay
LFTs	Liver Function Tests
LFx	Levofloxacin
LL	Lepromatous –lepromatous

LPA	Line Probe Assay
LPV/r	Lopinavir/ritonavir
LTBI	Latent Tuberculosis Infection
MABC	Mycobacterium Abscessus Complex
MAC	Mycobacterium Avium Complex
MB	Multi- bacillary (for leprosy)
MCAZ	Medicines Control Authority of Zimbabwe
MDR-TB	Multi – Drug Resistant TB
MDGs	Millennium Development Goals
M&E	Monitoring and Evaluation
MoHCC	Ministry of Health and Child Care
MOTT	Mycobacteria Other Than TB
MoU	Memorandum of Understanding
MTB	Mycobacterium tuberculosis
MUAC	Mid-Upper Arm Circumference
NAC	National AIDS Council
NCDs	Non Communicable Diseases
NFI	Nerve Function Impairment
NGA	Naso –gastric aspirate
NGOs	Non-governmental organisation
NLTP	National Leprosy and TB Control Program
NPA	Naso –pharyngeal aspirate
NSAIDs	Non-steroidal anti-inflammatory drugs
NTM	Non –Tuberculous Mycobacteria
NTPs	National TB Control Programmes
NVP	Nevirapine
OC	Out of Control
OIE	World Organization for Animal Health
OPD	Outpatient department
PB	Pauci-bacillary (for leprosy)
PHC	Primary Health Care

PHEs	Provincial Health Executives
PIs	Protease Inhibitors
PLHIV	People Living with HIV
PMD	Provincial Medical Director
PMDT	Programmatic Management of Drug Resistant TB
PP	Private (health) provider
PPD	Purified Protein Derivative
PPE	Personal Protective Equipment
PPM	Public –Private Mix (for TB care and prevention)
PTB	Pulmonary Tuberculosis
PTLC	Provincial TB and Leprosy Coordinator
PZA	Pyrazinamide
R	Rifampicin
RR-TB	Rifampicin Resistant TB
R&R	Recording and Reporting
Rif	Rifampicin
RDT	Rapid Diagnostic Test
SAE	Serious Adverse Event
SADC	Southern Africa Development Community
SAT	Self-Administered Treatment
SCC	Short Course Chemotherapy
SDGs	Sustainable Development Goals
SLI	Second Line Injectable
SL-LPA	Second Line (medicine) – Line Probe Assay
SMS	Short Message Service
STR	Short Treatment Regimen
TB	Tuberculosis
TB-CNR	Tuberculosis Case Notification Rate
TB-DRS	Tuberculosis – Drug Resistance Survey
TB-IPC	Tuberculosis Infection and Prevention Control
TB-LAMP	TB –Loop Mediated Isothermal Amplification Assay
TBM	Tuberculous Meningitis

TDM	Therapeutic Drug Monitoring
TBPT	Tuberculosis Preventive Therapy
TnC	Treatment not completed (a leprosy outcome)
TS	Treatment Success
TST	Tuberculin Skin Test
TT	Tuberculoid- Tuberculoid (for leprosy)
VM-ST	Voluntary Motor- Sensory Test
WHO	World Health Organisation
XDR-TB	Extensive Drug Resistant TB
Z	Pyrazinamide
ZIMA	Zimbabwe Medical Association
ZN	Ziehl – Nielsen (staining)

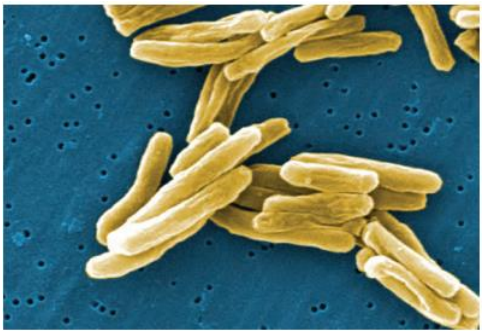
Chapter 1

Basics of Tuberculosis

Causative agent

Tuberculosis (TB) is an airborne disease caused by bacteria belonging to the *Mycobacterium tuberculosis* complex (Figure 1). The ***M. tuberculosis*** complex consists of ***M. tuberculosis*** and seven very closely related mycobacterial species *(M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti and M. mungi*). Most, but not all, of these species have been found to cause disease in humans but most TB disease is caused by *M. tuberculosis.*

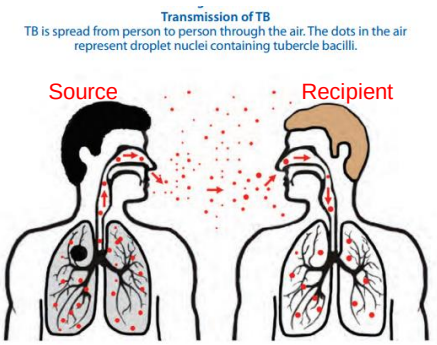
Figure 1 Mycobacterium Tuberculosis



Transmission of Mycobacterium tuberculosis

M. tuberculosis is carried in airborne particles, called droplet nuclei. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout or sing. Depending on the environment, these tiny particles can remain suspended in the air for several hours. Transmission occurs when a person inhales droplet nuclei containing ***M. tuberculosis***, and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs. The infectiousness of a person with TB disease is directly related to the number of bacilli they expel into the air.

Figure 2 Mechanism of transmission of Mycobacterium tuberculosis



Various factors determine the probability of transmission and acquisition of infection. These include host factors many of which are poorly understood, factors related to the pathogen and environmental factors. Table 1 below summarizes what is currently known about transmission of *Mycobacterium tuberculosis*.

Table 1 Factors that influence the transmission of Mycobacterium tuberculosis

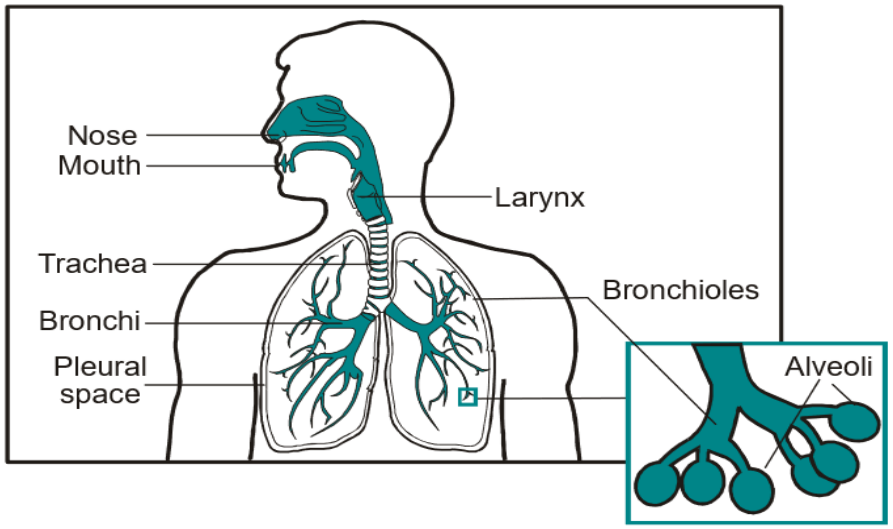
Factor	Description
Susceptibility	Immune status of the exposed individual
Infectiousness	Number of tubercle bacilli expelled into the air by the infectious individual
Environment	The sum total of the surroundings of a living organism which include the concentration of infectious droplet nuclei, space, ventilation, air circulation, lighting, air pressure and specimen handling in laboratory and related settings
Exposure	Duration, proximity and frequency of exposure to an infectious individual

Transmission of *Mycobacterium tuberculosis* is facilitated by exposure to a greater volume of droplet nuclei, in small enclosed spaces that are poorly lighted and ventilated and with long duration of contact and closer proximity to the infectious person

Pathogenesis of TB

When a person inhales air that contains water droplets containing M. tuberculosis, most of the larger droplets become lodged in the upper respiratory tract (the nose and throat), where infection is unlikely to develop. However, smaller droplet nuclei may reach the small air sacs of the lung (the alveoli), where infection is more likely to become established. (See Figure 3 below).

Figure 3 The anatomy of the respiratory system.



In the alveoli, some of the tubercle bacilli are killed, but a few multiply in the alveoli and enter the bloodstream and spread throughout the body. Bacilli may reach any part of the body. The areas where TB infection develops include the upper portions of the lungs, as well as the kidneys, brain and bone. Within 2 to 8 weeks of entry of the bacilli into the body, the body's immune system usually intervenes, halting multiplication and preventing further spread of the tubercle bacilli. When infection is established but the TB bacilli are not actively replicating and there is no apparent disease, the person is said to have Latent TB Infection (LTBI). LTBI is a function of a complex host –pathogen relationship that is poorly understood currently. In simple terms during LTBI the individual's immune system is able to keep the infecting bacilli under control and inactive through the development, production and activation of immune cells that surround the tubercle bacilli, forming a shell that acts as a fence and prevents the bacilli from replicating. People who have LTBI are NOT infectious i.e. they cannot spread the infection to other people. These people usually have a normal chest x-ray. It is important to remember that LTBI is not considered a case of TB. Major similarities and differences between LTBI and TB disease are shown in Table 2 below.

Table 2 Differences between LTBI and Active TB in the Lungs

Latent TB Infection (LTBI)	**TB Disease (in the lungs)**
Inactive tubercle bacilli in the body	Active tubercle bacilli in the body
Tuberculin skin test may be positive or negative	Tuberculin skin test may be positive or negative

Chest x-ray usually normal	Chest x-ray usually abnormal
Sputum smears and cultures negative	Sputum smears and cultures may be positive
No symptoms	Symptoms such as cough, fever, weight loss
Not infectious	Often infectious before treatment
Not a case of TB	A case of TB

Some people with LTBI progress on to develop TB disease. In general, it is accepted that persons who progress from LTBI to active TB have failure of immunological mechanisms that have hitherto prevented multiplication of MTB. The risk that TB disease will develop following infection is higher for some people than for others. Active TB disease that develops within a few months or years (1-2) after infection is labelled **primary TB disease**, while disease that develops many years (>2 years) after infection is called **post primary or reactivated TB**. The risk of developing TB disease following infection varies with various host factors such as concurrent infection with HIV, presence of diabetes mellitus, presence of chronic kidney and many others. In non HIV infected persons the lifetime risk of developing TB following infection is in the region of 10% which means that the majority of persons infected with MTB, currently estimated to be about a third of the world population, will never develop TB disease.

Further Reading

1. https://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf)

Chapter 2

The Burden of TB
Prevention, Care and Treatment Strategies

The Global Burden of TB

In the 2016 WHO Global TB report, WHO revised upwards the burden of TB disease globally that occurred between 2000 and 2015. This was based on evidence accruing from TB disease prevalence surveys and other epidemiological pieces of evidence. In 2015, an estimated 10.4 (range 8.7 -12.2) million people developed TB worldwide. Of these 61% were in Asia, 26% in Africa, 7% in the Mediterranean region, 3% in Europe and another 3% in the Americas. The estimated incidence of TB fell by 1.4% per annum between 2000 and 2015, however, the global decline in TB incidence increased marginally between 2014 and 2015 to 1.5%. Of the 10.4 million cases of TB that occurred in 2015, only 6.4 million were reported to national TB control programs, implying that nearly 4 million cases of TB were either not identified at all or if they were identified they were not reported to the relevant authorities in countries. Between 2000 and 2015, the incidence of TB declined by more than 4% in several countries including Zimbabwe (11%) , Lesotho (5%) , Tanzania (6.8%), Ethiopia (6.7%), Namibia (6.2%), Kenya 5.0% and the Russian Federation (4.2%).

In 2015, TB is estimated to have killed 1.4 (range 1.2 – 1.6) million HIV negative persons and an additional 0.4 (range 0.3 -0.5) million HIV infected persons globally, a total of 1.8 million deaths. Tuberculosis is thus the most common cause of death from an infectious diseases and the 5th commonest cause of death from all causes. Mortality rates from TB per 100,000 population fell by 34% between 2000 and 2015 and by 2.7% between 2014 and 2015. The WHO recently introduced the concept of the Case Fatality Ratio (CFR), defined as the number of TB deaths divided by estimated number of incident cases in the same year, expressed as a percentage. In the same year, CFR was estimated at 17%. If the targets of the End TB Strategy are to be achieved, the CFR will need to fall to 10% and 6% by 2020 and 2025 respectively.

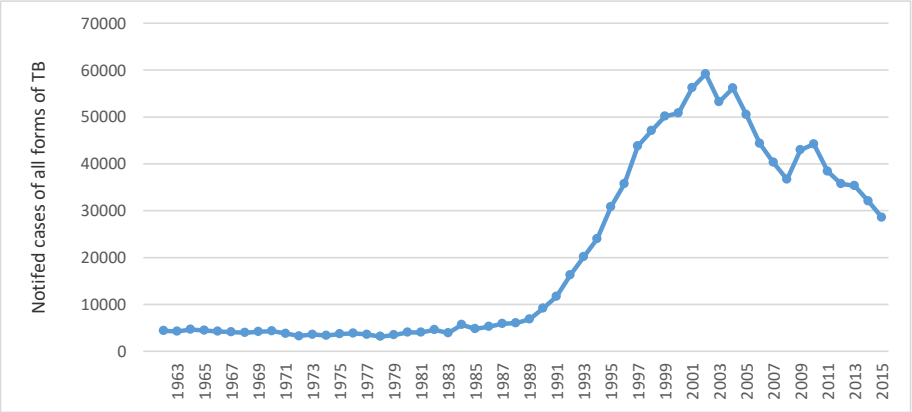
WHO estimates that in 2015, 3.5% (95% CI 2.7 -5.1%) of new patients and 21% (95% CI 15-28%) of previously treated patients had MDR-TB. This translates to 580,000 (range 520,000 -640,000) people having had MDR-TB in that year. It was also estimated that MDR-TB killed 250,000 (range 160,000-340,000) people in 2015. There is a worrying trend of increasing proportion of MDR-TB cases among notified cases.

Of the incident cases of TB that occurred globally in 2015, 11% were in persons who are concurrently living with HIV. Most of these cases (75%) were in the African region where the average HIV sero – prevalence among TB cases tested for HIV was 36% overall but with rates of greater than 50% in countries of Southern Africa.

Tuberculosis in Zimbabwe

Tuberculosis is a major public health threat in Zimbabwe. Tuberculosis Case Notification Rate (TB-CNR) was stable for several decades between the 60's and 80's at about 100/100,000, but this situation dramatically changed in the 90's when TB-CNR increased year on year until 2002 when a peak was reached (450/100,000). Since then the TB-CNR has been declining steadily with variations in the rate of decline on a year by year basis (212/100, 000 in 2015).

Figure 4 Tuberculosis Case Notification in Zimbabwe 1962-2015



In 2015, 28 225 TB cases were notified to the NTLP of which, 40% were bacteriologically confirmed pulmonary TB (PTB) cases, 46% were clinically diagnosed PTB cases and 14% were extra–pulmonary TB cases (EPTB). The proportion of re-treatment cases increased from 6% of all notified cases in 2007 to 12% in 2014. As in the rest of the world, the population most affected by TB was the economically productive age group between 25 and 44 years. In the population below 24 years, there were more females than males affected by TB and in the 25-34 years age group, rates of TB were similar in males and females, while in all other age groups TB rates were higher in males compared to females. There were district variations in TB case notifications with districts in the Southern parts of the country more affected by TB compared to Northern districts. These variations in TB–CNR appeared to be related to variations in HIV prevalence. Tuberculosis case notification in children of ages 14 years and below, as a proportion of

all notified TB cases, has averaged 5-6% in the last five years.

The Zimbabwe NTLP has identified the following groups of people as the vulnerable or key populations for active TB:

- Persons living with HIV Infection (PLHIV).
- Children, especially those 5 years of age and below.
- Current and ex-miners.
- Persons living in correctional facilities including inmates, the officers who work in these facilities and their families.
- Health Care Workers.
- Persons living with diabetes mellitus.
- Persons receiving immunosuppressive therapies.
- Persons with chronic kidney disease.
- Tobacco smokers.
- Persons living in urban slums.
- Persons living in remote rural areas with poor access to health services.

In 2015, 96% of all TB cases were tested for HIV; 70% were HIV positive. Of the HIV positive TB cases, 96% were put on Cotrimoxazole Preventive Therapy (CPT) and 86% were commenced on anti-retroviral medicines.

Principles of Tuberculosis Prevention, Care and Control

Tuberculosis prevention, care and control is based on the following key principles:

1. Early and complete identification of incident TB cases with prompt initiation of effective treatment so as to reduce TB morbidity including clinical illness that may result from long term sequelae of TB, prevent death and stop transmission of the causative agent.
2. Treatment of active TB disease with multiple medicines to prevent *Mycobacterium tuberculosis* from developing resistance to any medicine.
3. Providing appropriate support to persons being evaluated for TB or on treatment for TB to ensure full adherence to diagnostic processes and treatment until completion, while avoiding processes or procedures that have the potential to increase diagnostic or treatment costs to the patient and/or his/her family.
4. Providing an enabling environment, with adequate resources (human, financial, commodities and work environments) to ensure effective and efficient delivery of TB services.
5. Proactively and routinely screening and testing groups of patients known to be at risk of active TB and promptly linking those found to have TB to care and treatment.

6. Provision of Tuberculosis Preventive Therapy (TBPT) to individuals who are infected with *Mycobacterium tuberculosis* but, at the time of evaluation do not have clinical, radiologic and/ or bacteriologic evidence of active TB disease.
7. Engaging multiple partners and stakeholders in the TB response including private health care providers, non-governmental organizations, community based organizations and communities themselves in the TB response.
8. Vigorously pursuing efforts to eliminate poverty, which is the major driver of TB.
9. Providing an environment for creativity and innovation to thrive with rapid adaptation of new ideas, approaches and practices.

These principles have now been packaged into a comprehensive strategy called the End TB Strategy which is shown below:

Figure 5 The End TB Strategy

The End TB Strategy at a glance

VISION	**A WORLD FREE OF TB** — zero deaths, disease and suffering due to TB			
GOAL	**END THE GLOBAL TB EPIDEMIC**			
INDICATORS	MILESTONES		TARGETS	
	2020	2025	SDG 2030*	END TB 2035
Percentage reduction in the absolute number of TB deaths *(compared with 2015 baseline)*	35%	75%	90%	95%
Percentage reduction in the TB incidence rate *(compared with 2015 baseline)*	20%	50%	80%	90% (approximately 10 per 100 000 population)
Percentage of TB-affected households experiencing catastrophic costs due to TB *(level in 2015 unknown)*	0%	0%	0%	0%

PRINCIPLES

1. Government stewardship and accountability, with monitoring and evaluation
2. Strong coalition with civil society organizations and communities
3. Protection and promotion of human rights, ethics and equity
4. Adaptation of the strategy and targets at country level, with global collaboration

PILLARS AND COMPONENTS

1. INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION
   - A. Early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
   - B. Treatment of all people with TB including drug-resistant TB, and patient support
   - C. Collaborative TB/HIV activities, and management of comorbidities
   - D. Preventive treatment of persons at high risk, and vaccination against TB
2. BOLD POLICIES AND SUPPORTIVE SYSTEMS
   - A. Political commitment with adequate resources for TB care and prevention
   - B. Engagement of communities, civil society organizations, and public and private care providers
   - C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
   - D. Social protection, poverty alleviation and actions on other determinants of TB
3. INTENSIFIED RESEARCH AND INNOVATION
   - A. Discovery, development and rapid uptake of new tools, interventions and strategies
   - B. Research to optimize implementation and impact, and promote innovations

* Targets linked to the Sustainable Development Goals (SDGs).

Further Reading

1. Global Tuberculosis Report 2016
2. End TB Strategy

Chapter 3

The National TB and Leprosy Control Programme

Rationale for the new TB management guidelines

The Zimbabwe National TB and Leprosy Control Program (NTLP) last developed its TB management guidelines in 2010. These guidelines have served the NTLP well over the six years they have been in use. However, the landscape has significantly shifted in recent years in the field of TB prevention and care and the existing guidelines are no longer sufficient or comprehensive enough for the purpose for which they were developed. When the existing guidelines were developed, global TB care and control was based on the Stop TB Strategy which was intended to achieve TB control targets aligned to the Millennium Development Goals (MDGs) to be achieved by 2015. The Stop TB Strategy has since shifted to the End TB Strategy with new thinking about how TB prevention and care should be approached in order to achieve ambitious but achievable targets to end the global TB epidemic by 2035. A range of new TB diagnostic tests became available after 2010 and have been endorsed by WHO. These include the Xpert MTB/Rif assay (GeneXpert) which was endorsed by WHO towards the end of 2010 and the Lateral Flow Urinary Lipoarabinomannan assay (LF-LAM) , molecular Line Probe Assays (LPA) capable of providing susceptibility information for second line anti-TB medicines and the TB – Loop Mediated Isothermal Amplification Assay (TB- LAMP) which were endorsed by WHO in 2016. There has also been a greater focus on active TB case finding through routine and systematic screening of groups of persons known to be at risk of TB infection and progression to active TB disease. While previously the Chest X-Ray (CXR) was assigned lower priority in the TB screening and diagnostic process, experience gained in numerous TB prevalence surveys in various countries suggested that the CXR should be assigned a higher priority because of its higher sensitivity compared to symptom screening alone.

Finally, there has been a quantum leap in the development of new medicines for TB which has seen the introduction of two completely new medicines, Bedaquiline and Delamanid while a number of repurposed medicines including the fluoroquinolones, Linezolid and Clofazimine have found an increasingly important role in the treatment of TB, especially DR-TB. There have also been changes in global TB indicators with WHO recommending that countries adopt a set of ten key indicators to monitor the TB response as implementation of the End TB Strategy is pursued.

With all these developments, it was important that the NTLP revises its TB management guidelines to incorporate these changes in order to guide health care workers and program planners, managers and

implementers on the recommended modern approaches to the prevention, care and treatment of various forms of TB.

The results of the national TB disease prevalence survey and the recommendations of the recently conducted external program review and TB disease epidemiological assessment, provided additional reasons for the revision of the TB management guidelines.

National Tuberculosis and Leprosy Control Programme

The National Health Policy in Zimbabwe espouses equity and equality in health, consistent with the economic policy embedded in "Growth with Equity: A People's Right". The policy focuses on addressing inequitable access to health and health services to reduce TB incidence and mortality and to eliminate TB associated catastrophic costs in alignment with the global End TB Strategy.

The TB Policy

The five key points of the TB policy are:

1. Tuberculosis screening and diagnosis using the Xpert MTB/Rif assay and sputum smear microscopy for follow up, provided free of charge.
2. The laboratory diagnosis of TB and chemotherapy for all forms of TB, provided free of charge in the public health sector.
3. TB services available at all levels of the health delivery system and integrated into the primary health care system to ensure efficient case finding and case holding.
4. Collaborative TB/HIV activities carried out at all levels.
5. All patients on treatment for TB receive directly observed treatment either by a health care worker or a community health care worker.

The National Tuberculosis Control strategy

Vision: A TB-free Zimbabwe

Goal: To dramatically reduce the transmission, morbidity and mortality of tuberculosis in Zimbabwe, in line with the SDGs and the End TB Strategy.

Objectives:

1. To reduce TB incidence by 90% compared to 2015 baseline by 2035.
2. To increase TB treatment coverage from 72% in 2015 to at least 90% by 2035.
3. To increase treatment success rate from 81% in 2014 to at least 90% by 2035.
4. To reduce the absolute number of TB deaths by 95% compared to 2015 baseline by 2035.
5. To reduce catastrophic costs incurred by TB patients and affected families to 0% by 2025 and to sustain this target thereafter.

The expected impact of achieving and maintaining the above objectives and targets include:

- Rapid reduction of the burden of TB in the country.
- Prevention of the development and expansion of resistance to anti-TB medicines.
- Reduced social and economic burden due to TB placed upon affected patients, families and communities.

The Zimbabwean TB control strategy is based on the three pillars and principles of the Global End TB Strategy.

Structure and roles of the NTLP at various levels.

The Central Level

The central unit of the NTLP coordinates policy formulation and resource mobilization for TB prevention and care. The interventions pursued by the NTLP are guided by a strategic plan which is aligned to the Global End TB strategy. The central unit of the NTLP has strategic, managerial, leadership and technical roles to guide the implementation of the programme. These roles include but are not limited to:

- Development of national policies, strategies and interventions for TB care and prevention.
- Identifying and mobilizing resources, including financial, human and other types of resources for TB prevention and care.
- Coordination and harmonization of efforts by partners.
- Programme supervision.
- Defining, resourcing and coordination of TB research activities.
- Conduct of monitoring and evaluation activities.

- Strengthening collaboration between TB and HIV & AIDS programmes to ensure better management of co-infected patients.

Additional roles include strategic planning, development of annual work plans, preparation of budgets and preparation of technical and financial reports. The NTLP works closely with various directorates in the MoHCC such as laboratory, pharmacy and environmental health to ensure a comprehensive health sector response to TB. Efforts continue to be pursued to loop in other government ministries, the National AIDS Council (NAC), Non-Governmental Organisations (NGOs), the private sector and bilateral and multi-lateral organisations in the development and implementation of TB related strategies, interventions and activities to develop a strong multi–sectorial approach to TB prevention and care. Other responsibilities include recruitment of technical staff, training and compiling national and international reports.

Central Hospital Level

Central hospitals are ideally referral institutes for complicated TB cases who need specialised diagnostic and treatment services. They may, however, also serve as the health facilities where surrounding communities first seek care when they are unwell.

Practice Recommendation

All central hospitals should keep records of all TB patients managed in their institutions and regularly prepare and submit reports of these patients to the central level of the NTLP. This is best done by a TB focal person and therefore all central hospitals should appoint a TB focal person to coordinate TB services in the hospital including recording and reporting patients to the NTLP.

Central Hospitals should

- **Develop and implement a clear referral plan and strong feed-back mechanism to ensure that patients do not get lost when referred back to lower levels of the health care system.**
- **Ensure the TB focal person of the central hospital closely liaises with district and regional coordinators to ensure a) TB case notification of all patients diagnosed with TB at the institution b) treatment continuation after discharge or release from the central hospital and c) the conduct of contact identification, tracing, investigation and management.**

The Provincial Level and Metropolitan Cities (Harare and Bulawayo)

At provincial level, the Provincial Medical Director (PMD) is overall in charge of the TB programme, with technical assistance the provincial TB/HIV and Leprosy officer. The TB/HIV and Leprosy officer works with provincial TB & Leprosy coordinator (PTLC). At the local authority level the Director of Health Services takes overall responsibility for TB prevention and care and works with a TB focal person, who in turn is supported by TB coordinators.

Practice recommendations

All provincial health executive teams led by the PMD and assisted by the provincial TB/HIV/Leprosy officers and the provincial TB and leprosy coordinators should develop quarterly and annual TB prevention and care operational plans which are aligned to the national TB annual plan.

The plan should include:

- Activities to build capacity of health care workers on the full range of TB activities including uptake of new tools and approaches.
- The management of TB logistics and resources such as TB data collection tools, laboratory consumables and anti-TB medicines.
- Plans for the conduct of monitoring and evaluation of the TB programme to assess and track performance.
- Implementation of and enhancement of TB/HIV collaborative activities.
- Systematic screening of identified high risk or vulnerable populations, enhancement of community approaches and the engagement of the community in TB prevention and care.
- Plans for engaging and enhancement of the participation of non–state providers (PPM) in TB prevention and care activities.

The provincial plan should also include supervisory activities, the conduct of prioritized local level operations or implementation research and enhancement of TB data management including local data utilization.

The District Level

The District Health Executive (DHE) under the leadership of the District Medical officer (DMO) supervises the delivery of all health care services in hospitals and primary level centres. The DMO working with the District TB and Leprosy Coordinator (DTLC) has overall responsibility for the organization and implementation of TB prevention, care and treatment activities in the district.

Practice recommendations

All DHEs led by the DMO and assisted by the DTLC should develop quarterly and annual TB prevention and care operational plans which are aligned to the provincial TB annual plan.

The plan should include activities related to

1. Building capacity of health care workers on the full range of TB activities including the uptake of new tools and approaches.
2. The management of TB logistics and resources such as TB data collection tools, laboratory consumables and anti-TB medicines.
3. The conduct of monitoring and evaluation of the TB programme to assess and track performance.
4. Implementation of and enhancement of TB/HIV collaborative activities.
5. Systematic screening of identified high risk or vulnerable populations, enhancement of community approaches and the engagement of the community in TB prevention and care.
6. Engaging and enhancement of the participation of non-state providers (PPM) in TB prevention and care activities.

The district plan should also include supervisory activities, the conduct of prioritized local level operations or implementation research and enhancement of TB data management including local utilization.

Primary Care Level

Tuberculosis services are integrated into the Primary Health Care (PHC) system. The PHC facilities are responsible for:

1. Identification of presumptive TB cases through routine screening of all patients accessing care at that level.
2. Testing of presumptive cases for TB and treatment of confirmed TB cases with appropriate patient support to ensure adherence.
3. Linkages with the community directly or through community health care workers.
4. Patient recording and reporting

These functions are further outlined in sections of these guidelines that describe the responsibilities of clinicians and health care workers who work directly with patients to diagnose, treat and record and report patients.

The Community Level

A community-based approach remains a key pillar in the National Health strategic framework. The community based approach is undertaken by both government and non- government actors including NGOs and Community Based Organizations (CBOs).

Practice recommendations

The PHC facility is the entry point into the community and thus all organisations who are working or planning to work in the community to enhance the community TB response should ensure that the network of PHC facilities in the areas they work or intend to work are fully engaged in the development and implementation of community based interventions.

At the community health level community health care workers and volunteers work with communities to

- Raise knowledge and awareness about TB and thus reduce TB associated stigma and discrimination.
- Promote appropriate TB related health seeking behaviour.
- Identify presumptive cases of TB and support them to get tested for TB.
- Support patient on treatment to adhere to treatment.
- Identify and retrieve persons who have interrupted treatment.
- Identify and screen contacts of patients with TB to identify those who need to be tested for TB.

Further details on community engagement and the recommended practices are provided in chapter 12 of these guidelines.

Chapter 4

Tuberculosis Screening and Diagnosis at Health Care Settings

Screening for TB in health care settings

Practice Recommendation: All patients presenting to health care facilities should be screened for TB.

Justification: Although a recent study in Zimbabwe suggested that health system delays in TB diagnosis are uncommon, there is a persistent risk of delays in TB diagnosis as a result of health system factors if proactive action is not taken and sustained to promote TB screening among persons accessing care at the various levels of the health service delivery system. Delays in TB diagnosis or missed opportunities to diagnose the disease facilitates transmission of *MTB* and may lead to poor outcomes including deaths and the development of long term complications of TB such as post TB fibro- cavitary lung disease. To forestall health system delays in TB diagnosis, the NTLP recommends that all patients making contact with the health care system be screened for TB in order to contribute to early and complete diagnosis of this disease.

Situations where this recommendation may not apply

The provision of emergency care in patients presenting with life threatening conditions should not be delayed because of TB screening; screening and or testing should be carried out when patients have been stabilised.

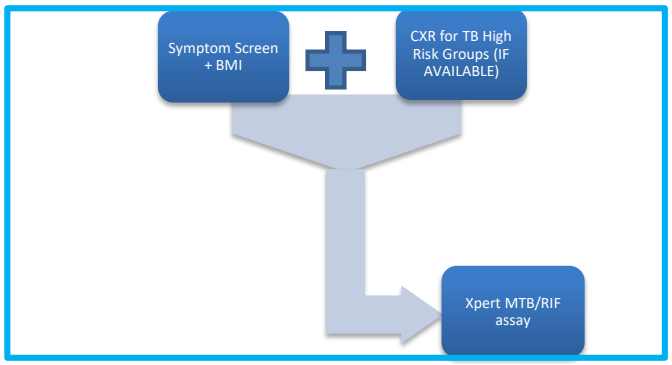
Steps to ensure successful implementation of the recommended practice

To enable successful screening of patients presenting at health care facilities, the NTLP will work with health facility managers to ensure that health care workers from all departments of the facility are trained on TB case management, screening tools are made available and become part of the facility's patient registration and triaging tools and TB diagnostic tests are always available or easily accessible.

Practice Recommendation: All adult patients should be screened for TB using a symptom enquiry of any of the following; fever, night sweats and loss of weight, in addition to cough of greater or equal to 1 week duration; for PLHIV, current cough of any duration. This is followed by the measurement of weight/height to calculate body mass index($BMI = \frac{weight}{height^2}$). If chest X-ray is available, this can also be used for screening among high risk groups.

Practice Recommendation: All adult patients with a positive symptom screen and/or a low BMI should have a chest x-ray (unless unavailable).

Figure 6 Tuberculosis screening and Testing Algorithm



Justification: While many patients with pulmonary TB will have fever, night sweats and loss of weight with a cough, these symptoms are neither sensitive nor specific enough for TB. The symptom screen using current cough, fever, night sweats and loss of weight has a low sensitivity for TB but a high negative predictive value for TB in HIV infected persons. The addition of BMI with a cut -off point of about 17 kg/m² may increase the sensitivity of symptom screening and allow optimization of the use of Xpert MTB/Rif assay. In TB prevalence surveys, including the one done in Zimbabwe, the CXR was more sensitive than symptom screening, however, non-targeted use of the chest x-ray at the health care setting level may lead to excessive use of this tool with the attendant increased radiation risk to patients and health care workers and costs.

Situations where this recommendation may not apply.

The CXR step in the screening algorithm should be omitted in those situations where access to this tool will entail a significant cost or time burden on the patient and could result in delays in confirming a diagnosis of TB.

Steps to ensure successful implementation of the recommended practice.

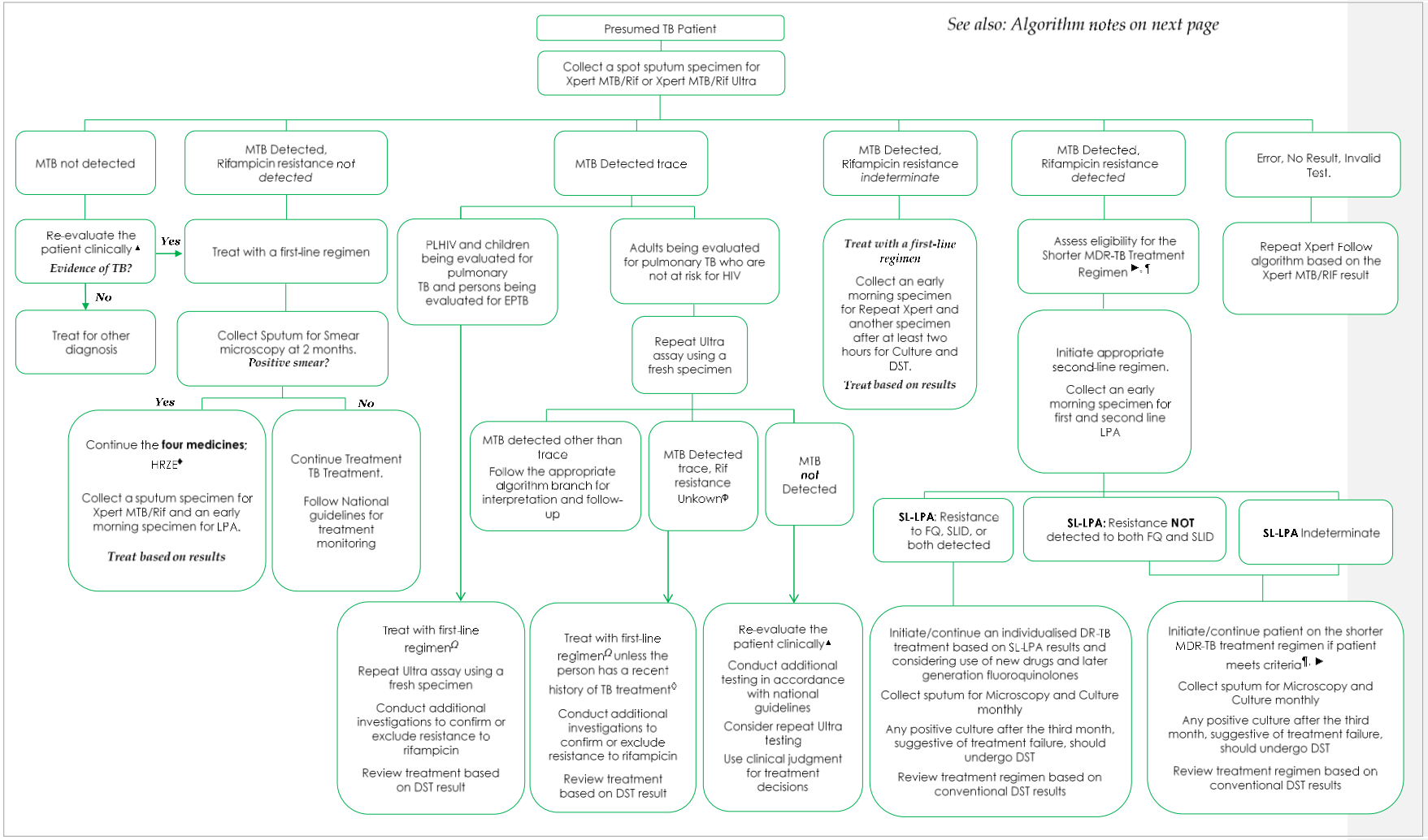
The NTLP will make efforts to make the CXR available to every Zimbabwean who needs this test. Naturally this process will take time but the commitment has been made and will be vigorously pursued in the course of implementation of these guidelines. The measurement of BMI should be possible even now, since nearly all health care facilities have weight and height measurement instruments. Going forward the NTLP will, working with others in the MoHCC and beyond, ensure that every health facility has these instruments which will serve not only the TB response but also the response to hypertension and diabetes which are among the most important non communicable diseases (NCDs) that Zimbabwe is confronting currently.

Diagnosis of Pulmonary TB (PTB) in adults.

Recommendation 4: All adult patients with a positive symptom screen and/or a low BMI and/or an abnormal chest x-ray should have ONE spot sputum sample collected and sent to the nearest Xpert MTB/Rif site. The sample is tested for TB using the Xpert MTB/Rif or Xpert MTB/Rif Ultra assay. The following are situations requiring collection of second specimen: i) MTB detected trace on Ultra; ii) error/no result/invalid test; iii) MTB detected Rifampicin resistance indeterminate (early morning and another one after at least two hours) and iv) MTB detected Rifampicin resistance detected (early morning for 1st & 2nd line LPA).

Justification: The Xpert MTB/Rif assay is a WHO recommended Rapid Diagnostic Test (RDT) with a high sensitivity and specificity for the diagnosis of disease due to *MTB* when compared to microscopy and in addition it provides information on rifampicin susceptibility which allows patients to be treated with appropriate medicine regimens. Figure 7 below summarises the possible outcomes from Xpert MTB/Rif testing and the course of action to be taken.

Diagnostic and Treatment Algorithm for Presumptive TB Patients



Algorithm Notes

▲ *Further investigations may include chest x-rays, additional clinical assessments, other biological specimens (tissue aspirates and biopsies), clinical response following treatment with broad spectrum anti-microbial agents and repeat Xpert MTB/RIF testing. For patients being evaluated for TB who are HIV positive and have a CD4 count of less 100 cells/µl or are seriously ill, perform TB-LAM test according to national guidelines.*

♦ *Treatment with the four drugs (HRZE) should be continued for the full duration of treatment unless results of LPA demonstrate susceptibility to isoniazid where the patient will be switched to continuation phase. The period extended on four drugs after the intensive phase, while awaiting LPA results, is considered as part of the continuation phase*

► *Patients may be initiated on the shorter MDR-TB regimen if they are assessed as being at low risk of having resistance to FQs and to SLIDs and meets the eligibility requirements. In patients at high risk of resistance, design of the treatment regimen to initiate may be guided by SL-LPA if the results can be obtained rapidly.*

¶ *The shorter MDR-TB regimen may be used in MDR-TB patients who do not have the following conditions:* ***i)*** *confirmed resistance, or suspected ineffectiveness, to a SLID or FQ* ***ii)*** *previous exposure for >one month to a SLID or FQ* ***iii)*** *A contraindication to any medicines in the shorter MDR-TB regimen* ***iv)*** *Pregnancy,* ***v)*** *Close contact with a patient that has resistance to FQ/ SLID*

φ *MTB detected trace results do not provide any information regarding rifampicin resistance or susceptibility.*

◊*For adults who successfully completed a course of therapy within the past 2 years (i.e., recent TB treatment), the possibility of both Ultra trace results being false-positive results because of the presence of non-viable bacilli must be considered. Clinical decisions must be made on all available information and clinical judgment.*

Ω*Patients should be initiated on a first-line regimen according to national guidelines with exception of the patient at very high risk of having MDR-TB or if a second Ultra assay indicates rifampicin resistance. Such patients should be initiated on an MDR-TB regimen.*

*****DST****=Drug susceptibility testing;* ***SL-LPA****=Second-line line probe assay;* ***FQ****=Fluoroquinolone;* ***SLID****=Second-line injectable drugs;* ***LAM test****=Lipoarabinomannan Test;* ***EPTB****=Extrapulmonary Tuberculosis;* ***PLHIV****=People Living with HIV;*

Diagnosis of Extra Pulmonary TB

Case finding among patients with presumptive extra-pulmonary (EPTB) forms of TB

Practice Recommendations: All patients presenting with non-respiratory symptoms especially in the presence of a fever, sweating at night and/or loss of weight should be evaluated for tuberculosis.

Justification: A high index of clinical suspicion is required for the diagnosis of EPTB. Symptoms of EPTB will of course vary with the organ that is involved, however, many patients will also experience a generalized systemic or constitutional disturbance including fever, night sweating and loss of weight. The presence of these symptoms especially in a patient with symptoms that have lasted several weeks (sub-acute or chronic presentation) should alert the clinician to the possibility of TB as the underlying diagnosis. Thus evaluation for TB should be carried out on all patients presenting with a generalized or systemic disturbance with or without organ specific symptoms. Extra- pulmonary TB carries a poor prognosis especially if it occurs in HIV infected persons and thus early diagnosis and initiation of effective treatment may be life-saving. Table 4 below shows the most common forms of EPTB and the preferred sample to collect for TB diagnostic testing.

Table 3 Clinical symptoms and signs and specimen selection for diagnosis of EPTB

	TYPICAL CLINICAL PRESENTATION	INVESTIGATIONS
TB adenitis	Asymmetrical, painless non tender lymph node enlargement usually for > 1month, +/- discharging sinus, especially in the neck	Fine needle aspiration (FNA) for Xpert MTB/Rif or Ultra assay and cytological examination. Node biopsy can also be sent for Xpert MTB/Rif or Ultra assay, TB culture and histological examination
Pleural TB	Chest pain, shortness of breath, reduced breath sounds and stony dullness on percussion	CXR to confirm pleural effusion, thoracocentesis (pleural fluid aspiration) and pleural fluid analysis (biochemistry and cell analysis), pleural biopsy submitted in saline and formalin for Xpert MTB/Rif or Ultra assay, TB culture and histological examination
TB meningitis	Headache, irritability/ abnormal behaviour, confusion, vomiting), lethargic/reduced level of consciousness, convulsions, neck stiffness, bulging fontanelle in young children, cranial nerve palsies, plus the constitutional symptoms of TB	Lumbar puncture obtain CSF for biochemistry, Xpert MTB/Rif or Ultra assay, microscopy, culture and sensitivity for other causes of meningitis

Miliary TB/ Disseminated TB	Non-specific, lethargic, persistent fever, wasting	Chest radiography and lumbar puncture to obtain CSF for biochemistry, Xpert MTB/Rif or Ultra assay /blood for TB culture, liver and or splenic aspirates and other tests
Abdominal TB/ Peritoneal TB	Abdominal swelling with ascites or abdominal masses	Abdominal ultrasound and ascitic tap for biochemistry, Xpert RIF assay/ ultra sound guided abdominal mass or organ sampling for cytological and bacteriologic testing including Xpert MTB/Rif or Ultra assay
Osteo-articular including spinal TB	Swelling of the end of long bones with limitation of movement/anterior collapse of vertebra on x-ray, para-spinal abscesses, cold psoas abscess /unilateral effusion of usually knee or hip joint	Radiography of joint or bone or spine, if there is a joint effusion tap or synovial biopsy for Xpert MTB/Rif or Ultra assay, biochemistry and cytology
Pericardial TB	Cardiac failure, distant heart sounds Apex beat difficult to localise, large and globular heart on the CXR	Echocardiography/Ultrasound and pericardial tap, send pericardial fluid for Xpert MTB/Rif or Ultra assay, biochemistry and cytology.

Cases where recommendation cannot be applied:

Where the facility does not have the clinical expertise to collect specimens for bacteriologic confirmation of TB in patients with a presumptive diagnosis of EPTB, these cases should be referred to the nearest facility where this capability exists.

What will be needed to successfully implement this recommendation?

Appropriate specimens, such as CSF, nodal aspirates, pleural biopsies, organ aspirates or biopsies, compatible with the clinical presentation should be promptly collected and submitted to the laboratory for Xpert MTB/Rif or Xpert MTB/Rif Ultra assay, histological examination and TB Culture. As far as feasible pleural biopsies and not pleural fluid should be submitted for the Xpert MTB/Rif or Ultra assay for patients presenting with a pleural effusion. The NTLP will train all relevant health care workers on the most common forms of EPTB to allow for prompt identification of these cases at all levels of the health care system. Effective referrals are unlikely to happen if health care workers are not familiar with the clinical presentation of common forms of EPTB. Additionally the NTLP will ensure that the capacity to process extra –pulmonary specimens for TB tests (molecular tests such as Xpert and LPA and culture) is built so that all patients who need these tests have access to them.

Diagnosis of TB in children

The diagnosis of TB in children relies on a thorough assessment of all evidence derived from a careful history of exposure, clinical examination and relevant investigations. Clinical signs and symptoms are generally non-specific. Health workers should therefore have a high index of suspicion.

Key risk factors for TB in children

The key risk factors for TB in children are as shown below:

Key risk factors for TB in children
• Household or other close contact with a case of pulmonary TB especially bacteriologically confirmed PTB. • Age less than 5 years • HIV infection • Severe malnutrition • Recent measles

Approaches to TB diagnosis in children

Practice Recommendation: All children presenting to health care facilities should be screened for TB using a symptom enquiry (current cough, fever and/or night sweats, failure to gain weight and/or loss of weight, fatigue/reduced playfulness plus history of contact with an individual with TB or chronic cough.

Practice Recommendation: All children presenting at health care facilities should have a nutritional assessment (weight for height, height for age, weight for age, Mid Upper Arm Circumference (MUAC)). This assessment should include reviewing the Child Health Card so as to pick growth faltering on the growth curve.

Practice Recommendation: All children with a positive symptom enquiry and/or are under nourished and or have a positive history of contact with TB, should have a chest x-ray.

Practice Recommendation: All children with a positive symptom enquiry and/or who are under nourished and/or have a positive history of contact with TB and an abnormal chest x-ray should have one a naso-

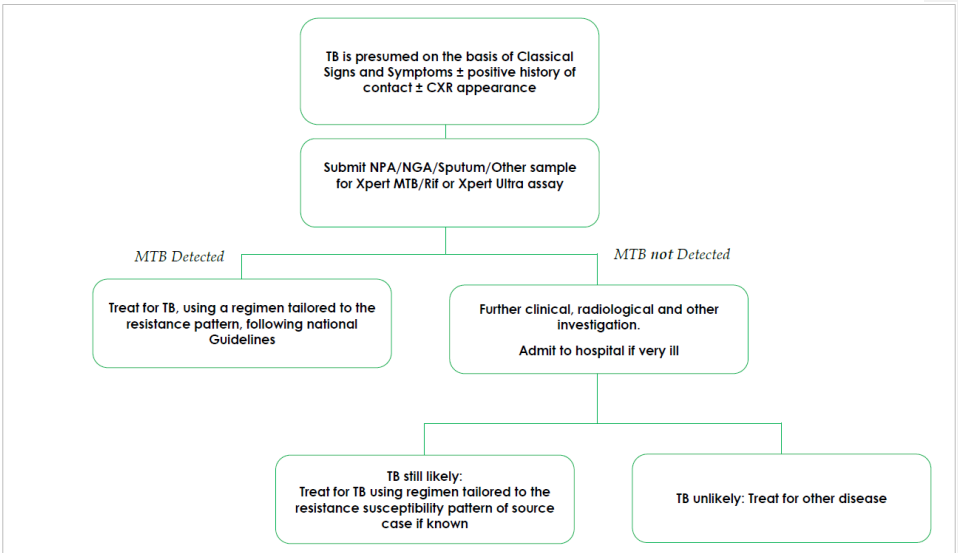
pharyngeal aspirate or a naso-gastric aspirate or a sputum (or induced sputum) specimen, of the child obtained and tested for TB using the Xpert MTB/Rif or Ultra assay. The specimen that is easy to collect should be prioritized and this will depend on the age

If the patient presents at the PHC level and CXR is not available, in an older child over 5 years who can produce sputum then collect sputum and send the specimen for Xpert MTB/Rif or Ultra assay. For children below five, refer to the next level of care for respiratory sample collection.

The Tuberculin Skin Test (TST) is useful to support a diagnosis of TB in children with suggestive clinical features who have a negative bacteriologic test for TB or who cannot produce sputum. However a positive TST only indicates that infection with MTB occurred and should not be interpreted to imply that TB disease is confirmed. A positive TST in any child is an induration of ≥10 mm irrespective of BCG immunization, however in an HIV-infected or a severely malnourished child, an induration of ≥5 mm should be considered positive. A positive TST is particularly useful to indicate TB infection when there is no known history of TB exposure on clinical assessment i.e. no positive contact history.

Caution: *Remember a positive TST does not distinguish between TB infection and active disease and a negative TST does not exclude TB disease.*

Figure 7 Algorithm for managing a child with a presumptive diagnosis of TB



Contact investigation and management

Practice Recommendation: All contacts of PTB patients, irrespective of bacteriological status should be identified, screened and investigated for the presence of TB disease and or infection.

Practice Recommendation: All children (under the age of 15 years) who are household contacts of a person with pulmonary TB should be screened for TB using symptom screening (current cough, fever, night sweating, fatigue/reduced playfulness, failure to gain weight or loss of weight), assessment of nutritional status and a chest x-ray (where available).

Practice recommendation 4.10: All children who are close contacts of a person with pulmonary TB and have a positive symptom screen AND/OR are undernourished AND/OR have an abnormal chest x-ray should have a NPA or sputum (or induced sputum) or a NGA or stool specimen collected and tested for TB using Xpert MTB/Rif or Xpert MTB/Rif Ultra assay.

Practice Recommendation: All contacts of children with TB, irrespective of site or bacteriological status should be identified, screened and investigated for the presence of TB disease and or infection.

Practice recommendation: All children who are household or close contacts of a person with pulmonary TB and have a negative symptom screen and / or a normal chest x-ray should be treated with six months of isoniazid to prevent TB.

Justification: Each person with infectious TB has on average of 10 contacts, of which 20%–30% have LTBI, and 1% have TB disease. Of contacts that will ultimately have TB disease, approximately 50% develop disease in the first year after exposure. Contacts of TB patients should therefore be investigated for the presence of TB infection and/or disease.

The aims of Contact Investigation (CI) are:

1. To reduce morbidity and mortality due to TB through early identification and appropriate treatment of active TB cases among contacts.
2. To stop further transmission by early detection of possible secondary cases.
3. To prevent future cases of tuberculosis in the population by detecting and offering preventive therapy of infected high risk contacts (children, immune compromised individuals) of index cases with active TB.
4. To counsel families and provide individual/ family education on infection control.
5. Identify all close and household contacts of MDR and extensively drug resistant (XDR) TB, without active disease for monitoring for at least 2 years following identification of the index patient.

Definitions for Contact investigation of TB[1]

Index Case: The first case or patient who comes to attention as an indicator of a potential public health problem. All Pulmonary TB cases should be regarded as index cases and their contacts investigated for TB. All children with TB should also be considered index cases. Since children are most often recipients of TB transmission from an older person, the purpose of contact investigation in children is to identify the source of TB transmission to them.

Source case or patient: The case or person who was the original source of infection for secondary cases or contacts. This may be but is not necessarily, the index case.

Contact: Someone who has been exposed to *MTB* by sharing air space with a person with infectious TB. The type of contact depends on the **closeness and duration of exposure to the index case**.

Household contacts, particularly, children less than 5 years of age should be assessed for TB.

High priority should also be given to those who are HIV positive and those with other underlying risk factors for TB such as diabetes, malnutrition, malignancy, alcoholism or long term corticosteroid therapy.

Contacts may also be found in aggregate settings such as workplace, schools (dormitories and classrooms), hostels and health facilities. Thus persons who have had prolonged contact with an index case beyond the household should be identified.

Process of Contact Investigation

The first step is to decide which contacts to evaluate first and the investigations which should be assigned a higher priority. The priority is to investigate contacts of patients who have characteristics and behaviours that increase the risk of TB transmission. These are:

a) Any adult with pulmonary and laryngeal TB; where prioritization is needed, consider especially those that are bacteriologically confirmed TB cases.
b) All children.

The index case should be interviewed to identify contacts and the place(s) of contact. Information gathered should be confirmed by a home, school or workplace visit as may be appropriate. Every effort should be made to investigate children, PLHIV and those with other conditions and situations associated with increased risk of TB. All identified prioritised contacts should have a symptom enquiry done at the point of identification and if feasible be invited to the health facility and investigated for TB including a CXR and Xpert MTB/Rif or Ultra assay on expectorated sputum. Alternatively sputum samples may be collected from contacts at home, school, workplace or other settings by community health care workers and/ or volunteers. All children and PLHIV should be assessed for TB more thoroughly, including disease at extra pulmonary sites. Children under 5 years and those at high TB risk should have a chest x-ray (if available). The likelihood of the presence of other medical conditions and social factors that increase the risk of TB should be determined. Provided below is a summary of the flow of events expected to occur in the process of contact management.

- Index case is asked about contacts especially household contacts and other close contacts with long periods of contact such as workmates, dormitory mates etc.
- Contacts are listed in a contact register for each index case.
- Index case is visited at home to identify contacts, or alternatively, though a weaker strategy, the index case may be requested to invite contacts to the health facility.
- Contacts are identified and cross checked with the list provided by the index case.
- Contacts are screened for TB using a symptom enquiry.

- Contacts with a positive symptom enquiry or risk factors for rapid progression to disease following infection are invited to the health care facility for an assessment of BMI, CXR and sputum (or other specimen) for TB bacteriology using the Xpert MTB/Rif or Ultra assay test.
- Contacts with a negative screen for TB are provided with TBPT if they are children under five or PLHIV.

Management options after contact investigation

There are 3 options:

1. Those who are diagnosed as having active TB should be initiated on TB treatment and registered.
2. Children <5 years with no evidence of TB disease should receive IPT.
3. Contacts who are 5 years and above who are healthy should be followed up on a clinical basis and educated to report any symptoms compatible with active TB such as persistent cough, fever, failure to gain weight or loss of weight to the nearest health facility.

Managing breastfeeding infants of mothers with infectious PTB

The priority is to immediately initiate treatment with effective anti-TB medicines to render the mother non –infectious. The baby should continue to breastfeed and mother and baby should not be separated. The baby should be screened for TB using a symptom screen, nutritional assessment, a TST if available and a CXR. If the baby has no evidence of active TB , IPT should be provided and regular TB screening be carried out during the period that the child recieves IPT. If the baby has not been vaccinated with BCG, this vaccine should be adminstered at the end of the IPT treatment.

Systematic Screening of at risk/vulnerable clinical groups in health care

Practice Recommendations

Tuberculosis screening with symptom enquiry, BMI and CXR (as per schedule, if available) should be regularly carried out at each health care visit by health care workers among the following vulnerable groups in the health care setting:

- Persons living with HIV.
- Previous TB
- Health care workers
- Patients receiving immunosuppressive treatment
- Persons with medical risk factors known to increase the risk of disease if infection has occurred such as post gastrectomy clients, chronic kidney disease clients and patients with diabetes.
- Alcoholics and intravenous drug users.

In these patients a positive symptom enquiry and/or a low BMI (<17 kg/m²) and/or abnormal CXR, a specimen should be collected for TB testing using the Xpert MTB/Rif or Xpert MTB/Rif Ultra assay.

Areas for operational research

1. The optimal approaches for contact management are not known and therefore implementation research to identify the most efficient and effective ways to find and investigate contacts is an area of research interest to the NTLP.
2. The NTLP will participate in research projects that examine the efficacy of new TBPT beyond IPT.
3. The NTLP will also want to study barriers to implementation of TBPT with a focus on IPT.

Further Reading

1. United States Centers for Disease Control and Prevention (CDC). Tuberculosis Education Curriculum. https://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf
2. Improving the diagnosis of smear negative pulmonary and extra pulmonary tuberculosis among adults and adolescents (Recommendations for HIV prevalent and resource constrained settings – by Stop TB Department of HIV/AIDS WHO.2006
3. National TB Management Guidelines 2014- Department of Health South Africa
4. Diagnosis and Treatment of EPTB by Ji Yeon Lee published on line 2015 April 2
5. Tuberculosis; Practical guide for clinicians, nurses, Laboratory Technicians and Medical auxiliaries, 2014 Edition MSF.
6. Zimbabwe Ministry of Health and Child Care National Tuberculosis Guidelines 2010.

Chapter 5

Systematic Screening of at risk / vulnerable populations

Introduction

While no person can be considered immune from TB infection and disease, this illness is known to disproportionately affect certain groups of people either because they are more likely to be exposed to infection or they have immune function defects that allows acquired infection to progress to disease. These people are collectively called TB risk groups or vulnerable populations. At risk populations whose vulnerability is related to the possession of a clinical condition that depresses their immune system and predisposes them to progression of MTB infection to disease have been dealt with in the previous chapter. In this chapter, attention is paid to those population groups that are not in the health care setting and whose vulnerability is primarily related to disproportionate exposure to infection in the community, residential setting or at work.

The major driver of TB in the world is poverty. Poverty leads to social deprivation with multiple consequences such as poor housing, insecure food supply and malnutrition, excessive exposure to indoor air pollution from use of biofuels for lighting and or cooking, tobacco smoking, substance abuse, a higher risk of HIV acquisition as a result of engagement in transactional sex and poor access to health care. These factors collectively increase the risk of exposure to infectious TB while at the same time increasing the probability of infection progressing to disease. This is the situation that prevails, for example, in urban slums, poor rural communities and in refugee camps.

Incarcerated populations such as those in correctional facilities also have a higher risk of acquiring TB infection and disease as a result of exposure to TB in the crowded conditions that prevail in most correctional facilities in low and middle income countries.

The health care worker is in a unique position. The mere fact that this person is working in an environment that attracts sick people including those with infectious disease makes the health care worker at a very high risk of exposure to MTB. Tuberculosis should therefore be considered an occupational hazard/disease in the health care worker. The most dramatic rates of TB are however seen in miners and ex – miners. Exposure to silica and other dusts together with other risk factors makes the miner or ex miner highly vulnerable to TB infection and disease.

Rationale for a targeted TB screening approach

Detecting TB cases only from among persons presenting themselves to health facilities with suggestive symptoms has until recently been the principal approach to case-finding in Zimbabwe and most other TB endemic countries in the world. This strategy has not worked and has contributed to the current case detection gap, particularly in certain vulnerable populations. Inadequate case finding and long delays in TB diagnosis leads to continued transmission of TB in the community, thus helping to maintain or grow the pool of future cases of TB. This highlights the need for a more active approach to detect TB early. While whole populations in a geographic area, may be screened and tested for TB, this approach would be costly and less effective. Systematic screening for active TB in selected risk groups is more likely to be effective and to provide a sustainable approach to early and complete TB case identification.

Screening is done to find persons with clinical disease in need of treatment. Therefore, appropriate follow-up, after initial screening, is essential. In addition, screening programs provide 1) epidemiologic data for assessing the extent of the tuberculosis problem and its trends, 2) data for assessing the value of continued screening, and 3) the opportunity to educate the public about tuberculosis. To some extent, members of high-risk groups and their health-care providers should be involved in the design, implementation and promotion of screening programs. Implementation may be enhanced by using health care workers or other staff (including volunteers) who have linguistic and cultural familiarity with the population at risk.

Objectives of targeted screening of at risk populations

1. To increase awareness and generate demand for TB screening among communities with a high risk of TB.
2. To screen and diagnose TB in communities that have a high risk of TB.
3. To link all people diagnosed with TB with primary health care services and ensure that they are promptly initiated on appropriate TB treatment.
4. To reduce transmission of TB through early detection of active TB cases and prompt TB treatment to eventually reduce the community burden of this disease.

Key principles of targeted TB screening

1. Tailor systematic and targeted screening to specific risk groups that are known to have high rates of TB.

2. Before screening is initiated, high-quality TB diagnosis, treatment, care, management and support for patients should be in place, and there should be capacity to scale these up further to match the anticipated rise in case detection that may occur as a result of screening.
3. Indiscriminate mass screening is expensive and probably undesirable and should be avoided. The continued prioritization of risk groups for screening should be based on a scientific approach that examines rates of TB in the risk group, feasibility and yield of various approaches (number needed to screen to identify a case of TB) and considering the cost effectiveness of the various screening approaches.
4. Tuberculosis screening should follow established ethical principles for screening for infectious diseases, observe human rights, and be designed to minimize the risk of discomfort, pain, stigma and discrimination.
5. The TB screening approach should be implemented in a way that optimizes synergies with the existing health care and social services and be in sync with regional and international best practices.
6. A screening strategy should be monitored and reassessed continually in order to inform re-prioritization of risk groups, re-adaptation of screening approaches and adoption of evidence based approaches.

Community TB screening

Tuberculosis screening by community health care workers using symptoms enquiry should be regularly carried out for the vulnerable populations listed below at the community level. **Case notification in a specific population, though not always a reflection of TB incidence, should be used to identify and prioritize population groups for TB screening.**

- Urban slum dwellers, poor rural communities, and other community groups known to have a high incidence of TB.
- Homeless people, people living in remote areas with poor access to health care, and other vulnerable or marginalized groups, including refugees.
- Household contacts and other close contacts of patients with infectious TB.

Zimbabwe is implementing community screening approaches that involve mobile CXR and Xpert MTB/Rif services and depending on the results of the pilot aspects of this approach will be adopted to regularly screen prioritized community groups with high rates of TB such as urban slum dwellers.

When a symptom enquiry by a community health care worker or volunteer suggests the presence of TB symptoms, several options may be pursued: a) the screened person may be requested to report to the

nearest health care facility where he or she will be managed as a presumptive case of TB; b) the community health care worker may collect a sputum sample from the screened person and convey the sample to the health care facility for TB testing using Xpert MT/Rif or Ultra assay. If the health care worker is the one who submitted sputum or other sample to the laboratory, he or she should take the responsibility to relay the results of the Xpert test back to the screened person and to support that person to access and begin treatment for TB treatment if the results are positive. If the TB bacteriology results of the screened and tested person are negative and the person's symptoms persist, the community health care worker should urge and assist that person to report to the nearest health facility for further evaluation by a clinician; c) where a van based mobile outreach service is being conducted, all screened persons should have a BMI and a CXR. The results of the symptom screening, BMI and CXR should determine if a sputum specimen should or should not be taken for TB testing.

Community TB screening should be carefully documented and monitored to track the following parameters:

- The number of people reached with screening services, against the target set (service coverage).
- The proportion of the population screened who have symptoms compatible with TB.
- The proportion of the population screened who have a BMI of <17 kg/m².
- The proportion of those with symptoms and or low BMI who had a CXR.
- The proportion of those x-rayed who had an abnormal CXR.
- The proportion of those screened who submitted a sputum sample for Xpert MTB/Rif or Ultra assay.
- The proportion of sputum samples that reached the laboratory and were positive for MTB on Xpert testing.
- The number needed to screen to identify one case of bacteriologically confirmed TB.

Several modifications of these approaches could be tested in formal operations or implementation research projects.

Screening and testing for TB in correctional facilities and police holding cells.

In correctional facilities, similar approaches as in the community will be used. However the process is easier in correctional facilities because of the captive nature of this population. At entry to a correctional facility, there is a legal requirement that all persons should undergo a medical assessment which is an opportunity to screen all such persons for TB. Thereafter routine medical checks are carried out on a

monthly basis. The recommended approach therefore for routine screening of inmates is monthly symptom enquiry, monthly BMI and annual CXR. If there are symptoms and/or a low BMI and/or an abnormal CXR a specimen is collected for TB testing using the Xpert MTB/Rif assay.

For the officers working in correctional facilities the recommended systematic approach to screening is six monthly checks using symptoms, BMI and CXR and sputum examination if symptom screen positive, low BMI or CXR is abnormal.

A similar approach with appropriate modification will be carried out for those in police holding cells, noting that screening programs in this population will be more challenging to manage because of the lesser degree of "captivity" as a result of more frequent movement of people in and out of these cells.

Screening of miners and ex-miners

Formal mining populations

Screening routines similar to those used in correctional facilities should work in formal mining settings. The NTLP will enhance its engagement with formal mining companies to ensure that routine TB screening is institutionalized in these populations. The NTLP recommends that screening of miners should be carried out every six months and CXR annually.

Screening among ex –miners

The major imperative is to be able to identify and locate ex miners so that they can participate in and benefit from TB screening programs. The NTLP will work with relevant organizations including but not limited to umbrella organization for ex–miners to ensure that all ex-miners are registered and their contact addresses (physical address, phone numbers etc.) known. Using local health services, ex-miners will be invited to local health facilities to be screened for TB using approaches similar to those used in persons who are still actively engaged in mining activities.

Screening of artisanal miners

As in ex-miners the major imperative is to overcome the challenge of identifying and locating artisanal miners so that they can participate in and benefit from TB screening programs. The NTLP will work with relevant organizations including but not limited to umbrella organization for artisanal miners, local leaders, NGOs and CBOs, to map artisanal mines, identify the miners, register them and obtain their

contact (physical address, phone numbers etc.) addresses. Depending on the numbers of miners identified in a particular geographic area, the NTLP on its own or through an intermediary may go to their workplace to carry out TB screening (outreach services) or follow an approach similar to that used for ex miners.

Screening persons with diabetes mellitus (DM)) for TB

People with DM should be systematically screened for TB. Ideally, screening should be carried out at every visit to a health facility. It is recommended that a TB symptom screen is used to identify presumptive TB patients among patients attending DM care. Persons with suggestive TB symptoms should then be referred to a TB clinic for investigations. A good quality sputum specimen should be collected and sent for Xpert testing (sputum smear microscopy if Xpert test is unavailable) and a CXR (which is helpful in monitoring treatment response in diabetic patients). It is important that health workers confirm receipt of the sputum test results, their interpretation and appropriate recording. Persons with TB (all forms) must be started promptly on correct TB treatment and informed of their condition.

Table 4 Summary of recommended frequency of TB screening and approaches for various at risk populations

Risk Group	Screening Frequency	Screening and testing approach
Congregated Settings (miners, residents of a correctional facility, health care workers, military and police cantonments)	Baseline and then Six monthly	Symptom enquiry, BMI + CXR (annually) then Xpert MTB/Rif or Ultra assay
Persons infected with the human immunodeficiency virus (HIV).	At diagnosis then at every health care visit	Symptom enquiry, BMI + CXR (annually if resources permit) then Xpert MTB/Rif or Ultra assay
Children under 5 who are contacts of an older person with TB	At point of diagnosis of index case or within 7 days of diagnosis of index patient and	Symptom enquiry, nutritional assessment/BMI, CXR, specimens (NPA, NGA

	again at six months when completing IPT	and others) for Xpert MTB/Rif or Ultra assay
Persons with medical risk factors known to increase the risk of disease if infection has occurred (Chronic kidney disease, diabetics, gastrectomy, patients receiving immunosuppressive treatment, others)	At every clinic visit	Symptom enquiry, BMI + CXR then Xpert MTB/Rif or Ultra assay
Current contact with TB	Within 7 days of diagnosis of the index case	Symptom enquiry, BMI + CXR (if available) then Xpert MTB/Rif or Ultra assay
Clients with a History of previous TB (those who remain in care and have abnormal chest x-ray)	Annually	Symptom enquiry, BMI, CXR in people with significant damage to the lungs at the beginning of treatment and Xpert MTB/Rif assay in symptomatic persons or those with progressive radiographic shadows
Health Care Workers	At entry into service, six-monthly, and at termination of service	Symptom enquiry, BMI + CXR(annually) then Xpert MTB/Rif or Ultra assay

Further Reading

1. https://www.cdc.gov/mmwr/preview/mmwrhtml/00001642.htm

Chapter 6

Management of Drug Susceptible Tuberculosis

Introduction

This chapter provides a summary of the management of drug sensitive tuberculosis. It looks at the aims and principles of treatment, standardized treatment regimens for drug sensitive TB including TB treatment in special situations, case holding strategies, use of adjuvant therapy, monitoring therapy, patient support systems that enable TB patients to adhere and complete treatment and post TB treatment care.

The aims of treatment are to:

- Cure the patient and ensure return to a full quality of life.
- Prevent death from active TB or its complications.
- Prevent relapse of TB.
- Stop transmission of TB to others.
- Prevent the development and transmission of drug resistant TB

Tuberculosis treatment policies in Zimbabwe

Practice Recommendations

- **Diagnosis and treatment of TB is offered for FREE in Zimbabwe.**
- **Treatment of TB should be supervised (DOT) throughout its duration.**
- **Both intensive phase (IP) and continuation phase (CP) must be completed.**
- **Multiple medicines preferably FDCs should be used to treat all forms of TB using standardised regimens.**
- **Every patient is treated under a designated class with either medicines that currently belong to the first line group (for treatment of drug susceptible TB) or to the 2nd line group (for treatment of drug resistant TB) guided by DST results.**
- **All patients on treatment need to be monitored both clinically and with laboratory assessment in addition to receiving appropriate support throughout treatment.**
- **Documentation of every step of the management process is critical.**

Justification

As part of the efforts to end TB in Zimbabwe, TB diagnostic and treatment services are offered at all levels of delivery of health services free of charge. This is one of the strategies of reducing catastrophic costs to TB affected patients and their families.

Treatment of TB should be supervised throughout its duration. The recommended approach is directly observed treatment (DOT) which requires a supporter to watch a patient swallowing the tablets. This ensures that the patient takes the right medicines, in the right doses and completes the treatment. The preferred order of DOT supporter is health workers, trained community health workers, trained family members/guardians.

NB: In highly motivated TB patients or those with special circumstances that impede DOT, self-administered treatment (SAT) can be employed. However, even when SAT is chosen every effort must be taken to ensure that the patient is fully aware of the obligation to adhere to treatment and to keep up with routine follow up and appointments. Video – observed treatment (VOT) is a new innovation that can be explored subject to guidance from NTLP.

Full TB treatment is delivered in two phases both of which must be completed:

- **Intensive Phase (IP):** the initial, intensive phase is designed for rapid killing of actively growing bacilli and killing of semi- dormant bacilli. The duration of this phase is 2 months.
- **Continuation phase (CP):** this phase eliminates bacilli that are persisters and reduces the rate of failure and relapses. The duration is between 4 -6 months depending on the organ affected by the disease.

It is important to use multiple medicines in the treatment of TB to avoid emergence of drug resistance. In a population of MTB bacilli that have never been exposed to anti-TB medicines, variable proportions of the bacilli will have spontaneous resistance mutations to any single drug, however, it is highly improbable that there will be bacilli that are resistant to multiple agents at the same time. If single medicines are used to treat TB, the bacilli with resistant mutations to the medicine used will be selected and allowed to replicate leading to failure of treatment. The three essential medicines for the treatment of drug susceptible TB are Isoniazid (H or INH), Rifampicin (R or Rif) and Pyrazinamide (Z or PZA) and they form the backbone of current short course chemotherapy (SCC) of TB. Ethambutol (E) is added in case there may be pre-existing resistance to one of these medicines.

The essential anti-TB medicines are available either as single medicine formulations or as fixed dose combinations (FDCs) that include two medicines (2-FDC), three medicines (3-FDC) or four medicines (4-FDC). The FDCs available in Zimbabwe are Rifampicin, Isoniazid, pyrazinamide and ethambutol (RHZE); Rifampicin, Isoniazid and Pyrazinamide (RHZ) and Rifampicin and isoniazid (RH).

While a recent systematic review has suggested that treatment with single drug formulations may confer some risk of acquired drug resistance, the risk appears to be small and thus the Zimbabwe NTLP has chosen to continue using FDCs for the following reasons:

- FDCs reduce the pill burden (maximum of 5 instead of 15-16 tablets per day) and are thus more convenient for the patient.
- FDCs also simplify both treatment and supply management system for these medicines.
- Finally FDCs reduce the risk of inappropriate treatment either through clinician error or selection by the patient of medicines to be taken on account of link between the medicine with an adverse event or even taste.

The number of FDC tablets to be taken by each patient is determined by the weight of the patient at the start of treatment with dose adjustment made as the patient's weight band changes with treatment.

All patients are treated with first line medicines in standardized regimen combinations. Standardized regimens have the following advantages over individualized prescription of medicines:

- Facilitate estimates of medicine needs, purchasing, distribution and monitoring.
- Reduce errors in prescription thereby reducing the risk of development of drug resistance.
- Facilitate staff training.
- Reduce costs.
- Facilitate regular medicines supply when patients move from one area to another.

Every patient should be treated with either first line (FLD) or second line medicines (SLD) as guided by DST results. First line drugs are used in patients whose DST results do not show resistance to at least rifampicin irrespective of whether they are new patients who have never taken anti-TB medicines or they were previously treated with one or more FLDs. Second line drugs are used for all patients whose DST results show resistance to R, either alone or in combination with other FLDs.

All patients on treatment need to be monitored throughout treatment for adherence, treatment response, and development of adverse events and at the end of treatment be assessed for treatment outcomes. The

progress of the patient, changes in clinical status, medication use and other clinical events should be documented at every stage using the patient TB treatment card.

Treatment of drug sensitive TB

Practice Recommendation

- **Initiate TB treatment immediately upon making a diagnosis of TB.**
- **All new or retreatment TB cases with rifampicin resistance not detected on Xpert MTB /Rif testing are treated for SIX months with FLDs using the regimen 2RHZE/4RH.**
- **All patients with meningo-cerebral TB and skeletal TB, which are difficult to treat forms of EPTB should be treated for at least 8 months using the regimen 2RHZE/6RH. Clinical evaluation at end of such treatment may lead to extension of treatment for up to 12 months.**
- **All other cases of EPTB are treated with the six month 2RHZE/4RH standard regimen.**
- **Doses of anti-TB medicines are weight based and remember to adjust doses when the weight band of a patient on treatment changes.**
- **All new or retreatment TB cases with rifampicin resistance detected on Xpert MTB/Rif assay should be treated with SLDs and second line DST must be done to guide treatment regimens (*refer to chapter 8 for details*)**
- **Treatment of TB is generally ambulatory (treatment received at an outpatient or community basis) except for special situations requiring admission.**

Initiation of treatment

Patients who are confirmed to have TB bacteriologically or clinically should be started on appropriate treatment by the clinician (doctors and nurses) at the point of diagnosis for the convenience of the patient. The patient must be notified and registered in the facility TB register. These patients should be monitored and followed up as recommended.

Treatment of drug susceptible TB in adults (FLDs)

Intensive phase 2RHZE

Continuation phase 4RH

Treatment for Extra-pulmonary TB (EPTB)

There have been no robust clinical trials to guide the choice of treatment regimens for EPTB. Experts recommend that most forms of EPTB are treated with the 2RHZE/4RH standard regimen except for patients with meningo-cerebral and skeletal TB where treatment may be extended for up to 12 months. This is primarily a result of the poor penetration of medicines to these disease sites and the consequences of either failure of treatment or recurrent disease should disease be insufficiently treated. The Zimbabwe NTLP has chosen to treat intracranial and skeletal TB with an 8 month regimen consisting of 2RHZE/6RH with the provision that clinicians can extend treatment beyond 8 months if in the judgement of the clinician an adequate response to treatment has not been achieved by the end of the 8th month.

Dosage of anti-TB medicines in adults

The dose of anti-TB medicines is based on the WEIGHT of the patient. Note: Adjust dosage as soon as the patient weight band changes to avoid under- or over-dosage.
Table 6 below gives estimates of number of FDCs per KG body weight:

Table 5 Weight based dosing of FLDs

Patient's weight	**Intensive phase for 2 months** 2(RHZE) daily (Isoniazid 75mg + Rifampicin 150mg + pyrazinamide 400mg + Ethambutol 275mg).	**Continuation phase for 4** months i.e. 4 (HR) daily (Isoniazid 75mg+ Rifampicin 150mg)
25-39 KG	2	2
40-54 KG	3	3
55-70 KG	4	4
70 KG +	5	5

Treatment of TB in Children

Practice Recommendations

- **All children with drug susceptible TB on DST (new or retreatments) are treated with FLDs in a similar way to adults using the regimen 2RHZE/4RH.**
- **In children with TB meningitis, osteo-articular TB and miliary TB, the continuation phase is prolonged for 10 months, thus the regimen used is 2RHZE/10RH.**
- **Commencement of TB therapy should be documented on the child health card for children under 5 years of age.**
- **Monthly weight should be documented on the TB treatment card and child health card where applicable. Failure to gain weight may indicate poor response to therapy.**
- **The treatment doses should be adjusted as soon as the child's weight band changes.**
- **The care giver and child should receive comprehensive information and education including the reasons why they must take the full course of treatment even if they are feeling better.**
- **Remember some children require to be hospitalised and others require pyridoxine supplementation during treatment (see below).**

Children weighing 25 kg and more should be treated using the adult treatment guidelines.

Children with severe malnutrition should be given medicines at the lower end of the dose range and closely watched for hepatotoxicity

Tuberculosis in children is treated in a similar way to that in adults with a few exceptions. The dose per weight in children is higher than in adults. The recently revised and accepted WHO daily dosage (range) recommendations are:

Rifampicin:	15 mg/kg/d (10 to 20 mg/kg/day)
Isoniazid:	10 mg/kg/d (10 to 15 mg/kg/day)
Pyrazinamide:	35 mg/kg/d (30 to 40 mg/kg/day).
Ethambutol:	20 mg/kg/d (15 mg to 25 mg/kg/d).

Table 6 Doses of paediatric formulations of anti TB medicines

Weight Band	Recommended Regimen		
	Intensive Phase		Continuation Phase
	RHZ (75/50/150)	E (100)	RH (75/50)
4-7kg	1	1	1
8-11kg	2	2	2
12-15kg	3	3	3
16-24kg	4	4	4
25kgs and above	Adopt adult dosages		

Reasons for hospitalization in children

Children with the following characteristics should be hospitalized

- Severe forms of TB such as TB meningitis (TBM).
- Severe malnutrition requires in-patient based nutritional rehabilitation.
- Signs of severe pneumonia such as chest in-drawing.
- Other co-morbidities e.g. severe anaemia.
- Social or logistic reasons likely to interfere with adherence to anti-TB medicines e.g. severe alcoholism in a parent or guardian and lack of appropriate social support at the home environment.
- Neonates.
- Severe adverse reactions such as hepatotoxicity.

Pyridoxine supplementation

Isoniazid (INH) may cause symptomatic pyridoxine deficiency, which manifests as peripheral neuropathy. The NTLP recommends that all children on INH as part of the anti-TB treatment regimen or for TBPT should receive pyridoxine.

It is however appreciated that the following categories of children are at an increased risk of developing peripheral neuropathy:

- malnourished
- breastfeeding infants
- adolescents
- Children on high-dose INH therapy (>10mg/kg/day)
- children with diabetes mellitus

- Children with renal failure

Treatment of TB in special situations

Practice Recommendations

- **All pregnant women with TB should be treated with a similar regimen to women who are not pregnant (2RHZE/4RH). FLDs are considered safe in pregnancy.**
- **FLDs are safe in breast-feeding mothers**
- **Breast feeding babies whose mothers are on treatment for pulmonary TB should be screened and tested for TB and only be initiated on preventive therapy using 6H (INH for SIX months) if active TB has been excluded. After completion of 6H, these babies should be vaccinated with BCG.**
- **Women in the child bearing age who are taking medicines for the treatment of TB should be advised to postpone getting pregnant until after the TB treatment is completed. Double contraception using a hormonal contraception and a barrier method should be recommended for such women.**
- **Patients with chronic liver disease should not receive pyrazinamide. Both INH and Rif are also hepatotoxic but less so compared with PZA and may be used with caution in patients with mild pre-existing liver disease. In severe pre-existing liver disease, PZA, INH and Rif should be avoided. These patients may be treated with an injectable , ethambutol and a fluoroquinolone with or without the addition of cyloserine for a total of 9-12 months. All such patients should be treated under the supervision of a medical specialist.**
- **Patients with renal failure can still use 2RHZE/4RH with adjusted doses and dosing intervals under specialist care. Pyridoxine is given to prevent INH-induced peripheral neuropathy**

Pregnant women

- All pregnant women with TB should be treated in a similar way to non-pregnant women. First-line anti-TB medicines are safe in pregnancy, except for streptomycin (which will be less often used as a first line medicine) which is ototoxic to the foetus.
- Note: Tuberculosis in pregnancy is associated with an increased risk of premature birth, low birth weight and perinatal death. For these reasons, women who develop TB should be strongly encouraged not to become pregnant while receiving treatment for TB and should be provided with appropriate contraception (using double protection as highlighted in the text box above)

Breastfeeding women

Full TB treatment is safe, and is the best way to prevent transmission of TB to the baby. If the mother has pulmonary TB then the baby should receive INH preventive treatment (10 mg/kg for 6 months) after TB screening using a symptom enquiry and a CXR with or without a TST. Once active TB is excluded, the child should be treated with 6H and pyridoxine. On completion of 6H, BCG vaccination should be provided. Mother and baby should not be separated on account of TB. As far as possible, mother and child should stay together for the entire duration of treatment.

Women taking hormonal contraceptives

Rifampicin reduces the efficacy of the contraceptive pill through induction of liver enzymes (cytochrome P450) which enhance the metabolism of many medicines including hormonal contraceptives. Therefore, providing an additional contraceptive method (dual protection) preferably a barrier method is recommended. However, this must be balanced against potential harms such as greater risk of acquisition of HIV for intrauterine implants/devices.

Patients with liver disorders and established chronic liver disease

Provided there is no clinical evidence of chronic liver disease which is associated with increased risk of anti-TB drug induced hepatitis, patients with the following conditions can receive the usual short-course chemotherapy: hepatitis virus carriage, a past history of acute hepatitis, and excessive alcohol consumption. Patients with chronic liver disease should not receive pyrazinamide. Patients may receive less hepatotoxic medicines such as INH and Rifampicin but must be clinically and biochemically monitored (AST, ALT and bilirubin) with the medicines promptly stopped if there is evidence of worsening of the liver disease. If INH and Rif are used without PZA, the treatment should be extended to 9 months, with the regimen therefore being 2RHE/7RH. If PZA, INH and Rif cannot be used because of severe existing liver disease, an injectable, Ethambutol and a fluoroquinolone with or without Cycloserine (note the overlap of symptoms between the central adverse events of Cycloserine and hepatic encephalopathy) may be used with the treatment lasting up to 9-12months.

NB: *All TB patients with pre-existing liver disease should be managed under the care or guidance of a specialist physician while being monitored clinically and or by biochemical tests to rapidly identify evidence of deterioration that requires modification of treatment.*

Acute hepatitis (e.g. acute viral hepatitis)

It may be prudent to defer treatment in some cases, while in others it may be necessary to continue with anti-TB treatment. All such patients should be referred to a specialist.

Patients with renal failure

Isoniazid, rifampicin and pyrazinamide are excreted almost entirely by the hepatobiliary system or metabolised into non-toxic compounds. However the metabolites of PZA, including Pyrazinoic acid and 5 hydroxy-Pyrazinoic acid are excreted by the kidneys and therefore dose adjustment is necessary for PZA in patients with chronic kidney disease (CKD). In severe renal failure, give pyridoxine to prevent INH-induced peripheral neuropathy. Ethambutol is excreted by the kidneys, and should be avoided or used under specialist care. Table 8 below shows the does adjustments that should be made when treating patients with CKD for TB.

Table 7 Drug doses and dosing frequency in patients with CKD.

Drug	Change in Frequency	Recommended Dose and Frequency for Patients with creatinine clearance of <30ml/min or patients receiving haemodialysis
INH	No	300 mg once daily
Rif	No	600 mg once daily
PZA	Yes	25-35 mg/Kg/dose 3 times/week (not daily)
Ethambutol	Yes	20-25 mg/Kg/dose 3 times/week (not daily)
Levofloxacin	Yes	750 -1000 mg/dose/ 3 times/week (not daily)
Moxifloxacin	No	400 mg once daily
Cycloserine	Yes	250 mg once daily or 500 mg/dose 3 times/week
Ethionamide	No	250-500 mg/dose daily
PAS	No	4g/dose twice daily
Streptomycin	Yes	15 mg /Kg/dose 2-3 times/week (not daily)
Capreomycin	Yes	15 mg /Kg/dose 2-3 times/week (not daily)
Kanamycin	Yes	15 mg /Kg/dose 2-3 times/week (not daily)
Amikacin	Yes	15 mg /Kg/dose 2-3 times/week (not daily)

Thus the regimen given to patient with CKD and drug susceptible TB remains 2HRZE/4HR but the dosing frequency for PZA and Ethambutol is adjusted to three times a week and not daily.

The key clinical practice points to remember when managing patients with TB and CKD are:

- Patients with CKD, on dialysis and following transplantation are at significantly increased risk of tuberculosis. As far as feasible these patients should be managed at the central level/highest level of care.
- All TB patients with concomitant CKD should be treated in the same way as patients without CKD, however medicines doses and dosing intervals need to be adjusted appropriately.
- Patients with TB and CKD should be cared for by or under the leadership of medical specialists familiar with the management of both TB and CKD.
- For patients with a creatinine clearance of 30 ml/min or less, dosing intervals should be increased to three times weekly for ethambutol, pyrazinamide and the aminoglycosides.
- For patients on hemodialysis, dosing intervals for ethambutol, pyrazinamide and the aminoglycosides should be increased to three times weekly to reduce the risk of drug accumulation and toxicity. All anti-TB medicines should be given after dialysis to avoid rapid clearance during dialysis.
- Rifampicin in particular can interact with immunosuppressive medicines, increasing the chance of graft rejection, and doses of mycophenolate mofetil, tacrolimus and cyclosporin may need adjustment. Corticosteroid doses should be doubled in patients receiving rifampicin.

Case holding

Practice recommendations

- **All TB patients must be enrolled, recorded and reported in the health information (recording and reporting) system used by the NTLP.**
- **All TB patients should receive treatment under DOT.**
- **Adequate information about TB should be provided regularly to TB patients**
- **Identifying and managing adverse events due to anti-TB medicines must be prioritized.**
- **Immediate follow up measures for all patients who interrupt treatment must be instituted.**
- **Ensure patient centred support systems are in place throughout the course of treatment.**

Following diagnosis and initiation of appropriate anti-TB treatment, it is the responsibility of HCWs to retain patients in care until they finish their treatment successfully.

- All TB patients must be enrolled, recorded and reported through the recording and reporting (health information and management) system used by the NTLP. Tuberculosis is a chronic disease which requires long duration of treatment. Thus, in order **to keep track of every patient** and to report on him/her appropriately, every step of the management process should be documented. The TB treatment card should be used for this purpose. Always capture the following key information:
    - Personal details of the patient.
    - Information about the diagnosis, classification and category of TB.
    - Details of the treatment regimen and actual doses prescribed.
    - Enter details of all clinical events that the patient experiences such as adverse events, inter-current illness, medication use, adherence to treatment, changes in medicine doses or dosing frequency etc.

Treatment of TB should be supervised throughout its duration. The recommended approach is DOT. The DOT observer should be chosen by the patient in consultation with the health care worker. The selected DOT observer should be a person who is trusted, reliable and acceptable to the patient and who is committed to supporting the patient over the entire period of treatment. In addition the DOT observer should, if he or she is not a health care worker, be willing to be trained and accept supervision by the health care workers at the treating health facility. For more detail, refer to chapter 12 on community TB care.

Adequate information about TB should be provided regularly to TB patients at diagnosis, prior to treatment initiation and during follow up visits as they receive their treatment. The information enhances their understanding of TB disease, helps them cope with the disease and its treatment and thus to remain in care. The information that should be provided to patients should focus on facts about TB to help dispel myths and misconceptions and should include the following:

- The cause of TB
- Transmission of TB
- Symptoms and signs of TB
- Diagnosis of TB
- Prevention of TB transmission
- The treatment of TB including the medicines used and the length of treatment
- Common adverse reactions of anti-TB medicines and how they are managed

- The association between TB and HIV
- The need for family and other contact screening and testing for TB
- Drug resistance in TB and how the patient can avoid acquiring drug resistant TB
- The patient's right and responsibilities

Identification and management of adverse events due to anti-TB medicines must be regularly carried out at every encounter with the patient through symptom enquiry and physical examination such as asking if the patient is nauseated or has vomited and looking at the eyes to see if there is jaundice. Patients must regularly be re-assured about adverse events so that they can develop and sustain confidence in the treatment and the ability of the health care worker and the health care system to "take care of things" should adverse events/reactions occur. This will enhance the patient adherence to treatment. Please see chapter 16 for more details of anti-TB medicines adverse reactions/events and how they should be managed.

Immediate follow up measures for all loss to follow up patients must be instituted for those patients who miss their appointments or discontinue treatment for whatever reason. Actions to take include: reminder telephonic messages (SMS); direct phone calls and home visits by HCWs or community-based health workers to establish the reasons for the missed appointment or treatment interruption. All these interventions depend on obtaining and recording detailed information about the patient in the TB treatment card.

In spite of efforts to prevent interruption of treatment, a proportion of patients (which should be minimal in a well- functioning TB prevention and care program) will still interrupt treatment for various reasons. A proportion of these patients will come back to care either on their own or following retrieval efforts by health care workers. Outlined below are the practice recommendations for patients who come back to care after a period of treatment interruption.

- The first and essential step is to establish the reasons for the interruption of treatment and to attempt as far as feasible to address those reasons in order to prevent a recurrence of treatment interruption. The most common reasons for treatment interruption include poor understanding of TB and its treatment, difficulties with coping with treatment schedules especially health facility based DOT due to distances and transport costs, negative attitudes of health care staff, feeling well and therefore assuming that treatment is no longer needed, perceived or experienced stigma and discrimination, experience of medicine adverse reactions/events and work schedules.

- Re-inforce patient education on TB and its treatment with an emphasis on adherence to treatment.
- Continue treatment with anti-TB medicine if the treatment interruption lasted less than a month
- If the treatment interruption lasted more than a month, collect a sputum specimen and send it over to the laboratory for smear microscopy, the Xpert MTB/Rif assay and SL-LPA.
    - If the Xpert MTB Rif assay comes back positive for MTB but with no Rif resistance, restart treatment with first line medicines, recording this patient in the register as a re–treatment case.
    - If the Xpert MTB /Rif assay come back with a positive MTB result and Rif resistance start treatment for RR/MDRTB using the recommended short RR/MDRTB treatment regimen as results of the SL-LPA are awaited. Treatment should be adjusted accordingly when the SL-LPA results are received.
    - If the Xpert MTB/Rif assay comes back negative for MTB consider the initial test results, the amount of treatment that patient had received and thus the time point when treatment interruption occurred. Patient who had a negative Xpert at the beginning of treatment should not be continued on treatment but be investigated for other diseases. Those who have received more than 4 months of treatment may also not be re-treated while patients who have a negative Xpert but have clinical symptoms and radiological features compatible with TB should be re initiated on treatment and recorded as clinically diagnosed re treatment cases of TB.

Summarized in the table 9 below is the recommended approach to managing patients who interrupt treatment but are retrieved back into care.

Table 8 Management of patients who interrupt treatment but are retrieved back to care

Duration of interruption	Sputum microscopy	Molecular DST or Culture &DST	Treatment way forward	Changes in outcome to be entered in the TB register	Re-registration
Less than 4 weeks	No need	None	Continue as before & extend total duration by number of days missed	None	No

4-8 weeks	Needed	Both needed	-Continue as before for negative results, and extend duration by adding the total days missed. - Adjust as per culture/DST results	None	No
Longer than 8 weeks	Needed	Both needed	- Re-start treatment with FLDs if positive with NO resistance or if clinically TB. Start SLDs treatment if resistance is identified. -If negative, consider 1st test results and time during treatment at which interruption occurred	Enter as lost to follow up	Yes as re-treatment

Ensure patient centred support systems are in place throughout the course of treatment. All patients on treatment for tuberculosis should have a psycho-social and economic assessment done to identify those who need to be provided with psychological and social support such as transport and food to prevent treatment interruption and to reduce treatment associated costs.

Adjuvant Therapy

Corticosteroid therapy is beneficial and improves outcomes in TB meningitis, TB pericarditis, patients with massive lymphadenopathy as part of paradoxical reaction if used concurrently with effective TB medicines. It is also useful in patients with severe hypersensitivity reactions to anti-TB medicines.

Steroids are beneficial as adjuvant therapy in some forms of TB disease. They work by targeting the host immune response, dampening it and thus reducing pathogen induced, host driven damage to the affected organ. On the other hand, corticosteroid therapy used in patients with TB without concurrent effective anti-TB therapy is hazardous.

Indications for steroids

- TB meningitis.
- TB pericarditis.
- Massive lymphadenopathy with pressure effects.
- Severe hypersensitivity reactions to anti-TB medicines.
- More rarely: hypo-adrenalism, renal tract TB (to prevent ureteric scarring), TB laryngitis with life-threatening airway obstruction.

For large TB pleural effusion with severe symptoms, urgent referral to a facility where the effusion can be drained using a chest tube and under water seal drainage system is critical. Drainage using needle and syringe should be avoided because of the risk of introducing air and infectious agents into the thoracic cavity. If the patient already has an empyema when the initial thoracocentesis is done, chest tube placement with under water seal drainage system should be carried out in addition to consultation with a surgeon for consideration of a decortication procedure to prevent massive pleural thickening and chest wall restriction.

Doses for steroid therapy

Table 9 Recommended doses for adjuvant steroid therapy

Indication	Prednisolone treatment
TB meningitis	60 mg/d for 4 weeks then taper off. Alternatively- Dexamethasone 8-12mg/d tapered over 6-8 weeks in cases of patients who cannot swallow prednisolone
TB pericarditis	60 mg/d for 4 weeks, then 30 mg/d for 4 weeks then taper off over several weeks
Hypersensitivity reaction to TB medicines	20-80mg (average 60mg)/d tapering off over 2-8 weeks

Note: for children the dose of prednisolone is 1-2mg/kg for 4 weeks with appropriate dose tapering thereafter over 2-4 weeks.

Monitoring therapy

Practice Recommendations

1. All TB patients on treatment must be monitored frequently for:

- Adherence

- Response to treatment (bacteriologically and or clinically)

- Adverse drug events (early identification and management)

2. Sputum smear microscopy is used to monitor response to treatment and is done at: a) end of 2 months of intensive phase, b) end of 5 months and c) end of treatment at 6 months.

3. Chest radiographs and Xpert MTB/Rif assays are only used for screening and diagnosis of TB respectively and NOT recommended for follow up and monitoring of TB treatment.

4. At the end of treatment, assessment of outcomes is mandatory for all TB patients.

5. All TB deaths should be audited (guided by death audit forms) within 7 days at the facility where it happened and reported to the next level within the next 7 days while the province will report quarterly to national level.

Once a patient with TB is started on treatment, he/she must be followed up regularly. The frequency of monitoring depends on the level of care. At the health facility level, this is usually at every visit (two-weekly or monthly depending on medicines refill schedules) by the clinician and daily by the DOT nurse while at the community level, the treatment supporter should monitor the patient daily during the intensive phase and at least weekly during the continuation phase.

Adherence to medicines

As stated before, each patient must take the right regimen at the right dose for the right duration until end of treatment. It is not only the duty of the patient to take his/her medicines but it is also the duty of the health care system, particularly the facility health care workers who are treating the patient, to ensure this. Thus adherence to medicines is an on-going activity that the patient must be continually reminded of and supported to achieve. Every health care worker must use every contact with a TB patient to ensure that adherence to medicines is as near 100% as possible.

Therefore at every contact with the patient assess and support adherence by doing the following:

1. Ask the patient if he/she is taking the medicines.
2. Carry out a pill count: ask the patient how many pills are left, request to see the tablets he/she has brought in and count them and compare with what was dispensed and what is expected to be remaining.
3. Ask what time he/she takes each medicine and whether he/she takes the medicines before meals or after meals.
4. Check and see if the patient is regularly obtaining treatment: review his/her tuberculosis treatment card and see if medicines were collected and taken at the scheduled times.

Response to treatment

The primary aim of treatment is to cure the patient. Treatment should result in improvement/decrease of the patient symptoms, resolutions of documented fever and gain in weight if there was significant weight loss due to the disease. These improvements should in most patients, begin to occur within two weeks of treatment. Most patients will be almost completely well within 1-2 months of being on treatment and any patient whose symptoms have not subsided and clinical status has not improved within that time should be evaluated for either a concurrent disease (such as, diabetes), a complication of the disease, poor treatment adherence or drug resistance. Meanwhile, clinicians should review results of the diagnostic tests and ensure that the diagnosis is correct. Monitoring the response to treatment involves clinical monitoring and bacteriological monitoring.

Clinical monitoring

Clinical monitoring must be done for all patients. For cases of TB where bacteriological monitoring cannot be done such as in most forms of EPTB, this is the only way of monitoring response to treatment. Clinical monitoring consists of re-taking the clinical history and performing physical examination as appropriate.

Check the weight of the patient, ask about his/her well-being and ask if the previous symptoms are still present or not at each visit to the clinic. A patient who is doing well will progressively have increased energy, increased appetite, gain in weight, a decrease, if not disappearance, of symptoms and generally feel better.

Bacteriological monitoring

This is done using sputum smear microscopy to monitor the response to treatment. In drug resistant TB cases, mycobacterium culture is also used for bacteriological monitoring. Examination of sputum smears for conversion from positive to negative is the best indicator that the treatment is being taken regularly and that it is effective. **Xpert MTB/Rif assay is only used for diagnosis of TB and is not recommended for monitoring treatment response**.

After 2 months of chemotherapy, more than 80% of new pulmonary bacteriologically confirmed cases should be smear-negative (seroconversion) and after 3 months, the rate should increase to at least 90%.

NOTE: Routine use of chest radiographs in monitoring patient response to treatment is unnecessary, wasteful of resources and is not recommended. Chest radiographic shadows may not resolve at the same pace as symptoms and or mirror bacteriologic clearance.

A positive sputum at the end of the intensive phase should trigger a review of the quality of supervision and support provided by the programme and adherence to treatment by the patient and if needed should trigger the provision of an appropriate remedy. This will, however, lead to prolongation or continued use of ALL four medicines used in intensive phase treatment awaiting results of repeat Xpert and LPA.

The schedule of sputum smear examination, what the results mean and what to do with the obtained results is shown in table 11 below:

Table 10 Schedule of sputum smear microscopy for monitoring patients on TB treatment

Category	Sputum examination, interpretation & action to take
All Pulmonary TB cases, resistance ruled out on FLD- DST	Examine sputum at end of months 2,5,6 months **If positive at:** End of month 2 then: • Continue RHZE. • Assess and address issues with adherence. • Send sputum specimen for culture and DST. • Repeat Xpert looking out for rifampicin resistance and send a specimen for LPA. Refer to the Clinical Guidelines for the Management of Drug Resistant Tuberculosis for INH mono-resistance End of month 5 or 6: • Assess and record outcome as treatment failure. • Close current patient's treatment card. • Assess and address issues with adherence. • Send sputum specimen for culture and DST. • Send specimen for LPA and repeat Xpert; looking out for rifampicin resistance. • Switch to an appropriate SLD treatment regimen depending on DST results.
Extra-pulmonary TB cases, with no resistance suspected	• Clinical monitoring. • If no change in clinical condition, re-evaluate and investigate further.
Children	• Examine sputum at the end of months 2, 5, 6 in children who produce sputum. • Manage as for adults above.

Adverse drug events monitoring

All patients on TB treatment must be monitored and managed appropriately for emerging adverse drug events. *Refer to chapter 16 on Pharmacovigilance for details of management of adverse events.*

Outcome assessment and recording

The performance of the TB control programme may be assessed in various ways and at different levels but of paramount importance is the ability of the program to assess and record outcomes of every patient diagnosed, registered and treated for TB. Every patient must be accounted for and a treatment outcome recorded in the patient treatment card and in the facility register. Treatment outcome assessment shall be done for all patients at the end of the treatment. Accurate and complete recording of the treatment outcome in the TB treatment card and the TB register will enable the NTLP to monitor progress of individual patients, performance of individual health care facilities, districts and provinces

and track Zimbabwe's performance towards achieving national and international targets to which the country has committed.

Death audits

All TB deaths should be audited within 7 days at the facility where the patients were being treated and reported to the next level within the next 7 days. The district level should report to the provincial level within 7 days of receiving the death audit report from the health care facility while the provincial level should compile all the data and report quarterly to the national level. The NTLP will provide death audit forms and the reporting format to be used. *Refer to chapter 17 on Monitoring & Evaluation for outcome case definitions*

Post TB treatment care

Practice Recommendations

At the end of TB treatment:

- **Pulmonary TB patients with significant lung damage and cavitations on the initial CXR should have a follow up CXR at the end of treatment.**
- **Where available a spirometric lung function test should be carried out in patients whose end of TB treatment CXR shows significant lung damage.**
- **Appropriate plans should be made to link patients completing treatment for PTB who have significant lung damage visualized at the end of treatment CXR and or have significantly abnormal spirometric lung function test to chronic respiratory care.**
- **Patients with TB pericarditis should have a CXR and echocardiogram carried out.**
- **Patients with TB meningitis associated with neurological deficits should have a brain CT scan carried out**
- **Patients with osteo-articular TB should be evaluated for physical function to identify the need for rehabilitation.**
- **Patients with genito-urinary TB should have urea & electrolytes plus creatinine done. Ultrasound scan can also be performed where affordable.**

While for a large proportion of TB patients the experience of the TB episode will lead to no significant illness after the TB is cured, for a significant proportion of patients, the episode of TB becomes the beginning of a journey characterised by chronic ill health and in some patients, premature deaths. National TB Control programs have hitherto not paid attention to the group of patients who develop long term complications of TB. Tuberculosis is associated with multiple, acute and chronic complications that are the result of structural, metabolic and vascular changes due to the disease. Despite successful cure

of TB, confirmed by the absence of MTB in the involved organ, chronic complications can arise such as lung scarring (fibrosis), bronchiectasis, chronic pulmonary aspergillosis, airway stenosis, chronic obstructive pulmonary disease (COPD), skeletal deformities, genito-urinary complications or focal neurologic deficits from healed tuberculomas.

Little is known about what drives the long term complications of TB. While delays in TB diagnosis may be associated with these complications, it appears that in some patients an exuberant and destructive immune response, determined by host-pathogen relationship may be playing a role. It is for this reason that several research groups are studying the immunological response to MTB and testing various host directed therapies to attempt to modify the immune response to MTB and make it less destructive. While this is going on, NTPs need to play their role by identifying patients who, at the end of TB treatment, require continued care to manage long term complications of TB. The Zimbabwe NTLP is among the pioneer TB control programs to include a statement and make a commitment to begin a systematic evaluation of patients at the end of TB treatment that goes beyond a search for bacteriological cure to identify patients who may be at risk of chronic morbidity post TB treatment. At this stage the burden and type of disease post TB treatment is not known and therefore elaborate plans for testing and providing care to these patients cannot be made. In the life time of the guidelines efforts will be made to attempt to define the burden and characteristics of post TB treatment chronic disease with a focus on the lung. Table 12 below provides a summary of the common chronic complications of TB that have been cited in the medical literature.

Table 11 Common chronic complications of TB and their management.

Complication post TB treatment	Investigation	Common clinical features	Proposed management
COPD	Lung function test (spirometry)	Shortness of breath, cough and wheeze	Bronchodilators (Long Acting Beta Agonists /Long Acting Muscarinic Agents (LABA/LAMA)
Bronchiectasis	CXR Lung function test (spirometry) High Resolution Chest CT Scan where available	Persistent productive cough which is copious & purulent Recurrent haemoptysis;	Physiotherapy; broad spectrum antibiotics when exacerbated by bacterial infection
Chronic Pulmonary Aspergillosis (CPA)	CXR Chest CT Scan (where available) Aspergillus precipitins serology	Aspergilloma (mycetoma) in the residual cavities; Malaise, cough, recurrent haemoptysis	Antifungal drugs e.g. itraconazole Surgical excision
Constrictive pericarditis	CXR, ECHO	Dyspnoea, oedema, fatigue, pleural calcification on CXR, changes in cardiac chamber sizes on ECHO	Refer for surgery e.g. pericardiectomy
Intracranial tuberculoma	Brain CT scan	Stroke; epileptic seizures; cranial nerve palsies, motor deficits; cognitive impairment; hydrocephalus in children; etc.	Consider surgery/ anti-convulsants;
Obstructive uropathy	U&E+ creatinine; USS	Genitourinary symptoms of obstruction	Surgical treatment by urologists
Osteo-articular deformities	Clinical evaluation	Various deformities	Physiotherapy

Further Reading

1. WHO Treatment of Tuberculosis guidelines, 2010
2. Bulletin of the WHO 2012;90:63-66. doi: 10.2471/BLT.11.092320 (Eliminating the category II retreatment regimen from NTP guidelines: the Georgian experience)
3. DOL: 10.4103/0028.3886.72182 (Duration of anti TB treatment in TBM: challenges and opportunity)
4. Adjunctive corticosteroid therapy for tuberculosis: A critical reappraisal of the literature by David P Dooley, John L Carpenter and Steven Rademacher

Chapter 7

Preventing and Managing HIV Associated Tuberculosis

How HIV changes the clinical picture of TB

The association between TB and HIV is now well documented. In persons infected with *Mycobacterium tuberculosis* the annual risk of TB disease in PLHIV is about 10% (ranges from 3-13), but it is only 10% for the entire lifetime of an HIV-negative individual. Tuberculosis is a leading killer of HIV-positive people. In 2015, 72% of notified TB patients in Zimbabwe were co-infected with HIV with 1 in 3 HIV reported deaths resulting from TB.

The clinical presentation of TB in PLHIV depends on the degree of immunosuppression. In persons with relatively well preserved immune function with a high CD4 T cell count, TB presents in a similar manner as in persons not infected with HIV. As immune function deteriorates, typical presentations become less common with more middle and lower lobe disease in the lung as opposed to upper lobe disease, less cavitations on the CXR, a higher frequency of intrathoracic lymph node enlargement and higher rates of EPTB including pleural, pericardial and disseminated disease. In the pre-ART era, TB in PLHIV carried a very high mortality. This mortality risk still persist today but has significantly been reduced by ART even though early mortality in HIV infected TB patients remains a major clinical and public health challenge.

The risk of active TB is highest in HIV co-infected patients who are not on ART and in those who have recently been enrolled in HIV care. The TB risk decreases significantly as the person's immune function recovers but it does not decline back to the same level as that of HIV negative persons. Both ART and Isoniazid Preventive Therapy (IPT) are effective in preventing HIV associated TB individually and with additive effects when combined. Both TB and HIV care and control programs need to develop robust approaches for prevention, identification and treatment of TB especially in newly diagnosed HIV infected persons entering care with low CD4 T cell counts. Similarly, to prevent early HIV associated TB mortality, early initiation of ART in HIV infected TB patients is a major imperative. The package of interventions that NAPs and NTPs together with their partners need to carry out to confront the burden of HIV associated TB are contained in the 12 component WHO policy on TB and HIV collaborative activities shown in Table 13 below.

Table 12: 12 components of TB HIV collaboration

A. Strengthening the mechanisms for delivering integrated TB and HIV services	
A.1	**Strengthening coordinating bodies for collaborative TB/HIV activities functional at all levels**
A2	**Determining HIV prevalence among TB patients and TB prevalence among people living with HIV**
A3	**Carrying out joint TB/HIV planning to integrate the delivery of TB and HIV services**
A4	**Monitoring and Evaluating collaborative TB/HIV activities**
B. Reducing the burden of TB in people living with HIV and initiate early antiretroviral therapy (the *Three I's for HIV/TB*)	
B1	**Intensifying TB case-finding and ensure high quality anti-tuberculosis treatment**
B2	**Initiating TB prevention with Isoniazid preventive therapy and early antiretroviral therapy**
B3	**Ensuring control of TB infection in health-care facilities and congregate settings**
C. Reducing the burden of HIV in patients with presumptive and diagnosed TB	
C1	**Providing HIV testing and counselling to patients with presumptive and diagnosed TB**
C2	**Providing HIV prevention interventions for patients with presumptive and diagnosed TB**
C3	**Providing cotrimoxazole preventive therapy for TB patients living with HIV**
C4	**Ensuring HIV prevention interventions, treatment and care for TB patients living with HIV**
C5	**Providing antiretroviral therapy for TB patients living with HIV**

Strengthening the mechanisms for delivering integrated TB and HIV services

Both the NTLP and the NAP will continuously work towards setting up and or strengthening TB/HIV coordinating committees at all levels (national, provincial and district) to support the integrated delivery of high quality TB and HIV services. These committees are responsible for planning, coordinating implementation, surveillance, monitoring and evaluation as well as support and supervision for the two programmes.

Practice Recommendation: There should be a functional TB/HIV coordinating mechanism (e.g. a committee) at the national, provincial and district level.

Reducing the burden of TB in people living with HIV and initiate early ART (the Three I's for HIV/TB)

Intensify TB case finding among PLHIV

Practice recommendations

1. **All PLHIV should be screened for active TB using the symptom enquiry** (current cough, night sweats, loss of weight, fever and history of TB contact) **and/or measurement of the BMI** at every encounter with a health care worker **and/or CXR (annually if possible or as indicated).**
2. **All PLHIV with a positive enquiry to any one of the symptoms on the checklist** (current cough, night sweats, fever, loss of weight and history of TB contact) **and/or a BMI of less than 17** Kg/m^2 should have a CXR taken (unless it is unavailable)
3. **All PLHIV with** a **positive enquiry to any one of the symptoms on the checklist** (current cough, night sweats, fever, loss of weight and history of TB contact) **and/or a BMI of less than 17 Kg/m2 and/or abnormal CXR** should have specimen collected and submitted to the laboratory for Xpert MTB/Rif or Xpert MTB/Rif Ultra assay.
4. All **newly diagnosed HIV positive patients** should submit one spot sputum sample for Xpert MTB/Rif or Xpert MTB/Rif Ultra to rule out active TB disease even if they have a negative symptom screen and or a BMI of >17.
5. **All PLHIV who are seriously ill and or have a CD4 T cell count of equal or less than 100** should have the Urine Lateral Flow - Lipoarabinomannan Assay (LF-LAM).

TB Preventive Therapy (TBPT) in PHIV

Practice recommendations

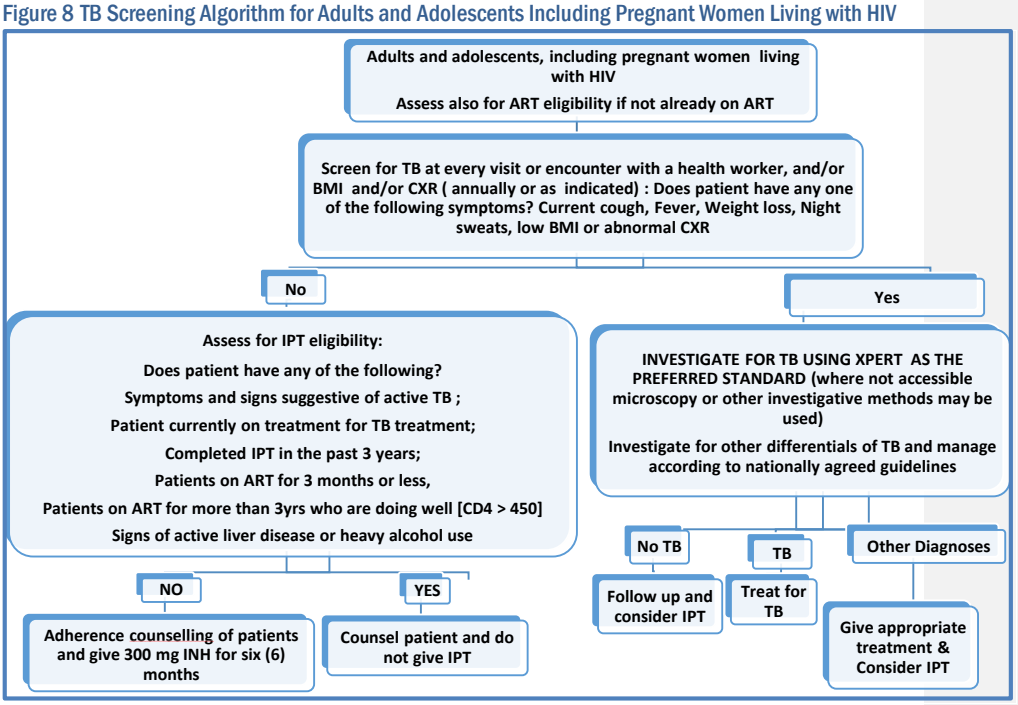
6. **All PLHIV who have active TB excluded on symptom enquiry, measurement of BMI and CXR** should be provided with TBPT preferably using isoniazid at 300 mg given once daily for six months (IPT/6H)

Practice Recommendations

7. **All people with presumptive and diagnosed TB should be tested for HIV at first contact with a HCW.**
8. **All presumptive and diagnosed TB patients who test negative for HIV should be linked with HIV prevention services.**
9. **All TB patients who test HIV positive should be started on ART within 2-8 weeks of commencement of TB treatment. HIV care should be provided preferably under the same setting and patients transferred for continuation of HIV care to the OI/ART clinic after completion of TB treatment.**
10. **Patients co-infected with TB and HIV should be managed for both conditions concurrently with TB treatment taking precedence over ART initiation.**
11. **All HIV infected persons with active TB should be initiated on anti-TB treatment promptly followed by Cotrimoxazole prophylaxis (CPT) and then an Efavirenz based ART regimen within 8 weeks of commencement of TB treatment.**
12. **All HIV infected persons with active TB who have a CD4 T cell count of equal or less than 50 should be initiated on anti-TB treatment promptly and on an Efavirenz based ART regimen within 8 weeks of commencement of TB treatment.**
13. **All HIV infected persons with intracranial TB who have a CD4 T cell count of equal or less than 50 cells/µl should be initiated on anti-TB treatment promptly and have their ART initiation delayed until after 8 weeks of commencement of TB treatment to reduce the risk of intracranial TB–Immune Reconstitution Inflammatory Syndrome (IRIS) which could end fatally.**
14. **All HIV infected TB patients should be given cotrimoxazole preventive therapy (CPT) for the whole duration of TB treatment.**

NB. **Following observations made by the NAP, on occurrence of severe hepatic necrosis in 8 cases (4 of whom died) among PLHIV who had been on ART for longer than 3 years and had high CD4 T cell counts (unpublished), the TB/HIV subcommittee recommends that IPT SHOULD NOT BE PROVIDED to this target population due to high risks of severe hepatic reactions that could end fatally. With further characterization of these cases being done, an interim decision to exclude persons who fit this description will be upheld, in line with the principle "First Do No Harm".**

Figure 8 TB Screening Algorithm for Adults and Adolescents Including Pregnant Women Living with HIV



Prevention of TB Transmission in HIV Care Settings (TB - Infection Control)

This is dealt with in the chapter on infection control

Managing HIV Associated TB in Children

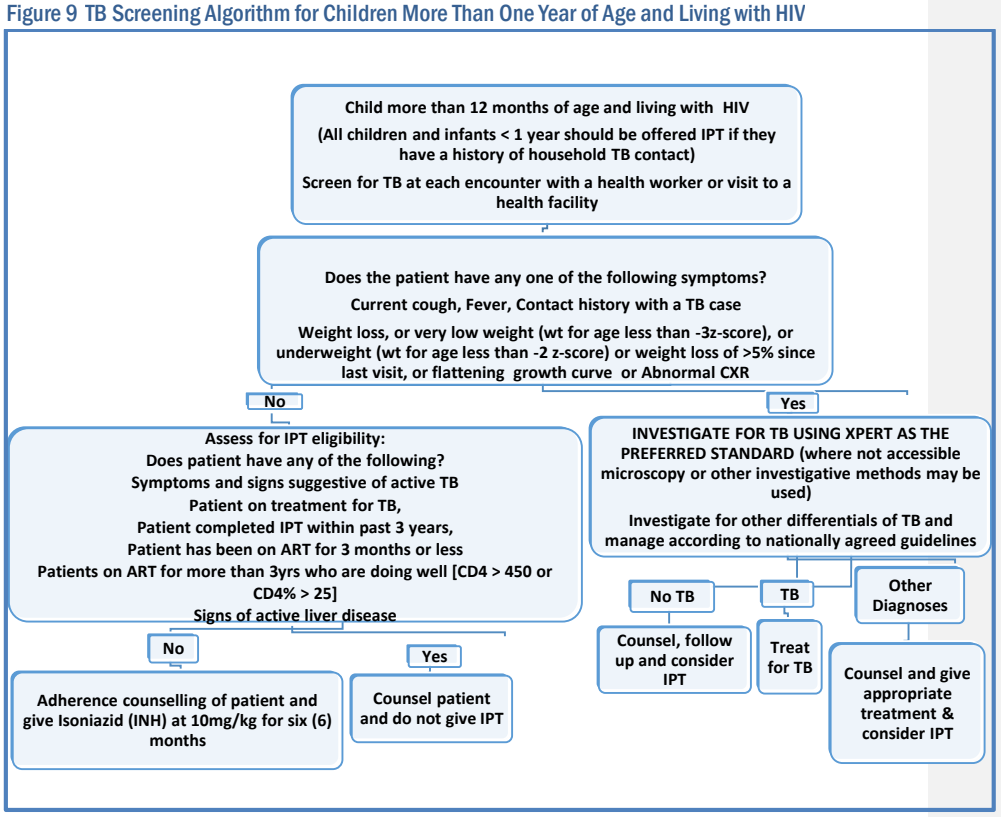
Note

- HIV infected children are at higher risk for TB infection and TB disease than HIV uninfected children.
- HIV makes the diagnosis and management of TB in children more difficult because:
    - HIV-associated chronic pulmonary disease and TB disease present in a similar way.
    - Tuberculin skin test is less reliable in the presence of HIV infection.
    - The HIV pandemic has led to increased prevalence of TB in adults and consequently increased risk of TB infection in children. Early mortality due to TB (and HIV co-infection) in adults has resulted in large number of orphans without adequate care.

Practice Recommendation

15. **All children who are presumed to have TB should be screened for HIV with adherence to the principle of counselling, consent or assent and confidentiality.**
16. **All HIV infected children receiving treatment for TB should also receive supplementary pyridoxine.**
17. **Recommendations for ART in HIV infected children being treated for TB remain the same as those in adults.**

Figure 9 TB Screening Algorithm for Children More Than One Year of Age and Living with HIV



Considerations for ART and TB treatment regimen

Note that drug–drug interactions can complicate TB and HIV treatment. The rifamycins used in TB treatment (Rifampicin, Rifabutin and Rifapentine) are hepatic enzyme inducers and will lower the serum concentration of many medicines used to treat HIV. This effect is most pronounced with Protease Inhibitors (PIs) and rifampicin. For these reasons the following recommendations have been made:

Practice Recommendation

18. **In patients receiving PIs for the treatment of HIV, rifabutin given at a dose of 150 mg once daily, should be substituted for Rifampicin. If Rifabutin is not available the doses of Ritonavir boosted Lopinavir (LPV/r) should be doubled or the doses of ritonavir increased to 400 mg twice daily (super boosting). Clinicians should be aware that both double dosing and super boosting are associated with increased risk of adverse drug reactions.**

Table 13 Weight adjusted dosing for TB/HIV co-infetced patients on ATZ/r

Weight (Kilograms)	Intensive Phase (2 months)	Continuous Phase (4 months)
40-54 kg	RFB* 150mg x 1 (3 times a week) Isoniazid 300mg x 1 daily Ethambutol 400mg x 2 daily Pyrazinamide 400mg x 2 daily	RFB 150mg x 1 (3 times a week) Isoniazid 300mg x 1 daily
55-70 kg	RFB 150mg x 1 (3 times a week) Isoniazid 300mg x1 daily Ethambutol 400mg x 3 daily Pyrazinamide 400mg x3 daily	RFB 150mg x 1 (3 times a week) Isoniazid 300mg x 1 daily
Above 70kg	RFB 150mg x 1 (3 times a week) Isoniazid 300mg x1 daily Ethambutol 400mg x4 daily Pyrazinamide 400mg x4 daily	RFB 150mg x 1 (3 times a week) Isoniazid 300mg x 1 daily

*RFB - Rifabutin

Practice Recommendations

19. **In children being treated for TB with a Rifampicin- based regimen, using a triple NRTI regimen (such as AZT+3TC+ABC) may be considered. This regimen may however be inferior in children with high plasma viral loads.**
20. **Bedaquiline is primarily metabolised by CYP3A4, therefore, its concomitant use with EFV and PIs for patients with XDR/MDR TB can interfere with drug concentrations and should be undertaken with extreme caution and close clinical, bacteriological and virological monitoring. Therapeutic drug monitoring should be considered in these patients (note this capacity is available at the University of Zimbabwe).**
21. **There is limited information on the use of EFV 400mg among TB patients on ART and as such an EFV 600mg based triple ART regimen once daily remains the recommended treatment regimen and dose of choice.**
22. **Rifampicin is known to significantly lower plasma concentrations of Dolutegravir (DTG) and therefore, in patients receiving TB treatment with a Rifampicin based regimen, the dose of DTG should be increased from 50 mg once daily to 50 mg twice daily.**

Further Reading

1. WHO Global Tuberculosis Report 2016
2. WHO, TB/HIV: A Clinical Manual, 2004

Chapter 8

Management of Drug Resistant TB

This chapter presents a summary of the current guidance on programmatic management of drug resistant TB (PMDT). Please refer to the PMDT guidelines for further information.

Definitions

Drug-resistant tuberculosis (DRTB) is confirmed through laboratory tests that demonstrates *in-vitro* growth of isolates of Mycobacterium tuberculosis in the presence of one or more anti-TB medicines. It can also be confirmed through molecular tests such the Xpert MTB/Rif assay, LPA or gene sequencing that detect mutations responsible for resistance to specific medicines (resistance conferring changes in the MTB's genetic code, the DNA). Cases are classified in categories based on DST results of clinical isolates confirmed to be M. tuberculosis:

Mono-drug resistance TB: resistance to one first-line anti-TB medicine only.

Poly-drug resistance TB (PDR): resistance to more than one first-line anti-TB medicine other than resistance to both isoniazid and rifampicin.

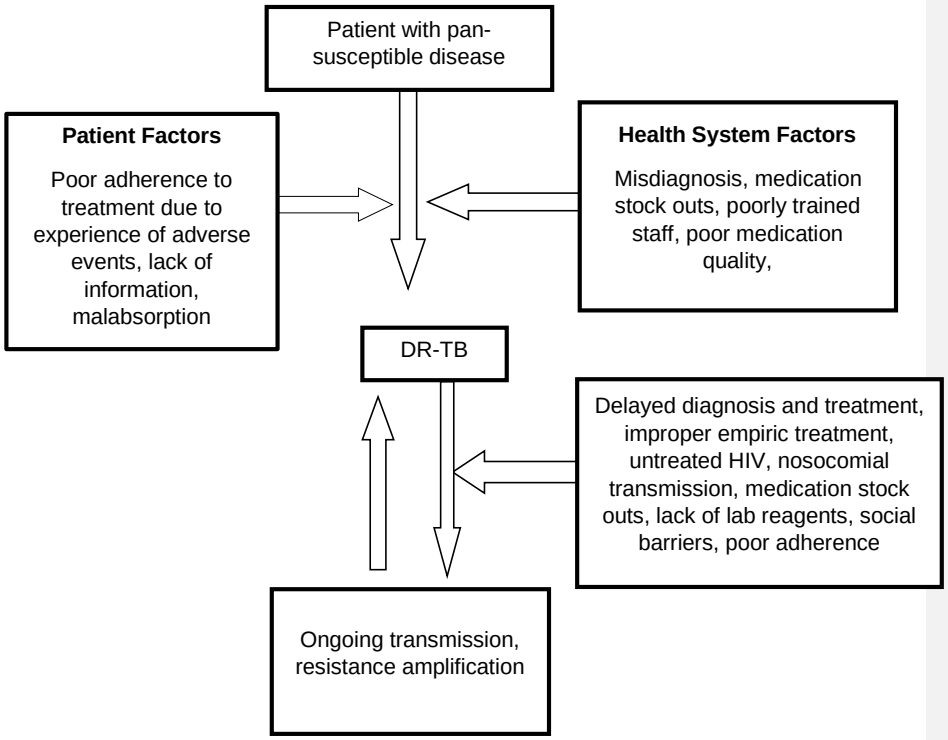
Multidrug resistance TB (MDR-TB): resistance to at least both isoniazid and rifampicin.

Extensive drug resistance TB (XDR-TB): multi -drug resistance that additionally is resistant to any fluoroquinolone and to at least one of three second-line injectable medicines (capreomycin, kanamycin and amikacin).

Rifampicin resistance TB (RR-TB): resistance to rifampicin detected using phenotypic or molecular (genotypic) methods, with or without resistance to other anti-TB medicines. It includes any resistance to rifampicin, whether mono-resistance, multidrug resistance, poly-drug resistance or extensive drug resistance. These categories are not all mutually exclusive. When enumerating rifampicin-resistant TB (RR-TB), for instance, multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are also included. While it has been the practice until now to limit the definitions of mono-resistance and poly-drug resistance to first-line medicines only, future drug regimens may make it important to classify patients by their strain resistance patterns to fluoroquinolones, second-line injectable agents and any other anti-TB medicines for which reliable DST becomes available.

Causes of DR-TB

Figure 10 Drivers of drug resistant TB



Prevention of DR-TB

Treating a case of MDR-TB is more than 25 times the cost of treating an uncomplicated drug-susceptible case. In the Zimbabwean setting of high HIV burden, an untreated case of MDR-TB can infect large numbers of individuals, rapidly leading to significant outbreaks of MDR-TB with high case fatalities. Prevention of DRTB depends on

- A robust TB control program that is able to treat successfully the largest possible proportion of identified new, previously untreated cases with first line medicines (a TB treatment success rate in excess of 90% for new cases)
- Correct usage of first line medicines in terms of regimens and doses in both the public and private health care sectors

- Rational use of anti-microbial medicines in general and anti-TB medicines in particular in both the public and the private sector.
- Ensuring the highest possible quality of all the anti-TB medicines used in the program in addition to optimised storage conditions.
- Ensuring every effort is made to promote and support full adherence to treatment for all patients treated with anti-TB medicines, both for first and second line medicines.
- Prompt and complete identification of patients with drug resistant TB and initiation of treatment with appropriate regimens and doses of second line medicines.

NOTE: The priority is prevention of MDR-TB plus early identification and appropriate management of MDR-TB.

The National TB Control Programme will ensure that regular and sufficient stocks of quality controlled anti-TB medicines are available in the country at all times. Provincial Health Executive (PHEs) teams led by the PMDs, central hospitals and local authority health departments should ensure all TB patients identified in their jurisdiction are registered to facilitate correct estimation of annual anti-TB medicines requirements.

In the event that a health care worker presumes that a patient has MDR-TB, a sputum sample must be sent for Xpert MTB/RIF testing. Screening of household contacts should be conducted and appropriate health education on infection control provided. Infection control measures as outlined in the chapter on TB infection should also be implemented.

Serious limitations of the quality of evidence prevent drawing any recommendations on MDR-TB preventive therapy as a public health measure. Strict clinical observation and close monitoring of contacts of patients with MDR-TB for the development of active TB disease for at least two years is preferred over the provision of preventive treatment. All contacts of patients with MDR-TB should be screened for TB in more or less the same way as in contacts of patients with drug susceptible TB. However even in the absence of symptoms and or a low BMI, it is recommended that contacts of MDR-TB cases have a CXR. The CXR should be repeated annually for two years in persons whose initial screening is negative for TB. The two year cut off is based on the risk of development of active TB following infection with MTB which is highest in the first two years.

Note: While clinical trials are underway to find an effective TBPT for persons latently infected with MTB that is MDR, currently such therapy does not exist.

Diagnosis of DR-TB

Principles of diagnosis of DR-TB

Practice Recommendations

1. ***Rapid DST, of at least rifampicin using rapid molecular tests such as Xpert MTB/Rif rather than conventional culture and DST, should be carried out in all adults and children at the time of TB diagnosis. Bacteriological diagnosis of TB without DST should as far as feasible be avoided.***

2. ***For patients with confirmed rifampicin-resistant TB or MDR-TB, SL-LPA must be used as the initial test, instead of phenotypic culture-based DST, to detect resistance to fluoroquinolones and the injectable medicines used to treat MDR-TB.***

Principles of the care and control of DR-TB

1. To detect DR-TB cases early and
2. To promptly initiate appropriate therapy for patients with DR-TB and thus
3. To avoid the spread of DR-TB strains
4. To select medicines and regimens for the treatment of DR-TB in a manner that prevents the emergence of further resistance to anti-TB medicines.

Table 14 Classification of TB medicines for DR-TB treatment

A. Fluoroquinolones		Levofloxacin Moxifloxacin Gatifloxacin	Lfx Mfx Gfx
B. Second-line injectable agents		Amikacin Capreomycin Kanamycin	Am Cm Km
C. Other core second-line agents		Ethionamide / Prothionamide Cycloserine / Terizidone Linezolid Clofazimine	Eto / Pto Cs / Trd Lzd Cfz
D. Add-on agents (not part of the core MDR-TB regimen)	D1	Pyrazinamide Ethambutol High-dose isoniazid	Z E H^h
	D2	Bedaquiline Delamanid	Bdq Dlm
	D3	*p*-aminosalicylic acid Imipenem-cilastatin Meropenem Amoxicillin-clavulanate (Thioacetazone)	PAS Ipm Mpm Amx-Clv (T)

Practice recommendations

1. *In the programme setting in Zimbabwe, all patients with RR-TB or MDR-TB who were not previously treated with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents is excluded or is considered highly unlikely, a shorter MDR-TB regimen of 9–12 months will be used instead of the longer regimens unless there are contraindications for some medicines in the shorter regimen.*

Subgroup considerations

2. *Rifampicin-resistant TB (RR-TB) without MDR-TB. In the programme setting in Zimbabwe, all patients, children or adult, with RR-TB in whom isoniazid resistance is not confirmed will be treated with the shorter MDR-TB treatment regimen.*

Resistance additional to MDR-TB.

3. *For patients infected with strains known or strongly suspected of being resistant to one or more drugs in the shorter MDR-TB treatment regimen (e.g. pyrazinamide), the shorter regimen will not be used, under routine programme settings in Zimbabwe, until more evidence becomes available about its performance in such a situation.*

Based on the following treatment principles and advise from WHO

a) *In patients with RR-TB or MDR-TB, a regimen with at least five effective TB medicines during the intensive phase is recommended, including pyrazinamide and four core second-line anti-TB medicines – one chosen from Group A, one from Group B, and at least two from Group C.*
b) *If the minimum number of effective TB medicines cannot be composed as given above, an agent from Group D2 and other agents from Group D3 may be added to bring the total to five.*
c) *In patients with RR-TB or MDR-TB, it is recommended that the regimen be further strengthened with high-dose isoniazid and/or ethambutol*
d) *It is recommended that any patient – child or adult – with RR-TB in whom isoniazid resistance is absent or unknown be treated with a recommended MDR-TB regimen, either a shorter MDR-TB regimen, or if this cannot be used, a longer MDR-TB regimen to which isoniazid is added*

The standard short treatment regimen for DR-TB treatment in Zimbabwe is:

4-6Km, Mfx$^{high\ dose}$, Cfz, Z, E, H$^{high\ dose}$, ETO / 5 Mfx$^{high\ dose}$, Z, CFZ, E

The initial treatment plan for all patients treated with the short MDRTB regimen will be to have a 4 and 5 months intensive and continuation phases respectively. Treatment will be extended to a maximum of 6 months in the intensive phase if culture conversion has not occurred by the fourth month of treatment. Similar considerations will be used to extend the continuation phase of treatment for a maximum total treatment duration (intensive and continuation phases) of 12 months. If patients have not achieved culture conversion by month 5 they will be declared treatment failures.

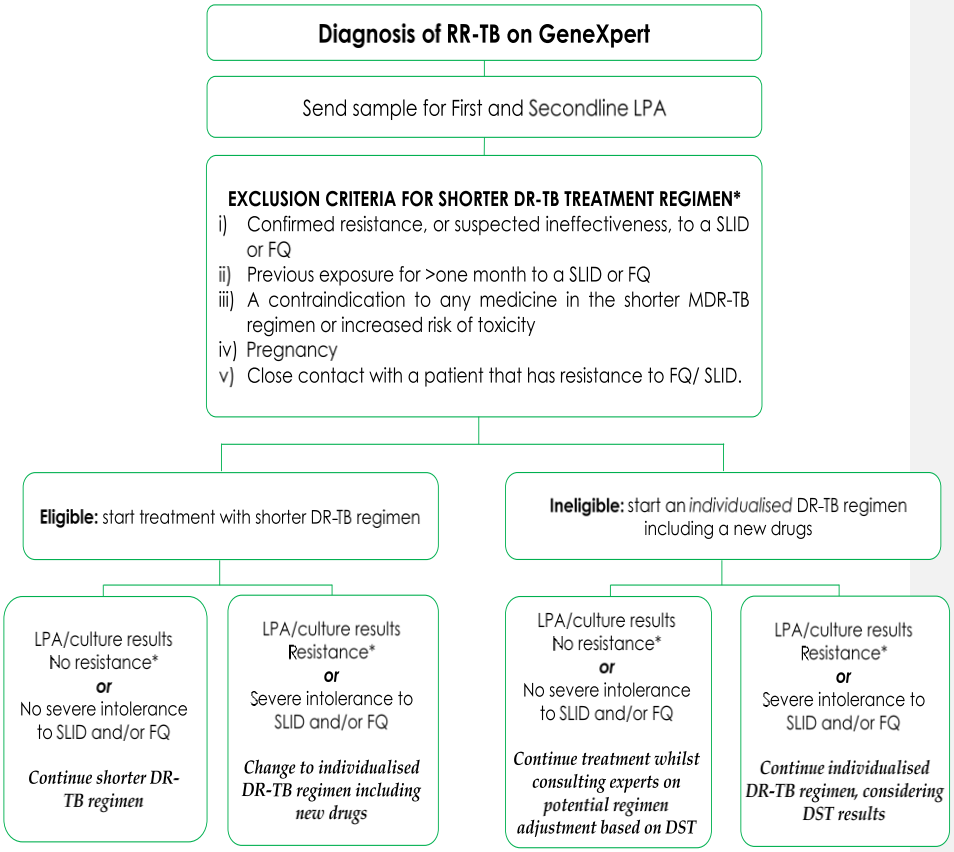
Regimen design steps for RR-TB patients who are not eligible for the Short Treatment Regimen (STR)

The steps shown below which are recommended by WHO, will be used to design a treatment regimen for the RR-TB patients who are not eligible for the STR.

Table 15 Step wise selection of SLDs for constituting regimens to treat MDR-TB

Step 1: Choose either Bedaquiline or Delamanid (Group D2). The choice of which drug (or potentially both drugs) is outlined in the section on 'special considerations' below.
Step 2: Choose a fluoroquinolone (Group A – Mfx or Lfx). If only ofloxacin resistance from DST is known, Mfx or Lfx (high dose is preferred) can still be added to the regimen, but should not be counted as one of the effective drugs. Treatment with a later generation FQ (Mfx or Lfx) significantly improves RR-TB or MDR-TB treatment outcomes; they should therefore always be included unless there is an absolute contra-indication for their use.
Step 3: Choose an injectable (Group B – Km, Cm, and Am). If clinical history or DST suggests resistance to all SLID, or in case of a serious adverse event (hearing loss, nephrotoxicity), the injectable should not be used or should be promptly discontinued. In children with mild forms of DR-TB disease, the harms associated with an injectable may outweigh potential benefits and therefore injectable agents may be excluded in this group.
Step 4: Choose at least two Group C drugs (Lzd, Cfz, Eto, and Cs) thought to be effective as additional core second line drugs to BDQ/DLM, FQs, and SLID. If efficacy is uncertain, the drug can be added to the regimen, but should not be counted as an effective drug.
Step 5: Choose D1 drugs (PZA, INH_{hd}, EMB) as add-on agents. PZA is routinely added to most regimens. High dose INH may further strengthen the regimen if DST shows INH sensitivity, or INH resistance is unknown. D1 drugs are usually added to the core second-line drugs, unless the risks from confirmed resistance, pill burden, and intolerance or drug-drug interaction outweigh potential benefits.
Step 6: Only choose D3 drugs if there are no other treatment options available due to highly resistant forms of DR-TB or multiple intolerances to other DR-TB drugs.
The final individualized DR-TB regimen will consist of at least 5 drugs with confirmed or high likelihood of susceptibility from the following list: Bdq or Dlm, Lfx or Mfx, Km (Am, Cm), Eto, Lzd, Cfz, Cs, Z, H_{hd}, E.

Figure 11 Algorithm for diagnosis and treatment of DR-TB



Patients started on the shorter treatment regimen and are failing, have drug intolerance or return after interrupting treatment for two or more months should be switched to the longer individualised regimen.

Patients may be initiated on the shorter treatment regimen, after assessment, while awaiting SL-LPA and treatment changed accordingly when results are available.

If a shorter treatment regimen is unavailable or contraindicated, patients with RR/MDR-TB should be treated with an individualised regimen.

The injectable is used during the intensive phase, a ***minimum of 6 months,*** and should be used up to a minimum of ***4 months after culture conversion***. The total duration of treatment must be ***at least 20 months***

NB. All patients treated with Cycloserine (Cs) should receive Pyridoxine (50 mg for every 250 mg of Cs) in order to prevent neurological adverse events.

Organization of the DR-TB case management system

There are three main strategies for the delivery of DR-TB treatment i.e. **hospitalization (institutional approach), clinic –based (OPD Model)** treatment and **community-based treatment.** Each patient must be assessed on an individual basis to choose the most appropriate care approach. The DMO is responsible in ensuring that this assessment is carried out. The assessment should include clinical and psychological condition of patient, home environment, infection control needs, distance from the health facility, transport logistics, availability of trained health care workers and community and family support potential.

Hospitalization: Institutional approach:

The main indications for hospitalization include the following:

- ✓ Patients too ill (clinically or psychologically) to commence DR-TB treatment on an ambulatory basis.
- ✓ DOT and adherence support not guaranteed.
- ✓ Implementation of adequate infection control measures not feasible at home.
- ✓ Patient monitoring cannot be implemented on an out-patient basis.

Where patients with DR-TB are admitted provisions for infection control must be strengthened and maintained at high levels according to the customised facility infection control plan. Patients may be referred to the provincial centre of excellence where clinical management dictates. Patients who meet the following criteria can be discharged for ambulatory care:

- ✓ Patients whose clinical status has improved to the extent that he/she can be managed on ambulatory basis.
- ✓ Adequate infection control measures in the home are ensured.
- ✓ Adequate nutritional and social patient support is available to the patient.
- ✓ Measures to ensure full implementation of DOT, adherence support and regular follow up have been put in place (including transport).
- ✓ The receiving facility has been oriented and mentored on the patient's management. This may include a visit by health care workers from the facility to the district hospital.

A discharge summary must be completed and a month supply of drugs must be provided to the responsible facility. Recording forms for treatment adherence and reporting of adverse events, patient information and education materials must be provided also. The district should arrange transport to the patient's home.

Clinic based (OPD Model) Treatment

This involves the patient visiting the clinic each day to receive DOT by the health care worker. Standard infection control measures must be implemented in facilities providing such DOT.

Community Approach

Trained community DOT observers may observe stable patients on treatment for DR-TB during the continuation phase. The specific tasks to be performed by these DOT observers are:

- ✓ Direct observation of treatment on a daily basis.
- ✓ Treatment literacy for DR-TB patients, including TB infection control and nutrition.
- ✓ Monitoring patients for side effects.
- ✓ Reminding patients of their follow-up dates.

These DOT observers are accountable to the DMO and are or should be supervised by the primary health care centre nurses. They should meet with the nurses at the supervising facility at least monthly to report on their activities. Additionally they should refer to the supervising health facility any patients who are getting worse or who are experiencing new symptoms, which could be due to adverse events of the SLDs.

NB: Infection control is also very important for ambulatory care in the intensive phase.

Patient Education

Adequate patient education and measures surrounding infection control include:

- ✓ Education on cough hygiene, including use of surgical masks by patients.
- ✓ Suspension of school or work attendance until culture conversion or first two months of intensive phase.
- ✓ Ensure measures for adequate ventilation in the home.
- ✓ Community and family education.

Decision making in DR-TB management MUST always be made by the district team led by the DMO. The model of care for each patient must be regularly reviewed as there maybe changes in the clinical condition or social circumstances.

Patient Support systems

All patients on DR-TB treatment should have a psycho-social and economic assessment to identify those who need to be provided with psychological and social support such as transport and food to prevent treatment interruption and to reduce treatment associated costs.

Monitoring Therapy

Table 17 below summarises the various investigations and schedules for monitoring therapy

Table 16 Schedule of evaluations and tests for monitoring patients on treatment for MDR-TB

	BL	Wk 2	M1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Clinical evaluation																						
Clinical evaluation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight[º]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Functional status	X	X		X				X *			X											X
PNP	X		X	X	X	X	X	X			X			X								
Audiometry	X		X		X		X		X													
Vision test**	X		X	X	X	X	X	X			X						X					
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BMI	X																					
Bacteriological																						
Smear/ culture	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Xpert[§]	X																					
LPA[#]	X	Repeat if smear or culture positive or presumption of failure																				
DST[@]	X	Repeat if smear or culture positive or presumption of failure																				
Laboratory tests																						
FBC[¶]	X																					
Cr/ electrolytes	X		X	X	X	X																
K	X		X	X	X	X																
Mg, Ca (if low K)	X		X	X	X	X																
ALT/AST	X		X	X	X	X	X	X														
TSH	X				X			X														
Albumin	X																					
HIV rapid test	X																					
VL (if on ART)	X							X						X						X		
Fasting glucose	X																					
HbSAg	X																					
CXR	X							X						X						X		

Clinical and bacteriological monitoring of patients on the shorter DR-TB treatment regimen

	BL	Wk2	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12
Clinical evaluation														
Clinical evaluation	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight[º]	X		X	X	X	X	X	X	X	X	X	X	X	X
Functional status	X	X		X				X*			X			
PNP	X		X	X	X	X	X	X			X			X
Audiometry	X		X			X		X		X				

Vision test**	X		X	X	X	X	X	X			X			
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BMI	X													
Bacteriological														
Smear/culture	X		X	X	X	X	X	X	X	X	X	X	X	X
Xpert[§]	X													
LPA[#]	X	Repeat if smear or culture positive or presumption of failure												
DST[@]	X	Repeat if smear or culture positive or presumption of failure												
Laboratory tests														
FBC[¶]	X													
Cr/electrolytes	X		X	X	X	X								
K	X		X	X	X	X								
Mg, Ca (if low K)	X		X	X	X	X								
ALT/AST	X		X	X	X	X	X	X						
TSH	X				X			X						
Albumin	X													
HIV rapid test	X													
VL (if on ART)	X													
Fasting glucose	X													
HbSAg	X													
CXR	X							X					X	

Patients coming from neighbouring countries who have already been diagnosed with MDR-TB have to be registered, have their treatment reviewed and either modified or continued with appropriate monitoring.

Post treatment care

All patients completing treatment for pulmonary TB should have a chest x-ray to determine if long term post TB pulmonary care is needed.

Further Reading

1. World Health Organization Treatment Guidelines for Drug Resistant Tuberculosis – 2016 Update
2. Guidelines for the Programmatic Management Of Drug Resistant Tuberculosis in Zimbabwe – 2014 Edition

Definitions and reporting framework for tuberculosis: 2013 revision (updated December 2014). Geneva: World Health Organization; 2013

Chapter 9

Confronting Zoonotic TB

Introduction

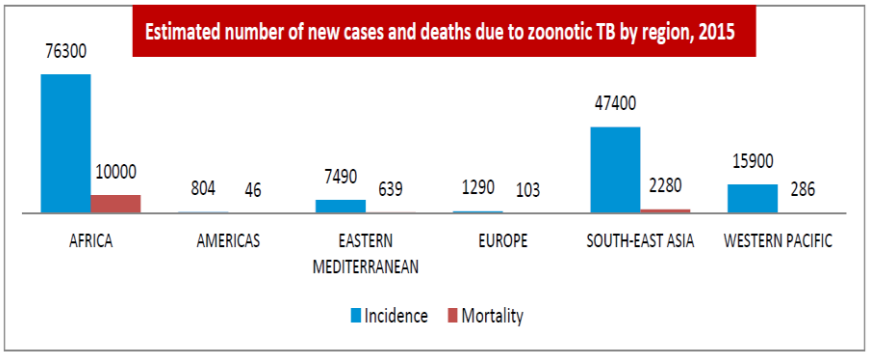
What is Zoonotic TB?

Zoonotic tuberculosis (TB) is a form of human TB caused by *Mycobacterium bovis*, which belongs to the *M. tuberculosis complex*. Cattle are the most important animal reservoir for *M. bovis* in relation to the zoonotic exposure of humans, but virtually all warm-blooded animals are susceptible to infection with *M. bovis* to a variable degree.

Epidemiology

According to the WHO Global TB report 2016, there were an estimated 149,000 new human cases of zoonotic TB globally, and 13 400 deaths due to zoonotic TB in 2015. The African region (figure 13 below) carries the heaviest burden of disease and death, followed by the South-East Asian region. The true burden of zoonotic TB is likely to be underestimated due to a lack of routine surveillance data from most countries. Studies from some countries have observed relatively high rates of *M. bovis* infection among patients with TB. For example in one study carried out in San Diego, USA, *M. bovis* accounted for 45% of tuberculosis cases in children and 6% of adult tuberculosis cases. Other studies have found variable proportions of *M. bovis* infection among assessed subgroups of tuberculosis patients, such as in Mexico (28%), Nigeria (15%), Tanzania (16%), Ethiopia (17%), India (9%), and Turkey (5%).

Figure 12 Global distribution of zoonotic tuberculosis



Transmission of zoonotic TB to humans

There are three routes of infection with *M. bovis* in human hosts: **ingestion**, **inhalation** or **direct contact**.

Oral transmission: traditionally, the consumption of contaminated unpasteurised milk from infected cows has been the main vehicle of *M. bovis* infections in humans. In theory, the consumption of undercooked or raw meat from animals with tuberculosis could also present a risk of transmission of *M. bovis* infection to humans.

Respiratory transmission: This involves inhalation of aerosolised bacilli excreted from the respiratory tract of infected animals. This is the most efficient method of transmission and the infectious dose is much lower than that for the oral route. A potential risk therefore exists for people who handle animals infected with *M. bovis* or their carcases. Bovine TB is an occupational zoonosis.

Cutaneous transmission involves the traumatic inoculation of *M. bovis* into the skin during manipulation of carcases or direct contact with infected animals, resulting in localised skin, tendon, mucosal or lymph node lesions.

Risk factors

While the most common route of transmission of *M. bovis* to humans is through food (unpasteurized milk and untreated animal products), airborne infections and direct contact with infected animals also pose an occupational risk to people with frequent direct contact with infected animals or contaminated animal products, including farmers, veterinarians, slaughterhouse workers and butchers. In the Zimbabwean setting the practices relating to consumption of unpasteurised dairy products and contact with animals should be explored as possible routes of transmission of M. bovis infection. Cow dung is also commonly used in rural Zimbabwe and the risk that this practice poses for the transmission of M. bovis infection should also be assessed in epidemiological studies designed to define the burden and risk factors for this disease.

Clinical management of zoonotic TB

Clinical features

Bovine TB often affects sites other than the lungs (extra-pulmonary), such as lymph nodes of the neck and gastrointestinal tract, and bovine TB should therefore be considered in persons who present with neck and or abdominal swellings and masses. However it is important to note that in many cases bovine TB is

clinically indistinguishable from TB caused by *M. tuberculosis. As in disease caused by MTB, symptoms include* a persistent cough, fever, night sweats and weight loss.

Laboratory diagnosis

Smear microscopy with Ziehl – Nielsen (ZN) staining and the Xpert MTB/Rif assay , the most commonly used tests for the diagnosis of TB do not differentiate between *MTB* and *M. bovis*. The relative lack of a specific and rapid test for *M. bovis* infection leads to under-diagnosis of zoonotic TB.

Practice Recommendation

In patients presenting with neck and or abdominal masses an appropriate clinical specimen, should be collected and submitted to the national TB reference laboratory for a line probe assay and mycobacterial culture able to speciate *MTB* further and to identify other Mycobacteria species. This is irrespective of the results of the Xpert MTB/Rif assay.

Justification

The Xpert MTB/Rif assay is a specific test for the MTB complex but is not able to identify or distinguish specific mycobacterial species in the MTB complex such as M. bovis.

Treatment of disease by M. bovis

Mycobacterial bovis is naturally resistant to PZA. For this reason 2RHE/7RH is recommended to treat patients with confirmed *M. bovis* infection.

Health care implications

Several clinical features of zoonotic tuberculosis present special challenges for patient treatment and recovery.

1. *M bovis* infection and zoonotic tuberculosis in human beings is often associated with extra-pulmonary tuberculosis that might be misdiagnosed or undiagnosed, and therefore initiation of treatment can be delayed.
2. *M. bovis* is naturally resistant to pyrazinamide, one of the four medications used in the standard first-line anti- TB treatment regimen. As most TB patients begin treatment without drug susceptibility testing, the risk of inadequate treatment of patients with *M. bovis* infection that is unconfirmed as a result of non-application of tests to speciate *MTB complex* further and to obtain drug susceptibility profiles is increased.

Further Reading

1. World Health Organization. Gear up to end TB—introducing the WHO End TB Strategy. 2015. http://www.who.int/tb/EndTBadvocacy_brochure/en
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Chapter 10

Managing Mycobacteria other than TB

Introduction

The Mycobacteria are a family of rod shaped bacteria that are classified into 3 groups depending on the disease they cause, the way they are diagnosed in the laboratory and the treatment that is provided:

1. *Mycobacterium tuberculosis complex* which cause the disease tuberculosis
2. *Mycobacterium leprae* which is the cause of leprosy
3. Mycobacterium other than tuberculosis (MOTT) or *Non Tuberculosis Mycobacterium* (NTM), also called *Environmental Mycobacterium* which may cause human pulmonary or extra-pulmonary disease including disseminated disease.

The Runyon classification places the MOTTs or NTMs into 4 groups based on growth and other characteristics on culture:

1. Photochromogens which develop pigment in or after exposure to light.
2. Scotochromogens which become pigmented in darkness.
3. Non chromogens which display no pigment in culture.
4. Rapid growers.

Mycobacterium other than tuberculosis are ubiquitous or widely distributed in the environment including being in soils and water. Human infection is currently believed to occur from environmental exposure and not from human to human transmission. For this reason, MOTTs have often also been called *Environmental Mycobacteria* and some clinicians believe the condition should be classified as an environmental health concern, like that caused by *Legionella species*.

The list of MOTTs that can cause human disease is long, however, Mycobacterium avium complex (MAC) predominates in most countries followed by *M. gordonae*, *M. xenopi*, *M. abscessus complex* (MABC) and *M. kansasii*. In Zimbabwe *MAC* is the most common MOTT that has been isolated from clinical specimens.

Without detailed clinical information, differentiating between contamination of specimens, colonization/infection, and disease is difficult. Laboratory reports of isolates do not always reflect the true incidence of disease. To determine if lung disease is present, sputum specimens and often a bronchoscopic sample of a patient's lower respiratory tract should be collected. In addition, computed tomography scanning of the chest and careful clinical evaluation by expert clinicians are needed to make what are often difficult clinical decisions. Accurate epidemiologic data is lacking globally because the

investigative processes to determine the presence of clinical disease are costly to the healthcare system and the patient. In recent years there has been an apparent increase in MOTTs related pulmonary disease, a situation that should be of interest to public health experts.

Practice Recommendations

1. **When a MOTT is isolated in the laboratory from a clinical specimen the clinical significance of the isolate should be established by a comprehensive clinical and radiological review of the patient and where necessary repeat sampling and testing. Repeated isolation of the MOTT increases the confidence with which MOTT lung disease is diagnosed.**
2. **When clinical disease by the MOTT isolate is considered highly likely appropriate treatment for the isolated MOTT should be provided based on in vitro DST results.**

Justification: Worldwide, pulmonary disease caused by MOTT appears to be increasing yet accurate data to support this assumption are difficult to produce. An isolate of MOTT in the laboratory could be the result of infection and disease, colonization of the respiratory system with no disease or a result of laboratory contamination from environmental sources.

Clinical Presentation

The symptoms of pulmonary disease due a MOTT are often nonspecific and include:

- ✓ Chronic cough
- ✓ Increased sputum production
- ✓ Dyspnoea
- ✓ Low-grade fever
- ✓ Malaise and weight loss

These symptoms overlap a great deal with the clinical characteristics of pulmonary TB.

Radiological Findings

Radiological imaging is important when MOTT lung disease is suspected. MOTT lung disease has two major manifestations:

- ✓ The fibro-cavitary form resembles pulmonary TB and typically affects elderly men with underlying lung disease. This form is characterized by cavities with areas of increased opacity, usually located in the upper lobes. Pleural thickening and volume loss resulting from fibrosis with traction bronchiectasis are frequent.

- ✓ The nodular bronchiectatic form shows bilateral, multi-lobar bronchiectasis, especially in the middle and lower lung fields, with small nodules on chest radiography and high resolution computed tomography (HRCT) scanning. This pattern of MOTT lung disease occurs predominantly in elderly non-smoking women without underlying lung disease, and appears more commonly in those with a thin body habitus.

It can be seen from above descriptions of pulmonary disease due to MOTT, the clinical and radiological picture of a MOTT lung disease are largely indistinguishable from those due to disease caused by MTB.

Laboratory Findings

Staining with ZN for Acid Fast Bacilli (AFB) on smear microscopy cannot differentiate between M. tuberculosis and MOTT. Culture remains the gold standard for laboratory confirmation of MOTT and is required for genotypic identification and drug susceptibility tests (DST). The culture media used for MOTT are similar to those used for M. tuberculosis. Since treatment and outcomes differ depending on the MOTT species, MOTT identification is clinically important. The role of DST is to guide the design of optimal treatment regimens. However, the DST for MOTT is difficult and controversial because of discrepancies between in vitro and in vivo clinical outcomes, with the exception of macrolides and amikacin.

Diagnosis of MOTT

Diagnosis of MOTT lung disease requires the clinician to integrate clinical, radiographic, and microbiological data.

Diagnosis can be confirmed by:

- ✓ at least two positive cultures from sputum, or
- ✓ one positive culture in the case of bronchoscopic wash or lavage, or
- ✓ A transbronchial or other lung biopsy with a positive culture for MOTT or compatible histopathological features such as granulomatous inflammation or stainable AFB and one positive sputum or bronchial wash culture for MOTT regardless of the mycobacterial strain.

Treatment of MOTT: Principles

The management of MOTT lung disease is a challenge that should be undertaken by experienced clinicians backed by reliable laboratory services for mycobacterial cultures and in vitro DST as it the requires prolonged use of costly combinations of multiple drugs with a significant potential for toxicity. The diagnosis of MOTT lung disease does not obligate the initiation of therapy against MOTT species and a decision must be made based on the potential risks and benefits of therapy for individual patients. Unlike pulmonary TB, clinicians may observe patients with minimal symptoms and stable radiographic disease closely without invasive workups or treatment, provided the patients do not have decreased host immunity towards MOTT and the patient is educated to avoid aggravating factors such as tobacco smoking. However, once the clinician decides to start treatment, the goal of curative therapy in MOTT lung disease is 12 months of culture negativity, and therefore, frequent sputum sampling every 1–2 months is needed. Simultaneously, clinicians should consider quality of life and a patient centred approach rather than solely targeting microbiologic eradication.

Practice recommendations

1. All patients with suspected pulmonary MOTT disease (those with clinical and radiological features compatible with MOTT pulmonary disease and a MOTT isolated from a clinical specimen) should, where feasible be reviewed by a multi-disciplinary team that at the bare minimum includes a specialist physician and a laboratory scientist to make the decision to or not to treat the patient and to select the medicine regimen to be used if treatment is chosen as the management option.

2. The national TB reference laboratories in Harare and Bulawayo should have their capacity adequately built to be able to isolate, speciate and carry out DST for MOTTs.

3. To begin to generate data on the burden and risk factors for MOTT pulmonary disease in Zimbabwe, MOTT laboratory and case registers should be developed and used to record and report cases to the central level.

Treatment of Mycobacterium Avium Complex (MAC)

MAC is by far the most common MOTT in Zimbabwe. Initial therapy should be triple oral therapy as listed in table 19 below.

Table 17 Recommended drug regimen and doses for the treatment of MAC

Drug	Dose
Rifampicin	450mg od (if <50kg) orally

Adults Children	600mg od (if >50kg) orally 10mg/kg (max 600mg) od orally
Azithromycin Adults Children	7.5mg/kg (max 500mg) bd orally 500mg od orally 10mg/kg (max 500mg) od orally
Ethambutol Adults and children	15mg/kg (max 1.5gms) od orally

Counselling – general

Patients must be counselled about the disease and its treatment including the regimens, potential benefits and adverse effects. They must be advised that treatment will be a minimum of 18 months or until they have been culture negative for a period of 12 months. Patients must be advised that they will receive regular monitoring throughout the duration of treatment. Female patients of child bearing age must be advised to use adequate contraception during treatment. Patients must be advised to report any potential side effects of treatment as soon as possible.

Monitoring – general

Full blood count and the patient's renal and hepatic function must be checked prior to initiating treatment. Renal and liver function should be checked at 12 weekly intervals. If LFTs rise to five times the upper limit of normal at any stage, all drugs should be stopped. Once LFTs return to normal, each drug should be re-introduced one at a time and LFTs measured daily.

Treatment of other MOTT

Treatment of other MOTT should be guided by in vitro sensitivities of the organism to commonly used anti-TB medicines and should include a combination of at least 3 medicines.

Futher Reading

1. Maiga M, Siddigui S, Diallo S, Dirra B, Traore B, et al. (2012) Failure to Recognise Nontuberculous Tuberculosis Leads to Misdiagnosis of Chronic Pulmonary Tuberculosis. PLOS ONE 7(5): e36902, doi:10,1371/journal.pone.0036902

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3. Yew W, Chiang C, Lumb R, Islam T. (2015) Are Pulmonary Non-tuberculous Mycobacterium of Concern in the Western Pacific Region? Int. J Tuberc. Lung Dis. 19(5):499-500, http://dx.doi.org/10.5588/ijtld.15.0118

Chapter 11

TB Infection Prevention and Control

Introduction

This chapter discusses the TB infection control (TB-IPC) measures to reduce TB transmission in health-care facilities, congregate settings and households. In the absence of appropriate infection control policy and practice, there is a high risk of transmission and spread of TB in healthcare settings, other congregate settings and in the community. The greatest risk of transmission occurs when TB patients remain undiagnosed and untreated. The most critical element or fundamental principle of infection control therefore is early diagnosis and prompt initiation of effective treatment of TB patients.

TB Infection Control in Healthcare Settings

A plan to prevent transmission of TB in a health care facility should be part and parcel of the overall facility infection prevention and control (IPC) programme. The plan should be guided by the Zimbabwe National Infection Prevention and Control policy. All health care facilities should develop and implement a facility specific TB infection control plan designed to:

- Ensure prompt identification of presumptive cases of TB.
- Appropriate, non-stigmatizing, immediate separation of presumptive cases or infectious TB cases from other patients.
- Prompt testing of presumptive cases of infectious TB with rapid and specific tests such as the Xpert MTB/Rif assay.
- Prompt initiation of treatment of bacteriologically confirmed cases of infectious TB
- Appropriate, robust and sustained implementation of simple but effective environmental infection transmission prevention measures.
- Judicious use of personal protective equipment (PPE)
- Ensure continuous monitoring and periodic evaluation of the TB-IPC plan and its implementation.
- Assess performance and achievements of monthly, quarterly and or annual targets.

To develop a robust and specific TB-IPC plan it is critical to carry out a baseline TB infection control risk assessment to identify the risk areas and what needs to be done in the various units or departments of the facility using a standardised TB-IPC risk assessment tool (see annex 1).

The task of developing, implementing and monitoring the TB –IC plan should be done by the IPC Committee of the health facility. Every health care facility, irrespective of size and portfolio of services offered should have such a committee in place whose tasks should include:

- Developing a written TB-IPC plan tailored to the specific health facility setting and needs.
- Assigning from within the IPC committee a designated TB-IPC officer to take responsibility for training of HCWs at the facility, supporting facility HCWs to implement and adhere to TB-IPC measures outlined in the TB-IPC plan, regular monitoring of the implementation of the plan and reporting to the facility IPC committee in addition to other IPC tasks that the committee identifies.
- Monitoring the implementation of the TB-IPC plan at the health facility including the achievement of facility specific TB-IPC targets.
- Periodically evaluating the facility TB-IPC plan to identify failures and successes, the reasons for these outcomes and to identify measures including innovations and modifications to the IC plan that need to be undertaken to achieve the desired results and outcomes.

Managerial and Administrative Controls

In health care settings, it is important to implement infection control measures designed to minimise the time that patients with possible TB symptoms (particularly cough) spend in clinics / health facilities. Ensure that those with a chronic cough are separated from other patients and investigated promptly and started as soon as possible on correct treatment if found to have TB. It is encouraged that all health facilities carry out symptomatic screening of all patients, so that persons with chronic cough, are identified, separated and investigated (triaging). The first and most important level of infection control is the use of administrative measures to prevent droplet nuclei from being generated, thus reducing the exposure of HCWs and patients to *M. tuberculosis*. Administrative controls are the cheapest and most effective interventions and they ensure early diagnosis and treatment of potentially infectious TB patients. These measures include:

- Setting up or strengthening facility IPC Committee
- Assessment of the risk of transmission of MTB in the various units or departments of the facility.
- The development of a health facility TB-IPC Plan or a unit SOP detailing what should be done, how it should be done and who should be responsible for each TB-IPC task.
- Assigning responsibility and authority for the coordination and monitoring of adherence to the implementation of the infection control plan to the TB-IPC officer with mechanisms for reporting back to the IPC committee and the implementation of appropriate corrective action.
- Adequate training of HCWs and other staff to implement the plan.
- Administrative support for procedures contained in the plan, including quality assurance.
- Ensuring that patient waiting areas are not congested.
- Ensuring that highly infectious or chronic TB patients (e.g. those failing treatment for MDR-TB) are reviewed by appointment with times scheduled at periods when facility patient volume is usually small.
- Implementing effective and efficient processes for the management of presumptive or confirmed TB patients including triaging, fast tracking of service delivery to potentially infectious patients (those who are coughing), isolation of potentially infectious TB patients and discharging patients when appropriate
- Organising appropriate patient movement through the facility to reduce the risk of cross-infection
- Prompt initiation of appropriate anti-TB treatment as soon as the TB diagnosis is made.

- Education of patients on TB and increasing community awareness including the use of cough hygiene to reduce the spread of infectious droplets into the environment.
- Designing health facilities e.g. wards, out-patient department to ensure adequate ventilation.
- Ensuring that HCWs who are at high risk of TB infection and progression to disease do not work in areas of the facility where exposure to MTB is very likely such as TB wards including wards for MDR-TB patients.

The infection control plan should include but not limited to the steps shown in Table 20 below.

Table 18 Five steps for managerial and administrative processes for patient management to prevent transmission of TB in Health Care Settings

Step	Action	Description
1	Screen	Early recognition of presumptive or confirmed infectious TB cases should be done through questioning patients about cough (and TB) on arrival.
2	Educate	Instruct presumptive or confirmed cases of infectious TB on cough etiquette and respiratory hygiene.
3	Separate	Patients identified to be presumptive or confirmed cases of infectious TB should be separated from other patients and requested to wait in a separate well ventilated waiting area.
4	Provide prompt health services	Triaging of patients with symptoms that could lead to the spread of infectious aerosols to the front of the line for the services they came for such outpatient consultation, TB/HIV counselling and testing services, and medical refills.
5	Investigate for TB or refer	TB diagnostic tests should be done on site and if not available on site, the facility should have an established link with a TB diagnostic centre to which collected sputum specimens should be sent

The following should also be part of the TB-IPC plan:

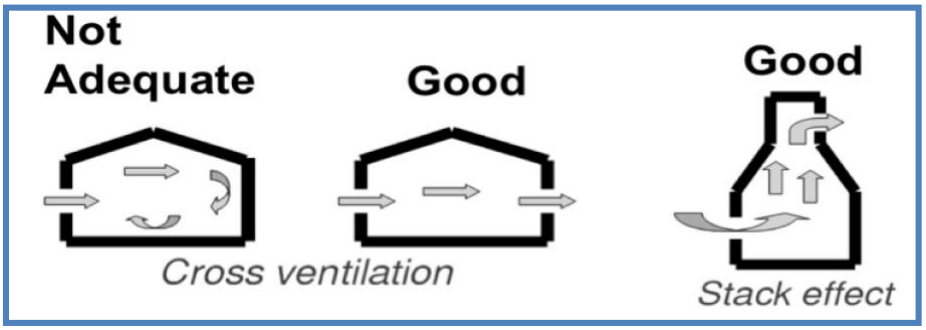
1. Using and maintaining environmental control measures.
2. Routine screening for TB using the TB screening tool (see Annex 3) and CXR/BMI among health care workers on an annual basis. This is best done as part of a health care worker wellness program (see annex 2).
3. Training and educating staff on TB, TB prevention and care and the TB –IC plan.
4. Job relocation of staff who are at risk of developing TB following infection, from high to low TB exposure areas.

Environmental Control Measures

It is often not possible to completely eliminate the exposure to infectious droplet nuclei, but various environmental control methods can be used in high-risk areas to reduce the concentration of droplet nuclei in the air. Such measures include:

- Maximizing natural ventilation by keeping facility windows and doors open at all times when providing care to patients even during winter and night time and promoting cross ventilation (opening of windows or doors on opposite walls) and "stack effect", which increases airflow using indoor/outdoor temperature difference (see Figure 14).
- Using open-air shelters with a roof to protect patients from sun and rain as waiting areas.
- Avoiding patients crowding in narrow, poorly ventilated and lighted corridors as they wait for services.
- Controlling the direction of airflow e.g. with strategically placed fans, which also cause air mixing which increases the effectiveness of other environmental controls.
- Utilizing an open plan in patient waiting areas and wards to let in sunlight. Sunlight is a natural source of ultraviolet light, which kills TB bacilli.
- Reducing crowding in patient waiting areas is very important. Waiting areas in open-air shelters should be favoured over enclosed corridors.

Figure 13 Promoting Natural Ventilation



- Organising sitting arrangements in consultation rooms to avoid airflow from patient to HCW.
- Attending to one patient at a time in the consultation room to minimise exposure to droplet nuclei.

Health staff should be mindful of the direction of airflow to ensure the patient is closest to the exhaust fans and the HCW is closest to the clean air source.

Personal Respiratory Protection

Personal respiratory protection protects HCWs, where concentration of droplet nuclei cannot be adequately reduced by administrative and environmental control measures. It protects the health worker from inhaling infectious TB droplet nuclei

When PPE is used the HCWs should wear N95 or FFP2 respirators to protect them from inhaling infectious air droplets. Respirators are worn by workers and visitors in high risk areas and situations. Patients with active TB should be encouraged to wear a surgical mask and practice cough etiquette to reduce the spread of infectious droplets (see Figure 15). Surgical masks reduce the spread of microorganisms from the wearer. Personal respirators are useful only when managerial, administrative and environmental controls are in place.

Performing a N95 fit test – Hold the mask in the palm of hand, with the cup facing upwards; place the mask on face covering the nose and mouth and secure the mask using the elastic bands. The top metallic margin should be above the nasal bridge; adjust the metallic section to tightly fit. Cup both hands over the mask gently and test the seal by exhaling forcefully after a deep breath. For a well-fitting mask, pressure build-up with no air blowing to your eyes or ears through the margins of mask should be felt. The mask should collapse on forceful inhalation.

The use of PPE should not replace, less expensive, administrative and environmental IPC measures. N95 masks are only indicated in specific settings, e.g. facilities nursing TB patients. All other infection control measures should be fully implemented; the use of personal protective equipment is the least effective of all infection prevention and control measures.

Figure 14 Face masks and Respirators.

Protection of Health Workers

All HWs should be screened for TB using a symptom screen, a BMI with a CXR on an annual basis and symptom screening every six months. This should be done free of charge and preferably as part of a routine medical evaluation as part of a health worker wellness program that also includes HIV testing and counselling services as well as screening for non-communicable diseases such as cancers, diabetes mellitus and hypertension. All presumptive TB cases (symptoms + BMI< 17 Kg/m^2 +abnormal CXR) should submit a sputum sample to be tested for TB using the Xpert MTB/Rif or Ultra assay.

TB Infection control is effective only if each person working in a facility understands the importance of TB infection control policies and his/her role in implementing them. All health facility staff, including medical and administrative staff, technicians and laboratory staff, laundry, cleaners and any other workers, should be targeted for training.

Construction of health facilities according to TB Infection Control measures

A multidisciplinary team should coordinate health facility demolition, construction, and renovation projects. During the developmental stages of health facility construction or renovation projects, the MoHCC should work closely with the Ministry of Public Works to proactively embed TB transmission

minimising designs for the new or renovated facilities. The engagement of the NTLP in this process may be done through a coordinating mechanism that includes aerosolized infection transmission prevention experts. Mandatory adherence to agreements for limiting transmission of pathogens that primarily use the aerosolized route to establish infection, should be incorporated into construction contracts, with penalties for non-compliance and mechanisms to ensure timely correction of errors.

Control of TB transmission in prisons, holding cells and other congregated settings

All the TB infection control measures described in this guideline apply also to medical services in refugee camps, correctional facilities and other congregated settings. This is because the spread of tuberculosis is worsened by the often poor living conditions in these settings such as overcrowding, malnutrition and HIV among inmates and residents of refugee camps. It is recommended that the following measures are routinely carried out:

- Regular TB screening of inmates and refugees to ensure early diagnosis of active TB and prompt initiation of appropriate treatment.
- Screening of all new inmates and new arrivals at a refugee camp using the TB screening tool and CXR (when available). All presumptive TB cases should submit a spot sputum sample for TB testing with the Xpert MTB/Rif or Ultra assay.
- Encourage all staff and their dependents working in congregated settings to undergo six monthly symptom screening and annual CXR screening as part of the comprehensive wellness programme.
- Separate inmates diagnosed with active TB from other inmates in an adequately ventilated area to prevent transmission to other inmates. Similar measures with appropriate modification may be carried out in refugee camps.
- Improvement in living conditions for inmates with special attention paid to reducing overcrowding.
- Offer TB information and HIV testing and counselling to all staff and inmates.
- There should be particular attention paid to integrating prison and civilian TB services so that there is continuation of care after discharge from the correctional facility.

Reducing TB transmission in households

The period of household transmission is greatest before the diagnosis of TB. Again, early case detection and prompt treatment is the key to reduction of TB in households. TB contact investigation should be undertaken as described in chapter 4. Information, education and communication messages including basic TB-IPC behaviour-change should be provided. Coughing etiquette and respiratory hygiene in the household before and after diagnosis of TB should be emphasised. Stigma reduction should not be forgotten. Environmental control measures to reduce exposure should be emphasized. Natural ventilation should be improved in households particularly in rooms where people with TB spend much time. Bacteriologically confirmed PTB patients in the first 2-4 weeks of treatment should spend as much time as possible outdoors, stay in a well-ventilated room, if possible, and spend as little time as possible in congregate settings. Children less than 5 years old should spend as little time as possible in the same living spaces as persons with bacteriologically confirmed PTB patients. . Children contacts of MDR-TB patients should be followed up regularly with TB screening and if possible culture and DST.

Home environment assessments should be conducted for TB-IPC adequacy to inform appropriateness of the home for TB care and to provide health education to families.

Chapter 12

Managing Latent Tuberculosis Infection

Introduction

Latent tuberculosis infection (LTBI) is the presence of Mycobacterium tuberculosis bacilli (MTB) which persist in an inactive state after inhalation but which remain viable in the human body. These bacilli may "reactivate" years after infection to cause active symptomatic and often transmissible TB disease. Concomitant infection with HIV is a leading risk factor for progression from LTBI to active disease. The rate of progression to active TB disease is 5 – 8% per year among HIV infected patients compared with a 10% lifetime risk in the general population. Hence prevention of progression to active TB disease among those with LTBI remains a high priority in HIV/TB care.

Diagnosis of LTBI

Identification of LTBI in at-risk populations is critical to reduce progression to disease. Latent TB Infection should only be diagnosed after active TB has been confidently excluded through symptom screening, measurement of BMI and obtaining a CXR. Those with symptoms, a BMI of less than 17 Kg/m^2 and an abnormal CXR should be investigated further with bacteriological and other tests to exclude active TB. There are two major tests for identification of LTBI.

The tuberculin skin test (TST)

The TST measures the delayed type hypersensitivity response to a purified protein derivative (PPD) from tubercle bacilli also known as tuberculin. **A positive TST indicates infection with Mycobacterium tuberculosis and not the presence of TB disease**. Tuberculin skin test, if available, should be done using the Mantoux technique where 0.1ml of PPD is injected intra-dermally on the volar aspect of the left forearm. In children and persons from low TB incidence countries (who may be visiting Zimbabwe for example) with clinical and or radiological features of TB disease a positive TST may provide supportive evidence of TB disease but it should never be used as a test for active TB or interpreted to mean the presence of TB disease.

Interpretation of the TST result.

A positive tuberculin skin test: Following BCG vaccination, a reaction to tuberculin usually persists for a few years. This reaction is usually weaker (diameter of skin induration is often less than 10mm) than the reaction to natural infection with M. tuberculosis. A tuberculin skin test is usually considered significant

or 'positive" when the diameter of skin induration is at least 10mm in HIV negative persons or 5 mm in HIV infected and severely malnourished persons.

A negative tuberculin skin test: A tuberculin skin test is negative or not significant when the diameter of skin induration is less than 10mm (or less than 5mm in an HIV infected or severely malnourished persons) regardless of whether the person had BCG vaccination or not. A negative TST does not exclude TB.

Conditions that may suppress the TST include:

- HIV infection
- Disseminated TB or TB meningitis
- Severe malnutrition, severe bacterial infection, including TB, viral infections (e.g. measles or chicken pox), cancers.
- Immunosuppressive drugs e.g. high dose steroid therapy
- Recent exposure to TB (2–3 months delay in conversion)
- Incorrect injection technique or storage of tuberculin

Interferon gamma release assay (IGRA) tests.

In June 2010, interferon gamma release assays (**IGRA**) were introduced for the diagnosis of LTBI. The main advantage of IGRA tests is their high specificity compared to TST. This significantly eliminates false positive results in BCG-vaccinated individuals and therefore avoids the costs and toxicity associated with unnecessary treatment. The sensitivity of IGRA tests is similar to that of TST. These tests measure interferon gamma released in response to stimulation of sensitized T-cells by mycobacterial antigens. Two tests are currently available:

1. **Quantiferon Gold In Tube Test (QGIT)**
2. **T-SPOT. TB Test**

Note: The IGRA tests are expensive and are unlikely to become routinely available in the public care setting in Zimbabwe in the short to medium term. Private health care providers in Zimbabwe may offer these tests and thus both health care professionals and patients need to know when to use these tests and how the results should be interpreted.

Management of Latent TB Infection

While a large number of people are likely to be latently infected with MTB in Zimbabwe, LTBI treatment for the general population is currently not recommended as a public health intervention. Treatment of LTBI in Zimbabwe is currently recommended for PLHIV and children 5 years and below who are household or close contacts of people with TB and who, after an appropriate clinical evaluation, are found not to have active TB. Ideally LTBI needs to be identified before treatment is provided but as a result of the challenges of providing the TST or the IGRA test under programmatic settings in Zimbabwe, a low resource setting, LTBI is usually not confirmed before PLHIV or under five contacts of persons with TB are treated with TBPT. This implies that a significant proportion of people who receive TBPT with IPT are treated for something that they may not have. This proportion is currently unknown. The benefits of TBPT given as a public health intervention however outweigh the risks of over treating people who are not infected with MTB.

Medicines Regimens for LTBI treatment

There are several medicine regimens that may be used to treat LTBI. The most common regimen is daily isoniazid given for 6 months (6H). Shorter regimens include 3 months of Isoniazid and Rifapentine (3HP) or 3RH or 3RZ or 3R. In HIV infected persons living in areas of the world where there is intense transmission of MTB, longer or even life-long TBPT may be needed. Some experts and NTPs in Sub – Saharan Africa have begun to re-dose 6H every 18 -24 months to overcome the waning off of protective efficacy that occurs within this period in HIV-infected persons who receive 6H. **Zimbabwe has chosen to treat PLHIV and under 5 child contacts of TB with 6H and re –dose those still unwell with CD4 T cell count less than 450 cells/ml after 24 months of completing the 6 month IPT course.**

Practice recommendations

- **All HIV infected persons, enrolling into HIV care and who on TB screening do not to have active TB should be provided with six months of isoniazid to prevent TB (IPT).**
- **The TB/HIV technical working group recommends that IPT should not be provided to people who have been on ART for longer than 2-3 years and have a high CD4 T cell count as a result of the observation (unpublished) that some of these persons experience severe hepatic reactions that could end fatally**

Recommended doses for INH

- Adults 5mg/kg body weight daily
- Children 10mg /kg body weight given daily.

Possible adverse effects of INH

Patients taking IPT commonly report minor side effects, mostly in the first month of treatment, which may include increased appetite, headache, itchy skin, joint pains, diarrhoea, nausea, stomach pains and/or decreased libido or energy. Though uncommon there are potentially serious side effects that may result from INH use which may include hepatitis, hypersensitivity rash, psychosis and convulsions. **Severe hepatotoxicity and death are rare if INH is stopped immediately when patients develop symptoms suggestive of hepatitis**.

Asymptomatic elevation of serum liver enzymes concentrations: Occurs in 10-20% of people but return to normal even when treatment is continued. It is generally recommended that INH be discontinued if a patient's transaminase levels exceed 3 times the upper limit of normal if associated with symptoms or 5 times the upper limit of normal if the patient is asymptomatic.

Clinical hepatitis

Occurs in about 0.1% of people taking INH and is more common when INH is combined with other hepatotoxic agents including some ART drugs. Consumption of alcohol, underlying liver disease and concomitant use of other medicines that are metabolized in the liver will increase the severity of hepatitis.

Peripheral neuropathy

Occurs in less than 0.2% of people taking INH at conventional doses. It is more likely in the presence of other conditions that cause neuropathy such as diabetes, HIV, renal failure and alcoholism. Pyridoxine supplementation is recommended only in such conditions or to prevent neuropathy in pregnant or breastfeeding women.

Patient Monitoring and Education during LTBI Treatment

To ensure safe and efficacious treatment for LTBI, the health care provider should periodically assess the patient's progress. This evaluation involves clinical monitoring and laboratory testing, as well as patient education.

Clinical Monitoring

- Patients should visit the health care provider who is managing their treatment on a periodic basis to be assessed for the following:
    - Signs of hepatitis
    - Adherence to the medication
    - Symptoms of possible adverse drug reactions or interactions

- **Patients being treated for LTBI who experience any possible medicine adverse reactions should report to the health care facility immediately and if the adverse medicine reaction is confirmed the health care provider is expected to manage the client appropriately based on severity of adverse drug reaction (see table 21 below)..**

Table 19 Common INH Adverse Events and Management

	Side Effect	Management
Mild	**Tingling/ burning sensation** **Joint pain** **Mild skin rash** **Abdominal pain**	**Continue with INH** **Reassure** **Reassess**
Severe	**Hepatitis/ jaundice (yellowing of eyes)*** **Severe skin rash with peeling skin** **Disabling peripheral neuropathy** **Convulsions**	**STOP INH** **Refer for further management**

Patients taking INH should be advised to stop this treatment on their own if there is obvious yellowness of the eyes and report immediately to the nearest clinic/hospital.

Patient Education

- Explain the disease process and rationale for medication in the absence of symptoms or radiographic abnormalities.
- Emphasize the importance of completing treatment for LTBI.
- Discuss possible side effects of LTBI medications that may include:
    - Fever
    - Unexplained anorexia

- Dark urine (color of coffee or cola)
- Jaundice
- Rash
- Persistent paresthesia of hands and feet
- Persistent fatigue or weakness lasting 3 or more days
- Abdominal tenderness, especially in right upper quadrant
- Easy bruising or bleeding
- Arthralgia
- Nausea and Vomiting

- Discuss management of common adverse effects and the need to report to the health care provider.

Laboratory Testing

- Baseline laboratory testing (measurements of serum AST, ALT, and bilirubin) is not routinely necessary.
- Laboratory testing at the start of LTBI therapy is recommended for patients with any of the following factors:
  - Liver disorders
  - History of liver disease (e.g., hepatitis B or C, alcoholic hepatitis, or cirrhosis)
  - Regular use of alcohol
  - Risks for chronic liver disease
  - Pregnancy or the immediate postpartum period (i.e. within 3 months of delivery)
- Baseline testing can be considered on an individual basis, especially for patients taking other medications for chronic medical conditions.
- After baseline testing, routine periodic re-testing is recommended for persons who had abnormal initial results and other persons at risk of hepatic disease.
- At any time during treatment, whether or not baseline tests were done, laboratory testing is recommended for patients who have symptoms suggestive of hepatitis (e.g., fatigue, weakness, malaise, anorexia, nausea, vomiting, abdominal pain, pale stools, dark urine, and chills) or who have jaundice. Patients should be instructed, at the start of treatment and at each monthly visit, to stop taking treatment and to seek medical attention immediately if symptoms of hepatitis develop and not wait until the next clinic visit to stop treatment.
- It is generally recommended that medication be withheld if a patient's transaminase level exceeds 3 times the upper limit of normal if associated with symptoms or 5 times the upper limit of normal if the patient is asymptomatic.

Assessing Adherence

Many variables affect a patient's adherence to the medication regimen for treatment of LTBI. Episodes of non-adherence should be recognized and addressed as soon as possible. Some examples of barriers to adherence are noted in the section that follows.

Health care facility Related Variables

- Long periods between clinic visits.
- Long waiting times at the health care facility.
- Inconvenient opening hours of the health care facility.

Patient-Related Barriers

- Misinformation or confusion about TB, LTBI and associated treatment such as
    - The distinction between active TB and latent TB infection (you do not have TB yet you need to take treatment "for TB").
    - Is the treatment a vaccine?
    - Modes of TB transmission and prevention.
    - Exposure versus becoming infected versus having TB disease.
    - Safety of family and friends around someone with LTBI.
- Residential instability for example in poor urban slum dwellers.
- Lack of financial resources to keep up with clinic attendance schedules.
- Poor access to health care.
- Stigma associated with tuberculosis.
- Co-existing medical conditions.
- Culture and language.
- Religious practices (e.g., fasting from food).

Treatment Barriers

- Complexity and duration of treatment.
- Medication side effects.
- Obtaining refills.
- Frequency of health facility visits.
- Cost, including insurance co-payment.

Strategies to Improve Adherence

- Collaborate with local health department to provide treatment.
    - Telephone reminders.
    - Home visits by health care workers.
    - Positive re-enforcements (for example “congratulations Mr. so and so, you have completed month 1 of IPT)
- Provide patient education and instructions in patient’s primary language at every visit.
- Ensure confidentiality.
- Visit appointment cards or diaries may be provided to patients as reminders.

Post-Treatment Follow-Up

- Patient should receive documentation that includes TST or IGRA results if done, chest radiograph results, names and dosages of medication and duration of treatment. The patient should be instructed to present this document any time in the future if TB testing is required.
- Providers should re-educate patient about the signs and symptoms of TB disease and advise them to contact the medical provider if he or she develops any of these signs or symptoms.
- Regardless of whether the patient completes treatment for LTBI, serial or repeat chest radiographs are not indicated unless the patient develops signs or symptoms suggestive of TB disease.

Any person who develops active TB during or after TBPT with IPT should have appropriate samples (sputum or other sample depending on site of disease) submitted to the laboratory for a full DST to First line medicines.

Chapter 13

Community Engagement

Community-based TB Care

Community TB Care (CTBC) is considered one of the most effective patient centred approaches to TB care and prevention. It allows communities to be involved in the TB response, become empowered and thus provide an effective partnership with TB control programs. In Zimbabwe CTBC has evolved into an initiative that involves the community to a wider scale than merely observing treatment. Effective CTBC contributes to increased case detection and rates of positive treatment outcome (Treatment Success) through active TB case finding and community education. Community education on TB aims at improving health care seeking behaviour, community support of TB patients and reduction in TB stigma and discrimination. ,. In addition, CTBC seeks to shift the worldwide perception of TB from only a medical disease to a more comprehensive socio-economic and community problem. Ultimately CTBC is expected to contribute to the goal of ending TB in the country

The aims of CTBC are:

- To improve cooperation and foster effective partnership between NTP, NGOs, CSOs and communities for patient and community empowerment.
- To facilitate access to health services and bring TB services to where people live.
- To create an enabling environment in which community members express their responsibility and solidarity towards those who are affected by TB.

Community TB Care activities

The following are some of the activities that should be implemented at community level:

- Awareness-raising, health education and community mobilization.
- Contact investigation.
- Screening and testing for TB and TB-related morbidity (e.g. HIV counselling and testing; diabetes screening) including home visits.
- Facilitating access to diagnostic services (e.g. sputum or specimen collection and transport).

- Initiation and provision of TB prevention measures.
- Referral of community members for diagnosis of TB and related diseases.
- Treatment initiation, provision and observation for TB and co-morbidities.
- Treatment adherence support through peer support, education and individual follow-up.
- Social and livelihood support (e.g. food supplementation, income-generation activities).
- Home-based palliative care for TB and related diseases.
- Community-led local advocacy activities

Who should be involved?

The implementation of CTBC constitutes strong partnerships between NTLP, health care providers, TB patients and the community. It utilises community structures and mechanisms through which community members, CBOs and other groups interact, coordinate and deliver their responses to the challenges and needs affecting communities.

Integrating CTBC with other programmes

Community based TB Care should be integrated with other community-based activities supporting primary health care services, including those for HIV infection, maternal and child health and non-communicable diseases to improve synergy and impact. Below are some of the activities that can be implemented through NGOs and CSOs:

Assisting early case finding

This involves identification of people who have symptoms suggestive of TB within the community and encouraging or supporting them to contact a health care worker or visit a health facility for TB testing. Community TB case finding also includes collection of sputum samples from identified presumptive cases of TB in the community and transporting these samples to the nearest health facility for TB testing.

Providing treatment support

Patients being treated for TB require support to take their medicines until treatment completion. Community-based treatment support (DOT) is usually provided by volunteers and family members who

should be oriented by NGOs and other CSOs supporting CTBC to carry out this function. . Effort should be done to provide patients with psychosocial and nutritional support when needed.

Preventing the transmission of TB

Implementers of CTBC such as NGOs, CBOs and other CSOs should support individual patients, their families and the community at large to implement community based TB-IPC measures such as cough etiquette and respiratory hygiene using various approaches including social communication media.

HIV programme

The implementation of CTBC should include encouraging and supporting every community member to know their HIV status and to support persons living with HIV to access HIV care and be screened for TB, depending on the result, helping them receive either treatment for active TB or TBPT.

Maternal and Child health programme

At the community level implementers of CTBC should encourage all pregnant women to test for HIV and to be screened for TB at the nearest health facility. All children under five in the community should be identified and those in contact with an older person with TB, especially infectious TB, should undergo contact investigation and managed as outlined in chapter 4 of these guidelines.

Education programmes and projects

Community TB care should incorporate information on TB prevention and care into primary, secondary and tertiary classroom learning. School children and tertiary students can be change agents and the opportunity they provide to enhance community TB case finding should be fully exploited. When well informed these children and students should be able to recognize TB symptoms in members of their families and communities and can encourage these persons to seek care and be tested for TB.

Approaches to community TB screening.

Tuberculosis screening at the community level should be carried out by community health care workers and or volunteers recognised by the MoHCC/NTLP. Symptoms enquiry should be regularly carried out when doing targeted TB screening at the community level. Specific actions for community TB screening include:

- Administration of the symptom screening tool to members of the community.
- Identifying presumptive TB clients who should then be referred using the NTLP recommended referral slips to the nearest health facility for TB testing.

- Carrying out door to door household screening.
- Screening at community meetings and events
- Screening of close contacts of prioritized index cases identified at the local TB testing centre as part of contact investigation. Tracking presumptive clients with the health facility whether they eventually underwent TB investigations. If not, they should immediately follow up the presumptive TB client to ensure that he/she undergo TB testing
- Communicate with client on the results of the TB investigation.
- Upon TB diagnosis, referred clients should be clearly recorded in the health facility TB register as community referrals to facilitate the reporting of the community contribution to TB case notifications (Proportion of notified TB cases, all forms, contributed by non-NTP providers - community referrals).
- The health facility should provide necessary recording and reporting tools to the community level cadres
- At the health facility, all persons referred by community health care workers and volunteers should be investigated for TB. All such presumptive TB clients should be recorded in the MoHCC/NTLP recording and reporting tools with the results of the TB testing clearly indicated in these tools.

Treatment Supporter

A patient's adherence to treatment instructions is an important factor in the achievement of treatment success. Directly observing treatment (DOT), that is, watching the patient swallowing every scheduled dose, is the most effective method to promote adherence. This could either be health facility based or community based DOT depending on the situation.

A TB patient who travels far each day to obtain treatment is unlikely to complete treatment. One of the aims of the NTLP is to organize TB services as a part of general health services expanded to the community, so that TB treatment is available as close to a patient's home or workplace as possible. Before the patient is sent to his/her community, the health care worker must educate the patient about the importance of adhering to treatment. For TB patients who live or work close to a health facility, a health worker will/should directly observe their treatment(health facility based DOT). However, for patients who live far from the health facility, a treatment supporter in the community is needed to directly observe treatment at a place and time more convenient for the TB patient (community based DOT).

Identifying a community TB treatment supporter

The HCW assists the patient to identify a treatment supporter who is acceptable to him/her. The patient and treatment supporter should enjoy a supportive relationship that motivates the patient to complete his/her treatment. A negative attitude can cause a patient to interrupt treatment. The community treatment supporter should listen empathetically to the patient's concerns and encourage the patient to complete treatment. The treatment supporter must be conveniently placed and must be able to manage medicines. The supporter must also have easy access to the health facility for reporting and obtaining resupply of medicines.

The treatment supporter may be selected from among the following, in order of preference;

- A health facility member of staff.
- A trained community/village health worker.
- A volunteer in the community or workplace.
- Or a family member, as the last resort.

When a treatment supporter has been identified, the HCW should set an appointment for the TB patient and family to meet with him/her. The community TB treatment supporter and the TB patient should then agree on the appropriate place and time where the patient will take the medicines. If a family member is available to directly observe the TB patient taking treatment, the community health worker then plays an oversight role by supporting the family and the patient. The treatment supporter must be oriented to give directly observed treatment, mark the TB treatment card, observe and record the patient's progress and regularly ask about and or observe the patent for symptoms and signs (yellow eyes , skin rashes for example) that may imply the occurrence of medicine adverse effects.

Roles of the Community TB Treatment Supporter

The community TB treatment supporter performs many functions all with the aim of enabling the patient to complete treatment.

These include:

1. Observing patient swallow medicines.
2. Recording on the patient's TB treatment card.
3. Collecting resupply of drugs on behalf of the TB patient, if the patient is unable to do so by him or herself.
4. Reporting any problems related to the patient to the health facility.

5. Following up on patients that miss an appointment or dose.
6. Supporting and encouraging the TB patient to take drugs and to work towards successfully completing treatment.
7. Monitoring the TB patient's progress and making enquiries about any side effects.
8. Referring the patient to the health facility for further information, management or review.
9. Informing and educating the patient, family and community about TB and related conditions.
10. Conducting contact tracing and referring presumptive TB cases to the health facility for further investigation.

Supervision of the community TB treatment supporter

The treatment supporter should visit the health facility once every month, to report on and discuss progress of the patients he or she is supporting. The treatment support should bring the TB patients' treatment cards for review and updating. If the treatment supporter fails to come to the health facility, the facility HCW should contact her/him by phone (call or SMS) followed by a visit to the home of the treatment supporter to ascertain the problem if phone contact does not yield satisfactory results.

The facility HCW should contact the patient, discuss with the patient to determine the quality of care being provided by the treatment supporter. Facility HCWs should find out if the treatment supporter has been offering timely and appropriate support to the patient and whether the patient wants to continue the engagement with the treatment supporter.

Effective community contributions to TB care, especially community based DOT, require a strong reporting system, access to laboratory facilities and a secured medicine supply, through district support. Effectiveness of CTBC interventions will include measuring the contribution of the community in TB case notification and treatment outcomes.

Note: The ultimate responsibility for community-based TB care remains with the health services.

Social Mobilisation

Social mobilisation is sometimes used interchangeably with community engagement. Social mobilisation believes a single effort has less impact than collective effort. It is the process of bringing together "allies" to raise awareness of and create demand for TB prevention, care and treatment

services, assist in the mobilization and delivery of resources and services and to empower communities to participate and be self-reliant in confronting TB.

Strategies for social mobilisation

Building partnership and networking

The NTLP will create alliances with organised institutions/groups, such as decision-makers, policy-makers, NGOs, CBOs, professional and religious groups, corporate bodies, development partners, the media, communities and individuals.

Community participation

Community players such as HCWs, CBOs, FBOs and other development partners working with various communities should engage with TB patients and affected communities to promote community participation, fight TB stigma and discrimination and thus contribute to ending TB as a public health threat. Communities should be placed in the forefront and must be engaged from planning, implementation to monitoring and evaluation.

Resource mobilisation

The NTLP and its partners will mobilize resources from domestic and external sources through the development of concept notes, proposals and dialogue with multiple partners to find the resources (financial, material resources, food and other inputs) needed, for effective social mobilization to create and sustain a social movement directed at ending TB within communities.

Further Reading

1. Engage TB operational guidelines, WHO, 2012
2. Advocacy, Communication and Social Mobilisation for Tuberculosis Control. A handbook for country programs, 2007
3. Patient centred Approach Strategy, USAID- TB CAP
4. National Guidelines for Community Engagement in TB prevention and care, MoHCC, Harare 2014

Chapter 14

Advocacy and Communication

Introduction

The aim of advocacy and communication together with social mobilisation/CTBC is to cause behavioural change. It involves activities targeted at different audiences.

- Advocacy is directed towards changing the behaviour of leaders, politicians, and decision-makers at all levels.
- Communication aims to change knowledge, attitudes and practices among various groups of people that result in positive behaviour change.
- Social mobilisation is targeted at communities to strengthen community participation for self-reliant and sustainable responses.

Advocacy and communication are very important in TB prevention and care as it helps to address the following four key areas:

- Improving prevention, case detection and positive treatment outcomes.
- Combating stigma and discrimination through appropriate messaging.
- Mobilising political commitment and resources for TB prevention and care.

Who should be involved in TB advocacy and communication?

For standardisation and accountability, the NTLP will continue to provide the stewardship required to undertake TB advocacy and communication activities and also to coordinate partners and stakeholders engaged in this area of work such as NGOs, CSOs, CBOs, private sector and communities at all levels. This partnership will continue to plan and implement advocacy and communication activities in the country.

Advocacy

Advocacy for TB is a broad set of coordinated interventions, designed to place TB high on the political and development agenda. It is directed at influencing policy makers, funders and decision making bodies both locally and internationally to increase and sustain financial and other resources for TB prevention

and care. The NTLP and its partners will continue to advocate for a strong commitment of the GoZ to support and sustain TB prevention and care efforts until the TB epidemic is brought to an end in the country.

There are different types of advocacy that the NTLP and partners will utilise for effective engagement. These are:

• *Policy advocacy* which informs senior politicians and administrators how an issue will affect the country, and outlines actions to take to improve laws and policies.

• *Programme advocacy* targets opinion leaders at the community level on the need for local action towards the creation of an enabling environment in the communities for both TB patients and the affected people.

• *Media advocacy* amplifies the TB program by putting issues on the public agenda, and encourages the media to cover TB-related topics regularly and in a responsible manner so as to raise awareness about TB, the challenges facing the country in its war against TB and possible solutions to overcome these challenges.

Activities for advocacy

The NTP and its partners will continue to focus on administrative and corporate mobilisation through:

- Policy dialogues with parliamentarians, policy makers, community, business and religious leaders.
- Press conferences and media briefings.
- Radio and TV talk shows.
- Publishing articles in the print media.
- Summits, conferences and symposia, partnership meetings.
- Use of celebrity spokespersons and TB champions.
- Meetings with various government ministries and departments, civil organisations, business entities.
- Official memorandum of understanding and
- Meetings with patient groups and health-care providers.

The NTLP will continue to highlight the challenge of TB in the country and its socio-economic impact to decision makers and community leaders so as to strengthen and sustain political commitment for TB prevention and care.

Communication

Communication can be used to inform the public of the services that exist for diagnosis and treatment of TB and relay a series of messages about the disease. The NTLP and its partners will use effective channels and messages primarily to inform, create awareness and improve knowledge among the general public about TB and related health services. It will also seek to improve interpersonal communication (IPC) between patients and health-care workers contributing to behaviour change. Communication should however convey more than medical facts as these on their own do not motivate individuals to seek health services. Rather, an attempt should be made to explore the reasons why people do or do not take action on information received. The focus should be on changing behaviour by addressing social norms and personal attitudes.

Various communication channels will be utilised to relay messages to the public and HCWs. These will include:

- Mass media: use of radio, TV, print media as distance-learning tools.
- Social media through Facebook, twitter, SMS, etc.
- Interpersonal communication (IPC): this includes peer education, traditional folk media, community drama and poems.
- IEC and promotional materials for mass distribution.
- Meetings and gatherings.
- Edutainment such as roadshows.

Basic health education messages

Basic TB health education messages should focus on the following:

Basic TB knowledge:

- Tuberculosis is an infectious disease caused by a bacteria called Mycobacterium tuberculosis and it commonly affects the lungs. Other parts of the body such as the heart, bones, brain, spine and the abdomen may also be affected.

Signs and Symptoms

- A person with TB commonly presents with a cough of at least a week or of any duration, associated with a fever, night sweating and loss of weight. There may or may not be a history of contact with a person who had TB.
- The messaging to the population should be "If you have any one of the above symptoms you are encouraged to immediately visit your nearest health care facility for TB testing.

Mode of Transmission

- TB is spread through small droplets in the air when people with infectious TB cough, sneeze, talk or sing.

Prevention

- Treat all TB cases
- Contacts of a confirmed positive TB case must get screened and or tested for TB.
- All TB patients should cover their mouths and noses when coughing and sneezing.
- Households with TB patients are encouraged to open windows of their houses at most times.
- Individuals, families and communities should practise good hygiene at all times.
- Effort should be made to prevent children from getting severe forms of TB by sending them for BCG vaccination.
- Children who are contacts of adult TB positive cases must receive preventive treatment if they do not show symptoms or signs of active TB.

Treatment and Care

- TB is curable and treatment is available at every health facility in Zimbabwe.
- TB treatment is FREE for everyone in Zimbabwe.
- Anti-TB medicines are now much easier to take with the introduction of fixed dose combinations(FDCs) meaning one now takes much fewer tablets at a time.
- It is very important to continue taking medicines and complete the treatment even when a person with TB starts feeling better for cure to be achieved and to avoid development of drug resistant TB.

- Patients who develop adverse effects of TB medication should visit the nearest health facility immediately for evaluation, advice and management of the adverse event.

Diagnosis

- All people with symptoms and signs of PTB should be investigated for TB by sputum examination at the nearest health centre.
- Sputum examination is FREE in Zimbabwe.

TB/HIV

- It is important to be tested for HIV when one has TB and to be screened for TB when one is HIV positive.
- TB is curable even in HIV positive people.

TB in high risk groups

- Everybody is at risk of getting TB but the most at risk are
    - Children under the age of 5 years.
    - People living with HIV.
    - Those who are malnourished.
    - People above 60 years of age.
    - People with diabetes mellitus.
    - People who drink alcohol excessively.
    - Miners and ex-miners.
    - People in congregate settings.
    - Inmates and correctional facility communities.
    - People living with diabetes mellitus.
    - Health care workers.

Establishment of a technical working group on advocacy, communication and social mobilization and CTBC

The NTLP will spearhead the establishment of a TWG to coordinate, harmonize and standardise implementation of activities among partners and to create a fora for sharing plans, experiences, and best practices and for resource mobilisation.

Composition of TWG

- Experts in ACSM from NTLP and partners involved in TB programming
- NTLP will be the secretariat
- A chairperson will be elected by the members of the TWG
- The TWG will meet on a quarterly basis

Although distinct from one another, advocacy, communication and social mobilization/CTBC (AC and SM/CTBC) are most effective when used together. AC and SM/CTBC activities should therefore be developed in parallel and not separately.

Chapter 15

Engaging all care providers

Introduction

Public-Private Mix for TB prevention and care (PPM) is the involvement of all health care providers, public and private as well as formal and informal providers, in the provision of TB care, in line with International Standards for TB Care (ISTC) for patients who have or are presumed to be having tuberculosis. The ISTC defines a set of standards which should be applied and adhered to by all health care providers who manage persons with presumed or confirmed TB.

The Goal of PPM

The goal of PPM in Zimbabwe is to contribute to reducing TB morbidity and mortality and prevent the development of drug resistance through standardized diagnosis and treatment of TB and TB/HIV patients by all health care providers in the country. This intervention will help in the expansion of coverage of services for TB care, thereby increasing the national TB treatment coverage (formerly TB Case Detection Rate) and treatment success rate.

The objectives of PPM.

- To increase TB case finding and treatment success.
- To optimize the use of all available resources to confront TB, a major public health problem.
- To improve quality, equity and access to effective and affordable TB services.
- To improve patient centered TB care, support and treatment.

Increasing case detection, in particular, will depend on involving the private sector in TB control to a much greater extent than at present. Since a significant number of patients first approach private providers, there is an opportunity to reduce diagnostic delay with a concurrent reduction in transmission. By enlisting private providers, the TB program can enhance patient access to NTLP supported services and build partnerships with mutual trust with the private health care sector which are expected to increase acceptance of national policies. The overall effect of this would be enhanced TB case finding and notification thereby decreasing gaps in TB treatment coverage, reduction of TB diagnostic delays which

will impact TB transmission, standardization and harmonization of care practices across the public and the private sector and thus reduce errors in TB case management. Errors in TB case management which include overreliance on the CXR for the diagnosis of TB, infrequent use of TB bacteriological tests for TB diagnosis, poor monitoring of patients on TB treatment and the use of sub-optimal anti-TB medicine regimens have been found to be common in the private care setting in many countries and have the potential to over or under diagnose TB but more importantly pose a great risk of inducing and expanding DR-TB.

There has been no formal assessment in Zimbabwe of the TB care practices of private health care providers especially those in the business of providing health care for profit but if what has been observed elsewhere also applies in this country, then PPM as a public health intervention, is a major imperative that should be prioritized and enhanced. The engagement of all care providers (PPM) offers the potential to share service delivery with the private sector and thus moderate the workload in the public health sector.

The NTLP will continue working with other public and private non NTLP healthcare providers and the corporate sector to offer TB diagnosis, treatment, and notification and contact screening. These will include the uniformed forces and their families, mining corporations, industrial clinics and NGOs.

The program will engage "for profit" health care providers to provide TB diagnosis, notification and full treatment, however, the task of contact investigation, which is primarily a public health intervention, will lie primarily with the NTLP. The NTLP will engage with professional associations such as the Zimbabwe Medical Association (ZIMA) to act as the PPM intermediary.

The role of the MoHCC

The MoHCC through the NTLP will provide the stewardship, financing and development of policy guidelines for the PPM effort.

The Provincial Medical Directorate/City Health Directorate will work with the NTLP to ensure that PPM national policy guidelines and recommended practices are adopted, appropriately adapted and implemented at the provincial and city health directorate level.

Defining the role of the private health care provider

Diverse care providers, ranging from traditional healers to chest physicians, may not have the capacity to undertake all the TB related tasks. For instance, a medical college or a private institution may be able to undertake most of the TB prevention and care tasks. Individual providers, including pharmacists and non-clinicians, may only be able to refer presumptive cases and, at times, supervise treatment, while trained clinicians could diagnose as well as initiate TB treatment. To guide this process, it is useful to map different providers, identify capacities of the various providers to undertake various TB tasks and allocate tasks appropriately. Defining a local task-mix should inform training and the level of technical support required by different care providers to carry out their allocated tasks. The mapping of the private practitioners will be done at district level. The district will in turn report to the provincial officer responsible for TB activities who will make a consolidated list of all private practitioners in the province.

Certification of Private for Profit Health Care Providers

Certification is the process by which the national control program will officially document that a provider, laboratory, or treatment institution of any size has met the appropriate criteria to provide the services being certified. Before certification, the NTLP together with members of the provincial team will assess private health care provider's capacity to provide the service allocated to them and thereafter will train and support the provider to be able to provide the highest possible quality for that service. Once a certain quality of care is achieved based on clear quality indicators, that provider will be certified as a provider for that specific task. If, for whatever reason, the provider does not maintain the minimum level of quality for the allocated service(s) and remedial measures by the NTLP have not worked decertification will be considered to protect public health.

Memorandum of Understanding (MoU) between the MoHCC (NTLP) and private providers

In order to manage expectations and clearly define roles and responsibilities, the NTLP will enter into formal MoU between it and willing private health care providers. These MoU will spell the tasks that the Private Provider (PP) has been allocated, the support the PP should expect to receive from the NTLP, commodities that will be provided and how the PP should manage these commodities and the reporting requirements. On the other hand, the MoU will highlight the obligations of the NTLP which will include providing training and technical support and ensuring that commodities and other supplies, including but not limited to recording and reporting tools are continuously available to the PP. The administration

of the MoU and private –public sector partnerships will be delegated to PMDs, city health directorates and DMOs at the provincial and district level.

It must be noted that the MoHCC has legal and regulatory mandates to protect public health and therefore from time to time the MoHCC may invoke these mandates to compel PPs to carry out tasks considered essential to the promotion or preservation of public health. These measures may include, for example, ministerial decrees on mandatory TB case notification.

PPM program enablers

For successful implementation of the PPM program, the MoHCC through the NTLP will provide the engaged PPs with program "enablers" to ensure that the TB services provided by the PPs are adherent to national norms and the ISTC. These will include BUT will not be limited to:

- Practice guides in user friendly formats.
- Training the health care practitioners on TB case management.
- IEC materials.
- TB medicines.
- Laboratory equipment and supplies in selected situations.
- Data collection/M&E tools.

The NTLP will also, resources permitting, disseminate lists of PPs that are engaged in the TB response and organize events in which the best performing PPs are recognized and/or awarded. The NTLP will avoid using financial incentives which in the long run are neither cost effective nor sustainable.

Supply of medicines and other consumables.

The NTLP will ensure that Zimbabwe has sufficient supplies of all anti-TB medicines for all Zimbabweans at all times and these medicines will be available to PPs who have partnered with the NTLP. **Engaged PPs will have to make a commitment, to be spelled out in the MoU, that they will pass these medicines to their patients for "FREE"**. However because PPs (at least the private for profit) are usually self–financing, the NTLP recognises the potential of constraining PPs financially if all TB services must be offered for free, in the knowledge that PPs need to pay for human resources for health, water, electricity and often rental fees for facility space. **For this reason the NTP will allow PPs to charge administrative fees for medicines and other products that they will receive from the NTLP**. The level of administrative fee to be charged will be negotiated and agreed upon in meetings of the national PPM task force that will be formed to guide the implementation of PPM interventions. The anti-TB medicines supply system that will be used will be

the same as the one in use for supplying commodities and supplies to public health care facilities. As in the public sector PPs receiving anti-TB medicines will be expected to report on their consumption of anti-TB medicines and other consumables monthly using the current reporting formats used by the MoHCC. **In the end the PPs will become part and parcel of the network of TB service providers in Zimbabwe and as far as feasible will not be treated differently from the other providers (no separate reporting lines for example).**

Coordination of PPM Activities

At the central level a PPM focal person is in place and will remain in place in the period covered by these guidelines. The MoHCC/ NTLP will establish a PPM coordination mechanism through the formation of a PPM task force. The membership of this task force will include the NTLP, other MoHCC programs and departments that are also engaging PPs, both technical and financial partners of the NTLP, professional associations and very importantly and in conformity with the principle of "Nothing for Us, Without Us", the PPs themselves. This task force will be tasked with the further development of national policies on PPM, defining parameters for task mix allocation, prioritization of PPs to be engaged, enabler and incentive packages and the required regulatory frameworks among other mandates.

Monitoring and Evaluation

It is essential to continuously monitor and evaluate PPM in order to assess the impact of this intervention on TB control targets. The key indicators that the NTLP will be monitoring include:

- The proportion of notified TB cases that are referred by PPs.
- The treatment success rate of TB patients treated by PPs.
- The proportion of TB patients managed by PPs who are tested for HIV and the proportion of HIV infected TB patients managed or treated by PPs who are placed on CPT and ART.
- Public Private Mix coverage, defined as the proportion of identified PPs in a given geographic area (district, province or national level) who are linked with the NTLP with linkage defined as the referral or treatment of at least one presumptive or confirmed TB case in a quarter.
- The proportion of presumptive TB cases managed in the private sector tested with a WHO recommended rapid diagnostic test.
- The NTLP will also keep track of the number of PPs trained and or supervised.

Practical tools to facilitate the process of implementing, monitoring and evaluation of PPM initiatives will include referral for-treatment forms, feedback or back-referral and transfer forms, monthly reporting forms etc. These tools will be developed and distributed by the NTLP.

Further reading

1. WHO -Guidance on Public- Private Mix for TB prevention and care
2. WHO - The PPM national PPM situation analysis
3. WHO- PPM implementation tool kit

Chapter 16

Enhancing and sustaining efforts to eliminate Leprosy

Introduction

Zimbabwe reached the WHO target of elimination of leprosy as a public health problem, defined as less than one case per 10,000 population, in 1987. However total eradication of the disease would be an unrealistic target at the moment. A strong surveillance system is required to maintain leprosy control at the elimination phase. Leprosy continues to a serious cause of morbidity and disability and the social stigma associated with the disease further compounds its control.

Objectives of the Leprosy Control Program

- To detect leprosy cases before patients develop grade two disabilities.
- To treat at all diagnosed PB/ MB leprosy cases using effective MDT.
- To develop and distribute data recording and reporting tools to all levels of health care and have the data uploaded into the DHIS2 system.

To prevent at least 95% of leprosy cases developing disabilities during treatment.

Basics of Leprosy

Leprosy, also known as Hansen's Disease, is a chronic, granulomatous infection caused by **Mycobacterium leprae (M. leprae)**, an acid-fast bacillus (AFB) related to the bacteria causing tuberculosis. It was discovered by the Norwegian, Gerhard A Hansen, in 1873 and principally affects the skin, mucous membranes of the nose and peripheral nerves including sensory, motor and autonomic nerves.

Mode of Transmission

Transmission of *M. leprae* is primarily from untreated Multi – Bacillary (MB) patients. The route of transmission is not however definitively known. Available evidence suggests that there are two main portals of entry: the skin and the upper respiratory tract. Nasal discharge from untreated patients with active leprosy has been shown to contain large numbers of AFBs. Leprosy has been successfully

transmitted to laboratory animals (mice) via aerosols in experimental studies and some evidence exists of *M. leprae* entering through breaks in the skin barrier.

Susceptibility to infection

Most people are not susceptible to leprosy and only a very small proportion of those exposed develop the disease. There are several factors that increase an individual's risks to development of leprosy. These include older age which may reflect either a weaker immune system or the increased likelihood of lifetime exposure to a multi-bacillary (MB) case.

Clinical features of leprosy

Manifestations of Leprosy depend on the infected person's immune response to the bacterium. In many patients, at the time of presentation there will often be signs of nerve damage such as weakness or anaesthesia due to a peripheral nerve lesion or a blister, burn or ulcer in an anaesthetic hand or foot.

Leprosy case finding

Case finding is primarily passive and health workers should have a high index of suspicion and rule - out leprosy in all patients presenting with dermatological lesions. Health workers should also ensure that, all households contacts of leprosy cases are traced and screened for leprosy and those who do not have symptoms or signs of the disease placed on surveillance for at least 5 years.

Diagnosis of Leprosy

Clinical assessment

A complete history and physical examination in addition to laboratory tests are essential for the diagnosis of leprosy. The main components of the clinical assessment are:

- History
- Skin examination
- Nerve palpation
- Nerve function impairment (NFI) assessment: voluntary motor sensory test (VM-ST)
- Eye examination
- Deformity, disability and psychological assessment

The three cardinal signs of leprosy

- **Definite loss of sensation in a pale (hypo-pigmented) or reddish skin patch.**
- **A thickened or enlarged peripheral nerve with loss of sensation and/or weakness of muscles supplied by the affected nerve.**
- **The presence of acid -fast bacilli (AFB) in a slit skin smear.**

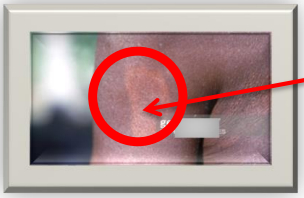


Figure 15 Tuberculoid Leprosy

One or a few well-demarcated, hypo-pigmented and anaesthetic skin lesions, frequently with active, spreading edges and a clearing center. Peripheral nerve swelling or thickening also may occur.

Figure 16 Border Line Leprosy

Lie in the middle of the polar TT to LL spectrum. This form is seen in those people with limited or variable resistance to *M. leprae*. Skin and nerve involvement is commonly seen, with only rare involvement of other structures

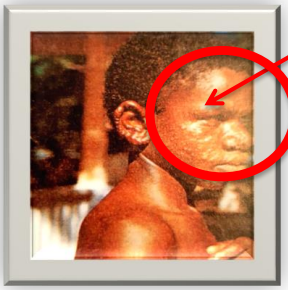


Figure 17 Lepromatous Leprosy

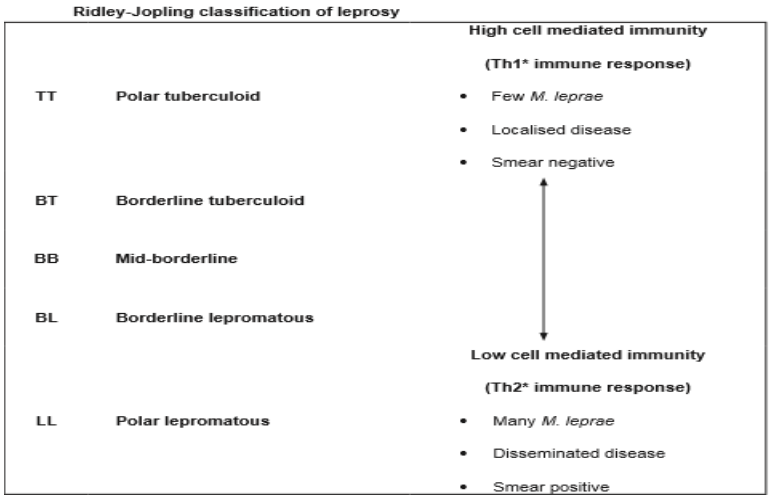
A number of erythematous papules and nodules or an infiltration of the face, hands and feet with lesions in a bilateral and symmetrical distribution that progress to thickening of the skin.

Leprosy Classification

Leprosy is classified into two treatment groups:

PB (Pauci-bacillary): **usually the PBs have one to five lesions and the skin smear is usually not required because most smears are always negative. These cases are diagnosed clinically based on the characteristic clinical presentation**

MB (Multi-bacillary): **MBs have more than six lesions and the skin smear is usually positive. The diagnosis of MBs is more bacteriological than clinical.**



Leprosy complications

Leprosy reactions

Leprosy reactions are immunologically mediated episodes of acute or sub-acute inflammation and are classified as either Type 1 (reversal) reactions or Type 2 (erythema nodosum leprosum (ENL)) reactions. They occur more commonly in MB leprosy than PB leprosy patients.

Type 1 (reversal or upgrading) reactions are due to a delayed hypersensitivity response to *M. leprae* antigens occurring in borderline lepromatous (BL), borderline (BB) or borderline tuberculoid (BT) cases. They are characterised by acute neuritis and/or acutely inflamed skin lesions. Usually with onset of type 1 reactions, there is an associated change in Ridley-Jopling classification towards the tuberculoid end of the spectrum. There is nerve tenderness with loss of sensory and motor functions. Redness and swelling

in pre-existing skin lesions occurs, and lesions which have not been visible may appear. Fever, malaise and peripheral oedema are additional features if the reaction is severe. Onset may be spontaneous though it is commonest after starting treatment.

Type 1 reactions should in general be treated by experienced clinicians using prednisolone 40mg, 30mg, 20mg, 15mg, 10mg, and 5mg daily, in this order, each dose for 2 weeks. Whenever prednisolone is being used precautions and prior screening for opportunistic infections must be carried out.

Type 2 (erythema nodosum leprosum or ENL) reactions are an immune complex response that develops due to an imbalance of the humoral immune system. They are the most serious complication of leprosy and occur in about 15% of patients with MB disease (LL and BL). Reactions may occur spontaneously or while on treatment. There is a sudden appearance of superficial or deep crops of new, tender, subcutaneous nodules on the back, the dorsum of the hands or the extensor aspects of the forearms and thighs that generally last for about 3 days. The whole episode usually lasts 2 weeks though it may be prolonged or recurrent over several years. ENL is commonly associated with systemic symptoms including:

- High fever peaking in the evenings
- Neuritis
- Leucocytosis
- Orchitis
- Nephritis
- Periostitis
- Iridocyclitis (eye inflammation)
- joint inflammation (arthritis)

Treatment of Leprosy

Leprosy can be cured with multi-drug therapy

Multi Drug Therapy (MDT) is the standard of treatment for leprosy worldwide and was first introduced in

1982. Multi drug therapy has been demonstrated in research projects to be the key to achieving cure in the individual, reducing the rates of drug resistance and breaking the cycle of transmission. Recommended regimens for treatment have been based on those highlighted in the WHO *Enhanced Global Strategy for further Reducing the Disease Burden Due to Leprosy* (2011-2015). It is recommended that if the classification of a case is in doubt, or the skin smear is positive, that the patient be treated as having MB leprosy.

Table 20 Recommended MDT regimens for the treatment of leprosy

Pauci-bacillary leprosy (PB): Duration of treatment 9 months			
Medicine	0-5years	6-14years	15 and over
Rifampicin Supervised	300mg (monthly)	450mg(monthly)	600mg(monthly)
Dapsone unsupervised	25mg (daily)	50mg (daily)	100mg (daily)
Multi-bacillary (MB) Duration of treatment 12 months			
Medicine	0-5years	6-14years	15 and over
Rifampicin Supervised	300mg (monthly)	450mg(monthly)	600mg(monthly)
Clofazimine Supervised	100mg (monthly)	150mg(monthly)	300mg(monthly)
Clofazimine unsupervised	50mg (twice a week)	50mg (twice a week)	50mg (twice a week)
Dapsone unsupervised	25mg (daily)	50mg (daily)	100mg (daily)

Adverse events of anti- leprosy medicines

Outlined below are the common adverse reactions of anti-leprosy medicines and the actions to be taken when they occur.

If a patient is receiving care at a PHC facility and is experiencing an anti–leprosy medicine adverse drug

reaction, the HCW should refer the patient to the district hospital for management of the adverse reaction.

Jaundice

In an MDT regimen the cause is usually rifampicin. All anti-leprosy medicines should be stopped immediately and the patients referred to the district hospital as stated above.

Anaemia

Anaemia may be caused by rifampicin and or dapsone. Other causes of anaemia such as parasites and malaria among many others should be ruled out.

Exfoliative dermatitis

This is usually caused by dapsone. The skin is itchy, and later peels off. The patient may be very ill. All anti-leprosy medicines should be stopped immediately and the patients referred to the district hospital as stated above.

Fixed drug eruption

A fixed drug eruption is an allergic reaction to a medicine that characteristically recurs in the same site or sites each time a particular drug is taken. This is usually caused by dapsone. The dapsone should be stopped immediately. The eruption will slowly clear after dapsone treatment is stopped.

Prevention of Disabilities

Leprosy disabilities can be prevented

Disability grading (0, 1, or 2) is carried out for the purposes of patient management, reporting to WHO and monitoring program objectives. The highest value for any body part is taken as the overall disability grading for the patient, e.g. if hands, feet, and left eye are graded 0, but the right eye is graded 2, then the overall grading for the patient is 2. It is sometimes expressed as an Eye-Hand-Foot (EHF) score where each hand, foot, and eye is graded 0, 1 or 2, and these grades are summed bilaterally for a maximum score of 12. Table 23 below shows the classification of leprosy disabilities.

Table 21 Classification of leprosy disabilities

Hands and Feet

Grade	Disability
0	No anaesthesia, no visible deformity or damage
1	Anaesthesia present, no deformity or damage
2	Visible deformity or damage
Eyes	
0	No eye problems due to leprosy; no evidence of visual loss
1	Eye problems due to leprosy, vision not severely affected (6/6 or better), can count fingers at six meters
2	Severe visual impairment (vision worse than 6/60, inability to count figures at six meters)

- Dry skin due to lack of sensation should be treated by soaking body part in water, followed by rubbing with emulsifying ointment or an oil based topical preparation.
- Ulceration and fissures (due to loss of protective sensation) lead to deep infection and osteomyelitis if not managed early, and loss of digits or limbs can result. These should be covered to allow them to heal.
- Joint contractures can occur when muscles are paralysed and active and passive exercises should be taught to patients to prevent this result. Involvement of specialist physiotherapy and orthopaedic care may be required.
- Eye damage occurs because eyes are vulnerable due to corneal sensory loss (trigeminal neuropathy) or lagophthalmos (facial neuropathy). Eyes should be inspected in a mirror daily for redness. Redness or visual deterioration should be assessed promptly by health staff. Use of lubricating eye drops or ointment should be encouraged where there is weakness in lid closure.

Daily regimen for the management of anaesthetic limbs

Health care workers should teach patients on management of anaesthetic limbs and emphasise the following;

- Look for reddened inflamed skin (hot-spots), blisters or ulceration of anaesthetic areas. Inspect footwear for foreign bodies with the potential to damage feet e.g. pebbles in shoe and nails in sole.
- Soak feet and hands if there is sensory loss, dryness, fissuring, callosity, or ulcer in water for 10-15 minutes daily.
- Pare after soaking, abraded areas of built up callus or hardened skin around an ulcer with a scotch-brite pad or pumice stone, until normal tissue is reached. (Health staff can assist this process periodically using a scalpel blade).

- Oil after soaking and paring to keep the skin supple and retain moisture. Eucerin, vitamin A, lanolin or vegetable oil are suitable types of emollient.
- Rest where hot-spots or blisters have occurred, avoid pressure to the affected part, e.g. rest with leg elevated or avoid another long walk until healed. Health staff may assist healing where ulceration has occurred by providing a sling, crutches, or a Bohler walking iron with plaster of paris cast or newer alternatives.

Enhanced leprosy case finding

To enhance case finding (complete and early case finding) the NTLP will develop a leprosy screening tool that should be administered to all patients in districts where leprosy is endemic and to all patients presenting with skin lesions in the other districts. This tool will allow HCWs to ask patients presenting to health care facilities several questions including the following:

- Does the patient have skin lesions?
- Is there loss of sensation in the skin lesion?
- Is there evidence of nerve damage?

If the answer is yes to any of these questions the patient should be considered a presumptive case of leprosy and should be tested for leprosy using skin slit smear microscopy or referred to a clinician familiar with leprosy for further clinical evaluation.

All contacts of patients with leprosy should be identified, screened and tested for the disease if there are symptoms and signs compatible with leprosy. Those with no symptoms or signs of leprosy should be placed under surveillance with 6 monthly reviews or earlier if they become symptomatic, for a minimum of 5 years.

Case holding

Medication should initially be dispensed weekly until full adherence with and understanding of the regimen is assured, and then a 4-weekly cycle of DOT and examination is established. Failure to attend a single 4-weekly DOT session requires an immediate effort to trace the patient and find an explanation. Health care workers at the local health facility should provide medication, assess adherence, monitor nerve function and trace patients who interrupt treatment. Patient on leprosy treatment should be reviewed every 3 months by a local medical officer.

Referral

Leprosy patients should be referred to the district hospital for further management if they have complications or if they require specialised services such as

- Management of adverse reactions to anti-leprosy medicines.
- Management of lepromatous reactions
- Management of deep ulcers
- Rehabilitation services

Monitoring and Evaluation/Surveillance

The health staff in charge of the tuberculosis or leprosy clinic is responsible for filling in and maintaining the following records and registers used for case reporting, analysis of treatment and defaulter tracing. Leprosy returns will be submitted to each level quarterly in sync with the National Health Information System timelines.

Quarterly report for leprosy patients on MDT

Name of District/Province:

Quarter:

	MB	PB	Total
1. Number of patients on register for MDT at the beginning of the quarter			
2. Added to MDT			
- New Patients			
- Change monotherapy to MDT			
- Restart after TnC, OC			
- Relapse after monotherapy			
- Relapse after MDT			
- Transferred in			
- subtotal			
3. Deducted from MDT			
- RFT			
- TnC			
- Died			
- Transfer			
- Subtotal			
4. No of patients on register for MDT at the end of quarter (1+2-3)			
	MB	PB	Total
No of new cases detected during the quarter			

No of new cases with WHO disability grade 2			
No of children (0-14 years) among new cases			

Name of Supervisor: Signature: Date:

TnC = Treatment not complete, OC = Out of control, RFT = released from treatment

Report form for MDT and Prevention of disabilities

District/Province/ Country Reporting Period

One dose MDT treatment = 4 week or a month medication		PB	MB	Total
101	Number of new cases detected during the reporting year and never been treated before			
101a	Amongst 101, number of cases with single skin lesion who received single dose ROM			
102	Amongst 101, number of children (0-14)			
103	Amongst 103, number of cases who have undergone a disability assessment at diagnosis			
104	Amongst 103, number of cases with WHO disability grade 1			
105	Amongst 103, number of cases with WHO disability grade 2			
106	Number of PB cases who started MDT during period 1 January – December 31, one year previously			
107	Amongst 106, number of cases who completed 6 doses of MDT within 9 months			
108	Number of MB cases who started MDT treatment during the period 1January – 31 December, two years previously			
109	Amongst 108, number of cases who completed 12 doses of MDT within 18 months			
110	Number of patients registered for MDT at the end of the reporting year			
Relapse after MDT recorded during the year				
111	Number of relapses after MDT recorded during the year			

Table 22 Leprosy Case Definations

PB	**Pauci-bacillary Leprosy**	**Leprosy patients with a maximum of 5 skin lesions and not more than one nerve trunk damaged. If slit-skin smears are examined they must be negative**
MB	Multi-bacillary Leprosy	Leprosy patients with more than 5 skin lesions or more than one nerve trunk damaged or with positive slit-skin smears
Pop	Total population in the covered area covered by the programme	Population in which leprosy cases occur. Please report the most recent reliable figure. If you treat patients from outside your official project area please specify this in an explanatory note
101-110	Patients registered for MDT	Patients who are receiving MDT that is treatment with any authorized combination of anti-leprosy drugs. E.g. Dapsone, Rifampicin, Clofazimine, Ofloxacin, Minocycline
101	New case of leprosy	A case of leprosy is a person showing clinical signs of leprosy with or without bacteriological confirmation of the diagnosis, and requiring MDT. A new case of leprosy is a person fulfilling the above criteria who have never been treated previously
101a	Single dose ROM	Single dose of a combination of Rifampicin and Minocycline. This combination is recommended in some countries for the treatment of single skin lesion PB leprosy
103	New cases who have undergone	Only report those who were assessed for disability in their eyes, hands and feet diagnosis
104	New cases with WHO disability grade 1	Hands and feet anesthesia present, no visible deformity or damage present. Eyes: eye problems due to leprosy present but vision not severely affected (vision 6/60 or better, ability to count fingers at 6m)
105	New cases with WHO grade 2	Hands and feet visibly deformed or damage present. Eyes: severe visual impairment (Vision worse than 6/60, inability to count fingers at 6m)
106-109	People completing MDT	Patients who have stopped their MDT after successfully completing the prescribed course of treatment. For PB patients, adequate treatment with the WHO recommended MDT regimen is completion of 6 doses of MDT within 9 months for the MB patients, adequate treatment with a WHO recommended MDT regimen is the completion of 12 doses of MDT within 18 months. In a country or project, some MB patients are treated with a 12 months MDT regimen and some other with a 24 month regimen, all patients should be considered having completed MDT once they have received at least 12 doses of MDT in 18 months
111	Relapse after MDT	Patients who had previously completed the course of MDT as prescribed but have now relapsed and are registered for chemotherapy. Relapses should be reported according to the original classification of the disease

Table 23 Leprosy Indicators

Indicators		Formulas	Calculations
Prevalence			
1	Total number of leprosy cases registered for chemotherapy at the end of the reporting year	110 Tot	
2	Prevalence rate of leprosy cases registered for chemotherapy at the end of the reporting year per 10 000 population	(110TOT div pop) x 10 000	
Case detection			
3	Total number of new leprosy cases detected during the reporting year	101 Tot	
4	Percentage of new MB leprosy cases amongst the total new leprosy cases detected during the reporting year per 10 000 population	(101 MB div 101 Tot) x 100	
5	Cases detection rate during the reporting year per 10 000 population	(101 Tot div Pop) x 10 000	
6	Percentage of children among the new leprosy cases detected during the reporting year	(102 Tot div 101 Tot) x 100	
Disability assessment			
7	Percentage of new cases who have undergone disability assessment	(103 Tot div 101 Tot) x100	
8	Percentage of new cases with WHO disability grade 1	(104 Tot div 103 Tot) x 100	
9	Percentage of new cases with WHO disability grade 2	(105 Tot div 103 Tot) x 100	
MDT completion			
10	Number of cases with single skin lesion who receive angle dose ROM	101a PB	
11	Percentage of PB patients completing 6 doses of MDT amongst those expected to complete their MDT treatment. To be calculated for one year cohort intake	(107 PB div 106 PB) x 100	
12	Percentage of MB patients completing 12 doses of MDT amongst those expected to complete their MDT treatment. To be calculated for one year cohort intake	(109 MB div 108 MB) x 100	

Relapses			
13	Total number of relapses after MDT treatment for MB leprosy recorded during the year	111 MB	
14	Total number of relapses after MDT treatment for PB leprosy recorded during the year	111PB	

District leprosy register

Date of Registration	Patient ID No	Name	Sex M/F	Age	Address	Name of Treatment Unit	Class	Date Start MTD	Categories						
									New	CHA	TnC	RLO	RLM	Trans in	OC

LEPROSY REGISTER (cont'd)

DISABILITY DIAGNOSIS						RESULT OF MTD AND DATE				REMARKS
EYES		HANDS		FEET		RFT	TnC	DIED	Trans out	

Key:

TnC = Treatment not completed CHA = Treatment changed from DOTS to MDT TRANS IN = Transferred in

OC = Out of Control RLO = Relapse after release from DOTS MT TRANS OUT = Transferred out

RFT = Released from treatment RLM = Relapse after release from MDT

Further Reading

1. World Health Organization, Regional Office for South-East Asia. *Enhanced Global Strategy for Further Reducing the Disease Burden due to Leprosy (Plan period: 2011-2015)*. 2009. http://www.searo.who
2. Zimbabwe Leprosy Control Programme Manual Second Edition 2000

Chapter 17

Pharmacovigilance

Prevention, identification and management of adverse reactions and events to anti- TB medicines.

Glossary of Terms

Adverse Drug Reaction (ADR) is a response to a medicine that is noxious and unintended, and which occurs at doses normally used in humans.

Adverse Event (AE) is any untoward medical occurrence that may present in a patient during treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with this treatment.

Serious Adverse Event (SAE) is an adverse event which either leads to death or a life-threatening experience such as hospitalization, prolongation of hospitalization, persistent or significant disability a congenital anomaly. SAEs that do not immediately result in one of these outcomes but that require an intervention to prevent it from happening are included. SAEs may require a drastic intervention, such as termination of the drug suspected of having caused the event.

Adverse event leading to treatment discontinuation or change in drug dosage is one that leads a clinician to stop, interrupt temporarily or change the dosage of one or more drugs, regardless of its seriousness, severity, or causal relationship to the treatment.

Causal relationship is a relationship between an exposure (A) and an event (B) in which A precedes and causes B. This may refer to the causal association between an exposure to a medicine and the occurrence of an adverse reaction.

Causality assessment is the evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction.

Therapeutic drug monitoring is a branch of clinical chemistry and clinical pharmacology that specializes in the measurement of medication concentrations in blood.

Pharmacovigilance of anti- TB medicines

Defining pharmacovigilance

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem (WHO).

Rationale of pharmacovigilance for TB medicines

The medicines used in the treatment of drug susceptible TB have been on the market for decades now. Clinicians and TB programmes around the world have an idea of the ADRs anti-TB medicines induce and the frequencies. However, in Zimbabwe locally generated data on the ADRs induced by these medicines are limited. Local data is crucial given that the occurrence and frequency of ADRs can be influenced by demographic, genetic and nutritional patterns. Some of the medicines used in the treatment of DR-TB are new or repurposed molecules whose ADR induction profile is not well understood. Moreover, studies have shown that patients on DR-TB experience at least one ADR during the duration of treatment. Systematically collecting data on ADRs and using the information to inform clinical practice helps to improve patient outcomes and promoting patient confidence in the health care system.

Prevention and management of adverse drug reactions (FLDs)

All health staff should be able to recognise and manage the common ADRs of first line anti-TB medicines. Tuberculosis patients should always be informed on starting treatment about the possibility of adverse reactions and what to do if they develop.

Patients at increased risk of ADRs

There are certain groups of patients who are at increased risk of medicine adverse effects. These include:

- The elderly
- The malnourished
- Those who consume excessive amount of alcohol
- Pregnant and nursing mothers
- Persons with liver failure
- Persons with a family history of ADRs
- Patients on other medicines
- Diabetics
- Patients with CKD
- HIV infected individuals
- Those with severe TB
- Patients with Anaemia
- Atopic persons

Carefully evaluate such patients before starting anti-TB treatment. Ensure that the medicine dosage is according to the weight of the patient in all cases. You may have to reduce the dose of the medicines in some cases, e.g. in renal failure and in the elderly (see chapter 6). Inform the patient and relatives on the possibilities of ADRs and advise the patient to report to a clinician immediately when a ADRs is suspected.

Adverse drug reactions induced by first line Anti-tuberculosis medicines

Adverse drug reactions (ADRs) of anti-TB medicines can be classified into major and minor ones and are shown in table 26 below. It shows a symptom-based approach to the diagnosis of ADRs and how to manage them.

Table 24 Symptom-based approach to identifying and managing ADRs due to FLDs

ADR	Drug probably responsible	Management
Minor		Continue anti-TB medicines, check medicine doses
Anorexia, nausea, abdominal pain	Pyrazinamide Rifampicin	Even though the NTLP recommends DOT for all TB patients in Zimbabwe, patients experiencing these minor AEs should be advised to take the medicines at night preferably with family member DOT. Ranitidine, omeprazole, or an antacid may also be prescribed.
Joint pains	Pyrazinamide	Give nonsteroidal anti-inflammatory drugs (NSAIDS) e.g. Aspirin or Ibuprofen
Burning sensation in feet	Isoniazid	Give Pyridoxine 100 mg daily
Skin rash with mild itchiness, no mucous membrane involvement or blisters	Rifampicin, Isoniazid & Pyrazinamide	Chlorpheniramine 4 mg tds or Promethazine 25-50 mg at night. Aqueous cream, Calamine skin lotion.
Peripheral neuropathy	Isoniazid	Pyridoxine 50 mg 1-3 times daily
Orange/red urine	Rifampicin	Reassure patient. Let patient know this at the beginning of treatment (before the first dose is taken).
Major		Stop responsible medicines. Refer patient to a medical officer and/or arrange admission to hospital.
Itching of skin with rash, mucous membrane involvement, blistering	Rifampicin, Isoniazid & Pyrazinamide	Stop anti-TB drugs. Refer to the next level if you cannot manage. Wait until the rash has resolved and resume medication at a hospital as advised below.
Jaundice (other causes should be excluded)	Most anti-TB medicines (especially Pyrazinamide, Rifampicin and Isoniazid	Stop anti-TB drugs. Do liver function tests. (See below) Test for Hepatitis A, B and C
Vomiting & confusion: suspect drug-induced	Most anti-TB medicines (especially	Refer to hospital for admission. Stop anti-TB medicines, do urgent liver function tests, Check for the presence of hepatitis viruses (A, B and C) and check the prothrombin

acute liver failure	Pyrazinamide, Rifampicin and Isoniazid	time/International Normalized Ratio (INR)
Hearing impairment (no wax on otoscopy)	Streptomycin	Stop Streptomycin
Dizziness (vertigo and/or nystagmus)	Streptomycin	Stop anti-TB drugs (Refer to Approach to management of adverse drug reactions section below)
Visual impairment (other causes excluded)	Ethambutol	Stop Ethambutol/ Refer to an eye specialist.
Shock, purpura (bleeding under the skin), acute renal failure	Rifampicin	Stop Rifampicin

Approach to management of adverse drug reactions

The first step in managing a patient with ADRs is to evaluate the severity of the adverse reaction, i.e. determine whether it is a minor or a major ADR. A patient who develops minor adverse effects should continue the anti-TB treatment, usually at the same dose while the ADR is treated symptomatically e.g. with an anti-histamine for itching. If a patient experiences a major adverse event, treatment with the offending medicine should be stopped immediately. Further management depends on the nature of the adverse reaction and is shown in table 26 above. Patients with major adverse reactions should be managed in a hospital. Tuberculosis treatment should be withheld until the affected organ or system returns to normal, which usually takes 2-3 weeks. After the adverse reaction has resolved a cautious reintroduction of the treatment should be attempted. This may be done using a desensitisation approach (see below).

Management of skin reactions

If a patient develops itching without a rash and there is no obvious cause (e.g. scabies), the recommended approach is to try symptomatic treatment with anti-histamines, continue anti-TB treatment and observe the patient closely. However, if a skin rash develops, then all anti-TB medicines must be stopped. Once the reaction has resolved, anti-TB medicines can be cautiously re-introduced (see below).

If a patient develops itching with a rash especially with a fever it is essential to stop all anti-TB medicines at once. Do not wait to see a widespread rash with peeling skin, blisters or raised red spots of a severe allergic reaction called Steven Johnson's syndrome. The eyes and/or mucous membranes may also be affected. Patients with Steven Johnson's syndrome are usually very ill with fever, hypotension and should

be treated as a medical emergency. Such a patient may need intravenous fluids and high dose steroids (60 mg prednisolone a day). In view of the gravity of this severe ADR, all health workers should take the presence of a generalized itchy skin rash in a patient receiving anti-TB medicines seriously and stop all medicines as indicated above. Chloramphenicol eye ointment should be applied to the patient's eyes if they are involved, in addition to giving a course of antibiotics (e.g. amoxicillin plus clavulanic acid) if the blisters look infected. Anti-TB treatment is only restarted once the skin reaction has completely resolved, which usually takes up to 4 weeks or more depending on the severity of the reaction.

Management of drug-induced hepatitis

Anti-TB medicines can damage the liver. Isoniazid, pyrazinamide and rifampicin are most commonly responsible. Ethambutol is rarely responsible. When a patient develops hepatitis during anti-TB treatment, it may be due to the anti-TB treatment or another cause. It is important to rule out other possible causes before deciding that the hepatitis is drug-induced. If the diagnosis is drug-induced hepatitis, then the anti-TB medicines should be stopped and the liver function tests checked regularly. After the hepatitis has resolved, the same regimen can often be re-introduced (see below).

If drug-induced hepatitis has been severe, then it is advisable to avoid pyrazinamide, rifampicin and isoniazid. Refer patient to a medical officer. A suggested regimen in such patients is a two-month initial phase of daily streptomycin, levofloxacin and ethambutol followed by a ten-month continuation phase of levofloxacin and ethambutol (2 [S + E + Lfx] / 10 [Lfx + E]). Note that this regimen's effectiveness has not been assessed in any clinical trial. Therefore, it is important that patients are closely monitored for clinical and bacteriological improvement. Patients should also be monitored for relapse post treatment completion.

Re-introduction of anti-TB medicines and desensitization following an adverse drug reaction.

The reintroduction of treatment and desensitisation should not be attempted in patients who have developed severe toxic reactions. In such cases that are life threatening, a new regimen not including the implicated medicine in the reaction should be used. Do not also reintroduce treatment in HIV co-infected cases.

The principles and steps for re-introduction of anti-TB medicines and desensitization following an adverse drug reaction are:

1. Reintroduce the treatment, medicine by medicine (one medicine at a time), in progressively increasing dose.

2. Start with the drug least likely to have caused the ADR. Add the other medicines from least to most likely to have caused the ADR.
3. Start with low dose of the medicine, often a sixth of the total dose and gradually increase the dose, for example, double the dose each day until the full dose is reached. This usually takes up to 4-6 days for full reintroduction of each drug, a time too short for the selection of resistant strains to the particular medicine.
4. When the full dose of a particular medicine is introduced without any ADR, then an additional medicine should be reintroduced in the same way as the previous medicine.

All reintroduction and desensitization must be done in a hospital setting under the care of an experienced medical officer. Before attempting to reintroduce treatment and desensitization, a plan should be established on how to proceed in the event of the adverse reaction reoccurring. Some recommend treating with prednisolone 40-60 mg for three days before re-introducing the medicine and continuing with the steroid for 2 weeks after reintroduction of anti-TB medicines.

Table 27 below shows the standard approach to re-introducing anti-TB medicines after a drug reaction. The medicine least likely to produce the side effect is started first and when its regular dose is achieved without any side effects the next less likely drug is introduced as shown in table 27 below.

Table 25 The standard approach to re-introduction of anti-TB medicines after an ADR

Drug	Day
Day 1	INH 25mg
Day 2	INH 50mg
Day 3	INH 100mg
Day 4	INH 300mg
Day 5	INH 300mg + R 150mg
Day 6	INH 300mg + R, 300mg
Day 7	INH 300mg + R 450mg
Day 8	INH 300mg +R 600mg (depends on weight)
Day 9	INH 300mg + R 600mg + E 400mg
Day 10	INH 300mg +R 600mg + E 800mg
Day 11	INH 300mg +R 600mg + E 1.2g (depends on weight)
Day 12	INH 300mg +R 600mg + E 1.2g + Z 400mg
Day 13	INH 300mg + R 600mg + E 1.2g + Z 800g
Day 14	INH 300mg + R 600mg + E 1.2g + Z 1.2g
Day 15	INH 300mg + R 600mg + E 1.2g + Z 1.6g (depends on weight)

The last medicine to be re-introduced before the recurrence of a reaction is the cause of the reaction and that medicine should be replaced. This may require a decision by a medical officer with extensive experience in management of TB. The patient may therefore have to be referred to the next level for further care.

Alternate regimens when first-line medicines cannot be used

It becomes extremely complicated when any of the first-line treatment medicines cannot be used. For this reason, it is advised that an experienced medical officer, be the one to care of patients in whom one or more of the first line medicines cannot be used. The principle is to use as many first-line medicines as possible in any treatment regimen.

In the event that one first-line medicine cannot be used, due for example to severe drug adverse effects to one medicine, the recommended regimens are shown in table 28 below:

Table 26 Alternate regimen when specific medicines cannot be used

Medicine that cannot be used	Alternate Regimen
Pyrazinamide	2HRE/7HR
Isoniazid	2REZ/10RE
Rifampicin	2HEZLfx/10HE
Ethambutol	2HRZLfx/4HR

NOTE:

1. **None of the above regimens have been assessed in a clinical trial setting. Therefore, it is important that patients are closely monitored for clinical and bacteriological improvement. Patients should also be monitored for relapse post treatment completion.**
2. **The recommended regimen above for situations where Rifampicin cannot be used refers to a state where there is intolerance to Rifampicin. In the event of resistance to Rifampicin patient should be managed with the recommend regimen described in chapter 8**

Managing ADRs when FDCs are used.

Medicine AEs are not any more common when FDCs are used compared to single drug formulations. However, an ADR to one of the components in a FDC is suspected, there will be a need for single-drug formulations. Limited stocks of single-drug formulations will be available in district/provincial/ referral hospitals where patients experiencing severe adverse event will be managed under supervision.

Drug interactions with first line anti-Tuberculosis medicines

Isoniazid interacts with anticonvulsants, and may cause their concentration in the body to increase to toxic levels. It is advisable to monitor serum concentration levels of anticonvulsant medicines, if possible. If this cannot be done, it may be necessary to reduce the dosage of anticonvulsant medicines during treatment with an isoniazid-containing regimen. The absorption of isoniazid is decreased by aluminium hydroxide. Medicines containing aluminium hydroxide should be taken at least 1 hour before or 2 hours after taking isoniazid containing treatment.

Rifampicin induces several liver enzymes of the cytochrome P-450 system that metabolise medicines thereby reducing their blood levels. This results in faster elimination and lower blood concentrations of many medicines ranging from anti-coagulants and cardiac medications to hormones, anti-fungals, oral

anti-diabetics and antiretroviral drugs (see table 29 below). Treating patients with rifampicin and these other medicines at the same time would result in lower blood levels and therefore loss of efficacy of these medicines.

Table 27 Rifampicin interactions with selected antiretroviral medicines

ARV drug	Effect of interaction with Rifampicin	Recommendation if patient is on Rifampicin-containing regimen
Nevirapine (NVP)	NVP level decreases by 37%. Rifampicin levels remain unchanged.	Avoid combined use of NVP and rifampicin, and therefore, switch patient to EFV if not contraindicated. If EFV is contraindicated consider switching patient to ATZ/r and switching from Rifampicin to Rifabutin (see Chapter 7)
Efavirenz (EFV)	The reduction of plasma concentration of EFV by rifampicin is not clinically significant.	If ART must be started whilst patient is still on a rifampicin-containing anti-TB treatment, EFV 600mg should be used instead of EFV 400mg.
ATZ/r	Plasma concentration of ATZ/r is reduced by up to 90% by rifampicin.	Use Rifabutin instead of Rifampicin for patients on second line ART
LPV/r	Plasma concentration of LPV/r is reduced by rifampicin.	Use Rifabutin instead of Rifampicin for patients on second line ART. In the absence of Rifabutin, LPV/r can be used with either double dosing or super boosting (see chapter 7 on TB/HIV).

Rifampicin and contraceptive methods

The effects of rifampicin on contraceptives are summarized in table 30 below. Dual protection should be recommended for all patients receiving rifampicin and hormonal contraceptives concurrently.

Table 28 Rifampicin interactions with hormonal contraceptive methods

Contraceptive method	Interaction with Rifampicin	Recommendation
Oral contraceptives containing < 50 mcg of ethinylestradiol	Efficacy reduced by rifampicin and pregnancy may occur	Change to high-dose OC, Depo-Provera or IUCD and use condoms correctly and consistently
Progestin-only-pill	Efficacy reduced by rifampicin and pregnancy may occur	Change to high-dose OC, Depo-Provera or IUCD and use condoms correctly and consistently

Depo-medroxyprogesterone (Depo-Provera®)	No known interaction	DUAL PROTECTION necessary
Hormonal implant	Efficacy reduced by rifampicin and pregnancy may occur	Use IUCD concomitantly or use condoms correctly and consistently
Intrauterine contraceptive device (hormone releasing or not)	No known interaction	May increase transmission of HIV DUAL PROTECTION necessary

Medicines that are ototoxic or nephrotoxic should not be administered to patients receiving streptomycin. These include other aminoglycoside antibiotics, amphotericin B, cephalosporins, etacrynic acid, cyclosporin, cisplatin, furosemide and vancomycin. Furthermore, streptomycin may potentiate the effect of neuromuscular blocking agents administered during anaesthesia.

Patient information about adverse drug reactions and interactions

To ensure good compliance during treatment, it is essential for patients, treatment supporters and family members to know basic facts about anti-TB medicines, their side effects and what to do in case of the occurrence of an ADR.

Because TB patients are seen daily for directly observed treatment, at least during the initial (intensive) phase of treatment, health staff are encouraged to use more than one consultation to explain the symptoms of side effects and check that patients have understood. It is also important to ask and look for any possible signs of side effects.

'Ready-made' messages adapted for local situations should be used as much as possible. The box below presents several examples of actual messages used in Bulawayo.

Example of health education messages

If you take all the anti-TB treatment with my (or the name of the treatment supporter) assistance and when I (s/he) can confirm that you have been able to swallow all the tablets, as instructed, and for the recommended period, you are going to get better. You will stop coughing, you will feel less tired, regain your appetite and gain weight.

It is very important to continue taking all the medications, even when you start feeling very well for all TB germs to be killed and for you to be permanently cured.

TB can be cured even if you are HIV-positive.

Anti-TB medicines are powerful and they can also cause side effects.

Common side effects include nausea, vomiting, abdominal pain and discomfort, joint pains, itching, skin rash, numbness, tingling or loss of sensation or burning sensation in feet and hands, yellow discolouration of eyes, diminished hearing or sight. Contact me or the clinic without delay and tell the doctor or nurse if you develop any of these symptoms.

Rifampicin colours all body fluids red or orange. This is not dangerous.

Note to Health Care workers

- If your patient is female and has had secondary amenorrhoea in spite of not being pregnant, inform her that it is likely that her monthly periods will start again as she recovers from tuberculosis.
- If your patient is female and is on modern contraception, find out what method she is using and discuss what additional method she should use during anti-TB treatment. Remember the importance of dual protection.
- Talk with all female TB patients about their reproductive plans and advise them about the benefits of starting to use contraception if she is not planning a pregnancy. This is particularly important if your patient is also HIV-positive.
- If your patient is taking anti-epileptic drugs: check what medication s/he uses and explain that the effect of anti-epileptic medication may be decreased. Suggest that the patient keeps a seizure diary, and s/he reports to you immediately if an increase in seizures is observed.
- If your patient is HIV-positive and is also on antiretroviral treatment: check what medication s/he uses and explain that added toxicities could occur and that it is important for the patient to contact you if nausea, vomiting, abdominal pain, skin rash or jaundice appears.

Key Points to Note:

At every contact with a TB patient, ask about symptoms, such as nausea, vomiting, abdominal pains and discomfort, itching, joint pains and numbness, tingling or burning sensation or loss of sensation in hands and feet

At every contact with a TB patient, look for skin rash, jaundice with continued nausea and vomiting.

If an ADR occurs diagnose it promptly followed by appropriate management of the ADR.

Modified from Health Services Department, Bulawayo materials

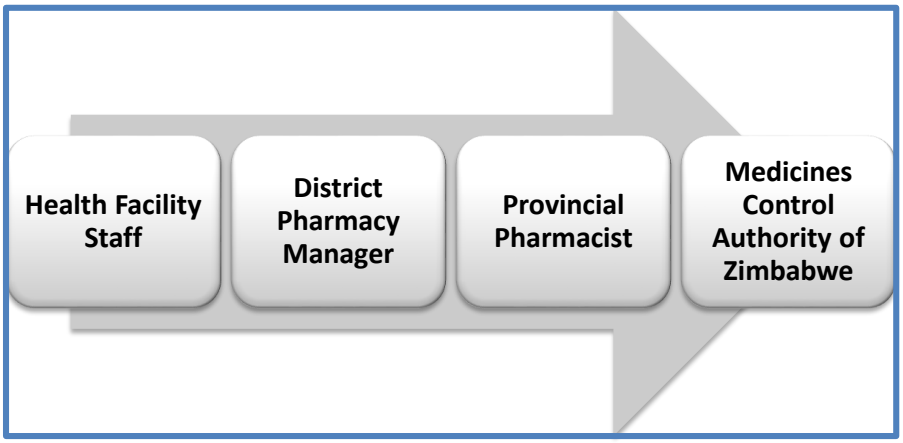
Reporting of ADRs to first line TB medicines

Spontaneous ADR reporting is recommended for ADRs suspected to be caused by first line anti-TB medicines. In spontaneous ADR reporting, reporting is the initiative of health care workers (HCWs). HCWs are encouraged to report all severe adverse events and adverse events of clinical significance.

How to report suspected ADRs and ADR reporting tools

An ADR report should be submitted to the Medicine Control Authority of Zimbabwe (MCAZ), as soon as possible after the reaction. To report an ADR, the MCAZ e-ADR reporting platform http://www.mcaz.co.zw/index.php/2016-01-08-06-40-00/e-reporting can be used. Once submission is made on-line, the e-ADR form is received by the MCAZ. A standard ADR reporting form can also be completed (Annex 11), and submitted to the MCAZ (see figure 19 below). All ADR reports once submitted, are treated in an anonymous manner i.e. information for both the patient and reporting health care worker are kept confidential.

Figure 18 A diagrammatic representation of the movement of the ADR form once completed



Prevention and management of ADRs for Second Line Medicines

There are multiple adverse events that can be seen in patients undergoing treatment for DR-TB. Prompt identification and management of AEs is important in maintaining patient health and adherence. Table 31 below lists the common adverse events seen in patients on therapy for DR-TB, presenting signs and symptoms, and the median time to onset of symptoms.

Table 29 Timing of onset for common AEs and symptoms

Adverse event	Signs and Symptoms	Average onset (in weeks)
Nausea and vomiting		2-8
Diarrhoea	Loose stool > 3 times a day	9
Hepatitis/ liver abnormalities	Nausea, vomiting, jaundice, anorexia	4-24
Hearing loss	Buzzing in ears, loss of ability to hear sounds, pressure in the ears, leaning forward when listening	6.5
Renal failure	Oedema, decreased urine output	16
Electrolyte imbalances	Tremors, muscle cramps	16

Seizure	Loss of consciousness, tonic-clonic movements	2
Psychosis	Hallucinations, loss of touch with reality	8
Hypothyroidism	Fatigue, decreased reflexes, constipation, dry skin,	16
Rash	Red skin or bumps over trunk, face or extremities	Anytime
Peripheral neuropathy	Tingling or burning in hands or feet	16
Arthralgia	Joint pain or swelling	13

Management of ADRs due to second line anti-TB medicines

Adverse reactions are common and to be expected in most patients treated for DR-TB. In order to ensure adherence, these should be quickly identified and managed with ancillary medicines provided free of charge to the patient. Studies have shown that careful management of adverse reactions improves overall treatment outcomes.

It is important to educate patients about what to expect during treatment and to encourage the patient to continue taking the anti-TB medicines if the symptoms are mild. Many AEs resolve spontaneously but some may need to be treated with supplementary medicines. Some adverse events are dose-dependent and can be managed by reducing the dosage. Significant dose reduction should be avoided (i.e. dose of the previous weight band), which can affect the efficacy of the medicine. Algorithms for the identification and management of common adverse reactions are discussed in table 32 below. Of note, pyridoxine should be prescribed to **all individuals** taking Cycloserine to prevent neurological adverse events (50 mg for every 250 mg of CS).

Table 30 Second Line medicine common adverse events, suspected agent(s) and management strategies

Adverse effect	Suspected agent(s)	Possible management strategies	Comments
Seizures	Most likely: Cycloserine (Cs), Less likely: Isoniazid (H), Fluoroquinolones (Fqs)	Suspend suspected agent pending resolution of seizures. Initiate anticonvulsant therapy (e.g. carbamazepine, phenobarbitone)). Increase pyridoxine to maximum daily dose (200 mg per day). Restart suspected agent or reinitiate suspected agent at lower dose, if essential to the regimen. Discontinue suspected agent if this can be done without compromising regimen.	Anticonvulsant is generally continued until MDR-TB treatment is completed or suspected agent discontinued. History of previous seizure disorder is not a contraindication to the use of agents listed here if a patient's seizures are well controlled and/or the patient is receiving anticonvulsant therapy. Patients with history of previous seizures may be at increased risk for development of seizures during MDR-TB therapy.
Peripheral neuropathy	Most likely: Cycloserine (Cs), Isoniazid (H), Streptomycin (S), Kanamycin (Km), Amikacin (Am), Less likely: Capreomycin (Cm), Ethionamide(Eto)/ Prothionamide (Pto), Fluoroquinolones (Fqs)	Increase pyridoxine to maximum daily dose (200 mg per day). Change injectable to capreomycin if patient has documented susceptibility to capreomycin. Initiate therapy with tricyclic antidepressants e.g. amitriptyline. Non-steroidal anti-inflammatory drugs or acetaminophen may help alleviate symptoms. Lower dose of suspected agent if this can be done without compromising regimen.	Patients with co-morbid disease (e.g. Diabetes, HIV, alcohol dependence) may be more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the agents listed here. Neuropathy may be irreversible; however, some patients may experience improvement when offending agents are suspended.
Hearing loss and vestibular disturbances	Most likely: Streptomycin (S), Kanamycin (Km), Amikacin (Am), Less likely: Capreomycin (Cm), Clarithromycin (Clr)	Discontinue suspected agent if this can be done without compromising regimen. Document hearing loss and compare with baseline audiometry if available. Change parenteral treatment to capreomycin if patient has documented susceptibility to capreomycin. Decrease frequency and/or lower dose of suspected agent if this can be done without compromising the	Patients with previous exposure to aminoglycosides may have baseline hearing loss. In such patients, audiometry maybe helpful at the start of MDR-TB therapy. Hearing loss is generally not reversible. The risk of further hearing loss must be weighed against the risks of stopping the injectable in the treatment regimen. While the benefit of hearing aids is minimal to moderate in auditory

		regimen (consider administration three times per week). Discontinue suspected agent if this can be done without compromising the regimen.	toxicity, consider a trial use to determine if a patient with hearing loss can benefit from their use.
Psychotic symptoms	Most likely: Cycloserine (Cs), Isoniazid (H), Less likely: Fluoroquinolones (Fqs), Ethionamide (Eto) / Prothionamide(Pto)	Stop suspected agent for a short period of time (1–4 weeks) while psychotic symptoms are brought under control. Initiate antipsychotic therapy. Lower dose of suspected agent if this can be done without compromising regimen. Discontinue suspected agent if this can be done without compromising regimen.	Some patients will need to continue antipsychotic treatment throughout MDR-TB therapy. Previous history of psychiatric disease is not a contra-indication to the use of agents listed here but may increase the likelihood of psychotic symptoms developing during treatment. Psychotic symptoms are generally reversible upon completion of MDR-TB treatment or cessation of the offending agent.
Depression	Most likely: Socio-economic circumstances, chronic disease, CS Less likely: FQs, H, Eto/Pto	Provide psycho-social support. Offer group or individual counselling. Initiate antidepressant therapy. Lower dose of suspected agent if this can be done without compromising the regimen. Discontinue suspected agent if this can be done without compromising regimen.	Socioeconomic conditions and chronic illness should not be underestimated as contributing factors to depression. Depressive symptoms may fluctuate during therapy and may improve as illness is successfully treated. History of previous depression is not a contraindication to the use of the agents listed but may increase the likelihood of depression developing during treatment.
Gastritis	Most likely: P-aminosalicylic acid (PAS), Ethionamide (Eto) Prothionamide (Pto), Less likely: Clofazimine (CFZ)	Give antacids, H2-blockers (ranitidine) or proton-pump inhibitors (omeprazole) depending on duration and severity; Stop suspected agent(s) for short periods of time (e.g., one to seven days). Lower dose of suspected agent, if this can be done without compromising regimen. Discontinue suspected agent if this	Severe gastritis, as manifested by hematemesis, melaena or haematochezia, is rare. Dosing of antacids should be carefully timed so as to not interfere with the absorption of anti-tuberculosis medicine (take 2 hours before or 3 hours after anti-tuberculosis medications). Reversible upon

		can be done without compromising regimen.	discontinuation of suspected agent(s).
Rash	Most likely: PZA, AMOX-CLV Less likely: INH, RIF, Pto/Eto, PAS, CFZ Any drug can cause rash	Assess for mucous membrane involvement; if mucous membranes involved discontinue all drugs and start prednisone. If rash is mild, can treat with nicotinamide, topical steroids	If rash is severe or if drug rash is suspected, discontinue all agents and restart the agents least likely to cause rash first. This can be done one at a time over short periods; alternatively, the three least likely agents can be started first followed by additional single agents.
Hepatitis (transaminases > 5X the ULN)	Most likely: Pyrazinamide (Z), Isoniazid (H), Less likely: P- aminosalicylic acid (PAS), Rifampicin (R), Ethionamide (Eto) Prothionamide (Pto), Ethambutol, FQs	Stop all therapy pending resolution of hepatitis (to < 2 x the upper limit of normal for the transaminases. Investigate to rule-out other potential causes of hepatitis (malaria, ART, viral causes). Consider suspending most likely agent permanently. Reintroduce remaining drugs, one at a time with the least hepatotoxic agents first, while monitoring liver function. If single drug introduction being used, must introduce the agents over 7-14 days; could also introduce 3 less likely drugs at once then add back additional agents	History of previous hepatitis should be carefully analysed to determine most likely causative agent(s); these should be avoided in future regimens. Generally reversible upon discontinuation of suspected agent.
Renal toxicity	Most likely: Streptomycin (S), Kanamycin (Km), Amikacin (Am), Less likely: Capreomycin (Cm),	Discontinue suspected agent. Consider using capreomycin if an aminoglycoside had been the prior injectable in regimen. Consider dosing 2–3 times a week if drug is essential to the regimen and patient can tolerate (close monitoring of creatinine). Adjust all anti-tuberculosis medications according to the creatinine clearance (see chapter 6)	History of diabetes or renal disease is not a contraindication to the use of the agents listed here, although patients with these co-morbidities may be at increased risk for developing renal failure. Renal impairment may be permanent.
Electrolyte disturbances	Most likely: Streptomycin (S),	Check serum potassium level If potassium is low replace both	If severe hypokalaemia admit patient. Amiloride 5–10 mg QD or

(hypokalaemia and hypomagnesaemia)	Kanamycin (Km), Amikacin (Am), Less likely Capreomycin (Cm),	potassium and magnesium. Check other electrolytes (i.e. calcium) if no improvement	spironolactone 25 mg 6 hourly may decrease potassium and magnesium wasting and is useful in refractory cases. Oral potassium replacements can cause significant nausea and vomiting. Oral magnesium may cause diarrhoea.
Optic neuritis	Most likely: Ethambutol Less likely: Eto, Pto, CFZ	Stop Ethambutol. Refer patient to an ophthalmologist to assess for other causes	Usually reverses with cessation of Ethambutol. Rare case reports of optic neuritis have been attributed to streptomycin.
ECG changes	Most likely: Bedaquiline (BDQ), Moxifloxacin, Levofloxacin Less likely: CFZ	Stop BDQ if there is worrying QT prolongation (>500ms), replete electrolytes, stop other medicines that affect the cardiac rhythm	
Arthralgias	Most likely: Pyrazinamide (Z), Less likely: Fluoroquinolones (FQs)	Initiate therapy with non-steroidal anti-inflammatory drugs. Lower dose of suspected agent if this can be done without compromising regimen. Discontinue suspected agent if this can be done without compromising regimen.	Symptoms of arthralgia generally diminish over time, even without intervention. Uric acid levels may be elevated in patients on pyrazinamide. Allopurinol appears not to correct the uric acid levels in such cases.

Drug-drug interactions of ARVs and second line anti-TB medicines

Fluoroquinolones and DDI: Reduced intestinal absorption of fluoroquinolones can be related to the concomitant administration of buffered DDI, which contains an aluminium/magnesium-based antacid. DDI is rarely used in the management of HIV except in extreme conditions. If the two must be used, this problem could be by-passed deferring the 2 administrations (DDI taken 6 hours before taking FQ or 2 hours later) or prescribing the enteric-coated formulation of DDI.

Clarithromycin: It is an inhibitor of cytochrome P3A. Consequently, it could have several pharmacological interactions with PIs and NNRTIs. On this basis and on the evidence of its poor activity against DR-TB strains, it should not be used in patients on ART.

Bedaquiline has not been extensively tested for use with ART. Dose adjustments are needed if it is used with EFV, as Bedaquiline has been shown to decrease the concentrations of EFV in the blood.

Furthermore, due to limited information on the co-administration of BDQ and ART, therapeutic drug monitoring (TDM) is recommended where available. It is also recommended to closely monitor the effectiveness of ART through monthly viral load testing.

Monitoring and reporting adverse events due to Second Line Anti-TB medicines

The World Health Organisation (WHO), recommends the use of active drug safety monitoring (aDSM) for the continuous monitoring and reporting of adverse events induced by second line TB medicines. The term 'active TB drug-safety monitoring and management' defines active and systematic clinical and laboratory assessment of patients while on treatment. Health programmes that systematically monitor patient safety are at an advantage to prevent and manage ADRs, as well as improve health-related quality of life and treatment outcomes. National tuberculosis programmes (NTPs) that actively pursue drug safety monitoring and management are also better prepared to introduce new tuberculosis (TB) drugs and novel regimens.

The primary difference with the spontaneous adverse event reporting system described earlier is that, with aDSM the health worker assesses meticulously for any perceived adverse events. The frequency of clinical and laboratory assessments to be done are described in Chapter 8. To report any adverse events to the MCAZ please use the ADR forms described in annexure 11 using the procedure described previously.

Further Reading

1. www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/ (Accessed November 2016)
2. A practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis: enhancing the safety of the TB patient (WHO 2012)
3. Bloss E et al. Adverse events related to multidrug-resistant tuberculosis treatment, Latvia, 2000–2004. International Journal of Tuberculosis and Lung Disease, 2010, 14:275–281.
4. Mallolas, J., et al., Pharmacokinetic interaction between rifampicin and ritonavir-boosted atazanavir in HIV-infected patients. HIV Med, 2007. 8(2): p. 131-4.
5. Nathanson, E., Gupta, R., Huamani, P., et al. Adverse events in the treatment of multidrug-resistant tuberculosis: results from the DOTS-Plus initiative. INT J TUBERC LUNG DIS 8(11):1382–1384. 2004.
6. Active tuberculosis drug-safety monitoring and management (aDSM): Framework for implementation (WHO,2015)

Chapter 18

Monitoring and Evaluating the TB and Leprosy Response

Introduction

Monitoring and Evaluating (M&E) is the key to the success of NTLP as it guides the programme to identify its strengths and weaknesses. It provides a continuous avenue for the systematic collection of data on specific indicators to inform programme management units and stakeholders at every level on the performance of the programme and whether selected interventions and activities are achieving the targets that have been set. Monitoring and evaluation is critical for tracking indicators in the performance framework including inputs, processes, coverage, outputs, outcomes and the overall impact of whatever is being done. The M&E system is also used to track utilization of programme resources to help monitor costs and expenditures and thus provide the ability to assess cost effectiveness and cost efficiency of interventions and activities.

Purpose of monitoring and evaluation of NTLP

Activities for M&E are carried out to continuously and periodically measure and evaluate progress of the programme vis-a-vis the set objectives and targets of the NTLP strategic plan. The purpose of M&E is to:

- Ensure that training, supervision, logistics management and communication activities are being carried out effectively at each level from the national level to the primary health-care level.
- Ensure that data needed to assess case notification rates and treatment outcomes are collected, analyzed and sent to the central unit by all health facilities.
- Help identify technical and operational problems, determine the reasons for the problems which will enable programme management units at all levels to take the necessary corrective actions.
- Provide evidence which will enable staff to improve standards of practice for patient care and support.
- Helps to understand the progress that has been made towards the achievement of an outcome at a specific point in time.

Recording and Reporting

Tuberculosis is a notifiable disease according to the Public Health Act [Chapter 15:09]. In addition to providing relevant information for planning, programme management, policy formulation and assessment of overall programme performance, recording and reporting is critical to satisfy legal requirements of the Public Health Act. Recording and Reporting (R&R) of TB cases is an essential component of the End TB strategy. The data used for M&E of the NTLP comes from the routine recording

and reporting of information from all levels of the health care delivery system. The collection of TB patient related data begins at the Out Patient Department (OPD) and other settings where TB screening is carried out. Thereafter data begins to move up the chain as seen in the figure 20 below. The tools used for collecting TB information include

1. The outpatient department register (T12) where all persons accessing at the OPD of any health facility are recorded.
2. All presumed TB clients are entered in the Tuberculosis Presumptive register
3. The laboratory sputum request form is used to inform the laboratory staff to examine the sputum specimens for Xpert MTB/Rif assay and document the findings on the form and returned it to the requesting clinician.
4. The laboratory register is used to document all results done in the laboratory and the patient information, provided in the laboratory request form for easier follow up of patients who are bacteriologically confirmed to be started on treatment on time.
5. The district and health facility TB register are used to record all types of TB patients diagnosed in the health facilities or in the district using unique serial numbers and treatment outcomes for each patient.
6. The TB case notification form is used by health facilities to notify the District Medical Officer about the newly diagnosed TB patients.
7. The TB outpatient treatment card is used by the patients to access treatment and by DOT observers to monitor patients' compliance/adherence to treatment

Note: Health Facilities use paper based TB quarterly report form, to report TB cases diagnosed in their health facilities during the reporting period (end of the quarter) to the District Medical Officer. The District TB/Leprosy Coordinator validates the data before it is entered in the DHIS2. The District Health Information Officer enters the data in DHIS2. After one week the data have been entered in the DHIS2; the DTLC counter checks that the data entered in the DHIS2 tallies with the data in the quarterly return forms. The health mangers are encouraged to analyse the data as a team at the end of each quarter and use the data for planning and decision making. This facilitates generation of feedback reports to the health facilities, district and provincial TB reports.

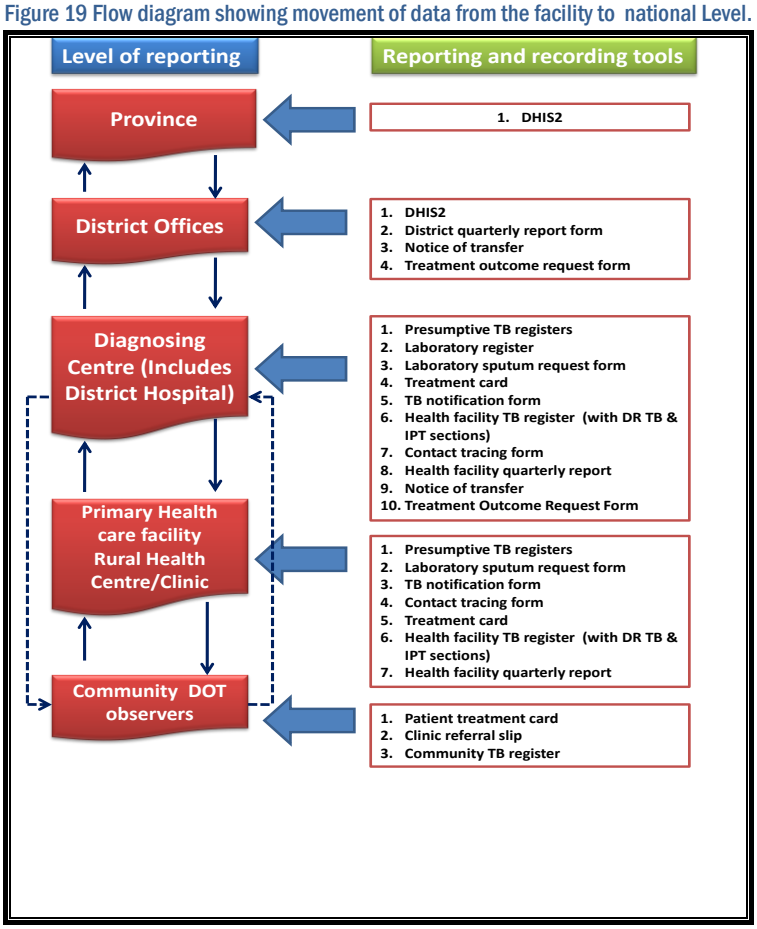
Table 31 The use of NTP data at each level of the Health Care System in Zimbabwe

Level	Use of Data
Health facility	Data is used for evaluation of case detection and case management. The data is also used to rapidly assess programme performance at the facility using the quarterly reports compiled from the health facility level recording tools. Individual patients records e.g. sputum examination for diagnosis and for treatment follow –up , HIV screening, ART initiating, Contact investigation, Lost to follow-up retrieving, treatment outcomes.
District	Data is used for comparisons between health facilities for programme performance, to identify health facilities with challenges in the implementation of programme mitigation intervention strategies and also for allocation of resources to health facilities and the provision of feedback to improve performance.
Provincial	Data is used for comparisons between districts for programme performance, to identify districts with challenges in the implementation of programme mitigation intervention strategies also for allocation of resources to districts and the provision of feedback to improve performance.
National	Data is used for comparisons between provinces and districts for programme performance, to identify provinces and districts with challenges in the implementation of programme mitigation intervention strategies and for allocation of resources to districts and the provision of feedback to improve performance. Data is also used for resource mobilization, international reporting requirements, formulation of TB policies and intervention strategies and advocacy for political commitment to the TB response and the TB prevention and care program.

Data flow and transmission

The District Tuberculosis and Leprosy Coordinator plays a key role in the coordination of the implementation of Tuberculosis interventions, both at health facility and community levels. The DHE and the DTLC under the guidance of the DMO ensures that all the diagnosing and treatment sites submit quarterly reports which are analysed and validated at local level. The district is responsible for entering the data in the DHIS2 after analysis and validation. The provinces analyses the data in the DHIS2 and generate reports for feedback to the districts. It is important that at each level data is analyzed and utilized at the point of collection to allow for quick action in order to improve programme performance.

Figure 19 Flow diagram showing movement of data from the facility to national Level.



Data generated is analysed and used differently at different levels as explained above.

Quarterly and annual reports will be generated from the routine TB data collected and shared with all stakeholders at district, provincial and national levels through TB/HIV newsletters, and quarterly and annual TB review meetings. Reports on TB will also be published in the MoHCC annual reports. Reports will also be shared with different stakeholders through NTLP Annual Reports, Global Tuberculosis Reports and SADC Regional TB surveillance report.

Cohort analysis and treatment outcomes

A cohort is a group of patients diagnosed and registered for treatment during a specific time period. The cohort analysis system is the key management tool for evaluating the performance of the NTLP. It allows

for the identification of problems with patient retention in care, so that the NTLP can institute appropriate action to overcome them and improve programme performance.

.The DTLC should perform cohort analysis of treatment outcomes every 3 months and at the end of every year. A typical cohort consists of all those new patients registered during a quarter i.e. 1 January to 31 March, 1 April to 30 June, 1 July to 30 September, and 1 October to 31 December. These are the 4 cohorts in a year. Cohort analysis can be disaggregated by type of TB e.g. for new bacteriologically confirmed TB cases or all TB cases among others.

The performance of the TB control programme is assessed at various stages and levels but of paramount importance is that an outcome is available for every patient registered and treated for TB. Treatment outcome assessment **MUST** be done for all patients at the end of TB treatment. This information, so far, is available on the patient treatment card, TB health facility register and district TB register. Accurate and complete recording of the treatment card thus enables the NTLP to monitor patients and the progress of the various health units with regards to achieving local and national targets. Various treatment outcomes are indicated on the reverse of the treatment card.

At the end of the treatment course, for each patient, the DTLC should record the treatment outcome in the district TB register, as per definitions.

All patients transferring from one health facility to another should be issued with **notice of transfer form**. It is the responsibility of the transferring unit to find out the treatment outcome of all patients that transferred out and this should be done in collaboration with the receiving facility.

Tuberculosis Programme Indicators

Indicators help measure the programme's performance. For the NTLP the indicators are based on the broad implementation framework. Indicator groups to be monitored are:

1. Input indicators: Human resources, equipment, finance and other material resources.
2. Process indicators: Training of staff, procurement of equipment and production of reports.
3. Output indicators: Availability of services such as laboratory services, to perform various activities, microscopy, culture and drug sensitivity testing.
4. Outcome indicators: Case detection rates, Treatment outcome rates, etc.
5. Impact indicators: Prevalence and incidence, mortality

Table 32 The main NTLP indicators

Indicator	Indicator definition	Target	Frequency
Community			
Number of People screened for TB by community health workers	Numerator = Number of People screened for TB by community health workers x 100,000 Denominator = Catchment population		**Quarterly**
Percentage/ Number of Presumptive TB clients referred to health facility by community health workers	Numerator = Number of Presumptive TB clients referred to health facility by community health workers Denominator = Number of People screened for TB by community health workers x 100		**Quarterly**
Percentage/Number of presumptive TB clients diagnosed with TB referred by the community health workers	Numerator = /Number of presumptive TB clients diagnosed with TB referred by the community health workers Denominator = Number of Presumptive TB clients referred to health facility by community health workers x 100		**Quarterly**
Percentage/Number of TB cases under DOT (health facility based and community based)	Numerator = Number of TB cases under DOT Denominator = Total number of all types of TB cases registered	**100%**	**Quarterly**
Case finding indicators			
Number of presumptive TB cases per 100,000 population	Numerator = number of presumptive TB cases recorded in register x 100,000 Denominator = Catchment population		**Quarterly**
Percentage of presumptive TB cases investigated using Xpert MTB/Rif who had positive results	Numerator = Number of presumptive TB cases tested with a positive X pert result x 100% Denominator = Total number of presumptive TB cases with Xpert MTB/Rif results		**Quarterly**
Percentage of presumptive TB cases investigated using culture who had positive result	Numerator = Number of presumptive TB cases with a positive culture x 100% Denominator = Total number of presumptive TB cases with results of culture		**Quarterly**
Notification rate all forms of TB cases per 100,000 population	Numerator = Number of all TB cases registered x 100,000 Denominator = Catchment population		**Annual**
Notification rate of new bacteriologically confirmed PTB cases per 100,000 population	Numerator = number of new pulmonary bacteriologically confirmed cases registered x 100,000 Denominator = Catchment population		**Annual**
Percentage of new and relapse TB patients tested using a who-recommended rapid test at the time of diagnosis	Patients tested using a WHO recommended rapid test at the time of diagnosis, divided by the total number of new and relapse TB patients, expressed as a percentage	90%	**Quarterly**
Contact investigation coverage	Number of household contacts of people with bacteriologically-confirmed TB who were evaluated	**90%**	**Quarterly**

	for TB, divided by the number eligible, expressed as a percentage		
Treatment Coverage			
TB treatment coverage	Number of new and relapse cases that were notified and treated, divided by the estimated number of incident TB cases in the same year, expressed as a percentage	**90%**	**Quarterly**
Treatment coverage, new TB drugs	Number of TB patients treated with new (endorsed after 2010) TB drugs, (Bedaquiline and Delamanid) divided by the number of notified patients eligible for treatment with new TB drugs, expressed as a percentage	**90%**	**Quarterly**
Treatment outcome indicators			
Treatment success rate	Numerator = Number of all forms of TB cases who successfully completed treatment (Cured and treatment completion) at the end treatment x 100% Denominator = Number of all forms of TB cases registered	**90%**	**After 12 months of treatment initiation**
Cure rate	Numerator = Number of new pulmonary bacteriologically confirmed TB patients declared cured at the end of treatment x 100% Denominator = Number of new bacteriologically confirmed pulmonary TB cases registered	**90%**	**After 12 months of treatment initiation**
Treatment completed	Numerator = Number of new pulmonary bacteriologically confirmed patients declared as treatment completed at the end of treatment x 100% Denominator = Number of new pulmonary bacteriologically confirmed cases registered	**90%**	**After 12 months of treatment initiation**
Failure rate	Numerator = Number of new pulmonary, bacteriologically confirmed TB patients declared as treatment failure at the end of treatment x 100 Denominator = Number of new pulmonary, bacteriologically confirmed cases registered	**<5%**	**After 12 months of treatment initiation**
Death rate	Numerator = Number of deaths of all forms of TB during/before treatment x 100 Denominator = Number of all forms of TB cases registers	**0%**	**After 12 months of treatment initiation**
Lost to Follow-up rate	Numerator = Number of all forms TB cases who were lost to follow-up during/before treatment x 100 Denominator = Number of all forms of TB cases registered	**<5%**	**After 12 months of treatment initiation**
Not evaluated rate	Numerator = Number of all forms of TB cases who do not have an outcome documented in the district TB register at the end of treatment x 100 Denominator = Number of all forms of TB cases registered	**0%**	**After 12 months of treatment initiation**

Six monthly Treatment Outcomes for Drug Resistant Cases			
MDR-TB cases on MDR-TB treatment that died	Numerator = Number of confirmed MDR-TB cases registered and started on MDR-TB treatment who died of any cause by the end of month 6 x 100% Denominator = total number of confirmed MDR-TB cases started on treatment for MDR-TB during the period.		**After 12 months of treatment initiation**
MDR-TB cases on MDR-TB treatment that interrupted	Numerator = Number of confirmed MDR-TB cases started on MDR-TB treatment who interrupted by the end of month 6 x 100% Denominator = total number of confirmed MDR-TB cases started on treatment for MDR-TB during the period.		**After 12 months of treatment initiation**
MDR-TB cases on MDR-TB treatment with negative culture	Numerator = Number of microbiologically confirmed pulmonary MDR-TB cases registered and started on MDR-TB treatment with negative culture at month 6 x 100% Denominator = total number of microbiologically confirmed DR-TB cases registered and started on treatment for DR-TB during the period.		**After 12 months of treatment initiation**
MDR-TB cases on MDR-TB treatment with positive culture	Number of microbiologically confirmed pulmonary MDR-TB cases registered and started on DR-TB treatment with positive culture at month 6 x 100% Denominator = total number of microbiologically confirmed DR-TB cases registered and started on treatment for DR-TB during the period.		**After 12 months of treatment initiation**
Annual Treatment outcomes for Drug Resistant Cases			
Treatment success rate	Numerator = Number of RR/MDR -TB cases who successfully completed treatment at the end of treatment period x 100% Denominator = Number of RR/MDR TB cases registered	**75%**	**After 24 months of treatment initiation**
Failure rate	Numerator = Number RR/MDR-TB patients declared as treatment failure at the end of treatment period Denominator = Number of RR/MDR cases registered	**<5%**	**After 24 months of treatment initiation**
Death rate	Numerator = Number of deaths of all MDR-TB patients during/before treatment x 100 Denominator = Number RR/MDR-TBTB cases registered	**<10%**	**After 24 months of treatment initiation**
Lost to Follow-up rate	Numerator = Number RR/MDR-TB cases who were lost to follow-up during/before treatment x 100 Denominator = Number of RR/MDR-TB cases registered	**0%**	**After 24 months of treatment initiation**
Not evaluated rate	Numerator = Number of RR/MDR-TB who not do not have an outcome documented in the district TB register at the end of treatment period x 100 Denominator = Number of RR/MDR- TB cases registered	**0%**	**After 24 months of treatment initiation**

TB& HIV Indicators			
LTBI treatment coverage	Number of people living with HIV newly enrolled in HIV care and the number of children aged <5 years who are household contacts of cases started on LTBI treatment, divided by the number eligible for treatment, expressed as a percentage (separately for each of the two groups).	**90%**	**Quarterly**
Documentation of HIV status among TB patients	Number of new and relapse TB patients with documented HIV status divided by the number of new and relapse TB patients notified in the same year, expressed as a percentage	**100%**	**Quarterly**
Number of TB patients who have HIV positive results recorded in the TB register	Numerator = Number of cases with an HIV- positive result recorded in the TB register x 100% Denominator = Total number of TB cases with an HIV test result		**Quarterly**
Proportion of HIV- positive TB cases initiated on CPT	Numerator = Number of TB patients with an HIV-positive result on CPT x 100% Denominator = Number of TB cases with an HIV positive result	**100%**	**Quarterly**
Proportion of HIV- positive TB cases initiated on ART	Numerator = Number of TB patients with an HIV-positive result on ART x 100% Denominator = Number of TB cases with an HIV-positive result	**100%**	**Quarterly**
Drug resistant TB			
Drug Susceptibility Testing (DST) coverage for TB patients	Number of TB patients with DST results for at least rifampicin resistance divided by the total number of notified bacteriologically confirmed (new and retreatment) cases in the same year, expressed as a percentage. DST coverage includes results from molecular (e.g. Xpert MTB/RIF) as well as conventional phenotypic DST results	**100%**	**Quarterly**
Total number of laboratory-confirmed RR/ MDR-TB cases identified			**Quarterly**
Number of laboratory-confirmed XDR-TB cases			**Quarterly**
Proportion of RR/MDR cases enrolled on treatment	Numerator=Number of cases on treatment Denominator=Total number of cases identified	**100%**	**Quarterly**
TB Drug Management Indicators			
Proportion of health facilities reporting stock outs of first line adult anti-TB medicines	Numerator= Number of health facilities reporting stock outs of at least RHZE or RH150/75 Denominator = Total number of health facilities managing anti-TB medicines	**< 5%**	**Quarterly**
Service Delivery			
Percentage of TB affected households that experience catastrophic costs due to TB	Number of people treated for TB (and their households) who incur catastrophic costs (direct and indirect combined), divided by the total number of people treated for TB	**0%**	**Periodic surveys**

Table 33 Tuberculosis case definitions

Disease category	Term	Definition
	Presumptive TB case (previously called "TB suspect")	Any person who presents with symptoms or signs suggestive of TB, in particular cough of two weeks or more and cough regardless of duration in HIV-positive persons
TB case categories		
By diagnosis	Bacteriologically diagnosed TB case	A patient with a biological specimen that is positive by smear microscopy, culture or WHO-approved rapid diagnostics (such as Xpert MTB/RIF). All such cases should be notified, whether TB treatment was started or not.
	Clinically diagnosed TB case	A patient who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extra-pulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.
By Site	Pulmonary TB patient	Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extra pulmonary TB. Note that pleura and pleural cavity are not part of the lung parenchyma or tracheobronchial tree. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of PTB.
	Extra pulmonary TB patient	Refers to any bacteriologically confirmed or clinically diagnosed patient with TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones and meninges.
By history of previous treatment	New TB patient	A patient who has never had treatment for TB or who has taken anti-TB drugs for less than one month.
	Previously treated patient	A patient who has received 1 month or more of anti-TB medicines in the past. They are further classified by the outcome of their most recent course of treatment (described below)
	Relapse patients	A patient who has previously been treated for TB, was declared *cured* or *treatment completed* at the end of their most recent course of treatment, and who is now diagnosed with a recurrent episode of TB.
	Retreatment after lost to follow up	A patient who has been previously treated for TB and was declared *lost to follow-up* at the end of their most recent course of treatment. (These were previously known as *treatment after default* patients.)
	Retreatment after treatment failure	A patient who has previously been treated for TB and whose *treatment failed* at the end of their most recent course of treatment.
	Other previously treated patients	A patient who has previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.
By HIV status	HIV-positive TB patient	Refers to any bacteriologically confirmed or clinically diagnosed case of TB who has a positive HIV test result from the time of TB

Disease category	Term	Definition
		diagnosis or other documented evidence of enrolment in HIV care, such as enrolment in ART register once ART has been started.
	HIV-negative TB patient	Refers to any bacteriologically confirmed or clinically diagnosed case of TB who has a negative HIV test result at the time of TB diagnosis. Any HIV-negative TB patient subsequently found to be HIV-positive should be reclassified accordingly.
	HIV status unknown TB patient	Refers to any bacteriologically confirmed or clinically diagnosed case of TB who has no result of HIV testing and no other documented evidence of enrolment in HIV care. If the patient's HIV status is subsequently determined, he or she should be reclassified accordingly.
Treatment outcome categories		
By outcome categories	Cured	A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear or culture negative in the last month of treatment and on at least one previous occasion.
	Completed treatment	A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.
	Died	A TB patient who dies for any reason before starting or during the course of TB treatment.
	Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment
	Lost to follow-up (previously called "defaulted")	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more
	Not evaluated	Patient for whom no TB outcome is assigned. This includes cases transferred out to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.
	Treatment success	Equals the sum of *cured* and *treatment completed*
Drug resistance TB		
	Presumptive MDR-TB cases	A patient in whom resistance testing should be done at least for rifampicin. This group of patients is defined by the NTLP and includes retreatment patients and household contacts of confirmed MDR-TB patients.
By Drug resistant TB	Mono-resistance	Resistance to one first-line anti-TB drug only
	Poly-drug-resistance	Resistance to more than one first-line anti-TB drug, other than both isoniazid and rifampicin.
	Multidrug-resistance	Resistance to at least both isoniazid and rifampicin.
	Extensive drug resistance	Resistance to any fluoroquinolone and to at least one of three second line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance.
	Rifampicin-resistance	Resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether mono resistance, multidrug resistance, poly-drug resistance or extensive drug resistance.
Definitions of treatment outcome and programme monitoring and evaluation indicators		

Disease category	Term	Definition
Case notification Rate	The number of TB cases reported to the NTLP per year per 100,000 population. Case notification rates are usually calculated for new bacteriologically confirmed pulmonary TB cases and all forms of TB cases	
Treatment success rate	Percentage of TB cases registered in a specified period and who completed treatment, whether with bacteriologic evidence of success ("cured") or without ("treatment completed")	
Treatment failure rate	Percentage of TB cases registered in a specified period who are smear positive at 5 months or later after initiating treatment	
Lost to follow-up rate (previously called "Default" rate)	Percentage of TB cases registered in a specified period who did not start treatment or whose treatment was interrupted for two consecutive months or more.	
Not evaluated rate	Percentage of TB cases registered in a specified period who were not evaluated for an outcome.	
Other useful definitions		
Xpert MTB/RIF	A rapid laboratory test that consists of two different tests to show if the specimen contains TB bacillus (Mycobacterium tuberculosis) and if the strain is resistant to rifampicin.	
Cohort	A group of patients in whom TB has been diagnosed, and who were registered during a specified time period (e.g. the cohort of new pulmonary bacteriologically confirmed patients registered in the calendar year 2014). This group forms the denominator for calculating TB treatment outcomes.	
Indicator	Measurable information obtained from routine TB recording and reporting that is monitored over time. The measure provides information on how well a certain aspect in TB control is functioning. Key indicators have been listed above, for example notification rate of all TB patients per 100,000 population	
Target	The value of an indicator that the NTLP sets as the goal to be reached by the end of a defined period. Targets are defined to focus efforts to improve TB control.	

Further Reading

1. Monitoring and Evaluation Plan (2015 – 2017)
2. Making Sense of TB Data – Data Collection Analysis and Use of TB Data

Chapter 19

Research and Innovation to Enhance Programme Performance

Introduction

The third pillar of the End TB Strategy focuses on innovation and intensified research which are essential for the achievement of the targets of this strategy. The TB research needs to achieve the targets of the End TB Strategy range from basic research with eventual development of new tools such as diagnostics, medicines and vaccines to the optimization of use of existing and yet to be developed tools through operations and implementation research. During the life of the End TB Strategy and the current TB management guidelines, Zimbabwe will play its role in the advancement of TB knowledge to enhance the TB response by developing a needs- based TB research agenda, mobilising and enhancing resources for the implementation of relevant research and wide dissemination of research results to the global TB community.

Coordination of TB research

The NTLP will work with all relevant stakeholders to form and support an all-inclusive national TB research network whose task will be to revise and or develop a national TB research agenda, mobilize financial and other resources for implementing the TB research agenda and enhance the capacity for the conduction of high quality TB research.

Situation Analysis

Following the revision and or development of the national TB research agenda, the national TB research network under the guidance of the NTLP will carry out a thorough assessment of the TB situation in Zimbabwe so as to identify programmatic bottlenecks that require a research approach to solve. The national TB data will be essential for this purpose.

The National TB Research Agenda

During the life span of these guidelines, there will be an annual review of the national TB research agenda based on a thorough review of the national TB data as highlighted above. Some of the research priorities that were identified include the following:

- Determining the optimal approaches for TB contact management to identify the most efficient and effective ways to find and investigate contacts.
- Examination of various TBPT approaches for efficacy and effectiveness in Zimbabwe where the risk of exposure and transmission of TB is high.
- Operations research to overcome barriers in the implementation of TBPT with IPT
- The additive value of BMI measurement for TB screening across various all level of care.
- Cross sectional study to assess practice of DOT and identify the most effective treatment supporter (health care worker, community worker and family members) in rural versus urban versus mobile populations.
- Cohort studies to define the proportion of TB patients who end up with significant organ damage that requires appropriate post TB treatment care.
- Studies on the clinical significance of MOTTs in the Zimbabwean situation.
- Studies to define the burden and risk factors for bovine TB in Zimbabwe
- Assessment of sample collection procedures and laboratory handling from children with a presumptive diagnosis of TB with a focus on NPA and stool.
- Studies to define the burden, risk factors and optimized screening approaches for occupational TB including TB in health care workers and miners.
- Operational studies on active TB case finding including effect of prioritization of at risk groups, rates of TB in at risk groups, feasibility and yield of various approaches (number needed to screen to identify a case of TB) and cost effectiveness of the various screening approaches.

Enhancing capacity for TB research

The national TB research network will be responsible for identifying TB research capacity gaps. Following identification of the research capacity gaps, the TB research network will work towards filling these gaps. This will include mobilizing financial resources, training and re –training of human resources, developing the physical infrastructure needed to support research etc. A proportion of the funding that becomes available to Zimbabwe for TB prevention and care will be used to fund TB research. This proportion should not be less than 10% of all available funding for TB prevention and care.

Annexes

Appendix 1: TB-IPC Risk Assessment Tool

INTRODUCTION

This is a tool to assess Healthcare workers' (HCWs) risk of acquiring *M. tuberculosis* infection within the facility where TB patients receive care (e.g., OPD OI, A&E, ICU, OT, NNU, wards, radiology, laboratory, pharmacy, waiting areas, etc.), based on the adequacy of control measures that are in place. Some areas within the facility are at higher risk. The results of this risk assessment will facilitate the revision of the facility infection prevention and control (IPC) plan and the development of specific ward/departmental SOPs. Information will be obtained mostly by inspection and observation of the facility, interviews with HCWs and clinical record reviews. The IPC Committee who include the IPC Focal Person, and other members such as the Quality Assurance officer, TB focal officer, Wellness program officer, in each facility should utilize this tool to assess the areas of risk and formulate facility specific infection control plans according to the results.

WHAT IS TB RISK ASSESSMENT?

A process of estimating the probability of TB infection within the facility

1.3 WHO SHOULD CONDUCT THE RISK ASSESSMENT?

The designated IPC focal person together with members of the IPC committee should conduct the risk assessment, with a view to obtaining information on where the gaps are in terms of TB infection prevention and control and the protection of HCWs so that the appropriate actions can be taken.

1.4 HOW OFTEN SHOULD THIS BE DONE?

Zimbabwe Infection Prevention and Control Policy, Strategic Plan & ME plan (2015) stipulates that facilities conduct the risk assessments at least annually

Step 1: Planning the risk assessment

The designated IPC focal person together with members of the IPC committee should:

1. Set aside time to conduct the risk assessment.
2. Review the facility TB profile (e.g. number of confirmed cases, number of Multidrug resistant (MDR) TB cases, etc.)
3. Familiarize themselves with the current infection control plan for the facility.
4. Understand that this tool will assist in improving the workplace conditions for all staff members.

N. B. Inform Management of the intended risk assessment but DO NOT inform the HCWs when the assessment will be conducted

Step 2: Conducting the risk assessment

The designated IPC focal person together with members of the IPC committee should:

1. Use the tool provided to conduct the risk assessment.
2. Collect the information by inspection, clinical record observation and interviews.
3. Ensure an objective approach to the assessment.

Step 3: Reporting actions and follow up

1. Evaluate the findings and identify the problem areas.
2. Document the findings in a report with recommendations
3. Present a copy of the report to the facility management team.
4. Address the problem areas with the appropriate actions to reduce risk of acquiring TB infection.

INSTRUCTIONS:

1. Tick the appropriate box.
2. Add the total score for each area and identify the actions to be taken.
3. **Red font indicates standards needed to be met for measuring national indicators**

KEY:

	Appropriate TBIC standard in place	**1**
	Inappropriate TBIC standard in place	**0**
	Not applicable	**1**

Please Note:

Achievement of these basic standards demonstrates the implementation of TB infection control measures and if any of these practices are not fully met then the facility should not qualify as having TB infection control standard

Health Facility Data

1. Name of Facility _____Type of facility _____
2. Assessors:
   _____
   _____
3. Date: _____Bed Capacity: _____
4. Total outpatient attendance in the previous year: _____
5. Total number of inpatient admissions in the previous year: _____
6. Total number of healthcare workers at facility (excluding those on secondment): _____

Laboratory/TB Register Information (Please enter total numbers from previous year for each of the following):

1. Number of AFB sputum smears performed: _____
2. Number of AFB sputum smears reported positive: _____
3. Number of smear-positive TB patients diagnosed: _____
4. Number of smear-negative TB patients diagnosed: _____
5. Number Gene Expert tests performed: _____
6. Number of TB cases positive for Gene Expert: _____
7. Number of TB cases with either MDR (or XDR) TB: _____
8. Number of health care workers diagnosed with TB disease: _____

Operational Research

Based on a review of the medical records, what is the average number of days for the following?

1. Presentation of patient until collection of specimen _____ ___
2. Specimen collection until receipt by laboratory _____
3. Receipt of specimen by laboratory until smear results are provided to health-care provider __
4. Diagnosis until initiation of standard anti TB treatment _____
5. Receipt of specimen by laboratory until culture results are provided to clinician _____
6. Receipt of specimen by laboratory until drug-susceptibility results are provided to clinician ___

PART 1: Managerial Controls

Standards	Yes	No	N/A	Means of Verification	Recommended actions
1. A Trained IPC Focal person has been assigned to carry out infection control activities in the facility				Trained IPC focal person available	
1.2 There is a current stamped and approved written facility-specific annual infection control plan which includes TBIC and is available to all departments				Facility infection control plan available in all departments	
1.3 There is a designated person for monitoring and evaluating TBIC activities				IPC focal person TB nurse/ officer	
1.4 There is a budget allocated for infection control activities.				Budget and expenditure records	
1.5 There is a multi-disciplinary IPC committee responsible for implementing TBIC practices in the facility.				Record of minutes which include TBIC agenda	
1.6 A clearly defined annual training plan for TB prevention, care and control in place				Training Plan	
1.7 Designated TB focal person has received documented TBIC training (includes refresher training) within the past 2 years.				Training log/ HR record	
1.8 All HCWs have received documented TBIC training includes refresher training) within the past 2 years				Training log/HR record	
1.10. Staff get annual TB screening (note screening method)				Confidential HCW TB register/ Occupational health records	
1.11 TB symptoms occurring among HCWs are immediately investigated and, if TB is diagnosed, is treated, registered and reported in the confidential occupational health records or in the TB register.				Occupational health records HCW TB register	
1.12 Evidence exist that a high incidence of TB disease has been observed in the community that the health-care setting serves				TB incidence Demographic data	
1.13 There is a policy to provide N-95 or FFP2 respirators to staff who have contact with patients with suspected TB and other infectious airborne diseases				Policy document	
1.14 Admissions policy for infectious patients available				Policy document	
1.15 The following SOPs are available: a) Isolation precautions				SOP document	

b) Sputum collection				SOP document	
c)Admission criteria				SOP document	
d) Use of Personal Protective Equipment				SOP document	
e) Respirator fit checking				SOP document	
f) Reprocessing of reusable respiratory equipment				SOP Document	
SCORE					

PART 2 ADMINSTRATIVE CONTROLS

Standards	**Yes**	**No**	**N/A**	**Means of Verification**	**Recommended Actions**
2.1 Patients are routinely asked about cough or other TB symptoms upon entering the facility/ ward (TB screening tool routinely used for all patients)				Screening tool	
2.2 Patients with cough or other symptoms of TB are promptly separated from others				Observation IPC plan	
2.3 Patients with cough or other symptoms of TB are "fast tracked" to a care giver				Observation IPC Plan	
2.4 Health education given on cough etiquette				Monthly Health education record	
2.5 TB information for patients is readily available and offered by staff and there is clear display of messages on cough hygiene in all areas frequented by patients.				Observation IEC materials	
2.6 A package of HIV and HIV-associated TB prevention and care is available for HCWs on site including: a) confidential HIV testing				Observation Occupational health records HTC register	
b) Post-exposure prophylaxis for all HCWs				Workplace Register	
c) Provision of antiretroviral ART				Occupational health records	
d) Isoniazid preventive therapy (IPT) for HIV positive HCWs				Occupational health records	
2.7 There is a tracking mechanism for monitoring turn-around time from TB screening to diagnosis, and from TB diagnosis to treatment initiation				Records	
2.8 There is a person responsible for monitoring turn-around time from TB screening to diagnosis, and from TB diagnosis to treatment initiation				Person responsible	
2.9 Sputum smear results received within 24 hrs				Presumptive TB register and laboratory smear register	

2.10 Gene Xpert results received within 24hrs				Presumptive TB register and laboratory Gene Xpert register	
2.11 The time between actual diagnosis and treatment initiation is within 24 hours				Lab Register, TB Register, Presumptive TB register and/or patient records	
2.12 WHO recommended rapid diagnostics, e.g. Xpert MTB/RIF as the first TB diagnostic test for people living with HIV and HCWs				Algorithm Flow Chart Laboratory register	
2.13 HIV testing is offered to all patients with presumptive TB and evaluation for time to start ART is carried out if found HIV-positive.				HTC testing register, TB register, Presumptive TB register	
2.14 There is a formal system for linking patients diagnosed with TB in the inpatient setting to outpatient care for follow-up (or to TB/DOT clinic for follow-up)				Records	
2.15 Mothers admitted in kangaroo and paediatric wards are screened for TB				Patient's records	
SCORE					
PART 3: Environmental controls					
Standards	**Yes**	**No**	**N/A**	**Means of verification**	**Recommended actions**
3.1 The facility design, patient flow and triage system comply with what is outlined in the IPC guidelines				IPC plan/ policy Observation	
3.2 There is adequate ventilation (If natural ventilation, windows are open and good airflow is present; If mechanical ventilation, good air flow and equipment is functioning)				Observation	
3.3 If natural ventilation, signage is in place to keep doors and windows open				Observation	
3.4 Airflow is considered in relation to HCW patient placement				Observation	
3.5. Waiting area is well ventilated (i.e. windows and doors open)				Observation	
3.6 Patients are not crowded in hallways or waiting areas.				Observation	
3.7 Sputum samples are collected in a well-ventilated, clearly designated area away from others, outdoors.				Observation	
3.8 Proper packaging boxes are available for transporting sputum samples to the next level				Packaging boxes	
3.9 On admission patients with presumptive TB are cohorted or isolated				Observation	
3.10 There is adequate space between beds (2.5m)				Observation	

3.9 Diagnosed TB cases, who are hospitalized, are isolated or cohorted according to drug sensitivity status in rooms with adequate natural ventilation or negative pressure				Observation	
3.10 Patients with suspected drug-resistant TB are separated from other patients (in a separate room/ward)				Observation	
3.11 Diagnosed DR TB patients are separated from other patients (in a separate room/ward				Observation	
3.12 The OT/ICU ventilation is tested regularly				Records	
3.13 The ventilation in the OT/ICU is maintained regularly				Records	

PART 4: Personal Protective Equipment

Standards	Yes	No	N/A	Means of verification	Recommended actions
4.1 Supplies are readily available for coughing patients (tissues, surgical masks, cloths) and are being used.				Stock and stock record	
4.2 Lined waste bins for safe disposal of tissues and masks available				Availability of bin liners	
4.3 Respirators are readily available for and being used by HCWs, particularly for high-risk aerosol-generating procedures and for providing care to patients with diagnosed or suspected infectious MDR-TB and XDR-TB, as per national guidelines.				Observation, stock and stock records	
4.4 There have been no stock outs in respirators in last 3 months				Stock and stock record	
4.5 HCWs have been trained in the proper fit and use of respirators.				Demonstration Training records	
SCORE					

Part 5. Part Infection control in the laboratory

Standards	Yes	No	N/A	Means of verification	Recommended actions
5.1 The laboratory has a safety manual				Safety manual	
5.2 There a designated safety officer				Safety officer	
5.3 Trainings on safety are conducted for the staff members				Training Log	
5.4 Bio hazardous waste autoclaved before leaving the laboratory				Autoclave	
5.5 The laboratory has a level 102 Biosafety cabinet				Biosafety cabinet in place	
5.6 Bio safety cabinet placed appropriately within the laboratory				Position	
5.7 Biosafety cabinet maintained annually				Maintenance log	
4.3 Waste bins in laboratory for disposal of sputum mugs lined and labelled with bio-hazard sign				Availability of waste bins	
4.4 Daily biosafety cabinet monitoring				Daily log sheet	

6.Risk Prone Procedures					
6.1 The following TB risk procedures are performed at the facility and procedure manuals available for the following; a) Suctioning				Procedure manual	
b) Intubation				Procedure manual	
c)Bronchoscopies				Procedure manual	
d) Gastric lavage				Procedure manual	
e) Nebulization				Procedure manual	
6.2 Respiratory equipment is being properly reprocessed: (If so state how under comments) a) Ventilator tubings				State how:	
b) Oxygen tubings					
c)Oxygen face masks					
d)Nebulization equipment					
e) Neonatal penguin sucker					
Score					
TOTAL SCORE	**...../ - (NA) ..... = ... /..... .....%**				

Actions to be addressed following the problems identified during this risk assessment

	Action	Person responsible	Time frame
1.			
2.			
3.			
4.			
5.			

Annex 2: Draft Health Care TB Screening and Wellness Programme

National Policy for HCWs TB Screening AND THE WELLNESS PROGRAMME

Zimbabwe's Non-Communicable Diseases (NCD) Policy 2013, provides guidance on effective prevention and control strategies for common NCDs. MoHCC has established NCD programmes in every province so that linking Wellness programs for HCWs with prevention of healthcare associated TB will assist in reducing the stigma and contribute to early detection of communicable and non-communicable disease.

Policy development for TB screening among health workers

To create an enabling environment to institutionalize routine TB screening and wellness among HCWs a comprehensive policy for routine screening of HCWs, within the context of a comprehensive workplace wellness program will be developed.

Wellness Programme

Each province will establish provincial wellness teams. This will be done in consultation with the nursing, non-communicable diseases and communicable diseases departments of the MOHCC. These teams will spearhead provincial workplace wellness at all health facilities, primarily hospitals as a conduit to implementation of the policy framework for routine screening of health workers. TB screening will include use of GeneXpert MTB/RIF, and an annual Chest X-ray. Screening and monitoring will also include as a minimum, HIV testing, Hepatitis B screening and vaccination, blood pressure, body mass index and diabetes, in order to inform appropriate public health responses to the emerging threat of NCDs. This will also minimize stigma associated with routine TB/ HIV care. Diagnosed HCW will be appropriately linked to care. This will include provision of TB preventive therapy for HCWs living with HIV and those diagnosed with latent TB infection.

Surveillance

Designated staff wellness clinics will be equipped with basic diagnostic equipment such as sputum specimen jars, thermometers, height-weight scales, glucometers, HIV test kits sphygmomanometers, laryngoscopes to facilitate routine confidential screening for TB, HIV, diabetes, among other communicable and NCD conditions. These clinics will be manned by a Medical Officer in the case of referral hospitals and Sisters in Charge for more peripheral primary care facilities. Routine TB screening will be offered at least twice a year. Customized M&E tools will be developed to facilitate confidential quarterly cohort, including zero reporting of surveillance activities, from facility through to national level through routine surveillance systems. Facility wellness teams will be responsible for regular analysis of generated data to inform decision making for improved service delivery at local level. HCWs diagnosed with TB, HIV or other conditions such as diabetes or needle stick injuries among others will be promptly initiated on appropriate treatment.

Annex 3: Tuberculosis Screening Tool

1. **Does the patient have any of the following**
    a. **Current cough (if HIV +) or cough of greater than 1 week?**
    b. **Fever**
    c. **Night sweating**
    d. **Loss of weight (>10%) or a BMI of less than 17Kg/m^2**
2. **CXR for TB High Risk Groups if available**

Notes:

Any person who has one or more of the above symptoms or an abnormal CXR is a presumptive TB patient.

Collect a sputum specimen for Xpert MTB/Rif or Xpert MTB/Rif Ultra assay (GeneXpert) from any presumptive TB patient.

Annex 4: Presumptive TB Register

Purpose of the register: It is used to record information of identified Presumptive Tuberculosis Clients.

Places where it is used: At all screening/entry points of the health facilities (OI Clinic, OPD and Wards)

Who maintains the register? Nurses .The SIC is responsible for the proper maintenance and updating of the presumptive register

Demographic Data for presumptive client								Demographic Data for next of kin			12.Xpert MTB/Rif Test					hh 13. Direct Smear Microscopy Examination					14. Culture, and Drug Susceptibility Testing 14. Culture Test				15. X ray done (yes/No)	16. Histology		17. HIV Testing		
1. Date of registration	2. Presumptive TB client Number	3.National I.D. Number	4. First Name Surname	5. Sex	6. Age	7. Physical residential/workplace Address Phone number	8. TB Risk groups (Use code below, multiple response allowed)	9. First Name and Surname of next of kin	10. Physical residential/workplace address of next of kin Phone number	11. Referred By (use code below)	Date specimen collected	Date specimen sent to the laboratory	Date result received	MTB Result /detected/ Rif Resistance not detected & lab serial number	Rif Resistance (detected/not detected/indeterminant)	Specimen collected	Date specimen collected	Date specimen sent to the laboratory	Date result received	Result & lab serial number	Date specimen collected	Date specimen sent to the laboratory	Date results received	Culture Results (use code below)		Type of specimen	Result & Date	Code 1	Code 0	Code 9
			Name			Address			Address							1st specimen	1st specimen	1st specimen	1st specimen	1st specimen										
			Surname			Phone number			Phone number							2nd specimen	2nd specimen	2nd specimen	2nd specimen	2nd specimen										
			Name			Address			Address							1st specimen	1st specimen	1st specimen	1st specimen	1st specimen										
			Surname			Phone number			Phone number							2nd specimen	2nd specimen	2nd specimen	2nd specimen	2nd specimen										
			Name			Address			Address							1st specimen	1st specimen	1st specimen	1st specimen	1st specimen										
			Surname			Phone number			Phone number							2nd specimen	2nd specimen	2nd specimen	2nd specimen	2nd specimen										
			Name			Address			Address							1st specimen	1st specimen	1st specimen	1st specimen	1st specimen										
			Surname			Phone number			Phone number							2nd specimen	2nd specimen	2nd specimen	2nd specimen	2nd specimen										
			Name			Address			Address							1st specimen	1st specimen	1st specimen	1st specimen	1st specimen										
			Surname			Phone number			Phone number							2nd specimen	2nd specimen	2nd specimen	2nd specimen	2nd specimen										
			Name			Address			Address							1st specimen	1st specimen	1st specimen	1st specimen	1st specimen										
			Surname			Phone number			Phone number							2nd specimen	2nd specimen	2nd specimen	2nd specimen	2nd specimen										

Annex 5: Specimen Examination Form

ZIMBABWE NATIONAL TB AND LEPROSY PROGRAMME
Laboratory Request/Report Form

N.B *Refer to the back of the for instructions on completing the form*

Health Facility Code ☐☐☐

Referring Health Facility/Department: _____

Date Specimen Collected: _____

Patient's Full Name:_____ ID Number:_____

DOB: _____ Age: ___ Sex: M [ ] F [ ] Patient Contact Number:_____

Complete Physical Address: _____

Next of Kin Full Name:_____ Contact number:_____

Presumptive TB or TB number: _____

HIV Status:

Code 0	Code 1	Unknown 9

TB Risk Group Codes ***(circle all that apply)***
1. Health Worker
2. Miners and ex-miners
3. Contact
4. Prisoner
5. Diabetic
6. Child Under 5 yrs
7. 60yrs +
8. HIV+
9. Drink alcohol excessively
10. Malnourished
11. Congregate settings
12. History of Residents in another Country
13. Other (Specify)

Specimen Type: Sputum [ ] Other (specify) _____

Examination(s) Required: Xpert MTB/Rif [ ] Smear Microscopy [ ]

Reason for Examination (tick box)

Initial diagnosis: [ ] Specimen *(indicate by ticking)* Spot [ ] Early Morning [ ]

Follow-up: [ ]

End of intensive phase [ ] End of 5 months [ ] End of Continuation phase [ ] Month for DR-TB Patients [ ]

Requested by (Full Name): _____ Phone: _____

Email Address: _____

RESULTS ***(to be completed in the laboratory)***

Laboratory Serial No. _____ Date Specimen Received: _____

Commented [U1]: How can we indicate results for Xpert MTB/Rif Ultra eg the 'trace'

XPERT MTB/RIF ***(for results tick appropriate)***

Date Examined	Visual Appearance*	MTB not detected	MTB detected/ Rif Resistance NOT Detected	MTB detected / Rif Resistance Detected	MTB detected/ Rif Resistance Indeterminate	Not done	Invalid/Error/No Result

SMEAR MICROSCOPY ***(for results tick appropriate)***

Date Examined	Visual Appearance*	SMEAR RESULT *(tick one)*				
		Negative	Positive			
			1 - 9	+	++	+++

***M** = mucoid, **MP** = mucopurulent, **SLV** = salivary, **S** = saliva, **MS** = mucosalivary, **BS** = blood stained and **P** = purulent.*
*+**FP** = with food particles*

Examined by (Full Name) _____ Date result released _____

Approved by (Full Name) _____Signature_____ Date _____

The completed form (with results) should be sent promptly to the requesting health facility

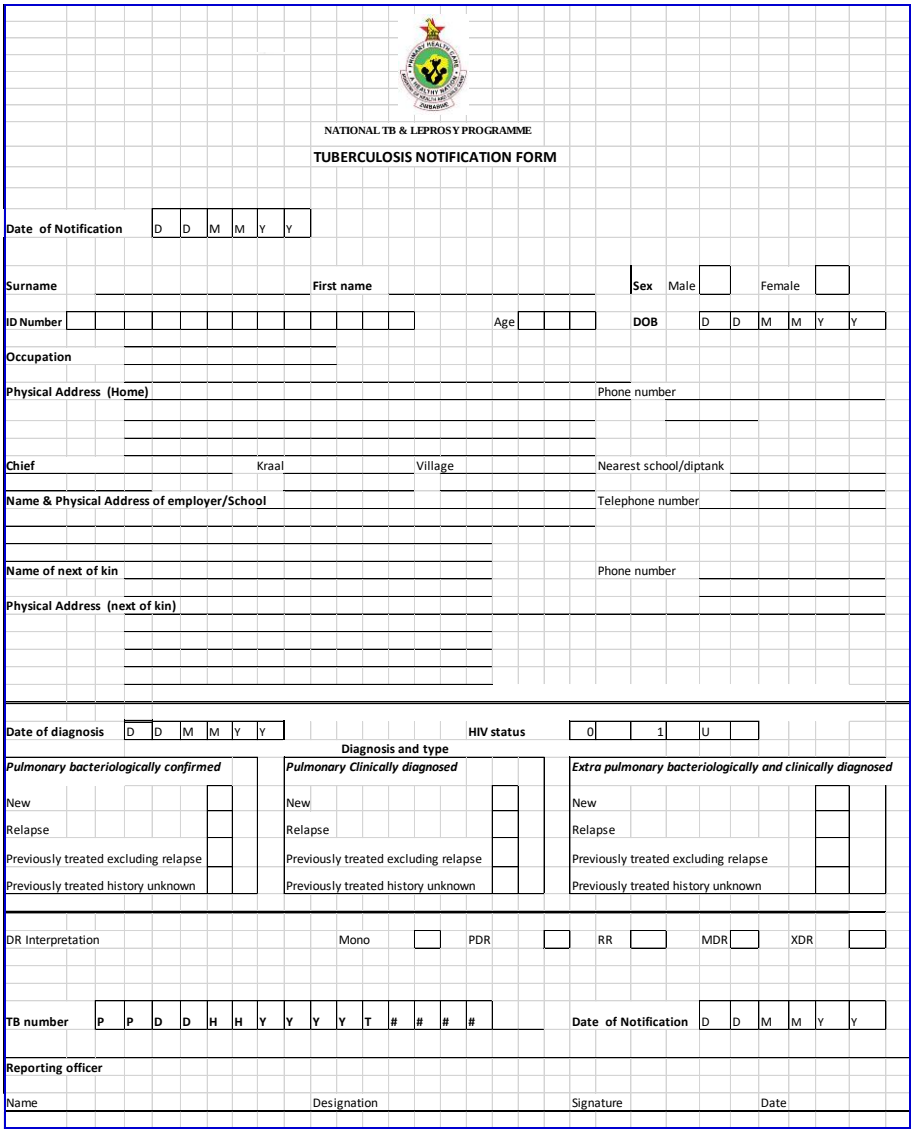
Annex 6: Tuberculosis Laboratory Register

The main function of the laboratory tuberculosis register is to record all specimens requiring laboratory examination for TB and their examination results. The laboratory personnel should maintain the Laboratory TB register. Purpose: To examine all specimens requiring Xpert MTB/Rif testing and microscopy.
Purpose: To enter results for patients at diagnosis of TB and follow up of treatment
Who maintains it? It is maintained by laboratory staff where there are Xpert MTB/Rif and Microscopy services
Where is it kept? It should be kept in the TB laboratory

1. Date of Entry	2. Lab Serial No.	3. Presumptive TB Number	4. TB Registration Number	5. First Name and Surname	6. National ID Number	7. Age	8. Date of Birth	9. Sex M/F	10. HIV Result (0,1,9)	11. Risk Group (use codes	12. Complete physical address + phone number	13. Name of referring Facility/Ward	14. Specimen					15. Xpert MTB/RIF Results			16. Smear Results					17. Name/Initials of Examiner	18. Date Result Sent to referring facility/ward & Person sending	19. Comments
																					Diagnosis		Treatment Follow-up Results					
													Type	Date collected	Date received	Date examined	Visual Appearan	MTB	Rif	Inavlid / No Result	1st	2nd	At end of Intensive	end of 5 mont	At end of Continuati			

Annex 7: Tuberculosis Notification Form

Purpose of the form: It is used to report confirmed susceptible and DR-TB cases.
Places where it is used: At all screening/entry points of the health facilities (OI Clinic, OPD and Wards)
Who fills the form? Nurses /Doctors



NATIONAL TB & LEPROSY PROGRAMME

TUBERCULOSIS NOTIFICATION FORM

Date of Notification D D M M Y Y

Surname _____ **First name** _____ **Sex** Male ☐ Female ☐

ID Number _____ Age ☐☐☐ **DOB** D D M M Y Y

Occupation _____

Physical Address (Home) _____ Phone number _____

Chief _____ Kraal _____ Village _____ Nearest school/diptank _____

Name & Physical Address of employer/School _____ Telephone number _____

Name of next of kin _____ Phone number _____

Physical Address (next of kin) _____

Date of diagnosis D D M M Y Y **HIV status** 0 ☐ 1 ☐ U ☐

Diagnosis and type

Pulmonary bacteriologically confirmed		*Pulmonary Clinically diagnosed*		*Extra pulmonary bacteriologically and clinically diagnosed*	
New	☐	New	☐	New	☐
Relapse	☐	Relapse	☐	Relapse	☐
Previously treated excluding relapse	☐	Previously treated excluding relapse	☐	Previously treated excluding relapse	☐
Previously treated history unknown	☐	Previously treated history unknown	☐	Previously treated history unknown	☐

DR Interpretation Mono ☐ PDR ☐ RR ☐ MDR ☐ XDR ☐

TB number P P D D H H Y Y Y Y T # # # # **Date of Notification** D D M M Y Y

Reporting officer

Name _____ Designation _____ Signature _____ Date _____

Annex 8: Health Facility Register

Purpose of the register: It is used to register confirmed TB cases and to monitor treatment

Places where it is kept: At the office of the TB Focal Person (TB Focal Nurse, TB Coordinator) at all health facilities

Who fills the form? Nurses / Doctors

Page 1

DEMOGRAPHIC DATA FOR PATIENT													DEMOGRAPHIC DATA FOR NEXT OF KIN		15.	16.
1. Date of registration	2. Date of diagnosis	3. Date of notification	4. TB Treatment initiation		5. TB Number	6. National ID Number	7. First Name	8. Sex (M/F)	9. Age	10. Physical residential/workplace address	11. Type of referral (use codes below)	12. TB Risk Group (use codes below - multiple responses allowed)	13. First Name	14. Physical residential/workplace address	Transferred from (facility/district/province/country name/ phone numbe & Date)	Pretreatment laboratory Results (use codes below)
			Yes/No	If Yes - Date			Surname			Phone number			Surname	Phone number		
							Name			Address			Name	Address	Facility District name Province Country	
							Surname			Phone number			Surname	Phone number	Phone & Date of transfer	

17. Diagnosis			18. Type of patient (use codes below)	19. Follow up laboratory results - Sputum smear examination with laboratory serial number			20. Other Tests Done During Treatment (culture/ rapid molecular tests/DST)					
							Test 1			Test 2		
17a. Pulmonary bacteriologically confirmed (use codes below)	17b. Pulmonary clinically diagnosed (use codes below)	17c. Extrapulmonary bacteriologically confirmed or clinically diagnosed (use codes below)		End of intensive phase	End of months	End of Continuation Phase	Type of test	Date	Result	Type of test	Date	Result
				Result	Result	Result						
				lab serial number	lab serial number	lab serial number						

21.TB-HIV CARE							22. No. of TB Contacts Identified			23. No. of TB Contacts Screened			25. Number of contacts found with TB			26. Transferred to/Date
HIV status	Date of HIV test	On CPT Y/N	CPT start date	On ART Y/N	ARTstart date & OI /ART No	ART initiated within 8 weeks (For patients starting treatment before ART initiation only) (Yes/No/N/A)	<5 years	5-14 Years	15years and over	<5 years	5-14 Years	15years and over	<5 years	5-14 Years	15years and over	
HIV result (0 or 1 or Uknown)																
																Name of health facility/district
																Date of transfer

Page 2

27. DOT ACTIVITIES																																			
	DATE																																		
MONTH	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	DOT (Yes/No)	Type of DOT evaluated at end of treatment (write in Full)	28. Treatment Outcome (Use Codes below) and date of death if outcome is death	29. Remarks
																																		Outcome	
																																		Date of death	

Annex 9: TB Patient Card

ZIMBABWE NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAMME
SENSITIVE TUBERCULOSIS TREATMENT CARD

Health Facility_____ **Patient TB Number**_____ **Date of Registration**_____/_____/_____

Name (surname, first name)	Sex (M/F)	Age
Phyical Address (in full)		
Name and Physical Address of next of kin or Treatment supporter		

Date of Diagnosis_____/_____/_____

Diagnosis [tick]
Pulmonary bacteriologically confirmed [ ]
Pulmonary clinically diagnosed [ ]
Extrapulmonary bacteriologically confirmed or clinically diagnosed [ ]

Type [tick]

New		Previously treated excluding relapse		Relapse		Previously treated history unknown	

Remember!
TB can be cured!
It is very important to complete the full course, even if you feel well!
Yeuka!!
TB inorapika!
Inwa mapiritsi sokurairwa kwaunenge waitwa kusvikira wapedza zvisinei kuti wava kunzwa zvirinani!!!
Nanzeleia lokhu!
Ufuba (TB) luyelapheka!!
Kuqakathekile ukuba uginye wonke amaphilisi owaphiwayo aze aphele laloba ususizwa ngcono!!.

Comments

	Laboratory results					
	Xpert			**Smesr**		
	Date	**Lab no.**	**Result**	**Date.**	**Lab no.**	**Result**
At notification						
At end of intensive phase						
At end of 5 months						
At end of continuation phase						

Pre-treatment weight .....kg

INTENSIVE PHASE Regimen – **FDC:**

		Adults	**Children**	SINGLE DOSES	
Date	**Weight in kg**	**Daily Dose in Tablets**	**Daily Dose in Tablets**	**Daily Dose in Tablets**	**Daily Dose in Tablets**

HIV RESULTS

0	1	u	
ART	Start Date		
	Regimen	1st Line	2nd Line

OI/ART number

ART medicines

NTENSIVE PHASE **Type of DOT* (Health facility based** ☐ **Trained community member** ☐

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

CONTINUATION PHASE **Type Type of DOT* (Health facility based** **Trained community member** ☐

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

Weight at start of continuation Phase .....kg

CONTINUATION PHASE (FDC)				SINGLE DOSES	
		Adults	**Children**	**Adults**	**Children**
Date	Weight in kg	Daily Dose in Tablets	Daily Dose in Tablets	Daily Dose in Tablets	Daily Dose in Tablets

Treatment Outcome

Date of discharge_____

- ☐ Cured
- ☐ Treatment completed
- ☐ Treatment failure
- ☐ Lost to Follow-up

Date stamp

_____

Name and designation

_____

Annex 10: Health Facility Reporting Form

MINISTRY OF HEALTH AND CHILD CARE

NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAMME

Health Facility Quarterly Report Form

Province _____

District_____

Name of health facility_____

Catchment Population: _____

Quarter: _____**Year**_____

Version: March 2017

SECTION A: CASE FINDING – TB screening, presumption, diagnosis and notification during the quarter

A (1) TB screening, presumption, diagnosis and HIV Screening (Source of data: T12, ART register, community level quarterly TB reporting form and Presumptive TB register)
(N.B. This table is for reporting cases not specimens) - Numbers

Category			Screening			Laboratory confirmation (numbers)										TB Clinical Diagnosis	HIV screening		
Clients	SEX	AGE	Total people screened for TB (Both symptomatic and X ray)	Clients who had a chest X-ray done	Presumptive TB clients identified	Xpert MTB Rif Testing		Direct Smear Microscopy Testing *(exclude cases reported under Xpert MTB Rif column)*		Culture examination		Presumptive TB clients Bacteriologically Confirmed				Presumptive TB clients clinically diagnosed with TB	HIV Testing for presumptive TB cases		
						Presumptive TB clients with specimen sent for Xpert MTB Rif	Presumptive TB clients with Xpert MTB Rif results	Presumptive TB clients with specimen sent for Smear Microscopy only	Presumptive TB clients with Smear Microscopy results only	Presumptive TB clients with specimen sent for culture	Presumptive TB clients with Culture results	Xpert	Microscopy	Culture	Total		Presumptive TB clients with HIV positive results	Presumptive TB clients with HIV negative results	Presumptive TB clients with unknown HIV status
Total *(including contacts, community and other)*	M	<5yrs																	
		5-14yrs																	
		15yrs+																	
	F	<5yrs																	
		5-14yrs																	
		15yrs+																	
Contacts Only *(part of total above)*	M	<5yrs																	
		5-14yrs																	
		15yrs+																	
	F	<5yrs																	
		5-14yrs																	
		15yrs+																	
Community Only *(part of total above)*	M	<5yrs																	
		5-14yrs																	
		15yrs+																	
	F	<5yrs																	
		5-14yrs																	
		15yrs+																	

A (2) Community Tuberculosis Care

Community Tuberculosis Care Indicators	Male		Female	
	0 -4 years	5 years and above	0 -4 years	5 years and above
Number of people in the **Community Health Worker's** catchment area screened for TB during the quarter under review.				
Number of presumptive TB clients referred to the clinic for TB investigation during the quarter under review (*among people screened for TB)*				
Number of presumptive TB clients referred to clinic diagnosed with TB during the quarter under review (*among presumptive client referred to health facility)*				

A (3) TB Notifications *(Source of data: TB Health Facility register)*

Age Group	TB patients tested using Xpert MTB/RIF				1. Pulmonary bacteriologically confirmed *(Smear, Xpert and culture)*										2. Pulmonary Clinically diagnosed										3. Extra pulmonary bacteriologically confirmed or clinically diagnosed										Grand Total (Add totals of column 1, 2 & 3)		4. HIV CARE										5. TYPE OF DOT			
	Total tested with Xpert/MTB RIF		With MTB detected		New		Relapse		Previously treated excluding relapse		Previously treated history unknown		Total		New		Relapse		Previously treated excluding relapse		Previously treated history unknown		Total		New		Relapse		Previously treated excluding relapse		Previously treated history unknown		Total				With recorded HIV results		HIV positive		Total on ART		HIV positive TB Patients initiated on TB treatment		On ART within 8 weeks		Health facility		Community	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
0 – 4																																																			
5-9																																																			
10–14																																																			
15-19																																																			
20-24																																																			
25-34																																																			
35-44																																																			
45-54																																																			
55-64																																																			
65+																																																			
Total																																																			

A (4) DST among Notified TB Cases *(Source of data Health Facility Register)*

Age Group	Total Notified Cases								Tested using Xpert MTB RIF / LPA							Patients with Full Phenotypic first line DST Only							
	New		Relapse		Previously treated excluding relapse		Previously treated history unknown		**New**		**Relapse**		**Previously treated excluding relapse**		**Previously treated history unknown**	New		Relapse		Previously treated excluding relapse		Previously treated history unknown	
	M	**F**	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
0 – 4																							
5-9																							
10– 14																							
15- 19																							
20- 24																							
25-34																							
35-44																							
45-54																							
55-64																							
65+																							
Total																							

A (5) Contact Investigations& IPT for children under 5 years of age *(Source of data: TB Health Facility register & IPT section of register)*

Number of index cases (Bacteriologically confirmed & all child TB cases under 5)	Contact screening and TB diagnosis							
	SEX	Age	Reported	Screened for TB	Diagnosed with TB	Started on TB Treatment	Eligible for IPT	Started on IPT
	M	0-4 years						
		5 years and above						
	F	0-4 years						
		5 years and above						

A (6) Key population screened and diagnosed with TB *(Source of Data: T12, OI/ART Patient Care Booklet, Presumptive and Health facility TB register)*

Indicator			
	Male	Female	Total
Number of health workers screened for TB			
Number of health workers diagnosed with TB			
Number of health workers started on TB treatment			
Number of miners and their household members screened for TB			
Number of miners and their household members diagnosed with TB			
Number of miners and their household members started on TB treatment			
Number of ex-miners and their household members screened for TB			
Number of ex-miners and their household members diagnosed with TB			
Number of ex-miners and their household members started on TB treatment			
Number of prison community members screened for TB			
Number of prison community members diagnosed with TB			
Number of prison community members started on TB treatment			
Number of Diabetic patients screened for TB			
Number of Diabetic patients diagnosed with TB			
Number of Diabetic patients started on TB treatment			

SECTION C: MEDICINE MANAGEMENT *(Source of data: Stock cards)*

C (1) MEDICINES NEEDS ACCORDING TO CASES REGISTERED DURING THE QUARTER *(Includes Transfer In)*

First-Line TB Medicines	Number of patients (A)	Factor (B)	Quarterly Needs (C=AxB)	Monthly Need (D=C/3)	Stock Status[1] in tablets (E)	Months of stock[2] (F= E/D)
RHZE tablets		168				
RH adult tablets		336				
RHZ paediatric tablets		112				
RH paediatric tablets		224				
Ethambutol 100mg tablets		112				

[1] *Count the quantities in both the store room and dispensing area*

[2] *NOTE: If MoS>6 – Overstocked, 3<Mos<6 – Adequately Stocked, MoS<3 – Understocked Place an order, MoS<1 – Place emergency order*

C (2): Stock Status of Second Line Anti-TB Medicines *(Source of data: Health Facility register- DR-TB section and Stock cards)*

How many patients do you have on DR-TB treatment? ☐

#	Medicine Name	Quantity (tablets/vial)
1.	Kanamycin 1g injection	
2.	Pyrazinamide 400mg tablets	
3.	Levofloxacin 500mg tablets	
4.	Ethionamide 250mg tablets	
5.	Ethambutol 400mg tablets	
6.	Isoniazid 300mg tablets	
7.	Clofazimine 100mg tablets	
8.	Cycloserine 250mg tablets	
9.	Moxifloxacin 400mg tablets	
10.	Para-Amino Salicylic Acid 4g sachets	
11.	Capreomycin 1g injection	

SECTION D: TREATMENT OUTCOMES

D (1): QUARTERLY REPORT ON TREATMENT OUTCOMES – for patients who were registered 12 months ago *(source data: TB Health facility register)*

All TB cases (sensitive TB)

TB patient type	SEX	Age Group	Cases registered	TB Treatment outcomes						Not evaluated	HIV CARE			TYPE OF DOT FOR ALL TB CASES	
				Cases					Total cases evaluated for outcomes		TB patients with HIV test results	TB patients with HIV positive results	TB patients on ART	Total Patients observed	Patients observed by trained community DOT observers *(including trained family members)*
				Cured	Treatment	Treatment failed	Died	Lost to follow							
All new and relapse cases (bacteriologically confirmed or clinically diagnosed, pulmonary or extra-pulmonary)	M	0 -14 years													
		15yrs+													
	F	0 -14 years													
		15yrs+													
Previously treated patients (excluding relapse Cases – retreatment after lost to follow up + retreatment after treatment failure	M	0 -14 years													
		15yrs+													
	F	0 -14 years													
		15yrs+													
All new and relapse HIV positive TB cases (bacteriologically confirmed or clinically diagnosed, pulmonary or extra pulmonary)	M	0 -14 years									[redacted]				
		15yrs+													
	F	0 -14 years													
		15yrs+													
		15yrs+													
	F	0 -14 years													
		15yrs+													

***D (2) IPT for under 5 years Outcomes* for patients who were registered 12 months ago (source of Data: TB Health Facility register – IPT section)**

Indicator	Number
Children under 5 years of age who were initiated on IPT	
Children under 5 years of age who were diagnosed of TB while on IPT	
Children under 5 years of age who completed IPT	
Children under 5 years of age who were lost to follow up	
Children under 5 years of age who died	

E: Data Analysis (In the table below record achievements, challenges and action points as informed by the analysis of data above)

Achievements	Challenges	
Action points to address challenges that were identified		
Action point	**Responsible person**	**Time line**

Report Compiled by:

1. **Name:_____Designation_____Signature_____Date_____**

Verified:

1. **Name:_____Designation_____Signature_____Date_____**

Date submitted to district_____

Annex 11: Medicine ADRs Reporting Form

MCAZ Medicines Control Authority of Zimbabwe

PVF 01

Spontaneous Adverse Drug Reaction (ADR) Report Form						
Identities of Reporter, Patient and Institute will remain confidential						
MCAZ Reference Number (MCAZ use only)						
Patient Details (to allow linkage with other reports)						
Clinic/hospital Name:			**Clinic/Hospital Number**			
Patient Initials:			**VCT/OI/TB Number**			
Date of Birth:			Weight (Kg)		Sex:	
Age:			Height (meters)			
Adverse Reaction						
Date of Onset:						
Duration:	Less than one hour	Hours	Days	Weeks	Months	
Description of ADR						
Serious: Yes ☐ No ☐	Reason for Seriousness	☐ Death		☐ Life-threatening		
		☐ Hospitalization/prolonged		☐ Disabling		
		☐ Congenital-anomaly		☐ Other medically important condition		
Relevant Medical History						
Relevant Past Drug Therapy						
Outcome of ADR	Recovered	Not yet recovered	Fatal	Unknown		
Current Medication						
Generic Name	Brand Name	Batch Number	Dose	Indication	Date Started	Date Stopped
Concomitant (Other) drugs taken, including herbal medicines & Dates/period taken:	Name of drug:				Date started	Date stopped
Suspected drug(s), if known:						
Laboratory tests results:						
Reported by						
Forename(s) & Surname:						
Designation:						
Address:						
Signature:			Date:			
Send to: The Director-General, Medicines Control Authority of Zimbabwe, 106 Baines Avenue, P O Box 10559, Harare **Tel**: +263-4-708255 or 792165, **E-mail**: mcaz@mcaz.co.zw, **website**: www. mcaz.co.zw						

NB. This form may be completed for any ADR related to medicines or medical devices
***Please attach any other additional information, including an anonymized picture of the ADR (with patient's consent)**