Democratic Republic of Timor-Leste

Ministry of Health

Comprehensive TB Guidelines for National Tuberculosis Control Program

V Edition
2020

Ministério da Saúde

END TB

World Health Organization
Timor-Leste

NTP Manual Timor-Leste

5th edition 2020

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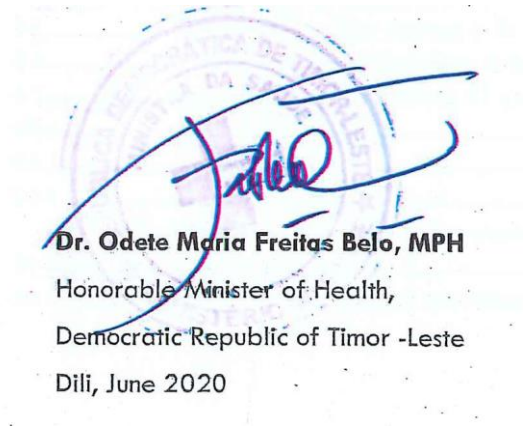
FOREWORD

Tuberculosis is one of the major public health problems in Timor-Leste. In order to address this problem, the National Tuberculosis Control Program (NTP) was established in 2000 through an NGO, Caritas Dili, and was then handed over to the Ministry of Health under the Communicable Disease Control (CDC) department in early 2006.

The NTP is now fully integrated within the Ministry of Health and works in collaboration with international organizations, national and international NGOs. The NTP receives technical support from the World Health Organization (WHO). The program has been successful in adapting to the rapidly changing circumstances whilst following internationally recommended best practices and standards in tuberculosis control. The country is now moving forward from control to end TB by 2030, and therefore it is important for everyone to support this collective vision of ending TB by proper implementation of the national TB guidelines and strategies.

The fifth edition of the NTP Manual (Revised TB/ DR-TB Guidelines) contains guidelines and updates in line with the WHO's latest recommendations for diagnosis and treatment of Tuberculosis, Latent Tuberculosis Infection (LTBI) Management and Drug Resistant Tuberculosis (DR-TB) patients in Timor-Leste.

I endorse this latest edition of the NTP Manual as an official document of the Timor-Leste Government and recommend it for use by ALL health care service providers, partners and stakeholders in Timor-Leste.



Dr. Odete Maria Freitas Belo, MPH
Honorable Minister of Health,
Democratic Republic of Timor -Leste
Dili, June 2020

MESSAGE FROM THE WHO REPRESENTATIVE IN TIMOR-LESTE

Timor-Leste has the 2nd highest TB incidence rate in the WHO South-East Asia Region after North Korea. According to data released by the WHO in 2018, total TB incidence rate in Timor-Leste is 498 per 100,000 population. As a comparison, the incidence rate in Indonesia is 316 per 100,000, in India 199 per 100,000, and in China 61 per 100,000 population.

One of the biggest challenges in eliminating TB is the increasing number of cases of Drug-Resistant TB (DR TB). It is estimated that 3.1 % of all TB cases in Timor-Leste are drug-resistant (DR) or Rifampicin-resistant TB (RR-TB). DR TB is significantly more difficult to treat compared to Drug-Sensitive TB with a lower success rate and a higher chance of adverse effects during the course of treatment. Because of this, treatment of DR TB needs to be given by highly trained medical personnel, competent in management of the DR TB regimen.

The WHO updated its guidelines for the management of Drug-Susceptible TB (DS-TB), Drug-Resistant TB (DR-TB), Patient Care, Latent TB Infection (LTBI) and Infection Prevention in 2018-19. These updated guidelines are important in the context of the End TB Strategy, which recommends treatment and patient support for all people with TB. Timor-Leste has a high TB burden, and this requires accelerated efforts for ending TB. The Revised TB and Drug Resistant (DR)-TB guidelines for Timor-Leste aligned with the recent updates to the WHO guidelines comes at an opportune time when the country is gearing up for implementing the End TB Strategy and is committed to ending TB by 2030.

The WHO is committed to support the NTP and the MoH in its efforts to end TB in the country and looks forward to the successful implementation of and adherence to the revised TB/ DR-TB guidelines (the fifth edition of the NTP Manual) by all TB care providers.

Dr. Rajesh Pandav
World Health Organization Representative in Timor-Leste
Dili, June 2020

PREFACE

The WHO updated its guidance for the management of Drug-Susceptible TB (DS-TB), Drug-Resistant TB (DR-TB), Patient Care, Latent TB Infection (LTBI) and Infection Prevention in 2018-19. These updated guidelines are important in the context of the End TB Strategy, which recommends treatment and patient support for all people with TB. Timor-Leste has a high TB burden, and this requires accelerated efforts for ending TB. Revision of the TB and Drug Resistant (DR)-TB guidelines for Timor-Leste aligned with recent updates to the WHO guidelines comes at an opportune time when the country is gearing up for implementing the End TB Strategy and is committed to ending TB by 2030. A consolidated guideline that will include all the recommendations on management of both TB and DR-TB, is currently the need of the hour for guiding the NTP, Timor-Leste, for accelerating its progress towards ending TB.

The policy recommendations in each of these guidelines have been developed by WHO-convened Guideline Development Groups (GDGs), using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to summarise the evidence, and formulate policy recommendations and accompanying remarks. The updated guidelines by WHO aim to use the best available new evidence on the management of Drug-Susceptible TB, Drug-Resistant TB, Patient Care, Infection Prevention and Latent TB Infection.

The key audiences for these guidelines are policy makers in the MoH and the managers of the NTP who formulate country specific TB and DR-TB guidelines. In addition, health professionals- including doctors, nurses, and educators working both in Govt. and Non-Govt. Organizations (NGOs) involved in treating TB patients and organizing treatment services – are expected to use this updated and consolidated guideline.

ACKNOWLEDGEMENTS

The Ministry of Health, Democratic Republic of Timor-Leste gratefully acknowledges the contributions from the WHO Country Office for Timor-Leste, especially Dr Rajesh Pandav, WHO Representative, Dr Debashish Kundu, Medical Officer (TB), and Dr Vineet Bhatia, Medical Officer (DR-TB), and the WHO SEARO and India Country Office for their valuable support and contributions in revising the 2020 NTP Guidelines for TB and Drug-Resistant TB (DR-TB) and Latent TB Infection (LTBI) Management.

Special thanks to the leadership at the Ministry of Health, Mr Constantino Lopez, the NTP Manager and his team in Dili and partners of the NTP who actively participated in five-day intensive in-country TB Guideline Revision workshop 19 April – 3 May 2019, deliberated, and provided suggestions for adapting context specific recommendations towards a consolidated TB and DR-TB guideline for Timor-Leste. The National Laboratory and National Hospital also provided valuable inputs to the TB Guideline Revision Workshop. The workshop was supported by the WHO and facilitated by a WHO Consultant - Dr. Holger Sawert, who developed the first draft of the revised 2019 TB Guidelines.

These revised guidelines were extensively reviewed by the regional green light committee members (r-GLC), specifically, Dr Fraser Wares, Dr Sanjay Sarin, Paran Sarimita Winarni, and then by the 2019 TB Mid-Term Review Expert Members – Dr Sarabjit Chadha on DR-TB, Dr Arax Hovhannesyan on revised Recording & Reporting (R&R) formats, Ms Blessina Kumar on Health Education, Advocacy, Communication and Social Mobilization (ACSM), and Dr Rina Triasih on Childhood TB. Dr Erlina Burhan, an expert on DR-TB management, also reviewed the DR-TB component, and Dr Siva Kumar, SNRL-Chennai, reviewed the diagnosis section of the guidelines. The final guidelines were reviewed by the WHO SEARO TB Unit and the NTP Team lead by Mr Constantino Lopez. The central NTP team provided background information on the NTP and the health system context in Timor-Leste. Dr Vineet Bhatia and Dr Debashish Kundu reviewed and compiled the final guidelines.

The Ministry of Health gratefully acknowledges the financial support provided from The Global Fund for TB, AIDS and Malaria (GFATM) and the continued technical support from the World Health Organization (WHO).

ABBREVIATIONS

AFB	Acid-Fast Bacillus
AIDS	Acquired Immunodeficiency Syndrome
ART	Anti-Retroviral Therapy
Am	Amikacine
ADR	Adverse Drug Reaction
BCG	Bacille Calmette-Guerin
Bdq	Bedaquiline
BSP	Basic Service Package
CHC	Community Health Centre
CHV	Community Health Volunteer
CPT	Cotrimoxazole Preventive Therapy
Cfz	Clofazimine
CBO	Community Based Organization
CMU-TB	Central Management Unit-TB
CP	Continuation Phase
Cm	Capreomycin
Cs	Cycloserine
DDC	Designated Diagnostic Centre
DMC	Designated Microscopy Centre
DOT	Directly Observed Treatment
DOTS	Directly Observed Treatment with Short-course chemotherapy
DR-TB	Drug Resistant TB
DRS	Drug Resistance Surveillance
DST	Drug Sensitivity Testing
DTC	District Tuberculosis Coordinator
DHIS	District Health Information System
Dlm	Delamanid
E	Ethambutol

Eto	Ethionamide
ECG	Electrocardiograph
EPTB	Extra-pulmonary TB
Eto	Etionamide
FQ	Fluoroquinolone
FDC	Fixed Drug Combination
GLC	Green Light Committee
H	Isoniazid hydrochloride
HAART	Highly Active Anti-Retroviral Therapy
H-DHO	Head of District Health Office
HIV	Human Immunodeficiency Virus
HNGV	Hospital Nacional Guido Valadares
IP	Intensive Phase
INS	Instituto Nacional da Saúde
JMM	Joint Monitoring Mission
MTR	Mid-Term Review
MDR-TB	Multidrug-Resistant Tuberculosis
NGO	Non-Governmental Organization
NTBS	National TB Strategy
NTP	National Tuberculosis Program
NHL	National Health Laboratory
Ofx	Ofloxacin
OPD	Outpatient Department
PAS	p-aminosalicylic acid
PHC	Primary Health Centre
PLWH	People living with HIV/AIDS
PNB	p-nitrobenzoic acid
PMDT	Programmatic Management of Drug-Resistant TB
R	Rifampicin
S	Streptomycin
SAMES	Serviço Autonomo Medicamento e Equipamento Saúde

SISCa	Integrated Community Health Services
SNRL	Supra-National Reference Laboratory
TB	Tuberculosis
TB-HW	Tuberculosis Health Worker
VCTC	Voluntary Counselling and Testing Centre
TB	Tuberculosis
UNFPA	United Nations Population Fund
UNHLM	United Nations High Level Meeting
WHO	World Health Organization
Z	Pyrazinamide
ZN	Ziehl-Neelsen

1 INTRODUCTION

1.1 THE BURDEN OF TB IN TIMOR-LESTE

The Democratic Republic of Timor-Leste has the highest TB incidence rate in the South East Asian Region - 498 per 100,000, which is the seventh highest in the world. In Timor-Leste TB is the eighth most common cause of death.

The salient observations are as follows:

- In 2018, 487 (12.5%) of the 3906 notified TB patients were tested for RR-TB and only 12 lab confirmed RR-TB patients were initiated on standard MDR-TB treatment of 20-months duration, (a 3-fold increase in RR-TB detection compared with 2017). This amounts to treatment coverage of only 17% of 72 estimated MDR/RR-TB among notified TB patients (3906) and 5% of 240 estimated incident MDR-TB patients as compared to 62% treatment coverage of 6300 incident drug sensitive TB patients estimated in TLS. The treatment success in the 2016 annual cohort of 6 MDR-TB patients has been reported at 83%. 80% of TB patients know their HIV Status with around 1% TB-HIV co-infection, 37/ 77 (48%) TB-HIV Co-infection Detected. Of the 387 PLHIV currently alive on ART, exact status on TB screening and testing is unknown. % of PLHIV newly enrolled in HIV care who received IPT is not known.
- In 2018, the mortality rate for TB was 94 deaths per 100,000 people (1200 per annum) in TL with an increasing mortality trend (Figure 1), despite TB services being available for nearly two decades.
- A survey of catastrophic costs due to TB (2016) highlights that 83% of TB patients are reported to be facing catastrophic costs due to the disease. This is the highest rate in the world.

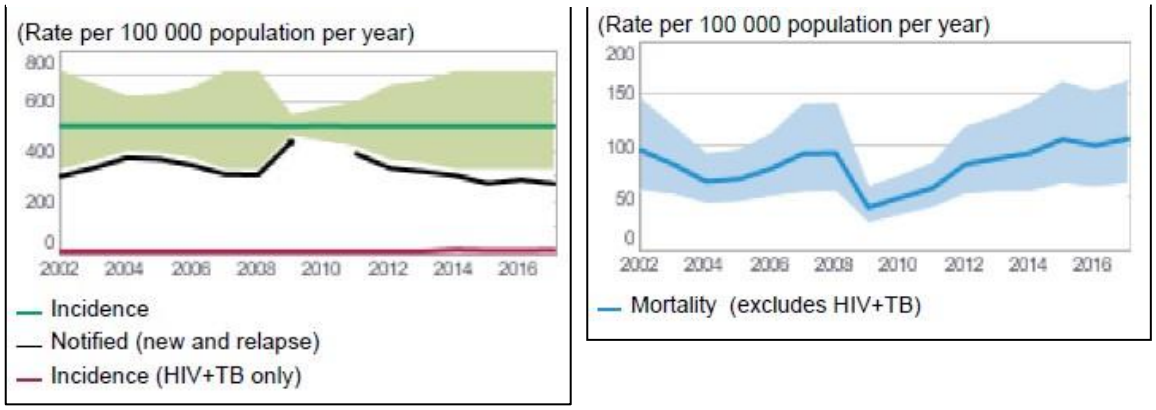


Figure 1: Trends of TB incidence, notification and mortality rates in Timor-Leste

MDR-TB is estimated to be 3.1% in new and 15% in previously treated patients, while the proportion with XDR-TB is unknown. This extrapolates to an estimated total of 240 RR/MDR-TB cases (19/100,000) in TL annually based on the WHO's Global TB Report for 2019. A national drug resistance survey was initiated from 21 January 2019 to measure the burden of M/XDRTB. The DRS enrolment was completed in early September 2019.

1.2 RISK FACTORS FOR TB IN TIMOR-LESTE

Key factors for continuing TB transmission from a social determinant lens include issues such as:

Malnutrition: Timor-Leste has one of the highest rates of malnutrition in the world, with children having high levels of stunting (50.2%), wasting (11.0%) and underweight (37.7%). The prevalence of low birth weight is 10%. One study noted that among pulmonary TB patients, the prevalence of malnutrition was very high and should be addressed in the fight against TB.[1]

Malnutrition increases the relative risk for active TB disease by 3 times (Lönnroth et al, Lancet 2010). Among mothers, an estimated 37% of pregnant women are anaemic (DHS, 2016); 25% of non-pregnant women are thin (UNICEF Nutrition Survey, 2013); while 38% of children aged 0-59 months are underweight, and 13% of children aged 6-11 months have acute malnutrition (wasting).

TB burden			$PAF = \frac{P \times (RR-1)}{P \times (RR-1)+1}$
Factors	**Relative risk for active TB disease**	**Weighted prevalence in % (adults 22 HBCs)**	**Population attributable fraction in % (adults)**
HIV infection	20.6/26.7*	0.8	16
Malnutrition	3.2 **	16.7	27
Diabetes	3.1	5.4	10
Alcohol use (> 40 g/d))	2.9	8.1	13
Active smoking	2.0	26	21
Indoor air pollution	1.4	71.2	22

Note: PAF: Population attributable fraction; RR: Relative risk

Source: *Lönnroth K, Castro K, Chakaya JM, Chauhan LS, Floyd K, Glaziou P, Raviglione M. Tuberculosis control 2010 – 2050: cure, care and social change. Lancet 2010 DOI:10.1016/s0140-6736(10)60483-7.*

Tobacco use: It is now known that tobacco smoking increases the risk of TB disease by 2.5 times.[2,3,4] Youth tobacco use in Timor–Leste is 69.9%, while smoking in males is substantial at 71.1%. The Global School

[1] Pakasi, T. A., et al. "Malnutrition and socio-demographic factors associated with pulmonary tuberculosis in Timor and Rote Islands, Indonesia." The International Journal of Tuberculosis and Lung Disease 13.6 (2009): 755-759. Available at: http://s3.amazonaws.com/academia.edu.documents/41617772/Malnutrition_and_socio-demographic_facto20160127-32283-8c2749.pdf?AWSAccessKeyId=AKIAIWOWYYGZ2Y53UL3A&Expires=1490149222&Signature=Xk28g0Nw465JXdjaGjCEfQHUJfI%3D&response-content-disposition=inline%3B%20filename%3DMalnutrition_and_socio-demographic_facto.pdf. Accessed on 23.03.2017

[2] Pai, Madhukar, et al. "Lethal interaction: the colliding epidemics of tobacco and tuberculosis." Expert review of anti-infective therapy 5.3 (2007): 385-391. Available at: https://www.researchgate.net/profile/DJ_Christopher2/publication/6288144_Lethal_interaction_The_colliding_epidemics_of_tobacco_and_tuberculosis/links/02e7e531c9092acc42000000.pdf. Accessed on 23.03.2017

Health Survey (GSHS) for Timor-Leste 2015, found that 27.6% of students (39.6% of boys and 15.6% of girls) have the highest current tobacco use rates in the world, with very high rates of second-hand smoke exposure (80%), including from parents at home;

Alcohol use: 16% of adolescents are alcohol users, the highest rate in the world (GSHS for Timor-Leste, 2015). Alcohol has a strong association with TB and increases its risk by 2.9 times.

All of these high-risk factors: malnutrition, alcohol and tobacco usage, can lead to the progression of latent TB infection in an individual to an active disease.

Diabetes: Diabetes has a strong association with TB and increases its risk by 3.1 times. It is essential to screen all TB patients for diabetes and manage them appropriately. Diabetes patients must be screened for TB regularly. It is also essential to provide treatment (drugs and life-style modification) and follow up facilities for diabetes patients.

Poverty: Timor-Leste is classified as an **upper lower-middle income country** with GDP wealth largely generated from offshore oil and gas reserves. However, 42% of people live in poverty with less than one dollar per person per day. Poverty rates are higher in western areas of Timor-Leste than in eastern areas and there is more variation within districts than between districts (World Bank Report).

Geographical access: 70% of the population in Timor-Leste is considered to be rural, mainly living in dispersed villages isolated by mountainous terrain and poor road conditions.

Migration:[5] Inter-district migration has been significant since 2010, with nearly 120,969 persons (14% of the population) having migrated from the municipalities of their birth for education, occupation or to follow other family members. Over one–third of the population of Dili are in–migrants (85,194 people or 36.4%) making it the municipality with the highest net intake of migrants. Timor-Leste and Indonesia share a 228-kilometre, porous land border. Multiple entry points, unpatrolled roads in hard to reach mountainous locations and limited capacity of law enforcement compromises effective border control.[6]

1.3 HEALTH SYSTEMS AND COMMUNITY SYSTEMS CONTEXT

1.3.1 Structure of the health care system

Patient services are delivered through a network of health care facilities. There are 320 health posts, one for each village with primary care services provided by a team of 3 – 4 health personnel including a doctor. Each of the 71 Community Health Centres (CHC) provides primary plus service and has 2 – 10 health posts in its catchment area. For secondary health services, there are 5 referral hospitals one located in the municipalities of Baucau, Bobonaro, Covalima, Oecusse and Ainaro. Dili has the National Hospital

[3] Zellweger, J. P. "Tobacco and tuberculosis." Monaldi Archives for Chest Disease 69.2 (2016). Available at: https://scholar.google.com/scholar?q=Zellweger%2C+J.+P.+%22Tobacco+and+tuberculosis&btnG=&hl=en&as_sdt=0%2C5. Accessed on 23.03.2017

[4] Slama, Karen, et al. "Tobacco and tuberculosis: a qualitative systematic review and meta-analysis [Review Article]." The International Journal of Tuberculosis and Lung Disease 11.10 (2007): 1049-1061. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17945060. Accessed on 23.03.2017.

[5] NSD and UNFPA (2012). Timor-Leste Population and Housing Census 2010. Analytical Report on Migration and Urbanization. Volume 7. Migration and Urbanization Monograph. Available at: http://www.statistics.gov.tl/wp-content/uploads/2013/12/Migration_Monograph.pdf. Accessed on: 23.03.2017

[6] IOM Timor-Leste discussions with local Chefes de Suco confirm irregular anecdotally indicate illegal border crossing crossings are rampant – including "official" illegal border crossings in which USD$3.00 is commonly received by security forces to permit entry without any documentation. Cross referenced from IOM: *Making a case: Pilot Project proposal on informing program and policy development on Human Trafficking in Timor – Leste – Indonesian border area. Unpublished.* Reference document attached as pdf.

known as Hospital Nacional Guido Valadares (HNGV), which is the largest referral and tertiary care facility in Timor-Leste.

Human Resources: Health professional workforce in each Municipality								
S.No	Municipality	Human Resource						Total
		Medical	Nurse	Midwife	Lab technician	Pharmacists	Nutritionist	
1	Aileu	44	31	24	10	12	1	**122**
2	Ainaro	27	36	25	10	12	6	**116**
3	Baucau	81	72	60	14	15	2	**244**
4	Bobonaro	43	56	31	11	8	2	**151**
5	Covalima	22	71	26	8	7	7	**141**
6	Dili	106	87	97	21	28	11	**339**
7	Ermera	62	54	34	12	18	8	**188**
8	Lautem	52	43	25	12	17	4	**153**
9	Liquiça	50	41	29	6	12	1	**139**
10	Manatuto	44	51	39	13	8	9	**164**
11	Manufahi	32	35	28	10	9	4	**118**
12	Viqueque	62	106	42	9	18	2	**239**
13	Região Oecusse	32	25	23	16	18	12	**126**
Total		**657**	**708**	**483**	**152**	**182**	**69**	**2251**

The administration and management of health systems is centrally managed by the MoH in Dili, the capital of Timor-Leste. The MoH is responsible for developing the policy, technical guidelines, and administration of complete health systems. Health services are based on delivery of a 'package of basic services' that includes maternal, neonatal and child health, immunization programs, TB, HIV and Malaria services.

In 2018 the doctor to population ratio was 8.9 per 10,000 population (Ref: HR Data Jan-Sep 2018), which is higher than the median for SEAR of 5.9 per 10,000 population. Timor-Leste also has 54 private health clinics that report to the Government on essential indicators. Anti TB medicines are not available in the private market. As a result, all TB cases are referred to the NTP or partner NGOs for treatment.

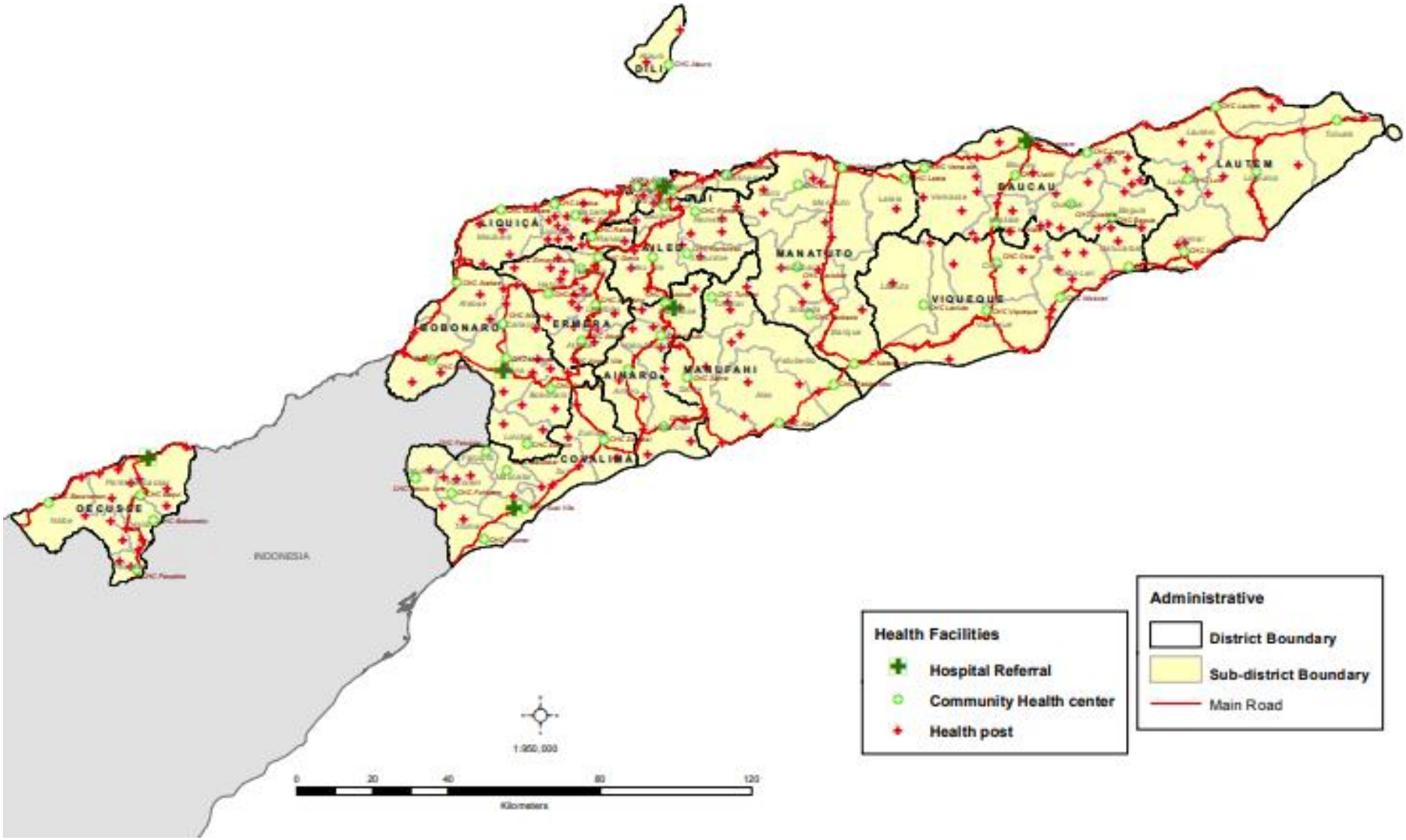
Both TB diagnostic and treatment services are fully integrated into the general MoH infrastructure using common health facilities such as health posts and health centres as well as general health staff such as health workers, nurses and doctors at implementing facilities. Only managerial staff are program specific, which is common practice for all health programs and is seen as an indispensable requirement for the effective functioning of the NTP.

The government provided health system is also complemented by non-government health providers and faith-based health service providers (mostly affiliated to the Catholic church).

Relationships between the government and non-government sectors are good. TB services are delivered, and reporting occurs, based on agreed government protocols and systems. Clinical referral systems exist, and referrals are made between services based in Dili and between Dili and the municipalities. For HIV services there are also connections made to community-based organizations. For example, when a person living with HIV begins treatment, service providers will contact social networks for people living with HIV

who will then actively promote their services and provide follow-up based in the community as needed, and similarly for TB/HIV patients.

Health Facilities of the Republic Democratic of Timor-Leste



1.3.2 **Common health system gaps**

There are major institutional challenges with translating policy, leadership and partnerships into operational systems and practices for Municipal Health Systems and Health Facilities (Referral Hospitals, Community Health Centres and Health Posts). These challenges are related to constraints in scaling up of management systems including systems for planning, budgeting, financial management, transport, quality controls and M & E.

Concerns about the quality of health care services and demand for these services will require more in-depth health systems and social research to uncover the reasons for limited utilization of the formal health care system. Despite positive trends nationally in utilization of facilities for maternal health services, there is a wide variance in utilization by location. The rate for delivery supported by skilled birth attendant ranges from 79% in Dili to less than 20% in some rural and remote municipalities. The prevalence of low birth weight is 10%. At 54.6 per 1000 live births, under-five child mortality remains high - 76% of which the cause is classified as unknown/other. The maternal mortality rate is also high at 557 per 100,000 live births. Malnutrition in women is high with 24.8% of women having a BMI less than 18.5.[7] Inadequate caring practices for women and children, inadequate use of preventive and nutrition services, high burden of childhood illnesses, inadequate dietary intake and food deficits account for these high malnutrition rates.[8] Hunger is a known driver for population migration and its associated effects.[9] One study noted that among pulmonary TB patients, prevalence of malnutrition was very high and should be addressed in the fight against TB.[10] Youth tobacco use in Timor–Leste is 69.9%, while smoking in males is substantial at 71.1%. Seven in ten students are exposed to second-hand smoke in public places in Timor-Leste which is one of the highest rates of exposure in the world. Exposure to second-hand smoke in public places has remained consistently high in 2006 (69.8%), 2009 (61.3%) and 2013 (69.9%) and equally impacts boys and girls.[11] In terms of hospital sector development, a principle MoH strategy will be to develop human resource skills, particularly in such areas as public health, health management and specialist medical and nursing skills. Structures and skills need to be developed for specialist areas including clinical care, nursing services, non-medical support, and finance and human resource management. There are significant variations in service access and coverage, indicating that greater emphasis is required on more equitable human resources distribution and capacity building. Service access is also an issue due to varying community acceptance of the relatively new system of health care. The community easily accepts and is more used to traditional care providers, which in turn gives rise to issues relating to health seeking behaviours.

7 Ministry of Health Timor – Leste. National Nutrition Survey 2013.

8 Democratic Republic of Timor-Leste and UNICEF. Situational Analysis of Children in Timor-Leste 2014.

9 Global Hunger Index, IFPRI, 2016. Available at http://ghi.ifpri.org/countries/TLS/. Accessed on 12 Dec 2016.

10 Pakasi, T. A., et al. "Malnutrition and socio-demographic factors associated with pulmonary tuberculosis in Timor and Rote Islands, Indonesia." The International Journal of Tuberculosis and Lung Disease 13.6 (2009): 755-759.

11 STEPs 2014/WHO Report on the Global Tobacco Epidemic, 2015

2 THE NATIONAL STRATEGIC PLAN (NSP)

2.1 ALIGNMENT WITH WHO'S GLOBAL STRATEGY FOR TUBERCULOSIS PREVENTION, CARE AND CONTROL AFTER 2015

NTP policies and strategies to date have been informed by international standards formulated by the World Health Organization, such as the directly observed treatment, short course (DOTS) strategy launched in 1993, and the Stop TB Strategy that underpinned the Global Plan to Stop TB 2006–2015. New multi-sectoral strategic approaches and new international targets for the post-2015 period have been approved by the Sixty-seventh World Health Assembly in May 2014. In developing the NTP's National Strategic Plan 2015-2020, successful efforts have ensured that the NTP's strategy takes full account of the WHO's post-2015 strategy. However, it should be noted that the targets of the post-2015 strategy involve long-term goals for incidence rate and mortality to be achieved by 2025 and 2035. Specifically, the reduction of TB incidence rates requires a long time-frame due to the prolonged presence of previously acquired infections in a population, which will not be affected immediately by any improvement to TB control activities. In defining a short-term goal for the period until 2024 covered by the NSP, the use of TB prevalence was deemed more appropriate as this epidemiological marker is more sensitive to changes in case-finding activities and treatment effectiveness. A summary of the WHO's post-2015 strategy is shown in the figure below.

END TB

Vision:

A country free of TB

Zero TB deaths,

Zero TB disease, and Zero TB suffering

Goal:

End TB epidemic in country

	MILESTONES		TARGETS	
	2020	2025	SDG* 2030	END TB 2035
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20%	50%	80%	90%
TB-affected families facing catastrophic costs due to TB (%)	0%	0%	0%	0%

Baseline – 83% (2016)

Translating the targets for Timor-Leste into specific numbers as follows:

Indicator	Baseline	Milestone	Targets	
			SDG	END TB
	2015	2025	2030	2035
Reduction in no. of TB deaths	1400	350	140	70
Reduction in TB incidence rate	498	249	100	50
TB affected families facing catastrophic costs due to TB (%)	83% (in 2016)	0%	0%	0%

2.2 DEFINITION OF NSP GOALS AND OBJECTIVES FOR 2020 - 2024

The objectives for the NSP 2020 - 2024 have been developed to cover the three pillars of the post-2015 strategy, and to specifically address the deficiencies identified in the gap analysis of this NSP. This is in alignment with the End TB strategy and UNHLM targets.

Vision: TB-free Timor-Leste with zero deaths, disease and catastrophic cost due to TB

2.3 GOAL OF NSP 2020-2024

To achieve a rapid decline in incidence, mortality and morbidity due to TB while moving along the path towards ending TB by achieving a reduction in the incidence of TB (all forms) by 50% by 2025 and 90% by 2035 (from the 2015 baseline figure)

The National Strategic Plan intends to achieve the following ***core impact, outcome and output indicators and targets*** as outlined in the Results Framework

Results Framework (Impact, Outcome and output indicators and targets)							
Indicator		Baseline (2018)	Target (2024)	Frequency	Data source	Layers of analysis	Level of indicator
IMPACT INDICATORS:							
1	To reduce estimated TB Incidence rate (per 100,000 population)	498 (322-711)	325	Annually	Global TB report	National	Impact
2	To reduce estimated mortality due to TB (per 100,000 population)	94 (56-142)	38	Annually	Global TB report	National	Impact
3	To ensure no family should suffer catastrophic cost due to TB	83% *(in 2016)*	0%	End of plan	Follow-up survey	National	Impact
OUTCOME AND OUTPUT INDICATORS:							
1. INTEGRATED PATIENT-CENTRED CARE AND PREVENTION							
1.1.	Active case finding at high load health facilities						
1.1.1.	Notification rate of new and relapse TB cases per 100,000 population	283	292	Annually	Routine TB notification quarterly reports	National	Outcome
1.1.2.	Coverage of population at risk with systematic screening for TB (Diabetes, PLHIV, malnourished children)	N/A	85%	Bi-annually	Survey among risk population	National Municipality	Output
1.1.3.	Proportion of presumptive TB cases among adult OPD visitor	1.6%	4.0%	Quarterly	Routine facility report& Routine TB notification quarterly reports	National Municipality	Output
1.2.Active case finding among vulnerable population – for TB, for LTBI							
1.2.1.	Contact investigation coverage	N/A	100%	Quarterly	Routine quarterly report (to be introduced)	National Municipality	Output
1.2.2.	LTBI treatment coverage among the household contacts of bacteriologically confirmed TB cases under 5 years of age	100%	100%	Quarterly	Routine quarterly report (to be introduced)	National Municipality	Output
1.3. Implementation of revised diagnostic algorithm							
1.3.1.	Percentage of notified new and relapse TB patients who were successfully treated	88.5%	>90%	Quarterly	Routine treatment outcome reporting	National Municipality	Outcome
1.3.2.	Percentage of newly notified TB patients tested using WHO-recommended rapid tests	15.0%	>90%	Annually	Routine TB notification quarterly reports	National	Output
2. BOLD POLICIES AND SUPPORTIVE SYSTEMS							
2.1.	DST coverage for TB patients	22.0%	>90%	Annually	Routine reporting	National	Output
2.2.	Percentage of RR- TB patients who were successfully treated	50.0%	>85%	Annually	Routine reporting	National	Outcome
2.3.	RR-TB treatment coverage	35.0%	100.0%	Annually	Routine reporting	National	Output
2.4.	Documentation of HIV status among TB patients	83.0%	>90%	Quarterly	Routine reporting	National Municipality	Output
3. INTENSIFIED RESEARCH AND INNOVATION							
3.1. Ensure adequate support for operational research to foster innovation							
	Number of operational researches conducted	N/A	>5	Annually	NTP annual report	National	Outcome

2.4 OBJECTIVES OF NSP 2020-2024

PILLAR 1: INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION

Objective 1:

Detect at least 85% of TB cases (all forms) by 2021 and at least 90% of all cases by 2022

Indicator: Notification rate of new and relapse TB cases per 100,000 population.

Numerator: Number of notified new and relapse TB cases available from the NTP's routine recording and reporting system. *Denominator:* Estimates of the underlying case incidence rate published annually in the WHO's Global TB Report.

Objective 2:

Ensure successful treatment for 90% of enrolled patients (all forms) by 2021, and more than 90% thereafter and; improve management of MDR-TB cases through country-wide implementation of the shorter MDR-TB treatment regimen

Indicator: Treatment success rate

The treatment success rate is available from the NTP's routine recording and reporting system. The rate has been regularly exceeding 85% during previous years, thus meeting WHO target levels. The objective of the NTP will be to make every effort to further improve treatment success rates to at least 90%.

PILLAR 2: BOLD POLICIES AND SUPPORTIVE SYSTEMS

Objective 3:

Provide MDR diagnostic services for 75% of the estimated persons with presumptive MDR TB by 2021 and 100% by 2022; successfully treat at least 85% of diagnosed MDR patients

Indicators: The NTP recording & reporting system will capture information on presumptive MDR-TB and testing for MDR-TB in the laboratory, and it will therefore be possible to define the proportion of cases with risk factors that received DST for at least Rifampicin. The treatment success rate will be available from the NTP's routine recording and reporting system for MDR-TB cases.

Objective 4:

Ensure timely and accurate recording and reporting from all (100%) of reporting centres by 2020

Indicator: The NTP to use DHIS2 / similar HMIS system to capture relevant data from each reporting centre, preferably real time. Case-based data available in electronic format with generation of routine program reports at national, district & sub-district levels. The NTP will coordinate with the MoH data management section to ensure regular and accurate entry of TB data into HMIS/ DHIS2.

Objective 5:

Ensure availability of quality TB services in line with current international standards and provided by qualified personnel at 90% of all facilities by 2021 and 100% of the facilities by 2022

Indicator: Number of health facilities with at least one qualified and trained staff managing TB patients.

Objective 6:

Scale-up patient support system to all TB patients including DSTB with an intent to reduce catastrophic cost prevalence by at least 80%

Indicator: Proportion of TB patients receiving support. Information to be documented and derived from program recording & reporting system. NTP to conduct follow-up patient cost survey to assess the catastrophic cost for TB patients.

Pillar 3: INTENSIFIED RESEARCH AND INNOVATION

Objective 7:

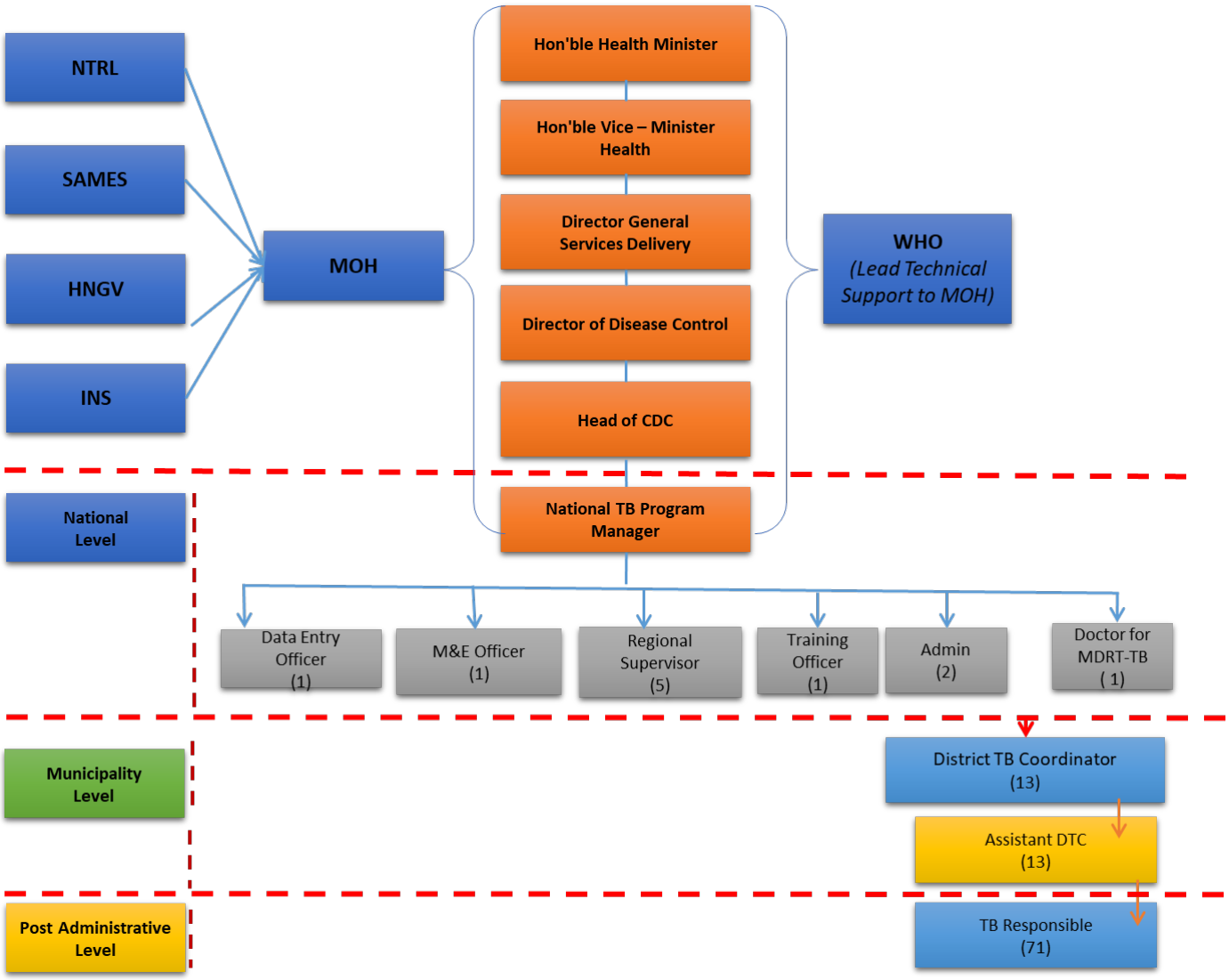
Ensure adequate support for operational research to foster innovation

Indicator: The NTP will develop an operational research plan specifying priority research areas. Emphasis will be given to operational research to assess the efficacy and cost implications of new active case finding activities.

3 STRUCTURE OF THE NATIONAL TB PROGRAM (NTP)

TB services are a part of the comprehensive service package and are delivered through all levels of the health system.

The Organogram of NTP in the MoH with coordination network: HNGV, INS, NHL, SAMES and WHO



Central level

The Central Management Unit for Tuberculosis (CMU-TB) under the Communicable Diseases Control (CDC) Department is located at the Directorate of Health Services Delivery in the Ministry of Health. It is the strategic focal point and has the overall responsibility for the NTP. The Central Management Unit is responsible for formulation of technical and operational guidelines and policies, planning and overall implementation of program activities in the country including coordination, monitoring and evaluation. The NTP is headed by the

National TB Officer working under the guidance of the Head of the Department of Communicable Diseases Control under the Directorate of Community Health of the MoH.

Currently the Central Management Unit for TB is staffed by a Program Officer, five regional supervisors (RS), one finance officer, and one monitoring and evaluation (M&E) officer, a data entry assistant, one training officer and an administrative assistant.

Key functions:

1. **Formulate national strategic plan, guidelines and policies**
2. **Advocacy for political commitment at all levels and community mobilization**
3. **Oversee program implementation at the municipality level**
4. **Provide necessary logistics to municipalities including:**
    a. **Anti –TB drugs**
    b. **Laboratory supplies**
    c. **Diagnostic equipment**
    d. **Educational materials**
    e. **NTP recording and reporting forms, registers and records**
5. **Provide technical assistance including training to health staff of government and non-government health care providers and to related departments**
6. **Regular monitoring, supervision, and evaluation of the NTP activities including quality assurance system**
7. **Collate and analyse all quarterly reports and provide feedback and recommendations to staff working in municipalities.**
8. **Engage national level partners and stakeholders**

<u>Municipality Level</u>

The Head of the Municipality Health Services (MHS) is the Municipality Director who is the principal for health activities, including control of TB. The Municipality TB Coordinator (MTC) is specifically responsible for the organization of TB activities in the municipality. The MTC is based at the MHS. The MTC with support from the Director is responsible for overseeing the implementation of the TB program in the municipality.

The program management unit at the Municipality level is the Municipality TB Unit (MTU). The MTU may be located at the municipal health service (MHS) office or the municipal CHC. The Municipal CHC does smear microscopy (designated microscopy centre-DMC), while the other CHCs receive sputum, do fixation and send smears to the DMC for microscopy. In the capital Dili, microscopy and treatment is done in all four CHCs, one private clinic and one church clinic.

The Municipality TB Committee is chaired by the Director of Municipal Health Services or his/her representative. The MTC is the member secretary of the MIC. The Municipality keeps sufficient stock of anti-TB drugs and laboratory reagents. There is stock for 6 months (3 months stock + 3 months reserve stock) at Municipality level. The Senior Laboratory Technicians (SRTs) at the Municipality level prepare and distribute laboratory reagents and ensure regular and adequate supplies of reagents and sputum containers in health facilities. The SRTs also supervise all laboratory activities in the Municipality and facilitate quality assurance in sputum microscopy.

Key functions:

1. **Advocacy for political and administrative commitment for the NTP at Municipality level**
2. **Implementation of TB activities as per the national guidelines for the NTP**
3. **Involving other health staff such as nurses and laboratory technicians in the NTP**

4. **Spending of funds received for NTP activities including: monitoring, supervision, evaluation, training of local staff and similar activities**
5. **Prepare and submit quarterly report to TB-CMU and analysis at Municipality level**
6. **Ensuring implementation of standardized NTP quality assurance system for laboratory network**
7. **Ensuring implementation of contact tracing and screening for high incidence areas in accordance with plans**

Administrative Post Level

The sub-Municipality (Administrative Post) covers a population of approximately 15,000 to 30,000. At the sub-Municipality level, the NTP is implemented through the sub-Municipality level community health centres (CHCs) or Health Posts. Each CHC has more than one doctor, and a team of 7 – 10 people, and at each Health Post primary care services are provided by a team of 3 – 4 health personnel including a doctor. CHCs which have been designated as diagnostic centres (see below) also have a laboratory technician. In addition, one doctor is placed on a rotating basis to be responsible for curative services and to act as the focal point for referral. Sub-Municipality facilities keep a stock for two months (one-month stock + one-month reserve stock). DOT is provided by health staff at the CHC (both Municipality and Administrative Post) health posts, and hospices working with community health promoters and community volunteers. The functions of the sub-Municipality level are implementation, monitoring and supervision of TB control activities within its designated geographical area. The Administrative Post CHCs and Health Posts maintain the 'TB Presumptive register' in which the names and information of all TB presumptives are entered. Delivery of health care for TB control is done by the primary health services, as per the policies stated in the NTP manual. Treatment supervision is provided by health workers in primary health care services (CHCs, Health Posts etc.), non-governmental organizations, hospices and community volunteers.

Key functions

1. **Organizing case-finding activities including identification of TB presumptives, their registration in the TB presumptive register and referral for sputum smear examination or Xpert MTB/RIF to designated microscopy or diagnostic centres**
2. **In cases where patients cannot travel to diagnostic centres, sputum fixation (for smear microscopy) or sample collection (for Xpert MTB/RIF) and timely transportation to designated microscopy or diagnostic centre for reading**
3. **Organizing patient-centred Direct Observed Treatment (DOT) activity**
4. **Support and work with non-governmental organizations, Church Clinic and hospices**
5. **Conducting NTP promotional campaigns**
6. **Supervision of community volunteers performing treatment supervision (DOT)**
7. **Proper management/referring for proper management of patients developing side effects to TB drugs**
8. **Conducting regular contact tracing and, organise screening activities for high incidence areas and identified populations twice a year**

Community level: *Programa Nacional Saúde na Família*

As part of the GoTL's constitutional commitment to rebuild the health infrastructure destroyed in 1999 and to fulfil the right to free universal health care of its people through a decentralized public health care system, the "Programa Nacional Saúde na Família" based on the Cuban model was launched in 2015 as a comprehensive service package of primary health care to the household level through domiciliary visits by a team made up of a doctor, a midwife and a nurse; clinical consultations; treatment and referral by the team of health professionals; as well as recording the household's and each of its member's clinical profiles, which are then

entered into an integrated digital medical record system. This aligns with the principle of the Sustainable Development Goals of "leaving no one behind". It covers all of the 296,483 households and 2,225 villages (Sucos) mapped in the 2015 Population and Housing Census.

Technical and implementation support to the NTP: WHO and Partners

The main technical support for the NTP is provided by the World Health Organization (WHO). The NTP has also received technical and commodity assistance from the Global Drug Facility (GDF), UNITAID, Green Light Committee (GLC), NIRT Chennai, and independent consultants.

The MoH initiated PMDT services with technical assistance from the WHO Country Office from 2008. PMDT services are available across all municipalities of TL with funding support from The Global Fund. Other partner organizations like Caritas Dili (Catholic Institution), Klibur Domin (NGO), Bairo Pite Clinic (NGO), International Organization for Migration (IOM), Korea International Cooperation Agency (KOICA) and Japan International Cooperation Agency (JICA) have also been supporting TL particularly in active case finding, laboratory expansion, and management of TB and DR-TB cases.

The general health system under the MoH is the primary provider of services for TB and DR-TB in TL. **In Timor-Leste, by legislation, TB medications are not sold in any private pharmacy nor available in any private/faith-based or NGO clinics.** However, smear microscopy facilities are available in 7 private clinics across TL. All TB patients seeking care in private clinics are notified to the NTP for provision of anti-TB drugs.

4 CASE FINDING AND DIAGNOSTIC SERVICES

4.1 FORMS OF TUBERCULOSIS

The etiological agent of tuberculosis is a bacillus belonging to the *Mycobacterium tuberculosis* complex. Other mycobacteria that occasionally cause diseases clinically indistinguishable from tuberculosis are identifiable only through culture.

Tuberculosis is most commonly transmitted by inhalation of infected droplet nuclei which are discharged into the air when a patient with untreated sputum smear-positive TB coughs or sneezes. If the tuberculosis bacillus succeeds in infecting a person, it can then spread from primary lung lesions to other parts of the body via the blood stream, lymphatic and bronchial systems and may thus affect any other organ. The initial infection usually goes unnoticed. Tuberculin sensitivity appears within a few weeks of the infection. Initial lesions commonly heal leaving no residual change except occasional pulmonary or tracheobronchial lymph node calcifications (primary complex).

About 10% of those who are infected with TB bacillus develop active disease. The remaining 90 % of those initially infected enter the latent phase with no tuberculosis disease from which there is life-long risk of reactivation. In approximately 5%, the initial infection may progress directly to pulmonary tuberculosis or by lympho-haematogenous dissemination of bacilli, to pulmonary, miliary, meningeal or other extrapulmonary tuberculosis. The initial infection has a serious outcome more frequently in infants, adolescents and young adults. Progressive pulmonary tuberculosis arises from endogenous reactivation of latent foci, which remained dormant since the initial infection or due to exogenous re-infection, and the disease, if untreated, leads to death within 2-3 years in at least half of these patients.

Tuberculosis affects the lungs in more than 85% of cases. This form of the disease is called pulmonary tuberculosis. Pulmonary tuberculosis is an infectious disease. People living with or coming in close contact with a patient who has undiagnosed or untreated infectious tuberculosis (in particular, smear-positive) have the risk of being infected. Therefore, it is very important to identify individuals with presumptive TB who have symptoms of pulmonary tuberculosis early in the course of the disease and ensure their treatment.

Tuberculosis of any organ other than the lungs such as the pleura (TB pleurisy), lymph nodes, intestines, genitourinary tract, skin, joints and bones, meninges of the brain etc. is classified as extrapulmonary tuberculosis. In extrapulmonary tuberculosis, the symptoms depend on the organs involved, for example:

- Swelling, occasionally with pus discharge when lymph nodes are affected
- Pain and swelling of the joints if these are involved
- Headache, fever, stiffness of the neck and mental confusion when there is tuberculous meningitis.

4.2 IDENTIFICATION OF PATIENTS WITH PRESUMPTIVE TB

Pulmonary tuberculosis is an infectious disease. People living with or coming in close contact with a patient who has undiagnosed and untreated infectious (particularly smear-positive) tuberculosis have the risk of being infected. Therefore, it is very important to identify people who have symptoms of tuberculosis early in the course of the disease and ensure their treatment.

When should pulmonary tuberculosis be considered?

The most common symptoms of pulmonary tuberculosis are:

- Persistent cough for more than two weeks usually with sputum, sometimes blood-stained
- Fever and chest pain
- Night sweats, lethargy, lassitude, loss of appetite and weight loss

A TB presumptive case is any person who presents with symptoms or signs suggestive of TB, in particular cough of more than two weeks duration. However, cough of any duration with other symptoms suggestive of PTB and of contacts should also be screened for TB

For the success of the NTP, it is of key importance that all TB presumptive cases receive diagnostic procedures as per the NTP diagnostic algorithms!

4.3 CASE DEFINITIONS

A **bacteriologically confirmed TB case** is one from whom a biological specimen is positive by smear microscopy **or** Xpert MTB/RIF or LPA or culture. All such cases should be registered and reported, regardless of whether TB treatment has started.

A **clinically diagnosed TB case** is someone who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extrapulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.

Bacteriologically confirmed or clinically diagnosed cases of TB are also classified according to:

- anatomical site of disease;
- history of previous treatment;
- drug resistance;
- HIV status.

4.3.1 Classification based on anatomical site of disease

Pulmonary tuberculosis (PTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Miliary TB is classified as PTB because there are lesions in the lungs. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of PTB.

Extrapulmonary tuberculosis (EPTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.

4.3.2 Classification based on history of previous TB treatment (patient registration group)

New patients have never been treated for TB or have taken anti-TB drugs for less than 1 month.

Previously treated patients have received 1 month or more of anti-TB drugs in the past. They are further classified by the outcome of their most recent course of treatment as follows:

> **Relapse** patients have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).
>
> **Treatment after failure** patients are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.
>
> **Treatment after loss to follow-up** patients have previously been treated for TB and were declared lost to follow-up at the end of their most recent course of treatment. (These were previously known as treatment after default patients.)
>
> **Other** previously treated patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

Patients with unknown previous TB treatment history do not fit into any of the categories listed above.

New and relapse cases of TB are **incident** TB cases.

4.3.3 Classification based on HIV status

HIV-positive TB patient refers to any bacteriologically confirmed or clinically diagnosed case of TB who has a positive result from HIV testing conducted at the time of TB diagnosis or other documented evidence of enrolment in HIV care, such as enrolment in the pre-ART register or in the 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 result from HIV testing conducted at the time of TB diagnosis or up to 6 months before 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.

4.3.4 Classification based on drug resistance

Cases are classified in categories based on the result of the Xpert MTB/RIF assay and any confirmatory DST results received from the NRL.

- **Rifampicin resistance (RR-TB)**: resistance to rifampicin detected in the Xpert MTB/RIF assay
- **Isoniazid resistance (HR-TB):** resistance to H (based on DST results from the NTRL)
- **Multidrug resistance (MDR-TB)**: resistance to at least both isoniazid and rifampicin (based on DST results from the NRL)
- **Extensive drug resistance (XDR-TB):** resistance to any fluoroquinolone and to at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance (based on DST results from the NRL).

4.4 INTENSIFIED (ACTIVE) CASE FINDING

4.4.1 Rationale

Passive case-finding relies on four actions: (1) a person with active TB experiencing and recognizing symptoms, (2) the person presenting to an appropriate health facility, (3) a health-worker correctly assessing whether the person fulfils the criteria for suspected TB, and (4) the successful application of a complete diagnostic algorithm with sufficient sensitivity and specificity. Barriers to early case detection may occur at each step, and the poorest people are at highest risk of not completing, or delaying, each step. They have the least access to high-quality services and face the highest costs from illness and for health care. Screening of groups who have limited access to health care may help reduce delays.

People living with HIV, young children, elderly people, people with diabetes, and other groups who have compromised immune systems face a high risk of poor outcomes from TB treatment, including relapse and death. The risk is augmented when diagnosis is delayed. Systematic screening can be particularly beneficial for these groups.

More than 50% of patients with bacteriologically confirmed pulmonary TB detected in prevalence surveys do not report symptoms that correspond to the commonly used criteria for suspecting disease and prompting diagnostic investigation (that is, cough lasting longer than 2–3 weeks); additionally, a large proportion of these cases do not report any symptoms at all. These individuals are less likely to seek care than people with more prominent symptoms. When they do seek care, they are less likely to be diagnosed.

Systematic screening for active TB is defined as the *systematic identification of people with suspected active TB, in a predetermined target group, using tests, examinations or other procedures that can be applied rapidly.*[12] Systematic screening for active TB is predominantly provider-initiated. It may target people who do not seek health care because they do not have or recognise symptoms, because they do not perceive that they have a health problem that warrants medical attention, because there are barriers to accessing care, or for other reasons. It may also target people seeking health care who do or do not have symptoms or signs compatible with TB and who may not be identified by "passive case-finding" as possibly having TB. People seeking care who may be eligible for TB screening include people with medical conditions that constitute risk factors for TB (such as people living with HIV and people with diabetes mellitus) who may seek care for reasons other than symptoms compatible with TB.

4.4.2 Objectives and goals of intensified case finding

The *primary objective* of intensified case finding is to detect active TB early; this can contribute to two ultimate goals:

1. To ensure that active TB is detected early and treatment is initiated promptly, reducing the risk of poor treatment outcomes, health sequelae, and the adverse social and economic consequences of TB for the individual. This reduces suffering, the prevalence of TB, and death from TB
2. To reduce TB transmission by shortening of the duration of infectiousness. This reduces the incidence of TB infection and consequently contributes to reduced incidence of TB disease.
3. Finding missing cases.

A *second objective* is to rule out active disease to help identify people who are eligible for treatment of latent TB infection.

Furthermore, screening can help identify people who are at particularly high risk of developing active disease in the future and thus may require repeat screening; for example, this group includes people with an abnormal

[12] *Systematic Screening for Active TB, Principles and Recommendations, WHO 2013*

chest radiograph that is compatible with TB but who were not diagnosed with active disease at the time of screening.

4.4.3 **Principles of systematic screening for active TB**

- Before screening is initiated, high-quality TB diagnosis, treatment, care, management and support for patients should be in place, and there should be the capacity to scale these up further to match the anticipated rise in case detection that may occur because of screening.
- Targeting of risk groups with high risk of TB
- Prioritization of risk groups for screening based on *vulnerability assessment*
- *Indiscriminate mass screening should be avoided*
- TB screening should follow established ethical principles for screening for infectious diseases, observe human rights, and be designed to minimise the risk of discomfort, pain, stigma and discrimination.
- The TB screening approach should be developed and implemented in a way that optimises synergies with the delivery of other health services and social services.
- A screening strategy should be monitored and reassessed continually to inform re-prioritization of risk groups, re-adaptation of screening approaches when necessary and discontinuation of screening at an appropriate time.

4.4.4 **Target populations for active case finding in Timor-Leste**

A risk group for TB is any group of people within which the prevalence or incidence of TB is significantly higher than in the general population. A risk group may be a group of people sharing a specific individual-level risk profile (for example, being in close contact with a person who has active TB; or living with HIV or having diabetes; or being a migrant). A risk group can also be defined as all people living in a specific geographical location associated with a high burden of TB (for example, all people living in an urban slum) or a specific type of institution (such as all prisoners in a country). An absolute level of TB prevalence or incidence may be used as a cut-off to define a risk group in a given epidemiological situation. Any absolute level must be adapted to the local situation, and it may also change over time as the burden and distribution of TB change.

The following risk groups should always be screened for active TB, in all settings:

1. Close contacts of people with TB;
2. People living with HIV;
3. Workers in silica exposed workplaces.

Tuberculosis risk groups have been categorized according to the places where they can be reached for screening and depicted in the table.

Category	TB risk groups
Community	• Geographical areas with high prevalence and subpopulations with poor access (poor populations, urban slums, remote areas, refugees, homeless, etc.
Hospital outpatient and inpatient departments and primary health care centres	• People previously treated for TB • People with an untreated fibrotic lesion • PLHIV and people attending HIV testing • People with diabetes mellitus • People with chronic respiratory diseases and smokers • Undernourished • People with gastrectomy or jejunoileal bypass • People with an alcohol-or drug-use disorder • People with chronic renal failure • People with immunocompromising treatements • Elderly people

	• People in mental health clinics or institutions
Residential institutions	• Prisoners and prison staff • People residing in shelters • Other congregate settings (such as the military)
Immigration and refugee services	• Immigrants from settings with high prevalence of TB • People in refugee camps
Workplaces	• Health care workers • Miners or others who are exposed to silica • Other workplaces with high prevalence of TB

In Timor-Leste, systematic community level screening by PSF's and Saúde na Família team to rule out TB and to gather data from the at-risk targeted population for TB, using the vulnerability assessment tool, should be considered in Timor-Leste in accordance with the existing risk factors for developing TB. This can be done by:

- Going door to door to screen households for vulnerability assessment, both for latent and active TB;
- Systematically screening individuals in shelters, refugee camps and other specific locations.

4.4.5 **Vulnerability assessment for TB: Timor-Leste**

The overall idea of doing vulnerability assessment of every individual in Timor-Leste is to personally meet approximately 1,200,000 individuals living in 200,000 households (HH) in Timor-Leste using the vulnerability assessment tool (Figure 3). This is required to:

(1) Generate TB awareness in every member
(2) Assess the TB vulnerability of every member
(3) Generate a vulnerability or TB risk profile data base for TB surveillance
(4) Prioritization of TB risk groups for screening
(5) Actively search for TB cases & latent TB.
(6) Tuberculosis Preventive Therapy (TPT) for adults, PLHIVs and children contacts.

Vulnerability factors (with their weighted scores in brackets) are: Household Contact (5), Immunosuppressive therapy (4), Malnutrition (4), Health Care Worker (3), Diabetes (3), Organ dysfunction (3), Worked/Lived in districts/sub-districts (CHCs) with TB notification rates ≥100/100,000 (3), Street Dweller (3), Migrant labour (Cross Border Migrants) (2), Chronic lung disease(2), Smoking/ Use of Solid Fuel in HH – Firewood etc. (2), Alcoholism (2), Prison inmate (2) Age above 60 (1), Slum dweller (1). If the total score is 5 or above, the person is classified as highly vulnerable and requires symptom screening once every 3 months. If the total score is 1 to 5, the person is moderately vulnerable and should be screened for symptoms once every year. For creating a database of chronically ill patients (diabetics, organ dysfunction, immunosuppression etc.) who were admitted in the 6 referral hospitals (1 National and 5 Referral Hospitals), review of 5 years hospital OPD and IPD registration records will be undertaken by the CV/PSFs and data will be entered digitally. If any of the following symptoms are found during vulnerability assessment, then individuals are referred immediately to the nearest TB diagnostic centre:

1. Two weeks of cough or cough of any duration with other symptoms (2-4)
2. Fever
3. Weight loss
4. Haemoptysis

Vulnerability assessment for the entire country and ACF can be conducted simultaneously. This can be done by establishing a digital surveillance system, including GIS mapping with digital entry of vulnerability assessment according to the ICT plan.

Once TB is diagnosed among the vulnerabilities, contact investigation should be done in their households for all children and adult contacts, and accordingly, latent TB infection (LTBI) management should be initiated, after ruling out active TB.

Figure 2: Vulnerability screening tool

Address of the household:

House No/Name: No. of HH members: No. of Children < 5 years: BCG Vaccination Status (Yes/ NO): BCG Scar Status (Yes/ No): Estimated Distance from the Health Post/CHC:	Phone numbers 1 2 3	**Reg. Number:** XXXX2020/ Name of the Village……../ House No…….. Or XXXX2020/ Name of the Hospital/ Health facility…….. Name of the nearest CHC: Name of the Village: Name of the Interviewer Interviewer occupation (PSF/ TB Responsible/ Nurse/ KP/ Other):

Name *Naran*	Sex M/F/TG	Age	1. a Slum	1.b Past H/o TB **(3 Yr)/** Present TB	1.c Health Worker	2a. PLHIV status	3a. Malnutrition Status (MUAC)	3b. Migrant Labour (Cross Border/ Intl. Migrants)/ Prisoner	3c. Diabetes (In Health Facility/ Hospital)	3d. COPD /asthma (In Health Facility/ Hospital)	3e. Liver/ kidney disease (In Health Facility/ Hospital)	3f. Bed ridden/palliative care (In Health Facility/ Hospital)	3g. Smoking/ Use of solid Fuels in HH: Firewood wood etc.	3h. Alcohol	4a. Symptoms present: -Cough -Fever -Weight Loss - Haemoptysis	4b Sputum collected and sputum examination form filled	Asymptomatic, but identified vulnerable requiring X-ray *(For Example – Asymptomatic contacts with Bac+ve, malnourished, smoker, alcohol use etc.)*	**SCORE**

[Reference: https://www.who.int/tb/features_archive/action-plan-launched-72-regional-committee/en/]

4.5 DIAGNOSIS OF TB

4.5.1 Organization of diagnostic services

The mainstay of TB diagnosis is sputum smear microscopy. There are 76 TB laboratories including 69 in CHCs and 7 in private clinics. There are 8 GeneXpert® machines in the country - 2 at NGOs: Klibur Domin and Bairo Pite; 6 at public health facilities: 1 located at the National Tuberculosis Reference Laboratory (NTRL), 1 each at Oecusse, Bobonaro and Ainaro Referral Hospitals, and 1 at Viqueque. There is one additional GeneXpert ® machine pending installation at the Baucau Referral Hospital for linking these far-off districts to GeneXpert®. The NTRL has a BSL 3 culture and DST laboratory requiring accreditation for full independent functioning. There is one MGIT 320 machine recently installed at the NTRL. There is currently no LPA facility available in the NTRL, however, there is adequate PCR capacity and space available in the national hospital laboratory where the NTRL is co-located. Under the revised NSP 2020-24 / End TB Strategy for TL, laboratory expansion has been proposed with additional GeneXpert® machines and 1st and 2nd line LPA for NRTL to meet the diagnostic demands of TL for universal DST.

Quality assurance for smear microscopy centres is provided by the NTRL, regional and municipality level Senior Laboratory Technicians and TB Coordinators through on-site supervision and external quality assurance.

X-ray facilities are available at the five referral and national hospitals. Other diagnostic facilities like Fine Needle Aspiration Cytology (FNAC) and biopsy facilities are currently not readily available.

4.5.2 Laboratory methods used by the NTP for the diagnosis of TB

Options for the initial screening include screening for symptoms (screening either for cough lasting for longer than 2 weeks, or screening for any symptom compatible with TB, including cough of any duration, haemoptysis, weight loss, fever or night sweats) or screening with chest radiography. If symptom screening is used initially, then chest radiography can be used as a second screen to improve the pre-test probability of the subsequent diagnostic test, and to reduce the number of people who need to undergo further diagnostic evaluation.

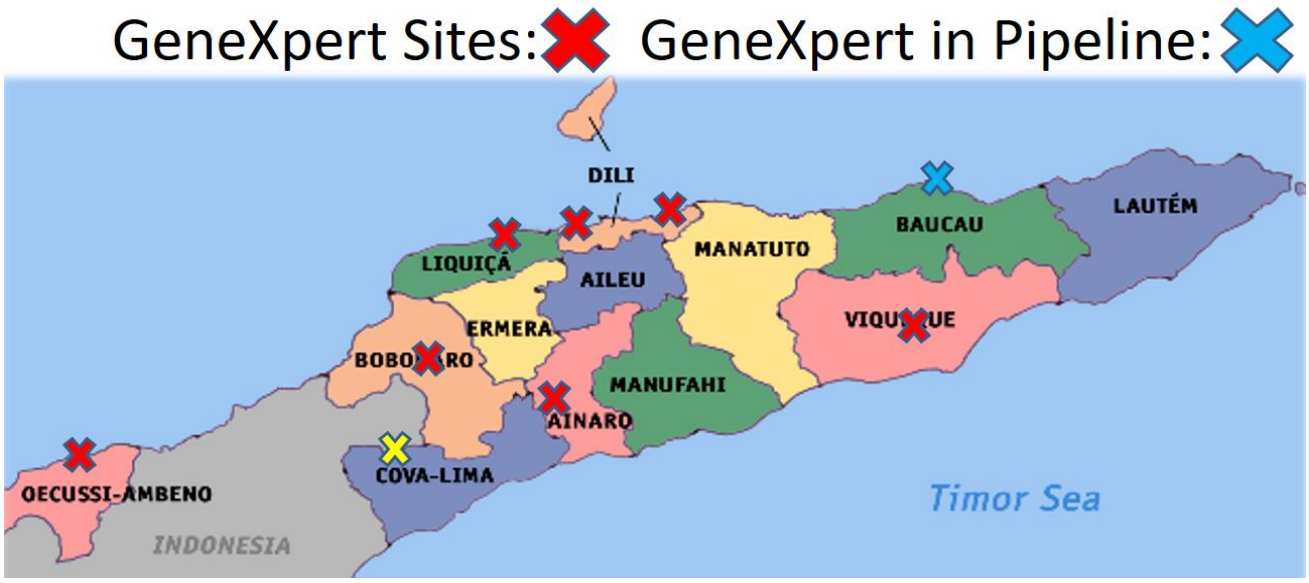
Starting in 2014, the NTP has implemented the Xpert MTB/RIF assay as an additional test for diagnosis of non-resistant and resistant forms of TB. The assay is simple to use and provides results directly from sputum in less than 2 hours. Xpert is currently available at 8 locations throughout the country, and further expansion will be planned according to funding availability. Smear-microscopy as the initial diagnostic test will gradually be phased out. Universal Drug Susceptibility Testing (U-DST) for all notified pulmonary TB cases by GeneXpert testing is proposed from 2020 *(WHO Rapid Communication January 2020)*. This will be extended to all presumptive TB patients by 2021. Smear microscopy is anticipated to be phased out for initial diagnosis by 2021 but will continue to be used for follow-up examination. In addition, the NTP will gradually replace the current Xpert MTB/RIF assay with the new XpertUltra assay. XpertUltra is non-inferior to the Xpert MTB/RIF assay for the detection of MTB and for the detection of rifampicin resistance, however, XpertUltra has a higher sensitivity than Xpert MTB/RIF particularly in smear-negative culture-positive specimens and in specimens from HIV-infected patients.

LPA (GenoType MTBDRplus and GenoType MTBDRsl; Hain Lifesciences, Nehren, Germany) is used to detect genetic mutations that render *M. tuberculosis* strains resistant to H, R (first-line LPA, FL-LPA), SLIs and FQs (second-line LPA, SL-LPA). As per the WHO recommendation, Isoniazid (INH) and Rifampicin (RIF) needs to be tested for smear positive cases to avoid transmitting the resistant bacilli. Novel technologies for rapid detection of anti-TB drug resistance have therefore become a priority in TB research and development, and thus, molecular LPA focusing on rapid detection of rifampicin resistance (alone or in combination with isoniazid) is the advanced molecular technology, which can be utilized for both first and second line DST results within 72 hours in the country. The 2019 TB Mid-Term Review (MTR) recommended that the NTP should consider introducing an LPA facility in the NTRL which will be essential for rapid diagnosis of INH and second line drug resistance.

Since the Xpert MTB/RIF essay only allows for the diagnosis of rifampicin resistance, LPA should be used in addition to Xpert as the initial DR diagnostic test for all sputum positive TB cases as per the proposed diagnostic algorithm (Figure 7) to GeneXpert.

Achieving U-DST would require establishment of an efficient sample collection and transport system. Sputum samples are to be transported from all the municipalities to the 8 Xpert sites *(See Map: Figure 6)* and NTRL within the prescribed timelines through human carriers who could be adequately incentivized for this work. The sputum collection and transportation (SC&T) mechanism from the DRS can be replicated for transporting samples from the microscopy labs to the Xpert sites.

Figure 3: GeneXpert Sites in Timor-Leste



Details of the CHCs feeding to Xpert with distance and time taken for sputum transportation is ***(Sample collection and transportation to Xpert sites)***:

Sl. No.	Municipality	Community health centre	Gene Xpert facilities	Distance to Xpert facility (km)	Travel time to Xpert facility
1	Aileu	Laulara	NTRL	2	30 min
		Remixio	NTRL	4	45 min
		Aileu Vila	Ainaro (Maubisse)	2	30 min
		Liquidoe	Ainaro (Maubisse)	20	1 h
2	Ainaro	Ainaro Vila	Ainaro (Maubisse)	20	1 h
		Hautio	Ainaro (Maubisse)	10	30 min
		Hatu-udu	Ainaro (Maubisse)	2	1.5 h
		Maubesse	Ainaro (Maubisse)	0	5 min
3	Covalima	Suai Vila	Ainaro (Maubisse)	1	2 h

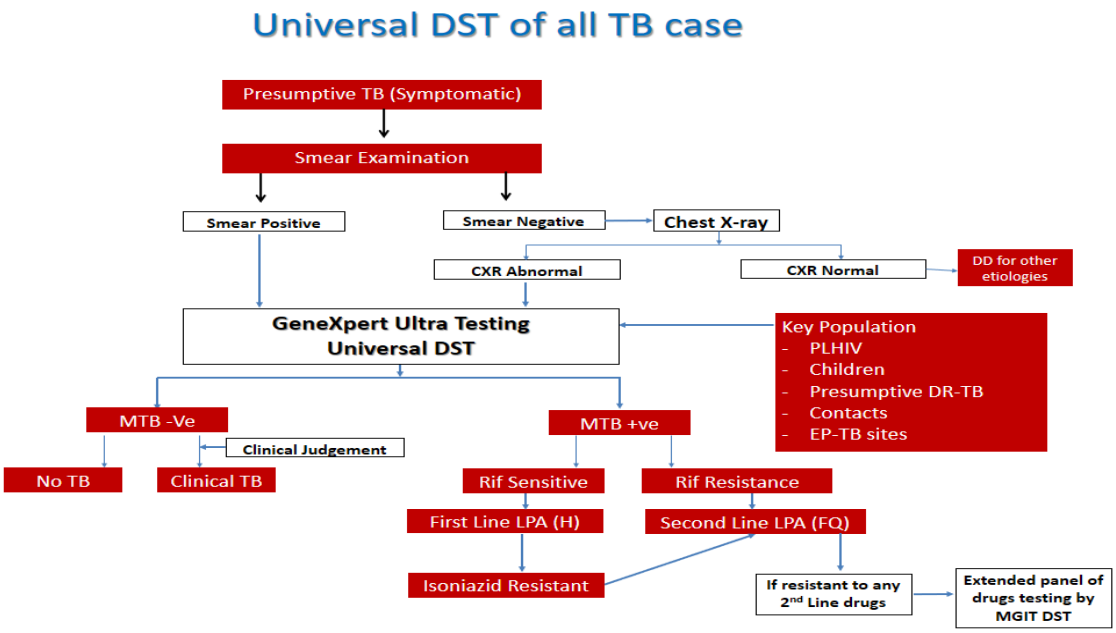
		Tiliomar	Ainaro (Maubisse)	5	2.5 h
		Fatululik	Ainaro (Maubisse)	20	3 h
		Fohorem	Ainaro (Maubisse)	20	3 h
		Maucatar	Ainaro (Maubisse)	30	2.5 h
		Zumalai	Ainaro (Maubisse)	20	2 h
4	Manatuto	Manatuto Vila	NTRL	30	4 h
		Laclubar	NTRL	20	2 h
		Soibada	NTRL	30	3 h
		Laclo	NTRL	30	3 h
		Laleia	NTRL	30	3 h
		Natarbora	Viquque	30	3 h
5	Baucau	Riamare	NTRL (In Future Baucau)	30	3 h
		Laga	NTRL (In Future Baucau)	40	4 h
		Baquia	NTRL (In Future Baucau)	50	7 h
		Vemace	NTRL (In Future Baucau)	40	3 h
		Uailili	NTRL (In Future Baucau)	30	4 h
		Bucoli	NTRL (In Future Baucau)	40	3 h
		Venilale	NTRL (In Future Baucau)	30	4 h
6	Lautem	Lospalos Vila	NTRL (In Future Baucau)	200	8 h
		Lautem	NTRL (In Future Baucau)	150	6 h
		Luro	NTRL (In Future Baucau)	175	7 h
		Iliomar	NTRL (In Future Baucau)	200	8 h
		Mehara	NTRL (In Future Baucau)	250	9 h
7	Viqueque	Viqueque Vila	Viqueque	5	6 h
		Lacluta	Viqueque	0	6 h
		Uatulari	Viqueque	0	7 h
		Ossu	Viqueque	0	6 h
		Uatucarbau	Viqueque	0	7 h
8	Manufahi	Same Vila	Ainaro (Maubisse)	4	45 min
		Alas	Ainaro (Maubisse)	10	1 h
		Fatuberliu	Ainaro (Maubisse)	6	1.5 h
		Turiscai	Ainaro (Maubisse)	10	2 h
9	Oecusse	Pante Makasar	Oecusse	3	30 min
		Oesilo	Oecusse	10	1 h
		Passabe	Oecusse	10	30 min
		Boknana	Oecusse	20	2 h
10	Dilli	Vera Cruz	NTRL	2	20 min
		Becora	NTRL	3	15 min
		Formoza	NTRL	2	15 min
		Comoro	NTRL	4	30 min
		Mitinaro	NTRL	2	15 min

		Motal	NTRL	11	30 min
		Atauro	NTRL	3	3 h
		Bairo Pite	Bairro Pite	0	0
11	Ermera	Gleno	Klibur Domin (Tibar)	25	20 min
		Ermera Vila	Klibur Domin (Tibar)	14	45 min
		Letefoho	Klibur Domin (Tibar)	25	1.5 h
		Hatulia	Klibur Domin (Tibar)	11	3.5 h
		Atsabe	Klibur Domin (Tibar)	8	2 h
		Railaco	Klibur Domin (Tibar)	17	3 h
12	Liquica	Liquica Vila	Klibur Domin (Tibar)	25	30 min
		Maubara	Klibur Domin (Tibar)	13	35 min
		Bazartete	Klibur Domin (Tibar)	29	45 min
13	Bobonaro	Maliana Vila	Maliana	8	Closer
		Balibo	Maliana	12	30 min
		Cailaco	Maliana	6	2.5 h
		Lolotoe	Maliana	15	30 min
		Bobonaro	Maliana	10	30 min
		Atabae	Maliana	14	3.5 min
		Kakamia	Maliana	2	1.5 h

Diagnostic algorithms

The universal DST can be completed in a phased manner- initially doing DST for all notified TB patients by June 2020 *(Fig. 7)* and expanding Xpert Ultra to all presumptive TB cases by March 2021.

Figure 4: Diagnostic Algorithm on Universal DST of all TB cases by June 2020



Note: Line Probe Assay (LPA) should be used in addition to Xpert as the initial DR-TB diagnostic test for all MTB positive TB cases as per the proposed diagnostic algorithm

4.6 Criteria for identifying presumptive DR-TB cases and Risk category factors

Presumptive DR-TB cases are cases fulfilling one of the following criteria:

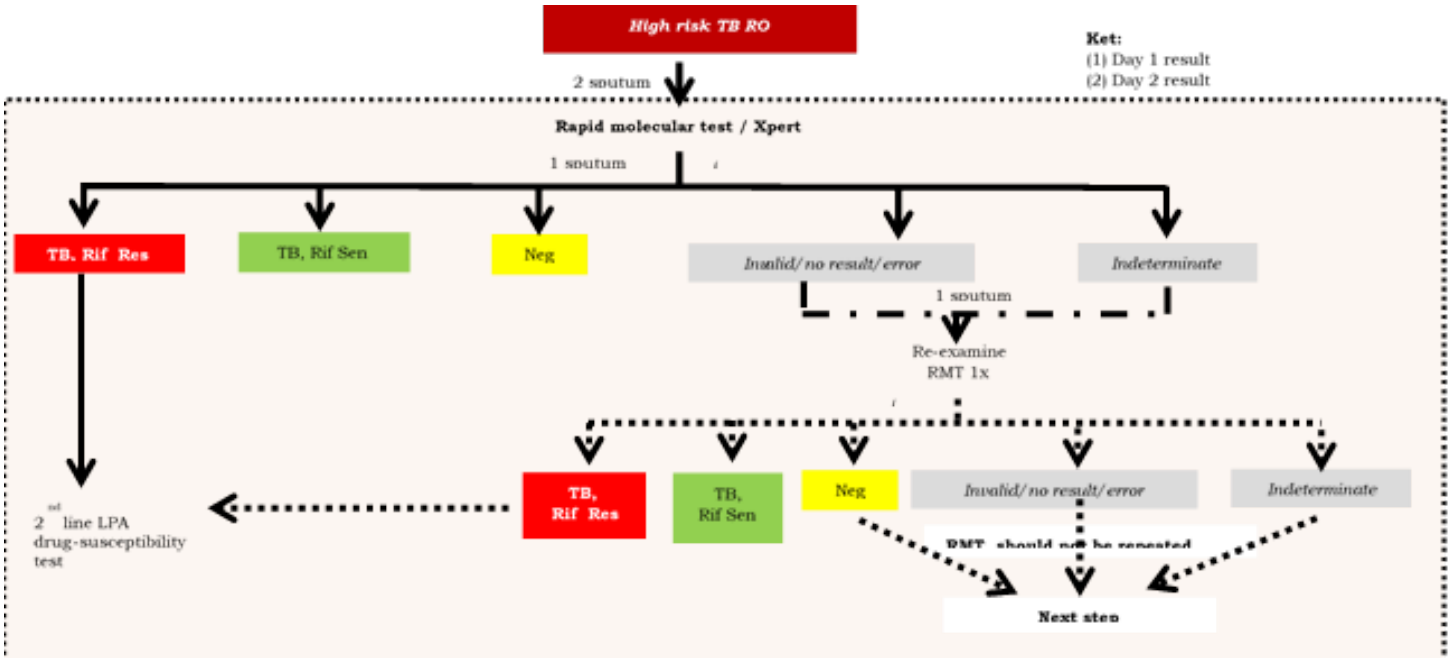
- TB patients found positive on any follow-up sputum examination during treatment with first line drugs
- Paediatric TB non-responders
- TB patients who are contacts of DR-TB
- Previously treated TB patients
- New TB patients with HIV coinfection

Risk category factors for DR-TB divided into two categories:

High Risk

- History of unstandardized anti-TB treatment and use of Quinolone and second-line injection drug at least 1 month
- Failed treatment in category 1
- Fail to convert in category 1

- Relapse case in category 1
- Patient returning after loss to follow-up
- Presumptive TB with history of close contact with DR-TB patient
- Co-infection TB-HIV which doesn't response either clinically or bacteriologically on anti-TB treatment



If from **high risk group** check for rapid molecular test/ RMT (Xpert) and if the test revealed:

- TB and Rifampicin resistant, then diagnosis is RR TB then do 1st and 2nd Line DST
- TB and Rifampicin sensitive, then diagnosis is drug sensitive TB (DS-TB)
- Negative, then diagnosis is not TB
- Invalid result/error and indeterminate to be re-examined and Xpert to be repeated with the 2nd sputum/ specimen collected. If the result is rifampicin resistant do culture and DST. If the result is Rifampicin sensitive, then the diagnosis is DS-TB. However, if the result revealed negative, diagnosis is not TB, and if the second result is invalid or indeterminate, Xpert test should not be repeated

Steps to be taken in high risk groups -

Result of 1st XPERT	Results 2nd XPERT	Final Results	Therapy
Invalid/no result/error	Rifampicin Sensitive	Rifampicin Sensitive	DS-TB
	Rifampicin Resistant	Rifampicin Resistant	DR-TB
	Negative	Negative	Other treatment
	Indeterminate	Indeterminate	Therapy by clinical judgement
	Invalid/no result/error	Invalid/no result/error	Therapy by clinical judgement
Intermediate	Rifampicin Resistant	Rifampicin Resistant	DR-TB
	Rifampicin sensitive	Rifampicin Sensitive	DS-TB
	Negative	Indeterminate	Therapy by clinical judgement
	Indeterminate	Indeterminate	Therapy by clinical judgement
	Invalid/no result/error	Indeterminate	Therapy by clinical judgement

Presumptive DR-TB in **low risk** category are

- Presumptive TB
- Children with presumptive TB
- TB in Diabetes Mellitus
- Presumptive TB with HIV positive

For any new case (i.e. without prior history of TB) found to be Rifampicin Resistant on Xpert, following are the recommendations *(TB MTR 2019)* -

- Elicit prior history of TB treatment. In some cases where the patient may not be aware of TB disease he/she (and family members) should be asked about any prolonged treatment the patient may have taken in the past, any treatment which caused orange discoloration of urine and also shown anti-TB drugs to confirm if the patient had taken them.
- Elicit history of contact with MDR/RR patient.
- In case the above are not elicited the patient should be **referred to the clinical management committee of DR-TB** for a detailed clinical and radiological assessment. The committee will take the decision for repeating Xpert (necessary steps are provided below) and the decision to initiate or defer the treatment in such cases.

Steps to be taken by the clinical management committee of DR-TB in low risk group for repeating Xpert (Re-examine – 2nd Xpert) -

Result of 1st XPERT	**Results 2nd XPERT**	**Final Results**	**Therapy**
Rifampicin Resistant	Rifampicin Resistant	Rifampicin Resistant	DR-TB
	Rifampicin Sensitive	Rifampicin Sensitive	DS-TB
	Indeterminate	MTB positive	DS-TB
	Invalid/no result/error	MTB positive	DS-TB
Invalid/no result/error	Rifampicin Resistant	-	Therapy by clinical judgement
	Rifampicin sensitive	Rifampicin Sensitive	DS-TB
	Negative	Negative	Other treatment
	Indeterminate	MTB positive, Indeterminate (Rif?)	DS-TB
	Invalid/no result/error	Invalid/no result/error	Therapy by clinical judgement
Indeterminate	Rifampicin Resistant	Rifampicin Resistant	DR-TB
	Rifampicin Sensitive	Rifampicin Sensitive	DS-TB
	Negative	Indeterminate	DS-TB
	Indeterminate	Indeterminate	DS-TB
	Invalid/no result/error	Indeterminate	DS-TB

Format for monitoring testing of presumptive MDR TB patients

Name of the Municipality:			**Quarter and Year:**		
Type of presumptive MDR/RR patients	Number eligible for DST (a)	Number Tested (b)	Percentage (a/b X100) (c)	Number diagnosed as MDR/RR	Number enrolled on treatment
Retreatment cases					
Sputum positive during follow up					
Contacts of MDR/RR patients					
TB-HIV					
Others					

4.7 PROCEDURES FOR SMEAR MICROSCOPY AND INTERPRETATION OF RESULTS

For all presumptive TB cases, smear diagnosis until NTP switches to U-DST for all presumptive TB by molecular diagnosis (figure 8) should be performed according to the following procedure:

Using the NTP laboratory form, the staff of the health facility sends the individual with presumptive TB for sputum examination to the laboratory of the nearest designated microscopy or diagnostic centre (DMC/DDC). In the DMC/DDC laboratory the patient receives sputum containers with instructions to provide sputum specimens, which are then subjected to sputum examination. The patient may be referred to the nearest DMC/DDC, or else the patient's sputum is collected and transported to the nearest DMC/DDC.

The number of specimens required for diagnosis of bacteriologically confirmed pulmonary TB is two, which are collected ***spot and spot on the same day, preferably in early morning, during the initial patient visit.***

One specimen positive out of the two is enough to declare a patient as bacteriologically confirmed TB by any methods – Smear Microscopy/GeneXpert

Guidelines for collecting sputum

It is important that the guidelines for sputum collection are followed. The clinician/health worker/laboratory technician (LT) should instruct the patient for proper sputum collection. If sputum is not collected in the correct manner and the patient has smear-positive pulmonary tuberculosis, the diagnosis may be missed, and the patient may continue to spread the infection to others. Results of sputum tests should be reported within a day.

The patient is given one wide-mouthed sputum container with Laboratory Serial Number written on its side. The person collecting the sputum demonstrates how to open and close the container, takes the patient to an open space away from other people, and demonstrates how to bring out sputum. The patient is instructed to wash or rinse their mouth with normal water to remove particles of food or betelnut, to inhale deeply 2–3 times with mouth open, cough out deeply from the chest, open the container and spit out the sputum into it, and then close the container.

To obtain good quality sputum specimens and to prevent contamination, health staff must perform certain tasks before, during and after sputum collection. The following are the details of the tasks to be performed.

1. Tasks performed before sputum collection

Before collecting the sputum specimen, the health worker should briefly explain to the patient the reasons for sputum collection. The laboratory form for sputum examination should be filled in completely by the clinician and given to the patient with instruction to go to the DMC. When sputum samples are collected or smear fixation done in a health facility, then the sputum samples/smears will be sent to the DMC along with the laboratory form. The results section, in the bottom half of the laboratory form is completed by the laboratory technician of the DMC after the sputum examinations.

2. Tasks performed during sputum collection

The person collecting the sputum specimen should adhere to the following guidelines:

- The person guiding the patient for specimen collection should stand behind and encourage him to cough and produce a good quality specimen. A specimen collected under supervision is likely to yield better results
- Whenever possible, sputum should be collected in an open place or well-ventilated room meant for this purpose
- Patients are usually more comfortable if they are separated from other persons at the time of sputum collection

- The patient should be given a sputum container with the laboratory serial number written on its side. When the sputum is being collected at a location other than the DMC, it will not be possible to give a laboratory serial number. In such cases, the patient's name is written on the side of the container
- The person collecting the specimen demonstrates how to open and close the container
- The patient is instructed to inhale deeply (2–3 times), cough out sputum from the chest, spit into the container and then close it
- The person collecting the specimen should make sure that no one stands in front of the patient who is trying to cough up sputum. Sputum should not be collected in closed rooms, toilets or poorly-ventilated rooms
- When a patient has only coughed up saliva or has not coughed up at least 2 ml of sputum, the patient should be encouraged to repeat the procedure in order to give a good (mucopurulent) specimen
- If the outside of the container is contaminated with sputum, the person collecting the specimen should wipe the container with disinfectant and destroy the material used to clean the container.

3. Tasks performed after sputum collection

   The person collecting the sputum specimens should follow the guidelines specified below:

- If the sputum specimens are to be sent immediately to the laboratory, the person should put the container into a special box meant for transport. If the sputum specimens are not being sent immediately to the laboratory, these should be stored at 2-8 degrees C (in a refrigerator) in the referring health facility. As far as possible the cold chain must be maintained for molecular and culture-based TB diagnosis.
- The person should wash their hands thoroughly with soap and water every time they handle specimens
- Patients should be told when to come back to receive the results of sputum examination.
- Alternatively, sputum results may be sent to the referring health facility by hand. The laboratory serial number should be clearly written on the side of the sputum container.

4.8 PROCEDURES FOR THE XPERT MTB/RIF TEST AND INTERPRETATION OF RESULTS

4.8.1 Sample collection and sample transport

Samples for the Xpert MTB/RIF assay can be collected at all CHCs in sputum cups used for smear microscopy and culture samples. One sputum specimen per patient should be collected. Patients should be instructed and supported in the collection of a good quality sputum specimen as described for the collection of smear microscopy samples above.

Transport to the nearest diagnostic centre offering Xpert MTB/RIF can be done using the sputum cups for sample collection. No cold chain is required if sputum samples are transported within 24 hours. Samples should be processed within three days following collection.

4.8.2 GeneXpert® MTB/RIF® Testing

The GeneXpert® MTB/RIF® assay provides the opportunity to identify RR-TB strains in a timely manner. The assay detects DNA sequences specific for *Mycobacterium tuberculosis* and rifampicin resistance (rpoB mutation) by polymerase chain reaction under 2 hours. It is based on the Cepheid GeneXpert® system, a platform for rapid and simple-to-use nucleic acid amplification tests (NAAT). As part of routine NTP procedures, the NTRL currently processes 156 samples each week on average (i.e. 26 samples daily).

Xpert® MTB/RIF® is performed on one sputum sample per patient following the manufacturer's instructions. In cases where only one of two sputum samples are positive by smear microscopy, the assay will be conducted on the SS+ sputum. Where both samples are SS+, Xpert® MTB/RIF® will be performed and the first ('spot')

sample. Results of the Xpert® MTB/RIF® assay should be reported back to health care facilities as soon as available initially using phone and later by sending the results to the health facilities for further communication with the patient using standard procedures. All results of examination will be informed to CHCs once the results are available.

Depending on the Xpert® MTB/RIF® test result, the following actions will take place:

- *MTB not detected*: Proceed to solid culture to confirm whether NTM. If still negative, then discard.
- *MTB detected:* Proceed with solid culture.
- *MTB and RR detected:* Proceed with solid culture and subsequently process for first-line and second-line DST once culture is positive. Second-line DST will also be conducted on all MTB-positive retreatment cases.
- *Test invalid:* Repeat testing from the sediment from the sample which has been stored as back up.

4.8.3 Interpretation of Xpert MTB/RIF results

The Xpert MTB/RIF assay provides diagnostic information with respect to the existence of the TB as well as the existence of resistance to rifampicin. Test results will be reported by the laboratory technician according to the table below.

Table 1: Classification of Xpert MTB/RIF test results

T = MTB detected; rifampicin resistance not detected

RR = MTB detected; rifampicin resistance detected

TI = MTB detected, rifampicin resistance indeterminate

N = MTB not detected

I = invalid / no result / error

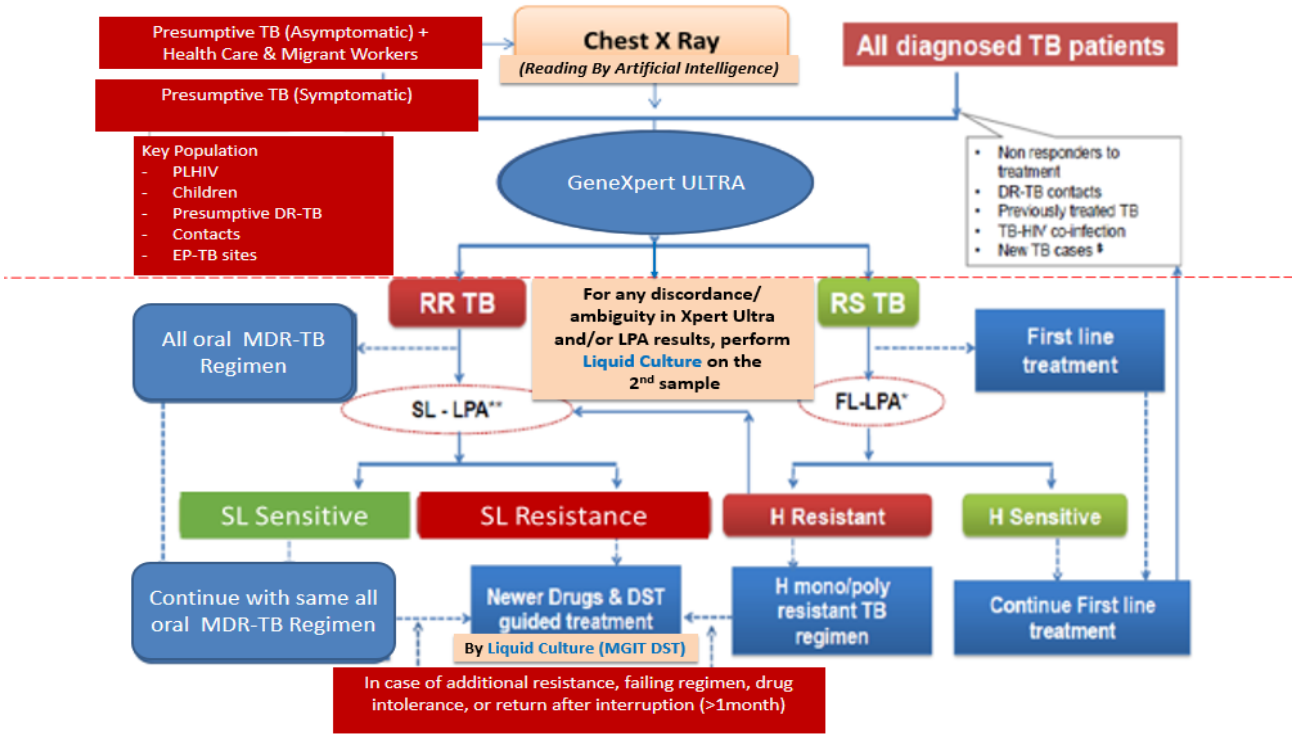
Whenever the test result is reported as "TI" or "I", the test should be repeated until a definite outcome can be observed.

All retreatment or failure cases with patients with a “T” results should also provide an additional sputum specimen for LPA testing to exclude INH resistance.

4.9 MOVING TOWARDS UNIVERSAL-DST

According to current WHO recommendations, molecular tests should be used as the initial screening test for tuberculosis.[13] The NTP expects that use of smear-microscopy as the initial diagnostic test will gradually be phased out. The following U-DST diagnostic algorithm for all presumptive TB cases is proposed:

Figure 5: Diagnostic algorithm in areas with universal Xpert MTB/RIF access (Universal DST of all Presumptive -TB cases by March 2021)



Key points on the Diagnostic Algorithm (U-DST for all presumptive TB cases):

- Chest X-ray (preferably with artificial intelligence to read the CXRs) should be used as the initial screening test for tuberculosis. Vulnerability assessment tool should be used to identify the risk groups for TB.
- Molecular tests should be used as the initial diagnostic test for tuberculosis.
- For any discordance/ ambiguity in Xpert Ultra results and/ or LPA results, perform Liquid Culture (MGIT) on the 2nd sample. Also, for any 2nd line drug resistance, failing regimen, drug intolerance, or return after interruption (>1 month) perform extended panel of drug testing by Liquid Culture (MGIT).
- The use of smear-microscopy as the initial diagnostic test could be gradually be phased out.

4.10 DIAGNOSIS OF EXTRAPULMONARY TUBERCULOSIS

Extrapulmonary TB diagnosis should be supported with relevant investigations and bacteriological examination. Positive contact history of TB is an indication for suspicion of TB when a patient presents with symptoms. Sputum is negative in most cases of extrapulmonary TB. Symptoms and signs of extrapulmonary tuberculosis usually depend on the site involved. The following table shows the common

[13] WHO RECOMMENDATIONS ON THE USE OF XPERT MTB/RIF, WHO 2016, http://www.who.int/tb/areas-of-work/laboratory/policy_statements/en/

signs and symptoms of EPTB. Extrapulmonary TB along with pulmonary lesions is classified as Pulmonary TB for reporting purposes.

Common symptoms of EPTB

1) Fever (found in up to 80% of all patients)
2) Weight loss
3) Night sweats
4) Loss of appetite

Table 2: Symptoms of Extrapulmonary TB by site of disease

Sites	**Symptoms and signs**
Pleural	1. Pleuritic chest pain 2. Shortness of breath 3. Effusions are usually unilateral
Lymphatic	1. Most common site of extra-pulmonary disease; 2. Usually presents as a painless swelling, most commonly in the neck. Any nodes can be involved; 3. Adenopathy usually occurs in a single lymph node or chain.
Central Nervous System	1. Headache, altered mental status, nausea and vomiting; 2. Meningeal signs, with characteristic neck rigidity; 3. Paralysis of the oculomotor nerve, leading to strabismus and/or ptosis (drooping/ floppy eyelids) and sometimes convulsions.
Bone and Joint	1) Most commonly effects the spine and the weight-bearing joints; 2) Insidious onset of joint pain and swelling; 3) Involvement of the cervical vertebrae may signal its presence by pain in the neck and shoulders. It may lead to rigidity of the neck, a cervical cold abscess behind the sterno-mastoid muscle, and more rarely neurological signs leading to progressive tetraplegia. Involvement of the dorsal vertebrae is indicated by localized back pain, deformity of the spine, and in extreme cases an angulated kyphosis (gibbus): the chief risk is spinal cord compression and paraplegia.
Genitourinary	1. Flank pain 2. Haematuria 3. Recurrent urinary tract infections 4. Pyuria
Abdominal	1. Abdominal pain and swelling
	2. Abdominal tenderness 3. Ascites
Disseminated	1. Clinical signs: general deterioration, high fever and dyspnoea. 2. Other organs may be affected including: pleural effusion, digestive problems, hepatosplenomegaly and sometimes meningeal signs.

5 PREVENTION OF TB

5.1 MANAGEMENT OF LATENT TUBERCULOSIS INFECTION (LTBI)

5.1.1 Background

Latent tuberculosis infection (LTBI) is defined as a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB. There is no gold standard test for LTBI. The NTP Manual considers the probability of progression to active TB disease in a specific risk group, the epidemiology and burden of TB, the availability of resources and the likelihood of a broad public health impact, based on recommendations published in recently updated WHO guidelines on LTBI.[14]

5.1.2 At-risk populations that should receive LTBI treatment

Based on recommendations published in the recently updated WHO guidelines on LTBI, the NTP considers the following to be at-risk populations that should receive LTBI treatment:

1. Adults, adolescents, children and infants living with HIV
   - Adults and adolescents living with HIV who are unlikely to have active TB should receive preventive treatment of TB as part of a comprehensive package of HIV care. Treatment should be given to these individuals irrespective of the degree of immunosuppression and also to those on antiretroviral treatment (ART), those who have previously been treated for TB and pregnant women.
   - Infants aged <12 months living with HIV who are in contact with a case of TB and are investigated for TB should receive preventive treatment of TB if the investigation shows no TB disease.
   - Children aged ≥12 months living with HIV who are considered unlikely to have TB disease on the basis of screening for symptoms and who have no contact with a case of TB should be offered preventive treatment of TB as part of a comprehensive package of HIV prevention and care.

2. HIV-negative household contacts
   - *HIV-negative children aged <5 years* who are household contacts of people with bacteriologically confirmed pulmonary TB and who are found not to have active TB on clinical evaluation should be given TB preventive treatment.
   - *Children aged ≥5 years, adolescents and adults* who are household contacts of people with bacteriologically confirmed pulmonary TB who are found not to have active TB by clinical evaluation may be given TB preventive treatment.

The NTP has developed a vulnerability assessment tool to help identify people who are at risk for progressing to active TB with the concept of treating other at-risk target populations in a shorter timeframe in order to reach the desired level of incidence decline as per the end TB strategy shown on the following page.

3. Other HIV-negative at-risk groups
   - Systematic testing for LTBI is not recommended and treatment for LTBI may be considered on a 'case to case basis' for the following HIV-negative at-risk groups - uncontrolled diabetes, people with harmful alcohol use, tobacco smokers and underweight (severely malnourished in mothers and adults, stunting in children). A close monitoring of such risk groups according to the vulnerability assessment tool is recommended.

[14] Latent tuberculosis infection: updated and consolidated guidelines for programmatic management, WHO/CDS/TB/2018.4

- Patients on anti-TNF (tumour necrosis factor) treatment, patients receiving dialysis, patients preparing for an organ or haematological transplant and patients with silicosis should be *systematically tested* and treated for LTBI.

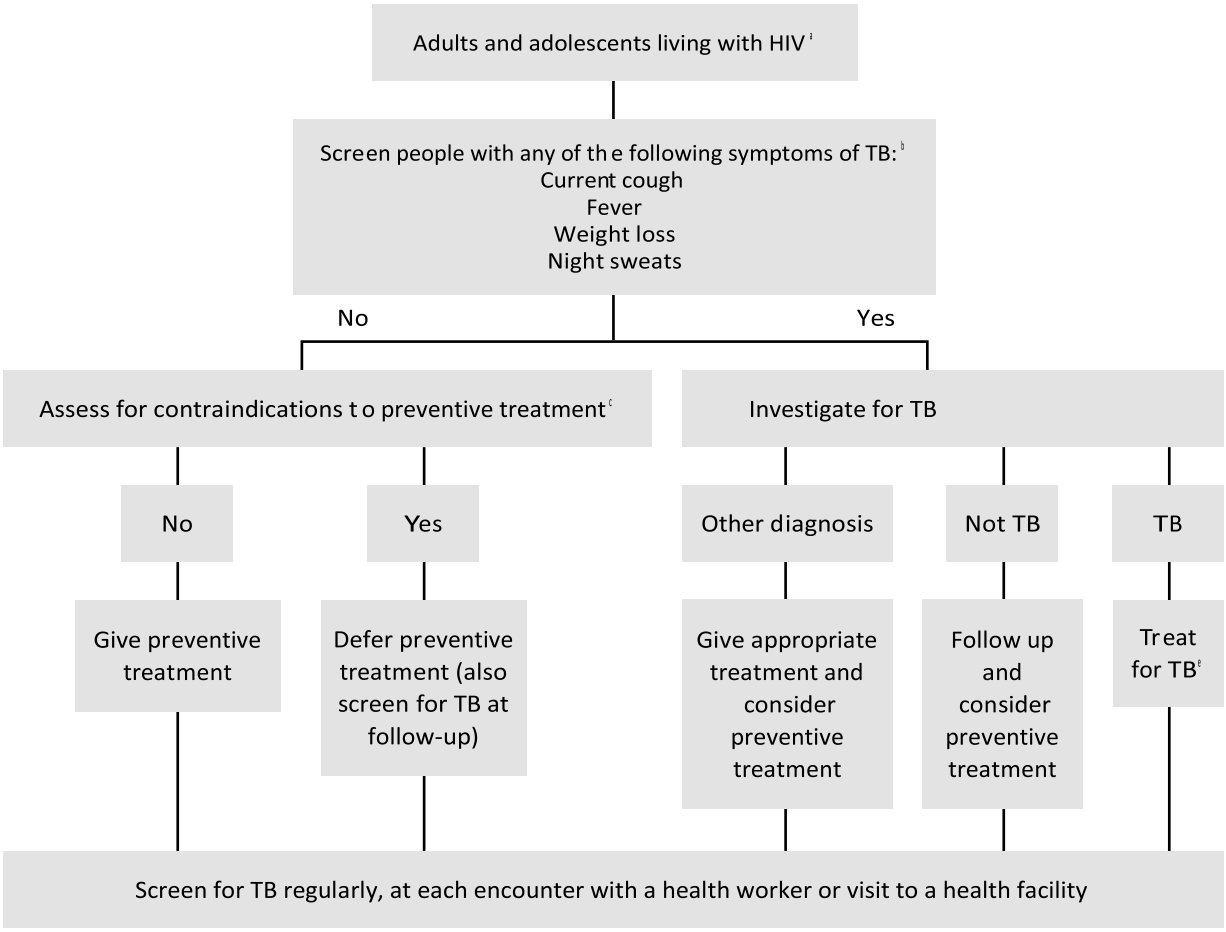
5.1.3 Algorithms for ruling out active tuberculosis disease

5.1.3.1 *Adults and adolescents with HIV*

Active TB disease must be excluded before initiating preventive treatment.

The algorithm for TB screening in adults and adolescents living with HIV shown in the figure below is based on recommendations published in the recently updated WHO guidelines on LTBI.

Figure 6: Algorithm for screening adults and adolescents living with HIV for TB



[a] Every adult and adolescent should be evaluated for eligibility to receive ART. Infection control measures should be prioritized to reduce *M. tuberculosis* transmission in all settings in which care is provided. [b] Chest radiography can be done if available, particularly for people living with HIV on ART, but is not required to classify patients into TB and non-TB groups.
Contraindications include: active hepatitis (acute or chronic), regular and heavy alcohol consumption and symptoms of peripheral neuropathy. History of TB and current pregnancy should not be contraindications for starting preventive treatment.
[d] Xpert MTB/RIF should be used as the initial diagnostic test for TB.

5.1.3.2 *Children living with HIV*

Infants and children living with HIV who have poor weight gain, fever or current cough or who have a history of contact with a case of TB should be evaluated for TB and other diseases that cause such symptoms. If the evaluation shows no TB, these children should be offered preventive treatment, regardless of their age.

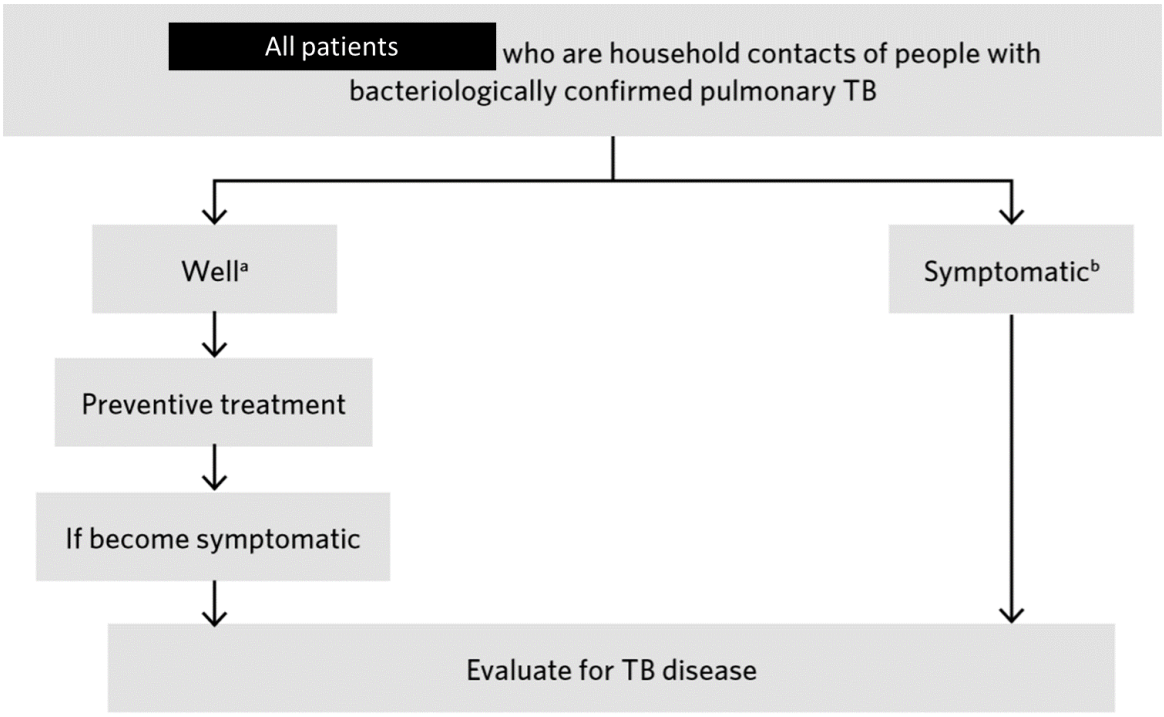
Poor weight gain is defined as reported weight loss, very low weight-for-age (< –3 z-score), underweight (weight for-age < –2 z-score), confirmed weight loss (> 5% since the last visit or growth curve flattening)

Children and infants < 1 year of age should be given preventive treatment only if they have a history of household contact with a TB case and active TB has been excluded in investigations.

5.1.3.3 *HIV-negative household contacts of a person with pulmonary TB*

On reviewing the evidence and considering the field conditions in Timor-Leste, and high TB incidence rate (498/100,000), the country consultation process during the guidelines revision workshop in May 2019 concluded that the implementation of a simple algorithm for ruling out active TB in household contacts before preventive treatment initiation would be feasible in Timor-Leste. The algorithm can be used by health workers at peripheral level. Research on symptom-based screening of children's TB contacts indicates that this contact management strategy is safe and more feasible in resource-limited settings than contact screening based on diagnoses. The algorithm shown below will therefore be used for HIV-negative household contacts of persons with pulmonary TB of all ages.

Figure 7: Algorithm for screening HIV-negative household contacts of a person with pulmonary TB



[a] Patients must be free of any TB and non-TB related symptoms to be considered well. [b] The most common TB-related symptoms are persistence of: cough, fever, weight loss and night sweats.

5.1.4 **Treatment for latent tuberculosis infection**

Based on recommendations published in the recently updated WHO guidelines on LTBI, the NTP will use the following drug regimes for at-risk populations that should receive LTBI treatment:

5.1.4.1 ***People living with HIV***

- Weekly rifapentine plus isoniazid for 3 months (3HP)

A new systematic review was conducted to compare the effectiveness of a 3-month weekly regimen of rifapentine plus isoniazid with that of isoniazid monotherapy. The review covered 4 RCTs, of which 2 RCTs involved adults with HIV from South Africa, Peru and in a number of countries with a low incidence of TB. No significant difference was found in the incidence of active TB between participants (adults with HIV infection, adults without HIV infection and children) given a 3-month weekly regimen of rifapentine plus isoniazid and 6 or 9 months of isoniazid monotherapy. Furthermore, the risk for hepatotoxicity was significantly lower with the 3-month weekly regimen of rifapentine plus isoniazid in adults with HIV.

5.1.4.2 ***HIV-negative household contacts of a person with pulmonary TB***

- Weekly rifapentine plus isoniazid for 3 months (3HP) for children above 2 years

This recommendation is based on recommendations published in the recently updated WHO guidelines. The advantage of 3HP is minimum number of doses (12) among other regimens hence higher acceptability, well-tolerated, high treatment completion rate and higher efficacy than other INH and INH-Rifampicin combined regimens. 3HP would likely be most suitable in Timor-Leste settings where the need of preventive treatment coverage and its completion is relatively higher than other regions.

It is crucial to strengthen HH contact investigations in contacts above 2 years by using the following regimen:

- Weekly rifapentine plus isoniazid for 3 months (3HP) for children above 2 years. In case, rifapentine is not available, daily rifampicin plus isoniazid for 3 months (3RH) should be provided

For children contacts below 2 years, daily rifampicin plus isoniazid for 3 months (3RH) should be provided. This regimen is based on recommendations published in the recently updated WHO guidelines indicating that the efficacy and the safety profile of 3–4 months' daily rifampicin plus isoniazid were similar to those of 6 months' isoniazid.

For adult contacts 3HP is recommended considering the ease of administration (once weekly, 12 doses instead of daily 90 doses of 3RH). In the long term 3HP (1 HP when it is formally recommended by WHO) may be the regimen to aim for considering treatment duration.

The shorter treatment duration is expected to facilitate the implementation of LTBI treatment in the country-specific conditions in Timor-Leste.

5.1.4.3 *Recommended dosages of drugs for the treatment of LTBI*

The recommended dosages of drugs for the treatment of LTBI are summarized in the table below.

Table 3: Recommended dosages of drugs for the treatment of LTBI

Drug regimen	Dose per kg body weight	Maximum dose
Isoniazid alone, daily	Adults, 5 mg Children, 10 mg (range, 7–15 mg)	300 mg
Daily rifampicin alone for 3–4 months	Adults, 10 mg Children, 15 mg (range, 10–20 mg)	600 mg
Weekly rifapentine plus isoniazid for 3 months (12 doses)	Individuals aged ≥ 12 years: Isoniazid: 15 mg Individuals aged 2–11 years: isoniazid: 25 mg Rifapentine: 10.0–14.0 kg = 300 mg 14.1–25.0 kg = 450 mg 25.1–32.0 kg = 600 mg 32.1–50.0 kg = 750 mg > 50 kg = 900 mg	Isoniazid, 900 mg Rifapentine, 900 mg
Daily isoniazid plus rifampicin for 3 months	Isoniazid: Adults, 5 mg Children, 10 mg (range, 7–15 mg) Rifampicin Adults, 10 mg Children, 15 mg (range, 10–20 mg)	Isoniazid, 300 mg Rifampicin, 600 mg

5.2 BCG VACCINATION

Bacille Calmette-Guérin (BCG) is a live attenuated vaccine derived from *Mycobacterium bovis*. In highly TB-endemic settings such as Timor-Leste, neonatal BCG vaccination provides substantial protection against the more severe types of disseminated TB, such as miliary TB and tuberculous meningitis, to which infants and young children are particularly susceptible. The NTP therefore recommends that:

- a single dose of BCG vaccine should be given to all infants as soon as possible after birth
- if BCG is given more than six weeks after birth, it should be evaluated whether the child had close contact to an active case of TB; if there is a contact history, the child should receive 6 months of IPT first, and be given BCG thereafter; if there is no contact history, the child should be vaccinated immediately
- in children who have not been vaccinated as infants, BCG should be given as a single dose up to 5 years of age

The provision of BCG to neonates of mothers with a recent diagnosis of active TB depends on the treatment history. If a pregnant woman with TB has been on treatment for TB for several weeks before delivery, it is less likely that the baby will become infected. The risk is highest if a mother is diagnosed at the time of delivery or shortly thereafter. The NTP therefore recommends that:

- **Neonates born to mothers with confirmed TB whose treatment was started less than two months before delivery should not receive BCG at birth. They should be assessed for signs of active disease. If asymptomatic, they should receive TB preventive treatment (TPT) for 3 Months (3RH). BCG should be given after completion of TPT.**

- **Asymptomatic neonates born to mothers with confirmed TB whose treatment was started more than two months before delivery can receive BCG at birth.**

There is no evidence that revaccination with BCG affords any additional protection, and revaccination is therefore not recommended.

5.2.1 BCG and HIV

BCG vaccine should not be used in children who are known to be HIV-positive because of the increased risk, reported from some settings, of severe and often fatal disseminated BCG disease. However, HIV infection cannot be reliably determined at birth, and there is a risk that BCG may be given to HIV-positive infants, e.g., those who experienced mother-to-child transmission from an HIV-positive mother. Nevertheless, since infants who are HIV-exposed but uninfected will be at increased risk of disseminated TB disease if not vaccinated with BCG, the NTP recommends that BCG should be given to infants who are born to HIV-positive mothers but who do not have any symptoms suggestive of HIV infection.

The diagnosis of **BCG disease** is difficult, and the treatment is specialized: *M. bovis* is inherently resistant to pyrazinamide and thus all forms of BCG disease must be treated using higher doses of other first-line TB medications. For example, some experts recommend a daily isoniazid dose of up to 20 mg/kg (maximum 300 mg) and a daily rifampicin dose of up to 20 mg/kg (maximum 600 mg) for at least 9 months of therapy, as well as continuous monitoring for drug toxicity and response to therapy. Children living with HIV and suspected of having BCG disease should be referred to a referral hospital for management.

5.3 INFECTION CONTROL

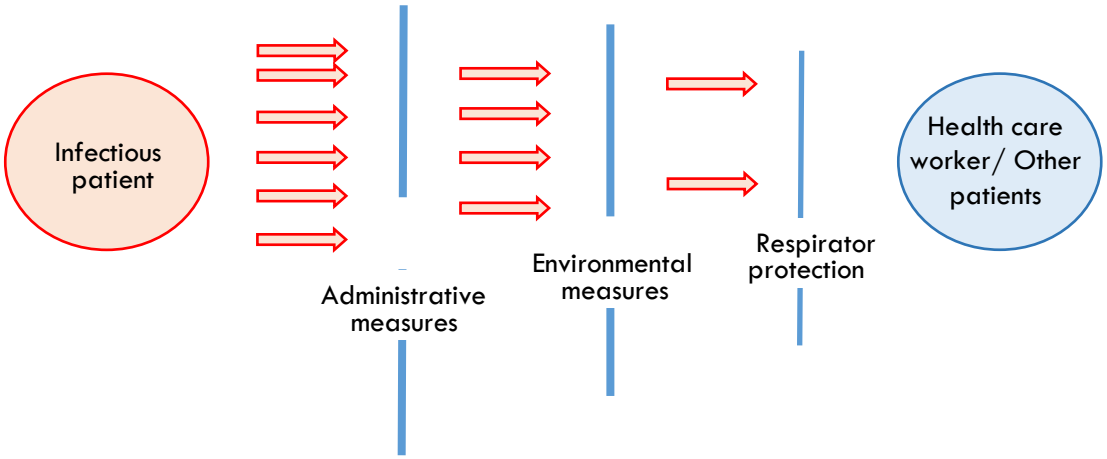
Worldwide, tuberculosis (TB) continues to be the most important cause of death from a single infectious microorganism.[15] Although recent decades have witnessed increased efforts in the fight to end TB, fundamental gaps are hampering these efforts, particularly in resource-constrained settings and in settings with a high burden of disease. The World Health Organization (WHO) estimates that close to 54 million TB deaths were averted between 2000 and 2017 because of improved disease prevention and management, and service delivery; nevertheless, up to 10 million people continue to fall ill with TB every year. One of the targets of the Sustainable Development Goals - SDG 2 for the period 2015–2030 is to end the global TB epidemic. In line with this target, the WHO End TB Strategy, approved by the World Health Assembly in 2014, calls for a 90% reduction in TB deaths and an 80% decrease in the TB incidence rate by 2030. The strategy emphasises the need for prevention across all approaches, including infection prevention and control (IPC) in health care services and other settings where the risk of *Mycobacterium tuberculosis* transmission is high. IPC practices are vital to reduce the risk of *M. tuberculosis* transmission, by reducing the concentration of infectious droplet nuclei in the air and the exposure of susceptible individuals to such aerosols.[13]

Infection prevention and control (IPC) is a **scientific approach** and **practical solution** designed **to prevent harm** caused by infection to hospitalized patients and health care providers. A three-level hierarchy of TB IPC comprising **administrative controls**, **environmental controls and respiratory protection** has been shown to reduce and prevent the risk of transmission and exposure to *M. tuberculosis*. The foundation of infection control is early and rapid diagnosis, and proper management of TB patients.

[15] WHO guidelines on tuberculosis infection prevention and control, 2019 update, Geneva: World Health Organization; 2019. License: CC BY-NC-SA 3.0 IGO.

5.3.1 General principles of infection control

The three-level hierarchy of infection control measures, operating at different points in the transmission process, with all being interdependent:



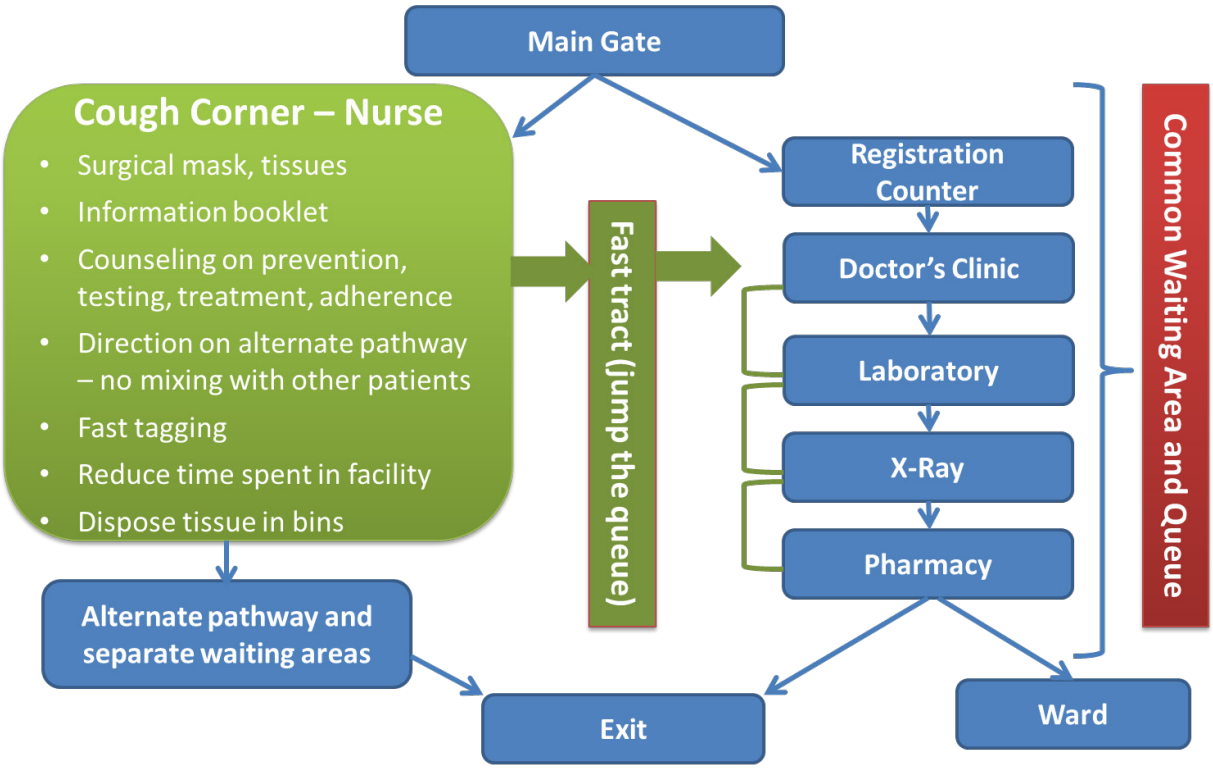
5.3.2 Administrative (managerial) controls: cough corners at OPDs

Administrative controls should be implemented as a priority because they have been shown to reduce transmission of TB in health-care facilities. Such controls are a vital part of sound infection control practices, which require people with TB symptoms to be promptly identified, separated and treated. The NTP has recommended the following strategy for fast tracking of chest symptomatic and infection control at high OPD load health facilities (1 National Hospital and 5 Referral Hospitals):

- All clients visiting hospital will be screened at cough corners by a **trained hospital designated staff** for TB symptoms and those identified presumptive TB patients would be fast tracked to the Microscopic Centre/ GeneXpert for diagnosis *(Triaging of the cough symptomatic)*
- The identified patient (presumptive TB patient) will be made aware of the basics of tuberculosis (symptoms and free diagnosis and treatment services) using the **IEC materials**
- The designated staff will **facilitate collection** of "spot-spot sample" or "front loading" sample in the Referral Hospitals + HNGV
- **CXRs for Presumptive TB Patients (PTBPs)** will be done for all or sputum negative at the hospital X-ray facility.
- The designated staff together with the ward nursing staff will **visit in-patients;** and staff will collect and transport samples from identified presumptive TB patients to DMC.
- The **designated staff will visit all departments** and advocate with doctors to refer PTBPs for diagnosis.
- All identified **TB patients will be linked to treatment** services under NTP

The strategy is summarized in the following diagram:

Figure 8: Cough Corner at Health Facility OPD – For Infection Control and Active Case Finding



Role of Administrative Measures: Administrative measures play a very important role in sustained efforts to prevent and control infection transmission by:

- Formation of multi-disciplinary Institutional IPC Committee as the first step
- Allocation of adequate budget to carry out IPC activity
- Ensuring uninterrupted supply of PPEs and other logistics required for IPC activities
- Preparation of a written manual with clear roles and responsibilities to implement IPC activities in the health care institution

Summary of recommendations from 2019 WHO guidelines on tuberculosis infection prevention and control:

1. **Triage of people with TB signs and symptoms,** or with TB disease, is recommended to reduce *M. tuberculosis* transmission to health workers (including community health workers), persons attending health care facilities or other persons in settings with a high risk of transmission. Triage is a simple and preliminary system of interventions for identifying people with TB signs or symptoms among those seeking medical attention in health care facilities. Triage is used to fast-track TB diagnosis and facilitate further separation or other precautions, when necessary, to minimise transmission from infectious patients.
2. Respiratory separation / isolation of people with presumed or demonstrated infectious TB is recommended to reduce *M. tuberculosis* transmission to health workers or other persons attending health care facilities.
3. Prompt initiation of effective TB treatment of people with TB disease is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.
4. Respiratory hygiene (including **cough etiquette**) in people with presumed or confirmed TB is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care

facilities or other persons in settings with a high risk of transmission. Cough etiquette is a series of actions to take if you are coughing or sneezing, which are designed to reduce the spread of respiratory illness to others. Guidance on implementation arrangements:

a. Provide a mask to those who are coughing
b. Designate an area in the waiting room for patients with respiratory symptoms or encourage them to sit at least three feet away from others
c. Consider isolating known TB patients and patients with other respiratory infections from staff during triage

5.3.3 Environmental controls

Environmental controls include methods to reduce the concentration of infectious respiratory aerosols (i.e. droplet nuclei) in the air, and methods to control the direction of infectious air. Such measures include:

- Use of ventilation systems, including natural, mixed-mode, mechanical ventilation and recirculated air through high-efficiency particulate air [HEPA] filters are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.
- Use upper-room germicidal ultraviolet irradiation (GUV) fixtures, at least when adequate ventilation cannot be achieved
- Identification of high-risk areas

Adequate ventilation in health-care facilities is essential for preventing transmission of airborne infections and is strongly recommended for controlling spread of TB. The choice of ventilation system will be based on assessment of the facility and informed by local programmatic, climatic and socioeconomic conditions. Any ventilation system must be monitored and maintained on a regular schedule.
Kind of ventilation systems:

- Natural
- Mechanical

Natural Ventilation

Created by the use of external airflows generated by natural forces such as:

- Wind
- Differences in temperature (stack)

Naturally ventilated rooms can achieve very high ventilation rates (Air Changes per Hour or ACH) under ideal conditions but natural ventilation is unpredictable. ACH is a measure of how many times the air within a defined space (normally a room or house) is replaced during a given time period. A well-ventilated spacious ward open to cross ventilation and > 6 ACH.

Maximise Natural Ventilation *(More appropriate for the context of Timor-Leste)*

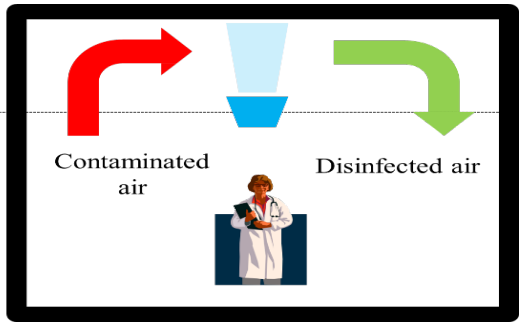
- Openings on opposite walls (cross ventilation)
- Openings are unrestricted (stay open)
- 10% of floor space should have openable window-area on each wall
- Use upper levels of the building
- Building and openings are oriented to use the prevailing wind, without obstruction by other nearby buildings

Mechanical ventilation

Well-designed, maintained and operated fans (mixed-mode ventilation) can help to obtain adequate dilution when natural ventilation alone cannot provide sufficient ventilation rates. In some settings, mechanical ventilation (with or without climate control) will be needed. This may be the case, for example, where natural or mixed-mode ventilation systems cannot be implemented effectively, or where such systems are inadequate given local conditions (e.g. building structure, climate, regulations, culture, cost and outdoor air quality).

Priority should be given to achieving adequate ACH using ventilation systems. However, in some settings it is not possible to achieve adequate ventilation; for example, because of climatic changes (e.g. in winter or during the night) or building structure, or because transmission of TB would pose a high risk of morbidity and mortality (e.g. in MDR-TB wards). In such cases, a complementary option is to use an upper room or shielded germicidal ultraviolet irradiation (GUV) devices. This environmental control does not provide fresh air or directional airflow.

HIGH RISK SETTING
TB Wards/
TB Contacts

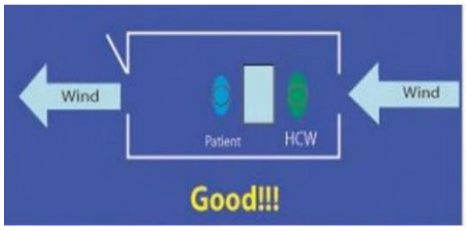


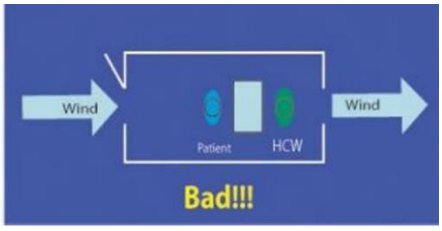
– TB Consultation Room; NTRL/ DR-Treatment Centre; Household with

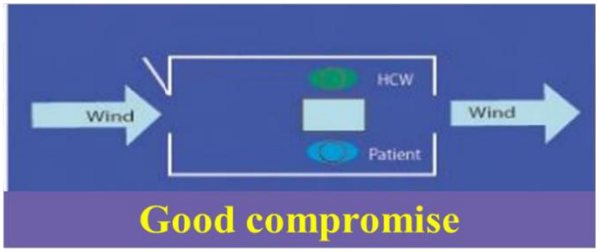
Infection control for TB consultation rooms

The rooms for TB consultation, counselling and health education should be arranged according to sound infection control principles:

- Both windows and doors should be open all the time.
- Direct sunlight gets into the room easily
- A stand fan ensures an airflow direction toward the opened window
- Patient and health staff sit in front of each other across the airflow
- Exhaust fan to extract the air
- One patient at a time should be received in the room
- The patient should wear a surgical mask
- Staff and family should wear N95 mask
- Appropriate cough hygiene must be observed by the patient







DR-TB Patient isolation room

The DR-TB isolation room should have large open windows allowing direct sunlight into the room, a closing door, a stand fan to establish an air flow direction toward the window, and preferably a GUV light installation with a shield to protect the eyes from direct exposure to it. The UV light should be turned on for 15 to 20 minutes every 12 hours (in the morning and evening), preferably with the patients not being in the room. An exhaust fan may help to extract the air from the room. The DR-TB room should be isolated from the other departments, especially the out-patient clinic, the HIV ward, the paediatric ward and other high-risk group departments.

DR-TB infectious patients in the isolation room must wear a surgical mask at all times. If no masks are available, patients should use a handkerchief or a piece of cloth to cover their mouth when talking, coughing, sneezing or speaking. Patients should refrain from spitting on the floor but should spit in a sputum cup that will be later burned.

Health workers must wear high filtration (N95) masks, fitted correctly, every time they meet DR-TB patients or enter the DR-TB ward.

Instructions on how to wear masks should be posted at all entrances to the DR-TB area for staff, patients and visitors

DR-TB patients should not receive many visitors and avoid contact with small children until sputum smear or culture conversion has occurred. Good infection control measures for visitors and small children include:

- Meeting in a room with good ventilation or meeting outdoors
- Patient wearing surgical mask and visitor wearing high filtration (N95) mask and room disinfected by appropriate use of GUV light

5.3.4 Respiratory Protection

Particulate respirators, within the framework of a respiratory protection program, are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. The use of respiratory protection control is the third level in the hierarchy of protections. It consists of the use of personal protective equipment in situations where there is a high risk of exposure to *M. tuberculosis*.

Personal respiratory protection aims to protect health workers in areas where the concentration of droplet nuclei cannot be adequately reduced by administrative and environmental controls. Health workers should use high filtration masks (N95) or "respirators" to protect them against the inhalation of airborne infectious droplets. Patients should wear a surgical mask to reduce the spread of droplets.

Respirators vs Surgical Masks

Respirators	Surgical masks
• Designed to filter out droplet nuclei from air being inhaled by health-care workers and other individuals.	• Designed to stop droplet nuclei from being spread (exhaled) by patients. • Should NOT be worn by health-care workers
• Should properly fit different face sizes and features.	

• Should NOT be worn by patients	

Personal respiratory protection on alone are insufficient to prevent TB transmission. They will not be worn continuously and are likely not to be in use when unsuspected TB cases are encountered. Administrative and environmental controls are more important.

It is important to conduct periodic surveillance for TB disease among health workers. Always follow recommended infection control procedures in your work in the health facility. Be aware of possible signs and symptoms of TB in yourself. If one or more of these develop, report promptly for assessment and care. If you are diagnosed with TB, start treatment promptly and adhere to treatment until it is completed.

5.3.5 Patient and patient household counselling regarding airborne precautions

Role of the TB patient in infection control:

- The patient should wear a surgical mask at all times when in contact with other people.
- Strict coughing hygiene must be observed by the patient, inside as well as outside the house.
- Known TB Patients are encouraged to spend little time in closed rooms, crowded places and public transport until smear/culture conversion.
- Known TB patients are advised to use disposable tissue paper to spit the sputum and dispose of this paper by burying or burning at the end of the day OR collect the sputum in sputum pots with lime/bleach and dispose of by burying
- TB patient to stop smoking and minimise intake of alcohol

Role of TB patient household in infection control:

- TB is completely curable with a full course of treatment – Family members should treat TB patients with empathy. Even though it spreads by airborne droplets, the risk of transmission can be minimized with adequate care.
- Avoid confining known TB patients in a closed room.
- Provide a nutritious diet to the patient. Motivate/remind the TB patient to take anti-TB medications.
- MDR-TB patients may take longer time to convert to smear/culture negative. Take adequate precautions till they convert to smear/culture negative.

5.4 BIO-MEDICAL WASTE MANAGEMENT

Waste is anything that is to be discarded. In laboratories, decontamination of wastes and their ultimate disposal are closely interrelated. In terms of daily use, few if any contaminated materials will require actual removal from the laboratory or destruction. Most glassware, instruments and laboratory clothing will be reused or recycled. The overriding principle is that all infectious materials should be decontaminated, autoclaved or incinerated within the laboratory.

The principal questions to be asked before discharge of any objects or materials from laboratories that deal with potentially infectious microorganisms or animal tissues are:

1. Have the objects or materials been effectively decontaminated or disinfected by an approved procedure?

2. If not, have they been packaged in an approved manner for immediate on-site incineration or transfer to another facility with incineration capacity?

3. Does the disposal of the decontaminated objects or materials involve any additional potential hazards, biological or otherwise, to those who carry out the immediate disposal procedures or who might come into contact with discarded items outside the facility?

An identification and separation system for infectious materials and their containers should be adopted. National and international regulations must be followed. Categories should include:

1. Non-contaminated (non-infectious) waste that can be reused or recycled or disposed of as general, "household" waste

2. Contaminated (infectious) "sharps" – hypodermic needles, scalpels, knives and broken glass; these should always be collected in puncture-proof containers fitted with covers and treated as infectious

3. Contaminated material for decontamination by autoclaving and thereafter washing and reuse or recycling

4. Contaminated material for autoclaving and disposal

5. Contaminated material for direct incineration.

Infected material should not leave the laboratory except when it has been properly packed for transport to another laboratory. All pathological material, smears, cultures and containers should at least be disinfected and preferably sterilized before disposal or re-use. Sterilization means the complete destruction of all organisms, while disinfection implies the destruction of organisms causing disease. Sterilization is usually accomplished by heat and disinfection by treatment with chemicals.

- **Disinfectants**

The time necessary for successful killing action of disinfectants depends on the population of organisms to be killed, the concentration used, the duration of contact and the presence of organic debris.

The proprietary disinfectants suitable for use in tuberculosis laboratories are those containing phenols, hypochlorites, alcohols, formaldehydes, iodophors or glutaraldehyde. These are usually selected according to the material to be disinfected. Sweet-smelling "antiseptics" should not be used. It is incorrect to assume that a disinfectant which has general usefulness against other microorganisms is effective against tubercle bacilli. A number of commercially available disinfectants have no or little mycobactericidal activity, while quaternary ammonium compounds are not effective at the recommended concentrations.

Disinfectant solutions should be prepared fresh each day and should not be stored in diluted form because their activity will diminish.

Phenol should be used at a concentration of 2% to 5% and contact time should be 15-30 minutes, depending on the type and volume of material to be disinfected. Phenol is useful in soaked paper towels to cover working surfaces. This minimizes spatter and aerosol formation in the event of spilling.

Hypochlorite should be used at concentrations between 1% and 5%, with a contact time of 15-30 minutes, depending on the type and volume of material to be disinfected. Hypochlorite solutions (5%) are useful for the disinfection of material containing organic debris because of their digesting action.

Glutaraldehyde does not require dilution but an activator (provided separately by the manufacturer) must be added. Glutaraldehyde is usually supplied as a 2% solution, while the activator is a bicarbonate compound. Glutaraldehyde is useful for decontaminating bench surfaces and glassware. The activated solution should be used within two weeks and discarded if turbid.

Alcohol usually 70% ethanol (methylated spirits) or propanol is used in alcohol- sands baths and for decontaminating benches and surfaces. It should also be used instead of water to balance centrifuge tubes.

When hands become contaminated, a rinse with 70% isopropyl alcohol followed by thorough washing with soap and water is effective.

Iodophor preparations should be used at concentrations of 3% to 5% and contact time should be 15-30 minutes, depending on the type and volume of material to be disinfected. Iodophors are useful for mopping up spills and for handwashing.

All of the above disinfectants are toxic and undue exposure may result in respiratory distress, skin rashes or conjunctivitis. However, used normally and according to the manufacturers' instructions, they are safe and effective.

- **Discarding contaminated laboratory supplies**

A container with appropriate disinfectant (see paragraph on disinfectants) should be present in the BSC into which used, contaminated pipettes, loops and grinding vessels should be placed. The container should be deep enough to ensure that discarded items are completely covered. Used pipettes, wire loops etc. should be soaked for two hours after which they can be washed, sterilized and re-used.

In the immediate proximity of the BSC there should be stainless steel buckets with lids, ready to receive discarded specimen containers and tubes with bacterial suspensions.

Contaminated fluids should not be poured down drains but discarded into autoclavable containers.

Glassware should be substituted with plastic whenever possible. Broken glassware should be removed by a brush and dustpan, tongs or forceps and decontaminated in an appropriate disinfectant before disposal.

- ***Sputum containers***

Plastic sputum containers should be disposed of by incineration. Used glass sputum containers can be recycled after boiling for 20 minutes, or preferably autoclaving at 121°C and thorough washing.

- ***Applicator sticks, pipettes, wire loops***

Wooden applicators and paper should be disposed of by incineration. Contaminated or used pipettes and wire loops should be soaked for two hours in a bactericidal specific solution (see paragraph on disinfectants), washed and sterilized before re-use. Positive slides should be broken and burnt/buried to prevent their re-use

- **Autoclaving**

Autoclaving is the optimal initial sterilization procedure and staff should be carefully instructed in the correct procedure. Ideally, the autoclave should be inside the tuberculosis laboratory to prevent contaminated material from being discarded or washed before decontamination. Autoclaves should be tested periodically to ensure that chamber temperatures are high enough to kill all microorganisms. Testing can be done by sterilizer indicator tubes that change colour during an adequate sterilizing process.

Articles should be autoclaved at a minimum temperature of 121°C for a minimum period of 15 minutes. Autoclavable disposal bags usually contain indicator strips that change colour to indicate adequate sterilization. After autoclaving waste material may be burned or buried. Re-usable articles may be washed and re-sterilized

- **Burning and Burial**

Peripheral laboratories may not have autoclaves and an alternative must be provided for the disposal of specimen containers and other items. The simplest methods for treating infected material are burning and burial.

6 CASE MANAGEMENT

6.1 TREATMENT OF CASES WITHOUT CONFIRMED DRUG RESISTANCE (DS-TB)

6.1.1 General aspects of chemotherapy

The objective of chemotherapy is to achieve a cure rate of at least 90% of all newly detected bacteriologically confirmed TB cases. The treatment regimens will cure all such cases if the requirements for chemotherapy are followed and unless the patient is in a critical condition, coming too late for treatment, or the bacilli are resistant to both isoniazid and rifampicin (multidrug-resistant TB). The main requirements for adequate chemotherapy are:

1. An appropriate combination of quality assured anti-tuberculosis drugs (which would ensure cure)
2. Prescription in the correct dosage
3. All doses to be taken regularly by the patient
4. Prescribed for period of time (to prevent relapse)

The NTP follows the WHO's recommendations for treatment of TB issued in the latest revision of the treatment guidelines published in 2017.[16] This implies important changes to the standard treatment regimens based on the following **WHO recommendations**:

- **In patients who require TB retreatment, drug-susceptibility testing should be conducted to inform the choice of treatment regimen. Category II regimen should no longer be prescribed**
- **Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment**
- **In patients with tuberculous meningitis, an initial adjuvant corticosteroid therapy with dexamethasone or prednisolone tapered over 6-8 weeks should be used**
- **In patients with tuberculous pericarditis, an initial adjuvant corticosteroid therapy may be used**
- **A package of treatment adherence intervention may be offered for patients on TB treatment in conjunction with the selection of a suitable treatment administration option**

6.1.2 Drugs used by the NTP

The drugs used by the NTP in the treatment of non-MDR TB are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E).

The following combinations are used by the NTP:

- Four fixed drug combination tablets (4FDC) in blister packs (R 150mg + H 75mg+Z 400mg + E 275 mg). This is used in the intensive phase of treatment
- Two fixed drug combination (2FDC): R150mg + H 75 mg. This is used in the continuation phase of treatment.

The dosages of drugs are based on the body weight. The recommended dosages for adults per kilogram of body weight for daily therapy are shown in the following table below:

[16] World Health Organization 2017. Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update. WHO/HTM/TB/2017.05

Table 1: Drug dosage for daily regimens for adults (with range)

Drugs	Dose and range (mg/kg body weight)
Isoniazid	5 (4-6)
Rifampicin	10 (8-12)
Pyrazinamide	25 (20-30)
Ethambutol	15 (15-20)

6.1.3 Standard Treatment Regimen

The NTP uses only one standard treatment regimen for drug-sensitive cases. Treatment of MDR cases is discussed in the relevant chapter.

The regimen is **2(RHZE)/4(RH)**. The prefix before the regimen is the number of months and the suffix is the number of doses in a week. Total duration is six months; 2 months intensive phase (IP) and 4 months continuation phase (CP).

Table 2: Standard treatment regimen for drug-sensitive cases: Drug dosage and number of tablets according to body weight for the treatment

Body weight (Kg)	**Initial phase (2 months) daily**	**Continuation phase (4 months) daily**
	4FDC: (RHZE) (150mg + 75mg + 400mg + 275 mg)	2FDC: (RH) (150mg + 75mg)
30-39	2	2
40-54	3	3
55-70	4	4
>70	5	5

6.1.4 Organization of treatment and treatment supervision

1. Organization of direct observation of treatment (DOT)

Direct observation of treatment (DOT) is a crucial component of the DOTS strategy. All regimens that contain Rifampicin should be taken by the patient under direct observation. Currently the WHO defines DOT as any person observing the patient taking medications in real time. The treatment observer does not need to be a health-care worker, but could be a friend, a relative or a lay person who works as a treatment supervisor or supporter. Community-based or home-based DOT has more advantages than health facility-based DOT while family members should not be the first or only option for administering DOT. DOT is better provided at home or in the community and by trained lay providers or health-care workers. There may be challenges in providing community- or home-based DOT by health-care workers because of the increased number of health-care workers required and the increased costs for staff time and daily travel to the community or patient's home. DOT provision in the community or at home by trained local lay persons is more feasible. ***A combination of lay provider and health-care worker for provision of community- or home-based DOT is also an option.*** Community-based or home-based DOT is more likely to be acceptable and accessible to patients than with other forms of DOT. However, stigma may continue to be an issue with community- or home -based DOT. Having a health-care worker coming regularly to a patient's house may be stigmatizing and the feeling of being "watched over" may be disempowering to patients. Other forms of DOT (e.g. administered by an

emotionally supportive relative or close friend) may be more acceptable but may still be stigmatizing. Health staff should discuss different options of facilities for treatment supervision (DOT centres) with the patient and the patient should select the most convenient place for DOT. The treatment should be provided in such a way that it is accessible to the patient.

The following strategies have been used in Timor-Leste and proven to be effective:

- If patients live close to a treatment facility, they come every day to that centre to receive treatment
- If patients live far away from a TB treatment facility, the patient may stay with relatives near the treatment centre, and come daily to the treatment centre for DOT
- If patients come from a place far away from treatment facility, they may stay in a hospice (temporary house).
- If a patient's condition is severe and does not allow him/her to visit TB clinic daily, and in the absence of a hospice, he/she may stay in a hospital.
- If patients live far away from a TB treatment facility, but there are trained community volunteers or family members closely supervised by a clinic providing NTP services in that area, these community volunteers or family members may observe treatment. In some sub-districts, there is a network of community volunteers. Community volunteers can also be organized through the family health promoters.
- Cured TB patients can also be encouraged to act as DOT providers

If the patient cannot come to the health facility for the sputum follow-up examinations during the treatment because of distance, health staff or community volunteer should organise collection and transport of sputum sample of the patient.

When a TB diagnosis has been made, the doctor or the clinical nurse of the health facility explains to the patient about the disease, about the drug dosage schedule, duration of treatment, importance of consuming all doses of drugs regularly for the entire course, possible drug side effects, need for examination of contacts and the frequency of monitoring the progress towards cure. The clinician should discuss with the patient from where and from whom he/she would prefer to receive DOT and reach an agreement with the patient about which DOT centre is most easily accessible to the patient.

The clinician should discuss with the patient about the patient's background and find ways of preventing the patient from discontinuing treatment. The patient should be convinced that cure depends on regular drug intake for the entire course of treatment. The same messages should be conveyed to the patient's relatives also so that they can take an interest in ensuring regular drug intake by the patient. It is best to agree on a plan for the whole course of treatment. Health education and motivation of the patient should be done periodically during follow-up visits. The district TB assistant, nurse or community volunteer will visit the house of the patient as early as possible for confirmation of patient's residence and will have a detailed dialogue with the patient and other members of the family. They will emphasise the treatment schedule, the importance of regular uninterrupted drug intake, completion of the course of treatment, possible intolerances and the need for check-ups household contacts. After this visit treatment is initiated by the health staff or community volunteer.

For DOT, a convenient location is decided mutually between the district TB assistant (or nurse or community volunteer) and the patient. The patient must consume the medicines in front of the DOT provider, but only in very exceptional circumstances when the patient is unable to come, the DOT provider will bring the medicines to the home of the patient. If the patient is receiving DOT from a DOT provider away from the treatment facility, then two treatment cards should be made. One card should be kept at the treatment facility and the duplicate treatment card should be with the DOT provider.

The district TB coordinator (DTC) will give the patient's medicine box for the entire duration of treatment to the sub-district CHC. The sub-district CHC staff will give medicines to the DOT provider, one-week stock during the intensive phase and one month for the continuation phase. The distribution of drugs to the community volunteers will be duly recorded in the special register maintained by the 'TB-responsible staff' at the community health centre.

If the patient does not come for the doses, he/she must be retrieved within one day of missing a dose during the intensive phase and at least within a week during the continuation phase.

2. Package of combined treatment adherence interventions

In its most recent TB Treatment Guidelines,[17] the WHO notes that treatment supervision is not always sufficient to guarantee better treatment outcomes while the combination of treatment supervision with other treatment adherence interventions (incl. social support, digital health interventions etc.) significantly improves treatment outcomes for TB patients. Therefore, the WHO recommends the use of a package of treatment adherence interventions in addition to health education and counselling as a means to improve patient adherence to treatment.

The NTP will use a mixture of types of adherence interventions depending on the specific patient situation. These include different combinations of patient education, staff education, material support (e.g. food, financial incentives, transport fees, bonuses for reaching treatment goals), psychological support and counselling. The treatment adherence interventions may also include tracer actions such as home visits, use of digital health communication (e.g. SMS, telephone calls) or a medication monitor. The interventions will be selected on the basis of the assessment of an individual patient's needs, the NTP's financial resources and conditions for implementation in specific locations throughout the country.

Table 3: Treatment adherence interventions

Treatment adherence intervention	**Description**
Patient education	Health education and counselling.
Staff education	Education, chart or visual reminder, educational tool and desktop aid for decision-making and reminders.
Material support	Food or financial support such as meals, food baskets, food supplements, food vouchers, transport subsidies, living allowance, housing incentives or financial bonus. This support addresses indirect costs incurred by patients or their attendants in accessing health services and, possibly, tries to mitigate the consequences of income loss related to the disease.
Psychological support	Counselling sessions or peer-group support.
Tracer	Communication with the patient, including home visits or via mobile telephone communication such as SMS or telephone (voice) call.
Digital medication monitor	A digital medication monitor is a device that can measure the time between openings of the pill box. The medication monitor can give audio reminders or send SMS to remind a patient to take medications,

[17] Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update, WHO/HTM/TB/2017.05

	along with recording when the pill box is opened.

3. IN-PATIENT VERSUS OUT-PATIENT TREATMENT

Hospitalization in itself has no added advantage or effect on the outcome of treatment unless the patient is seriously ill. A TB patient who consumes the drugs will do equally well whether treated in a hospital or at home. In-patient treatment is indicated (usually for a few weeks only) for seriously ill TB patients, those with complications of TB (e.g. haemoptysis, spontaneous pneumothorax), and for those TB patients with other serious accompanying diseases. Hospitalization may also be required to ensure that the intensive phase of chemotherapy is received without fail by patients who live far away from the health centre or health post and for whom visiting the DOT centre is difficult. The NTP policy prefers ambulatory treatment. Only in exceptional cases the patient may be admitted into a health care facility. Smear-positive patients should be given priority for in-patient care. During hospitalization, all drugs must be administered under direct observation by the hospital staff.

4. DOT in cities

In cities, (Dili and Baucau) diagnosis may also be made in a hospital, where microscopy and treatment administration is done by hospital staff. After the clinician decides on the category of treatment, he/she explains the treatment schedule and refers the patient to the CHC and from there to a health facility near the patient's residence for DOT.

If the patient is not coming for DOT, the DOT provider should visit the residence and have a dialogue with the patient to find out why he/she did not come and what can be done to ensure that the patient is taking the drugs regularly. As there are several health facilities run by the government and NGOs, most patients are likely to be within walking distances from the DOT facility in the area.

6.1.5 Monitoring during treatment of DS-TB

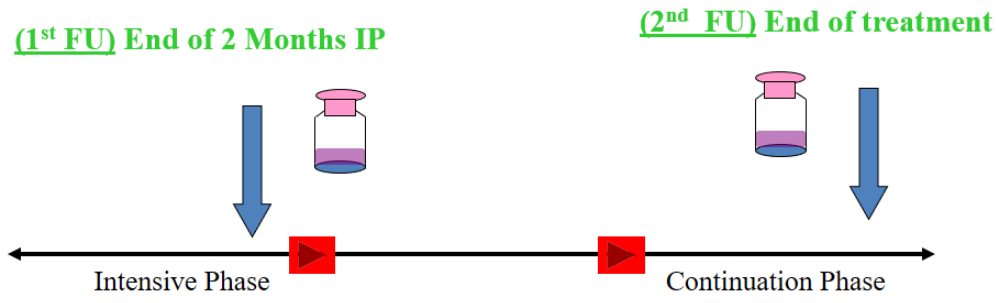
All patients should be monitored to assess their response to therapy. Regular monitoring of patients also facilitates treatment completion and allows the identification and management of adverse drug reactions. All patients, their treatment supporters and health workers should be instructed to report the persistence or reappearance of symptoms of TB (including weight loss), symptoms of adverse drug reactions, or treatment interruptions.

Patient weight should be monitored each month, and dosages should be adjusted if their weight changes. Additional monitoring and the actions it triggers are discussed below for pulmonary and extrapulmonary cases treated with first-line drugs. For monitoring of patients receiving second-line drugs, see 6.2.15.

A written record of all medications given, bacteriological response and adverse reactions should be maintained for every patient on the TB Treatment Card.

For all pulmonary TB patients treated with first-line drugs, sputum smear microscopy is performed at completion of the intensive phase of treatment. Sputum should be collected when the patient is given the last dose of the intensive-phase treatment. The end of the intensive phase is at 2 months. Sputum specimens should be collected for smear examination at each follow-up sputum check. They should be collected without interrupting treatment and transported to the laboratory as soon as possible thereafter; if a delay is unavoidable, specimens should be refrigerated or kept in as cool a place as possible.

Follow-up (FU) Schedule in the sputum positive and negative TB Patients



Among EPTB patients, sputum microscopy recommended only if patients have cough

Detection of a positive sputum smear remains important as a trigger for the patient assessment outlined below. The proportion of smear-positive patients with sputum smear conversion at the end of the intensive phase is also an indicator of NTP performance.

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

- the initial phase of therapy was poorly supervised and patient adherence was poor;
- poor quality of anti-TB drugs;
- doses of anti-TB drugs are below the recommended range;
- resolution is slow because the patient had extensive cavitation and a heavy initial bacillary load;
- there are co-morbid conditions that interfere either with adherence or with response;
- the patient may have drug-resistant *M. tuberculosis* that is not responding to first-line treatment;
- non-viable bacteria remain visible by microscopy.

The CHC staff should carefully review the quality of the patient's support and supervision and intervene promptly if necessary. Patient treatment records should be reviewed with the responsible health care worker, and reasons for any interruptions should be explored and addressed.

It is unnecessary, unreliable and wasteful of resources to monitor the patient by chest radiography.

Additional sputum monitoring is needed for new patients whose sputum smear is positive at the end of the intensive phase.

If the specimen obtained at the end of the intensive phase (month 2) is smear-positive, an Xpert MTB/RIF assay must be performed

The main purpose of obtaining samples for Xpert MTB/RIF at this stage is to detect drug resistance without waiting until the fifth month to change to appropriate therapy.

Figure 1: Sputum monitoring by smear microscopy in new pulmonary TB patients

Note: If a patient is found to harbour a multidrug-resistant strain of TB at any time during therapy, treatment is declared a failure and the patient is re-registered and should be referred to an MDR-TB treatment program.

months of treatment					
1	**2**	**3**	**4**	**5**	**6**
[========	========] • if sm +, obtain Xpert MTB/RIF[b]	[----------	----------	----------	----------] • [a] if sm +, obtain Xpert MTB/RIF[b]

Key:
[========] intensive phase of treatment (HRZE)
[----------] continuation phase (HR)
• Sputum smear examination
[a] omit if patient was smear-negative at the start of treatment and at 2 months.
[b] Smear- or culture-positivity at the end of the intensive phase, at the fifth month or later (or detection of MDR-TB at any point) is defined as treatment failure and necessitates re-registration and change of treatment

6.1.6 Recording standardized treatment outcomes

At the end of the treatment course for each individual patient, the District TB Officer records the treatment outcome in the District TB Register. The NTP has adopted the most recent revision of the standard recording and reporting system published by WHO.[18] The new treatment outcome definitions make a clear distinction between two types of patients:

- patients treated for drug-susceptible TB
- patients treated for drug-resistant TB using second-line treatment.

The two groups are mutually exclusive. Any patient found to have drug-resistant TB and placed on second line treatment is removed from the drug-susceptible TB outcome cohort. This means that management of the standard TB register and of the second-line TB treatment register needs to be coordinated to ensure proper accounting of the outcomes of treatment.

All bacteriologically confirmed and clinically diagnosed TB cases should be assigned an outcome from the following list (Table 7) except those with RR-TB or MDR-TB, who are placed on a second-line drug regimen (see section 6.2.2).

Table 4: Treatment outcomes for TB patients (excluding patients treated for RR-TB or MDR-TB)

Outcome	Definition
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.
Treatment completed	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.

[18] World Health Organization 2013. Definitions and reporting framework for tuberculosis – 2013 revision. WHO/HTM/TB/2013.2

Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Died	A TB patient who dies for any reason before starting or during the course of treatment.
Lost to follow-up	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A TB patient for whom no treatment 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	The sum of *cured* and *treatment completed*.

6.1.7 Management of treatment interruption

Supporting patients to prevent treatment interruption is discussed in section 6.1.4; this section covers what to do if treatment is interrupted.

If a patient misses an arranged appointment to receive treatment, the NTP should ensure that the patient is contacted within a day after missing treatment during the initial phase, and within a week during the continuation phase. It is important to find out the cause of the patient's absence so that appropriate action can be taken, and treatment can continue.

The management of patients who have interrupted treatment takes into consideration several factors, each of which, if present, will necessitate further caution and probably additional treatment:

- The patient is found to be smear- or culture-positive upon returning from treatment interruptions.
- Interruption occurs in the intensive, rather than the continuation, phase.
- Interruption occurs early (rather than later) in the continuation phase.
- The interruption is of long duration.
- The patient is immunocompromised (living with HIV or another condition).
- The patient had poor response to treatment before the interruption.
- Drug-resistant disease is known or suspected.

Xpert MTB/RIF should be performed in addition to smear microscopy for all patients returning after treatment interruption.

6.1.8 Transfer of patients

For patients who need to be transferred from one district to another, the 'transfer form' (see Annex) should be filled in triplicate at the centre where the patient is taking the treatment. One copy of this is to be given to the patient, another sent to the health facility where the patient proposes to continue treatment and the third is retained at the original health facility along with the treatment card of the patient. The centre to which the patient has been transferred receives and registers the patient as a "transfer in" case and returns the counterfoil of the transfer form back to the centre from where the case has been transferred out. The patient is registered in the district TB register in the new centre as a 'transfer in' case and given a new TB Number (old TB number may also be noted).

6.1.9 Complications of Tuberculosis

5. Complications of pulmonary tuberculosis

- Haemoptysis (coughing up of blood): In severe cases, the patient should be advised to rest, sedatives and antitussive administered and referred to the nearest hospital.
- Spontaneous pneumothorax (collapse of the lung due to damage caused by TB): The patient must be referred to the nearest hospital for further management.
- Pleural effusion: If the amount of fluid is not very large, the clinical condition will improve with chemotherapy alone. If there is too much fluid in the thorax, aspiration may be necessary for relief of symptoms and the patient should be referred to hospital.
- Cardio-pulmonary insufficiency (combined heart and lung disease – cor pulmonale): A doctor should be consulted regarding therapy.
- Bronchiectasis, fibrosis of the lungs: these are sequelae of extensive tuberculous disease and only symptomatic therapy is usually available.

6. Complications of extrapulmonary tuberculosis

Complications depend on the organs involved. A doctor must be consulted in case of complications.

6.2 TREATMENT OF CASES WITH DRUG-RESISTANT TUBERCULOSIS (DR-TB)

6.2.1 Definitions of drug resistance

DR-TB is **confirmed** through laboratory tests that show that the infecting isolates of *Mycobacterium tuberculosis* grow in vitro in the presence of one or more anti-tuberculosis drugs. Four different categories of drug resistance have been established:

• **Mono-resistance**: resistance to one anti-tuberculosis drug.

• **Poly-resistance**: resistance to more than one anti-tuberculosis drug, other than both isoniazid and rifampicin.

• **Multidrug-resistance**: resistance to at least isoniazid and rifampicin.

• **Rifampicin-resistant TB (RR-TB):** 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 monoresistance, multidrug resistance, polydrug resistance or extensive drug resistance.

Extensively drug-resistant TB (XDR-TB): resistance to any fluoroquinolones (FQs) and to the second-line injectables (SLIs) (amikacin, streptomycin), in addition to multidrug resistance

Pre-extensively drug-resistant TB (pre-XDR-TB): *resistance to any FQ or to at least one of the three SLIs (amikacin, capreomycin and kanamycin), in addition to multidrug resistance.*[19]

6.2.2 DR-TB patient registration groups

The introduction of the Xpert MTB/RIF assay has brought important changes to the standard TB recording and reporting system, which are reflected in WHO's 2013 revision to the reporting framework.[20] Accordingly, there is **no distinction between registration groups for DR- and non-DR patient groups** and the DR-TB registration groups are the same as described in section 4.3.

[19] Although this use of the definition for pre-XDR-TB is widespread, it is not officially recognized

[20] World Health Organization 2013. Definitions and reporting framework for tuberculosis – 2013 revision. WHO/HTM/TB/2013.2

6.2.3 Bacteriology and sputum conversion

Besides the use of Xpert MTB/RIF for rapid testing, bacteriological examinations used in patients with DR-TB include sputum smear microscopy and culture. Even if the Xpert MTB/RIF assay is positive, LPA or culture DST should be done at the start of treatment to assess the baseline status of the patient to monitor the response to treatment. Follow-ups every month until 6 months of BDQ, followed by quarterly follow-up cultures and smears.

Sputum conversion is defined as two sets of consecutive negative smears and cultures from samples collected at least 30 days apart. Both bacteriological techniques (smear and culture) should be used to monitor patients throughout therapy. The date of the first set of negative cultures and smears is used as the date of conversion and the date used to determine the length of the initial phase and treatment.

6.2.4 Definitions for DR-TB treatment outcomes

The following are mutually exclusive DR-TB outcome definitions that rely on the use of laboratory culture as a monitoring tool. Follow-up on DR-TB treatment will be based on culture results. They have been constructed to parallel the outcomes for drug-susceptible TB (see section 6.1.6). All patients should be assigned the first outcome they experience for the treatment being evaluated for recording and reporting purposes.

Table 5: Outcomes for RR-TB/MDR-TB/XDR-TB patients treated using second-line treatment

Outcome	**Definition**
Cured	Treatment completed without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.[a]
Treatment completed	Treatment completed without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.[a]
Treatment failed	Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of: • lack of conversion[b] by the end of the intensive phase[a], *or* • bacteriological reversion[b] in the continuation phase after conversion[b] to negative, *or* • evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, *or* • adverse drug reactions (ADRs).
Died	A patient who dies for any reason during the course of treatment.
Lost to follow-up	A patient whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A patient for whom no treatment outcome is assigned. (This includes cases "transferred out"

	to another treatment unit and whose treatment outcome is unknown)
Treatment success	The sum of *cured* and *treatment completed*

[a] For Treatment failed, lack of conversion by the end of the intensive phase implies that the patient did not convert within the maximum duration of intensive phase

[b] The terms "conversion" and "reversion" of culture as used here are defined as follows:

Conversion (to negative): culture is considered to have converted to negative when two consecutive cultures, taken at least 30 days apart, are found to be negative. In such a case, the specimen collection date of the first negative culture is used as the date of conversion.

Reversion (to positive): culture is considered to have reverted to positive when, after an initial conversion, two consecutive cultures, taken at least 30 days apart, are found to be positive. For the purpose of defining treatment failure, reversion is considered only when it occurs in the continuation phase.

6.2.5 Pre-treatment evaluation

The initial assessment comprises a medical examination, sputum smear microscopy, Xpert testing, SL-LPA (if available), culture and DST for first-line (H and R) and second-line (FQs and SLIs) anti-tuberculosis drugs, chest X-ray, audiogram, blood tests (creatinine, potassium, glucose, transaminase, blood cell count), pregnancy test for women of childbearing age and HIV testing. An electrocardiogram (ECG) should be performed and repeated a week after treatment initiation. An initial home visit also needs to be done to verify the address and meet the family members. Since the drugs used for the treatment of DR-TB are known to produce adverse effects, a proper pre-treatment evaluation is essential to identify patients who are at increased risk of developing such adverse effects. These include screening for diabetes mellitus, liver disease, drug or alcohol use, mental illness, renal insufficiency, thyroid function, pregnancy and lactation. Those DR-TB presumptives and cases who have a history of high-risk behaviour in relation to HIV infection, a sexually transmitted disease, or any HIV-related Opportunistic Infection, will be offered referral to the nearest voluntary counselling and testing centre (VCTC). Management of patients with any of these conditions is likely to vary from the standard practice depending on the condition and may require more intense monitoring. Patients should receive counselling on the nature and duration of treatment, the need for regular treatment, possible side effects of these drugs and the consequences of irregular treatment or premature cessation of treatment. It is advisable to involve close family members during the counselling since family support is an essential component in treatment management. Patients should be advised to report if they experience any unusual problem. Female patients should receive special counselling on family planning. It is preferable to screen all close family contacts of patients for presence of chest and extrapulmonary symptoms as per NTP norms. A DOT provider (who can either be a health care worker, a community worker or a community volunteer), should be identified for the patient in consultation with the patient. The DOT centre can be either at a health post or in the community. The DOT provider should be given training for drug administration and to identify possible adverse effects during treatment, and also the frequency of follow up.

6.2.6 Referral of a confirmed DR-TB case to the DR-TB treatment unit

A DR-TB presumptive confirmed to have DR-TB according to the diagnostic algorithms in Figure 7 & 8 requires treatment with the NTP DR-TB regimen containing second-line anti-TB drugs. Once confirmed, the DR-TB patient is referred to the **DR-TB Unit** at the national hospital, with their Xpert MTB/RIF results (and LPA/DST result if applicable) and request for DR-TB treatment.

6.2.7 Deciding on treatment

The DR-TB committee (a DR-TB clinical management committee) will review the patients' details, including previous history, LPA/DST result and concurrent illnesses, and make a decision in relation to treatment with a

DR-TB regimen. If the Committee decides on treatment with a DR-TB regimen, the patient is admitted to the designated in-door facilities (HNGV/ Klibur Domin), counselled in regard to their treatment, their treatment book is opened, and treatment initiated. Initial 6 months all oral DR-TB treatment duration as criteria for failure, and the timepoint to reduce the frequency of follow-up cultures if the patient is responding well to the treatment regimen.

The NTP is aiming for a fully ambulatory treatment delivery model for all DR-TB patients. However, this requires availability of facilities for monitoring the patients, which must be ensured by the program. In the interim, until all of these facilities are available, patients should be admitted into Klibur Domin (DR-TB Centre) for a period of 1 to 3 months.

6.2.8 Drugs used to treat DR TB and Principles of Treatment

In 2018, the WHO convened a GDG (Guideline Development Group) meeting and assessed the individual contribution to treatment outcomes of medicines used in MDR TB regimens using primarily the estimates of effects from 2018 individual patient data meta-analysis. Following a thorough assessment of relative benefits to harms, recommendations were made for each medicine and published in revised guidelines on drug-resistant tuberculosis treatment[21] in early 2019. Drugs were classified in to three groups:

Group A: Fluoroquinolones (Levofloxacin and Moxifloxacin), Bedaquiline and Linezolid were considered highly effective and strongly recommended to be included in all regimens unless contraindicated;

Group B: Clofazimine and Cycloserine or Terizidone were conditionally recommended as agents of second choice

Group C: included all other medicines that can be used when a regimen cannot be composed with Group A and B agents.

The composition of DR-TB regimens is guided by the selection of individual medicines considered to be effective and also by a need to combine sufficient medicines to maximise the likelihood of relapse-free cure without increasing toxicity. Regimens may be of standardized (fixed) composition or may be individualized to patient needs. Apart from ranking by balance of effectiveness and harms, choice is also determined by: a preference for composition of agents; the results of drug-susceptibility testing (DST); the reliability of existing DST methods; population drug resistance levels; history of previous use of the medicine in a patient; drug tolerability; and potential drug-drug interactions.

Table 6: Grouping of Medicines recommended for the treatment of RR-TB and MDR-TB

Groups	Steps	Medicines	Abbreviations
A	Include all three medicines in the regimen, if no contraindication	Levofloxacin OR Moxifloxacin	Lfx /Mfx
		Bedaquiline	Bdq
		Linezolid	Lzd
B	Add one or both medicines	Clofazimine	Cfz
		Cycloserine OR Terizidone	Cs, Trd
C	Add to Complete regimen and when medicines from Group A and	Ethambutol	E
		Delamanid	Dlm

[21] WHO consolidated guidelines on drug-resistant tuberculosis treatment, WHO/CDS/TB/2019.3

	Group B cannot be used	Pyrazinamide	Z
		Imipenem-cilastatin OR Meropenem	Imp,Cln, Mpm
		Amikacin (OR Streptomycin)	Am(S)
		Ethionamide OR prothionamide	Eto , Pto
		P-aminosalicylic acid	PAS

Important notes:

1. The recommended duration of use for Bdq is 6 months and its use beyond this duration is "off label"
2. Bdq can be used in children from 6 years and above
3. Dlm can be used in children 3 years and above
4. Bdq and Dlm can be used together to complete the regimen - such use is to be considered as "off-label"
5. Lzd preferably to be used for whole duration of treatment or less if not tolerated
6. If DST to Z, E shows susceptibility, can be part of regimen
7. Imipenem should always be used with Amox-Clv
8. Use Am and S; only to be used, if only susceptible and under close monitoring, preferably in patients who are 18 years or above and when a regimen cannot be designed with sufficient drugs from Group A and B, and other Group C drugs

6.2.9 Principles of MDR TB Treatment and Regimen Construction

The following general principles and precautions related to DR TB treatment have been taken into account for designing the NTP's standardized DR-TB regimen in line with WHO's 2019 DR-TB guidelines:

- It is recommended by the WHO that treatment should start with at least four medicines likely to be effective and that at least three agents are continued for the rest of the treatment after bedaquiline is stopped.
- Possibly all three Group A agents (Lfx/Mfx, Bdq, Lzd) and at least one Group B agent (Cfz or Cs) should be part of the regimen and if only one or two Group A agents are used, then both Group B agents are to be included in regimen.
- If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it.
- Bdq use beyond 6 months is considered as "off label" should be case by case keeping in view treatment response and the number of effective drugs on board after Bdq is stopped
- The use of three cardiotoxic drugs (Bdq, Dlm and Cfz) in combination should be with caution and with close monitoring. However, recent data shows that combined use of Bdq and Dlm is safe, and QTcF interval with co-administration of both drugs is clinically modest
- The use of Lzd for whole duration is associated with better treatment outcomes and lower mortality but is expected to cause toxic effects in significant number of patients. The neurological toxicity is associated with duration, while haematological toxicity/myelosuppression is dose related.

- For Lzd use in the regimen, baseline assessment by Blood CP and neuropathy screening should be done and if contraindicated, should not be part of regimen or, if possible, with the lower dose of 300 mg daily or 600 mg on alternative days

6.2.10 Standardized RR/MDR-TB treatment regimen & treatment duration

The NTP has updated the RR/MDR TB regimens for Timor-Leste based on the recommendations in the WHO's 2019 DR-TB guideline[21] - "Starting with five agents instead of four may be favoured in certain situations to avoid the need to replace a medicine after treatment has started, namely: (i) two of the four agents are likely to be stopped before the end of treatment; for instance, bedaquiline stopped at month 6 and linezolid stopped early because of toxicity; (ii) reliable DST is not available for one or more of the agents on the regimen but background resistance to the agent is known to be high. Accordingly, the following drug combination should be used as the standard *All Oral Longer RR/MDR TB Regimen* for adults and children 6 years and above:

6 Lfx/Bdq/Lzd/Cfz /Z, 12 Lfx/Cs/Cfz

Cs has been added for 12 months. This will cover in case Lzd has to be stopped before 6 months. It is proposed not to continue with Lzd beyond 6 months, considering the duration related side effects and the need for monitoring. *The Lfx, Cs and Cfz* combination is strong enough. Vit B6 to be added to all patients to potentially prevent possible ADRs.

Shorter DR-TB Regimen: MDR/RR TB patients who have not been previously treated for more than 1 month with second-line drugs used in the Shorter MDR-TB Treatment Regimen (STR) or in whom resistance to fluoroquinolone and second line injectable agents has been excluded, a shorter DR-TB regimen of 9-12 months may be used instead of the longer regimen (WHO recommendation 2019).

Shorter Treatment Regimen Criteria

1. There is no evidence of fluoroquinolone resistance / second-line injection drugs
2. There is no close contact with pre / XDR TB patients
3. Have never taken second line TB drugs for ≥ 1 month
4. There is no intolerance to standard short-term regimen
5. Not pregnant
6. Not a case of severe extrapulmonary tuberculosis (TB meningitis, brain tuberculoma, TB spondylitis)
7. Not a case of extrapulmonary tuberculosis (in patients with HIV-AIDS)
8. Not a case with poor predicted outcome

From the **rapid communication WHO December 2019**, for MDR/RR-TB patients – a) **Without** previous exposure to second-line treatment (including bedaquiline); b) **Without** fluoroquinolone resistance; and c) **No** extensive TB disease or severe extrapulmonary TB; the preferred treatment option is a shorter, all-oral, bedaquiline-containing regimen. In this group of patients, the national TB programs are advised to phase out use of the injectable-containing shorter regimen. Several countries (under operational research) are treating DR TB patients using all oral shorter regimen. Replacing second line injectables with oral bedaquiline.

South Africa is one of those countries (Lzd-Bdq-Lfx/Mfx-Eto-E-Z-HH-Cfz). This regimen intensively started by using seven drugs: Linezolid, High dose isoniazid, Bedaquilin, Levofloxacin, Clofazimine, Pyrazinamide, and Ethambutol. Linezolid will only be administered during the first 2 months of intensive phase. Bedaquiline is included to replace injectables, for a duration of 6 months, and Levofloxacin is included to replace Moxifloxacin.

The country consultation was conducted from 16-18 December 2019 with MDR-TB global expert, Dr Erlina Burhan, on clinical management of DR-TB with all oral new DR-TB regimen and the way forward. An effective

shorter all oral drug regimen for DR-TB treatment was constructed based on the country context and with reference to the South African all oral STR. Since isoniazid high dose is not available in Timor-Leste, the regimen for all-oral shorter treatment regimen is proposed below under the Operational Research conditions while the updated WHO guidelines are being adopted. Moreover, this regimen is being tried in South-Africa with considerable success.

6 months: Lzd (2 months only)/ **BDQ** (total 6 months)/ **Lfx / Cfz / Z / E** (total 6 months)
5 months: Lfx/ Cfz/ Z/ E

To summarize, all patients with MDR/RR-TB including those with additional resistance to fluoroquinolones stand to benefit from effective all-oral treatment regimens, either **shorter or longer,** implemented under programmatic conditions –

- MDR/RR-TB patients with extensive TB disease, severe forms of extrapulmonary TB those with resistance to FQ or who have been exposed to treatment with 2nd line drugs will benefit from an **individualized longer regimen** designed using the WHO priority grouping of medicines recommended in 2018. Proposed standardized regimen for all-oral longer regimen:

  6months **Lfx/Bdq/Lzd/Cfz /Z, 12**months **Lfx/Cs/Cfz**

  The following principles for the determination of treatment duration apply:

  - A total minimum duration of 18 months depending on patient's response
  - A treatment duration of 16 months is recommended after culture conversion
  - The treatment duration may be modified as per patient's response to treatment
  - Prolonging the treatment longer than 20 months may be considered in patients with additional resistance or late converters, extensive disease and other risk factors for failure or relapse of treatment.

- For MDR/RR-TB patients without previous exposure to second-line treatment (including Bedaquiline) without FQ resistance and no extensive TB disease or severe extrapulmonary TB the preferred treatment option is **a shorter, all oral, Bedaquiline-containing regimen** using seven drugs:

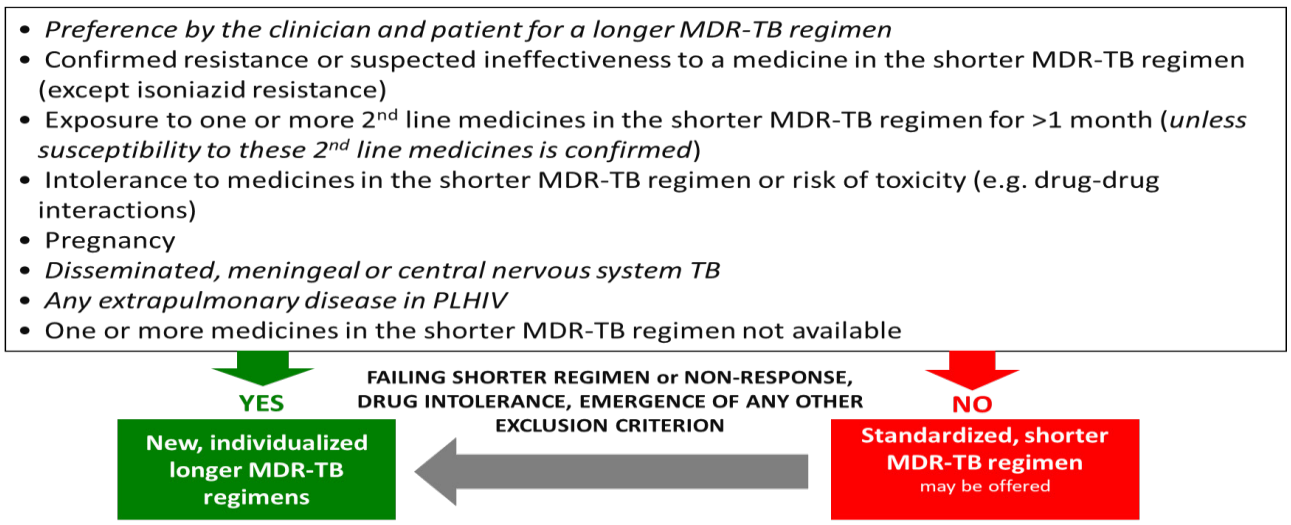
  Regimen for all-oral shorter treatment is proposed as below:

  4 - 6 months: Lzd (2 months only)/ **BDQ** (total 6 months)/ **Lfx / Cfz / Z / E** (total 6 months)

  5 months: Lfx/ Cfz/ Z/ E

Linezolid will only be administered during the first 2 months. Bedaquiline is included to replace injectables, for a duration of 6 months. Levofloxacin is included to replace moxifloxacin. Total duration of all oral short treatment is 9-11 months. All treatment should be delivered under WHO-recommended standards, including patient-centered care and support, informed consent when necessary, principles of good clinical practice, active drug safety monitoring and management and regular patient monitoring to access regimen effectiveness

Criteria to be followed for shorter, all oral, Bedaquiline-containing regimen:



6.2.11 Treatment of RR/MDR TB with additional resistance (Pre-XDR and XDR)

A pre-XDR- and XDR-TB treatment regimen is not for a failing second-line regimen but when resistance is detected at the start of the treatment.

- A drug with high early bactericidal activity, such as linezolid, to protect Bdq and to prevent resistance amplification. Because of its toxicity, Lzd should only be used in the intensive phase and its use should be carefully evaluated if given throughout treatment. Possible alternatives are meropenem or imipenem/cilastatin plus amoxicillin/ clavulanate. These need an implantable venous access device, which is problematic in most endemic settings. Another possible option is amikacin if still susceptible.
- A companion drug with bactericidal activity, such as delamanid, to protect the action of the other drugs and to prevent resistance amplification. This is presently an off-label use. Possible alternatives are meropenem or imipenem/cilastatin plus amoxicillin/clavulanate if available.
- A sterilizing drug, such as clofazimine, to prevent relapse after treatment cessation. In the case of resistance to clofazimine, cycloserine is an option. However, its low sterilizing activity must be taken into account. Pyrazinamide may be added because of its sterilizing activity.
- High-dose isoniazid should also be added in the intensive phase for its bactericidal properties, except in the case of confirmed high H resistance (mainly double katG and inhA mutations or katG deletion).

Prolonged use of bedaquiline with concomitant use of delamanid is considered off-label, as both drugs have been registered to be used for a maximum duration of 24 weeks. Data on the simultaneous use of the two drugs in the same patient remains limited, but the use of the two drugs has proved effective and safe to date. Nevertheless, the risk of creating additional drug resistance with a weak regimen is very real and the proposed approach seems justified. An all oral individualized regimen is preferred whenever possible. As an example, a regimen may be composed as follows: Bdq-Lzd-Hh-Dlm-Cfz-Z for a total duration of 18-20 months.

In the case of high H resistance:

Bdq-Dlm-Lzd-Cs-Cfz-Z for a total duration of 18-20 months

6.2.12 MDR-TB in children

6.2.12.1 *Diagnosis*

Diagnosis of MDR-TB among children can be challenging and requires a high level of suspicion. Under field conditions, it may take several weeks from the time a child first presents with signs and symptoms of TB and

the receipt of test results, during which time a child can rapidly deteriorate. Thus, it is important to consider initiating MDRTB therapy in the absence of bacteriologic confirmation in line with consultation with a paediatrician expert in TB/MDR TB. GeneXpert and culture in liquid media should be prioritized in children. All relevant and available tests should be considered; performing multiple tests on one or more samples of a variety of specimen types significantly increases the diagnostic yield. Collecting the respiratory specimen at optimal times is important to enhance the yield e.g. early morning fasting gastric aspirate, before mobilization; induced sputum after fasting 2-4 hours; expectorated sputum early morning. Of note, sputum (induced or expectorated) should be minimum 3 ml, gastric aspirate 5 ml, gastric lavage 10 ml, BAL 3 ml, nasopharyngeal aspirate 2 ml.

In addition to that there are extrapulmonary samples useful for testing with Xpert for diagnosis in children and which can be obtained any time, e.g. CSF, Stool, Urine (use of the urinary lipoarabinomannan (LAM) may be a useful test to diagnose TB in children or individuals living with HIV with low CD4 counts). Moreover, there are imperative and developing data to show that Xpert testing done on stool after simple decontamination procedures can have a diagnostic yield closer to gastric aspirate and are not invasive. For testing purposes CSF 2 ml and stool 5gm is enough. Serosal fluids including pleura, pericardium, peritoneum, and synovium may also be helpful in diagnostics, but bacteriological yield is higher in tissues than fluids.

It is important that TB should be included in the differential diagnosis list of any child with a persistent non-settling cough or fever, weight loss/failure to thrive, or focal findings that are suggestive of TB, such as lymphadenitis, spinal deformities, ascites, and joint effusions. Danger signs of possible meningitis include lethargy/sleepiness, loss of consciousness, and seizures MDRTB in children can either be confirmed (they have clinical TB disease and a sample taken from the child shows MDR-TB) or clinically diagnosed (the child has clinical TB disease and has risk factors for drug resistance).

6.2.12.2 ***Treatment***

The treatment regimens for children are identical to those for adults. Use of paediatric formulations where available should be preferred. For drugs which do not have paediatric formulation currently available tablets may be cut into fragments and crushed or, capsules may be opened, and the contents fractioned. The drugs may be mixed with small amounts of liquid or soft food. The treatment regimens for children are as follows:

6 Lfx/Bdq/E/Cfz, 12 Lfx/Cs/Cfz (>6 years)

6 Lfx/Dlm/E/Cfz, 12 Lfx/Cs/Cfz (<6 years)

6.2.13 **Dosages of medicines by weight band by medicines used in MDR-TB regimens in adults and children**

Dosing of medicines used in second-line MDR-TB regimens by weight band in patients older than 14 years

Group	Medicine	Weight-based daily dose	Formulation	Weight bands for patients older than 14 years[a]					Usual upper daily dose[b]	Comments
				30–35 kg	36–45 kg	46–55 kg	56–70 kg	>70 kg		
A	*Fluoroquinolones*									
	Levofloxacin	-[c]	250 mg tab	3	3	4	4	4	1.5 g	
			500 mg tab	1.5	1.5	2	2	2		
			750 mg tab	1	1	1.5	1.5	1.5		
	Moxifloxacin	standard dose[c,d]	400 mg tab	1	1	1	1	1	400 mg	
		high dose[c,d]	400 mg tab	1 or 1.5	1.5	1.5 or 2	2	2	800 mg	as used in the standardized shorter MDR-TB regimen
	Bedaquiline	-[c]	100 mg tab	4 tabs od for first 2 weeks; then 2 tabs od M/W/F for 22 weeks					400 mg	
	Linezolid	-[c]	600 mg tab	(<15 y)	(<15 y)	1	1	1	1.2 g	
B	Clofazimine	-[c]	50 mg cap or tab	2	2	2	2	2	100 mg	
			100 mg cap or tab	1	1	1	1	1	100 mg	
	Cycloserine or terizidone	10–15 mg/kg	250 mg cap	2	2	3	3	3	1 g	

Group	Medicine	Weight-based daily dose	Formulation	Weight bands for patients older than 14 years[a]					Usual upper daily dose[b]	Comments
				30–35 kg	36–45 kg	46–55 kg	56–70 kg	>70 kg		
C	Ethambutol	15–25 mg/kg	400 mg tab	2	2	3	3	3	–	
	Delamanid	–[c]	50 mg tab	2 bd	2 bd	2 bd	2 bd	2 bd	200 mg	
	Pyrazinamide	20–30 mg/kg	400 mg tab	3	4	4	4	5	-	
			500 mg tab	2	3	3	3	4		
	Imipenem-cilastatin	–[c]	0.5 g + 0.5 g vial	2 vials (1 g + 1 g) bd					–	To be used with clavulanic acid
	Meropenem	–[c]	1 g vial (20 ml)	1 vial 3 times per day or 2 vials bd					–	To be used with clavulanic acid
	Amikacin	15–20 mg/kg	500 mg/2 ml vial[e]	2.5 ml	3 ml	3 to 4 ml	4 ml	4 ml	1 g	
	Streptomycin	12–18 mg/kg	1 g vial[e]	Calculate according to the dilution used					1 g	
	Ethionamide or prothionamide	15–20 mg/kg	250 mg tablet	2	2	3	3	4	1 g	Once daily dose advised but can start with 2 divided doses until tolerance improves
	p-aminosalicylic acid	8–12 g/day in 2–3 divided doses	PAS sodium salt (4 g) sachet	1 bd	1 bd	1 bd	1 bd	1 to 1.5 bd	12 g	
			PAS acid (4 g) sachet	1 bd	1 bd	1 bd	1 bd	1 to 1.5 bd		
Other medicines[f]	Isoniazid	4–6 mg/kg (standard dose)[d]	300 mg tab	2/3	1	1	1	1	-	100 mg isoniazid tablet can facilitate the administration of certain dosages Pyridoxine given with isoniazid in patients at risk (such as those with HIV, malnutrition)
		10–15 mg/kg (high dose)[d]	300 mg tablet	1.5	1.5	2	2	2		
	Clavulanic acid[g]	–[c]	125 mg tab[g]	1 bd	1 bd	1 bd	1 bd	1 bd	–	Only to be used with carbapenems

Group	Medicine	Weight-based daily dose	Formulation	Weight bands for patients older than 14 years[a]					Usual upper daily dose[b]	Comments
				30–35 kg	36–45 kg	46–55 kg	56–70 kg	>70 kg		
Other medicines[f]	Kanamycin	15–20 mg/kg	500 mg/2 ml vial[e]	2 to 2.5 ml	2.5 to 3 ml	3 to 4 ml	4 ml	4 ml	1 g	M/W/F dosing of aminoglycosides at 25 mg/kg/day may limit toxicity and inconvenience when the injectable agents are used in longer MDR-TB regimens
	Capreomycin	15–20 mg/kg	500 mg/2 ml vial[e]	2.5 ml	3ml	3 to 4 ml	4 ml	4 ml	1 g	
	Gatifloxacin	–[c]	400 mg tab	2	2	2	2	2	800 mg	Not used in <18 year olds (no quality assured product currently available)
	Thioacetazone	–[c]	150 mg tab	1	1	1	1	1	–	Not used in <18 year olds (no quality assured product currently available)

(<15 y) = follow the separate dose schedule for patients younger than 15 years of age; bd = two times a day; cap = capsule; g = gram; im = intramuscular; iv = intravenous; kg = kilogram; ml = millilitre; mg = milligram; M/W/F = Monday, Wednesday, Friday; soln = solution; susp = suspension; tab = tablet

[a] Dosages were established by the Guideline Development Group for the *WHO treatment guidelines for rifampicin- and multidrug-resistant tuberculosis, 2018 update* and the WHO Global task force on the pharmacokinetics and pharmacodynamics (PK/PD) of TB medicines and other experts. They are based on the most recent reviews and best practices in the treatment of MDR/RR-TB. For certain agents the dosages were informed by pharmacokinetic modelling results based on the principle of allometric scaling (Anderson BJ, Holford NH. Mechanism-based concepts of size and maturity in pharmacokinetics. Annu Rev Pharmacol Toxicol 2008;48:303–32). Due to the pharmacokinetic properties of certain medicines the doses proposed may exceed the mg/kg/day ranges shown here in order to achieve blood concentrations similar to target levels in an average adult patient. In patients <30 kg follow the schedule for <15 year olds unless otherwise indicated. If multiple dose options are given for one weight band select the lower or higher option depending on whether the patient is at the lower or higher limit of the body weight range. Dosing more closely to the target mg/kg/day should be aimed for, and is more feasible with oral or parenteral fluids and when solid forms of different dosages are available. Fractioning of tablets into halves or less should be avoided, if possible. Therapeutic drug monitoring is advised when the dose is at the upper and lower ends of the range to minimize the adverse therapeutic consequences of over- and under-exposure, respectively (especially for injectable agents, linezolid and fluoroquinolones).

[b] Clinicians may decide to exceed these values in particular cases to improve therapeutic effect.

[c] No weight-based dosing is proposed.

[d] Unless there is risk of toxicity, the high dose may be used if antimicrobial levels may be lowered because of pharmacokinetic interactions, malabsorption or other metabolic reasons or if the strain has low-level drug resistance.

[e] Weight-based daily dose is for 6 or 7 days/week administration (M/W/F scheduling may permit higher dosing). Volumes shown may differ by preparation. Streptomycin may be diluted in three different ways. For iv use, the volume may be increased.

[f] In the 2018 WHO treatment guidelines, these agents are either no longer recommended (kanamycin, capreomycin), only recommended as a companion agent (amoxicillin/clavulanic acid) or not included because of lack of data from the latest analysis on longer MDR-TB regimens in adults (gatifloxacin, isoniazid and thioacetazone).

[g] Only available in combination with amoxicillin as co-amoxyclav (e.g. 500 mg amoxicillin/125 mg clavulanic acid fixed dose combination). It is given with each dose of carbapenem, either as 125 mg bd or 125 mg 3 times daily.

Dosing of medicines used in second-line MDR-TB regimens by weight band in patients under 15 years[a]

Group				Weight bands among patients not yet 15 years old[a]							Usual upper daily dose[b]	Comments
				5–6	7–9	10–15	16–23	24–30	31–34	>34 kg		
A	*Fluoroquinolones*											
	Levofloxacin	15–20 mg/kg	100 mg dt	1	1.5	2 or 3	3 or 4	(>14 y)	(>14 y)	(>14 y)	1.5 g	
			250 mg tab	0.5	0.5	1 or 1.5	1.5 or 2	2	3	(>14 y)	1.5 g	
	Moxifloxacin	10–15 mg/kg	100 mg dt[c]	0.8	1.5	2	3	4	(>14 y)	(>14 y)	400 mg	
			400 mg tab[c]	2 ml[c]	3 ml[c]	5 ml[c]	0.5 or 0.75	1	(>14 y)	(>14 y)	400 mg	Use 10 mg/kg in <6 months
	Bedaquiline	–	100 mg tab	–	–	-	2 tabs od for two weeks; then 1 tab od M/W/F for 22 weeks		4 tabs od for 2 weeks; then 2 tabs od M/W/F for 22 weeks		–	Only in patients >5 years old (lower dose from 15–29 kg; higher dose from >29 kg)
	Linezolid	15 mg/kg od in <16 kg 10–12 mg/kg od in >15 kg	20 mg /ml susp	4 ml	6 ml	8 ml	11 ml	14 ml	15 ml	20 ml[d]	600 mg	
			600 mg tab[c]	0.25	0.25	0.25	0.5	0.5	0.5	0.75[d]		
B	Clofazimine	2–5 mg/kg	50 mg cap or tab	1 alt days	1 alt days	1 alt days	1	2	2	(>14 y)	100 mg	Give on alternate days if dose in mg/ kg/ day is too high
			100 mg cap or tab	M/W/F	M/W/F	1 alt days	1 alt days	1	(>14 y)	(>14 y)	100 mg	
	Cycloserine or terizidone	15–20 mg/kg	125 mg mini capsule	1	1	2	3	4	(>14 y)	(>14 y)	1 g	
			250 mg cap[c]	4–5 ml[c]	5–6 ml[c]	7–10 ml[c]	2	2	2	(>14 y)	1 g	
C	Ethambutol	15–25 mg/kg	100 mg dt	1	2	3	4	-	-	(>14 y)	–	
			400 mg tab[c]	3 ml[c]	4 ml[c]	6 ml[c]	1	1 or 1.5	2	(>14 y)		

Group				Weight bands among patients not yet 15 years old[a]							Usual upper daily dose[b]	Comments
				5–6	7–9	10–15	16–23	24–30	31–34	>34 kg		
C	Delamanid	–	50 mg tab	–	–[c]	–[c]	–[c]	1 bd	1 bd	2 bd	200 mg	Only in patients >2 years old (25 mg bd in 3–5 years; 50 mg bd in 6–11 years; 100 mg bd in 12–17 years)
	Pyrazinamide	30–40 mg/kg	150 mg dt	1	2	3	4 or 5	-	-	(>14 y)	–	
			400 mg tab	0.5	0.75	1	1.5 or 2	2.5	3	(>14 y)		
			500 mg tab	0.5	0.5	0.75 or 1	1.5	2	2.5	(>14 y)		
	Imipenem-cilastatin	–	0.5 g + 0.5 g vial	–	–	–	–	–	–	–	–	Not used in patients <15 years (use meropenem)
	Meropenem	20–40 mg/kg iv every 8 hours	1 g vial (20 ml)	2 ml	4 ml	6 ml	8-9 ml	11 ml	(>14 y)	(>14 y)	–	To be used with clavulanic acid
	Amikacin	15–20 mg/kg	500 mg/2 ml vial[d]	0.4 ml	0.6 ml	0.8 - 1.0 ml	1.2 - 1.5 ml	2.0 ml	(>14 y)	(>14 y)	1 g	
	Streptomycin	20–40 mg/kg	1 g vial[d]	Calculate according to the dilution used						(>14 y)	1 g	
	Ethionamide or prothionamide	15–20 mg/kg	125 mg dt (ethionamide)	1	1	2	3	4	4	(>14 y)	1 g	
			250 mg tab	0.5	0.5	1	2	2	2	(>14 y)	1 g	
	p-aminosalicylic acid	200–300 mg/kg in 2 divided doses	PAS acid (4 g) sachet	0.5–0.75 g bd	0.75–1 g bd	1–2 g bd	2–3 g bd	3–3.5 g bd	(>14 y)	(>14 y)	–	Full dose can be given once daily if tolerated
			PAS sodium salt (4 g) sachet	0.5–0.75 g bd	0.75–1 g bd	1–2 g bd	2–3 g bd	3–3.5 g bd	(>14 y)	(>14 y)		
			PAS sodium salt 60% (9.2g) SACHET	1.5 g bd	2–3 g bd	3–4 g bd	4 or 6 g bd	6 or 8 g bd	8–12 g bd	8–12 g bd	–	

Group				Weight bands among patients not yet 15 years old[a]							Usual upper daily dose[b]	Comments
				5–6	7–9	10–15	16–23	24–30	31–34	>34 kg		
Other medicines[g]	Isoniazid	15–20 mg/kg (high dose)	50 mg/5 ml soln	8–10 ml	15 ml	20 ml	–	–	–	–		300 mg isoniazid tablet can be used in patients >20 kg
			100 mg tab	1	1.5	2	3	4	4	(>14 y)		Pyridoxine is always given with high-dose isoniazid in children (12.5 mg od in <5 y olds and 25 mg od in >4 y olds)
	Clavulanic acid[h]	–	250 mg amoxicillin/62.5 mg clavulanic acid/5 ml susp[h]	2 ml bd[h]	3 ml bd[h]	5 ml bd[h]	8 ml bd[h]	10 ml bd[h]	(>14 y)	(>14 y)		Only to be used with carbapenems
	Kanamycin	15–20 mg/kg	500 mg/2 ml vial[f]	0.4 ml	0.6 ml	0.8–1.0 ml	1.2–1.5 ml	2.0 ml	(>14 y)	(>14 y)	1 g	
	Capreomycin	15–20 mg/kg	500 mg/2 ml vial[f]	0.4 ml	0.6 ml	0.8–1.0 ml	1.2–1.5 ml	2.0 ml	(>14 y)	(>14 y)	1 g	
	Gatifloxacin	–	400 mg tab	–	–	–	–	–	–	–	–	Not used in <18 y olds (no quality assured product currently available)
	Thioacetazone	–	–	–	–	–	–	–	–	–	–	Not used in <18 y olds (no quality assured product currently available)

(>14 y) = follow the separate dose schedule for patients older than 14 years of age; alt = alternate; bd = two times a day; cap = capsule; dt = dispersible tablet; g = gram; im = intramuscular; iv = intravenous; kg = kilogram; ml = millilitre; mg = milligram; M/W/F = Monday, Wednesday, Friday; soln = solution; susp = suspension; tab = tablet

[a] Dosages were established by the Guideline Development Group for the *WHO treatment guidelines for rifampicin- and multidrug-resistant tuberculosis, 2018 update* and the WHO Global task force on the pharmacokinetics and pharmacodynamics (PK/PD) of TB medicines and other experts. They are based on the most recent reviews and best practices in the treatment of MDR/RR-TB. For certain agents the dosages were informed by pharmacokinetic modelling results based on the principle of allometric scaling (Anderson BJ, Holford NH. Mechanism-based concepts of size and maturity in pharmacokinetics. Annu

Rev Pharmacol Toxicol 2008;48:303–32). Due to the pharmacokinetic properties of certain medicines the doses proposed may exceed the mg/kg/day ranges shown here in order to achieve blood concentrations similar to target levels in an average adult patient. In patients >30 kg follow the schedule for >14 year olds unless otherwise indicated. If multiple dose options are given for one weight band select the lower or higher option depending on whether the patient is at the lower or higher limit of the body weight range. Dosing more closely to the target mg/kg/day should be aimed for, and is more feasible with oral or parenteral fluids and when solid forms of different dosage are available. Fractioning of tablets into halves or less should be avoided if possible. Therapeutic drug monitoring is advised when the dose is at the upper and lower ends of the range to minimize the adverse therapeutic consequences of over- and under-exposure respectively (especially for injectable agents, linezolid and fluoroquinolones).

[b] Clinicians may decide to exceed these values in particular cases to improve therapeutic effect.

[c] Dissolving in 10 ml of water may facilitate administration in patients in lower weight-bands and avoids fractioning solid formulations, although bioavailability is uncertain (use of dispersible tablets is preferred if available).

[d] In individuals >44 kg a dose of 600 mg od is proposed.

[e] May be used in children 3–5 years of age. Giving half a 50 mg adult tablet in these children does not result in the same blood levels observed in trials using the special 25 mg paediatric tablet. Bioavailability may further be altered when the 50 mg tablet is split, crushed or dissolved.

[f] Weight-based daily dose is for 6 or 7 days/week administration (M/W/F scheduling may permit higher dosing). Volumes shown may differ by preparation. Streptomycin may be diluted in three different ways. Dosing closer to the upper limit of the mg/kg/day is more desirable. For iv use, the volume may be increased.

[g] In the 2018 WHO treatment guidelines, these agents are either no longer recommended (kanamycin, capreomycin), only recommended as a companion agent (amoxicillin/clavulanic acid) or not included because of lack of data from the latest analysis on longer MDR-TB regimens in adults (gatifloxacin, isoniazid and thioacetazone).

[h] Only available in combination with amoxicillin as co-amoxyclav. Only to be used with carbapenems, in which case they are given together, e.g. 125 mg bd or 125 mg 3 times daily in the 24–30 kg weight band.

See the text of the 2019 WHO Consolidated Guidelines on DR-TB Management for more details on the use of medicines.

6.2.14 Monitoring during treatment of patients diagnosed with Xpert MTB/RIF

Molecular tests, including Xpert MTB/RIF, are not suitable for patient monitoring as these tests also detect DNA from nonviable bacilli.

Follow-up of TB patients diagnosed with GeneXpert will be done by smear microscopy as described in the relevant chapters of treatment monitoring for specific types of patients below.

6.2.15 Management of INH (Hr) TB

Among the most potent and effective treatment of TB drugs, Isoniazid (H) plays vital role and because of its strong bactericidal activity, it is one of the most important first-line medicines for the treatment of active tuberculosis (TB) and latent TB infection (LTBI). Globally about 8% of TB patients are estimated to have rifampicin-susceptible, isoniazid-resistant TB (Hr-TB) with incidence ranging from 5 to 11% between the various WHO regions (WHO 2017). Thus, the emergence of TB strains resistant to isoniazid threatens to reduce the effectiveness of TB treatment (WHO 2016, 2018). Treatment of mono- and poly-resistance to H with WHO standardized first-line anti-TB drug regimens has been shown to increase the risk of treatment failure and even worse, contribute to amplification (acquisition of additional resistance) and multidrug resistance.

TB control programs generally focus on MDR-TB because these highly resistant strains are difficult to treat and cause much morbidity and mortality. However, at the same time, the significant number of Hr TB individuals who remain undiagnosed and inappropriately treated cannot be ignored. Moreover, in recent years based on the WHO recommendations, most countries are eliminating the Cat. 2 TB treatment and using the following as operational ways to treat patients:

- Patients with a history of previous treatment who have pan-susceptible disease to be treated with first-line drugs
- Patients with mono- or poly-resistance (other than RRTB) should be treated with appropriate regimens
- Patients with RR/MDR-TB should be treated with second-line therapy

6.2.15.1 *Diagnosis of Hr TB*

Hr Tb can be diagnosed using 1st Line LPA and phenotypic conventional DST to 1st line drugs. It has been observed that such cases are now being increasingly reported and early detection of such cases is crucial. The following are suggested to test for Hr TB;

1. Close contacts of patients who are being treated with mono/poly DR TB should be tested both by Xpert and by 1st Line LPA if Xpert shows no RR TB
2. DS TB retreatment patients when tested with Xpert and result is TB with no RR, such patient should be tested by LPA 1st Line
3. In DS TB non-converters when Xpert shows TB with no RR
4. Clinicians should request testing 1st line drugs by liquid/solid DST, where LPA is not available or non-interpretable and patient response to treatment is poor

Once mono and poly DR TB (other than RR TB) is reported, it is also imperative to request SL LPA to exclude resistance to FQs.

6.2.15.2 *Treatment of Hr TB*

In patients with confirmed rifampicin-susceptible isoniazid-resistant tuberculosis, treatment with rifampicin, ethambutol, pyrazinamide and levofloxacin is recommended for a duration of 6 months. However, if no REZ FDC is available then the suitable option is to use HREZ FDC. Intermittent or divided dosing of the 6(H)REZ-Lfx regimen is to be avoided and weight band dosing scheme for Lfx is recommended.

The implementation of this recommendation requires that the (H)REZ-Lfx regimen is administered only in patients in whom resistance to isoniazid is confirmed and resistance to rifampicin has been excluded. Preferably, testing for resistance to fluoroquinolones where possible prior to treatment initiation. It is also important to test for resistance to pyrazinamide and later treatment adjusted, while E and S has no practical implication on treatment as DST is not usually reliable. In line with the WHO recommendations, in practice the following situations apply at the field level:

1. Hr-TB is confirmed before TB treatment is started: treatment with the (H)REZ-Lfx is started immediately. If the diagnosis is strongly presumed (e.g. close contacts of a confirmed Hr-TB source case) but results of drug susceptibility testing are still pending, the regimen may be introduced. Should drug susceptibility test results taken at the start eventually show susceptibility to isoniazid, then levofloxacin is stopped, and the patient continues treatment in order to complete a 2HREZ/4HR regimen.
2. Hr-TB is confirmed after the start of treatment with 2HREZ/4HR regimen: This includes patients who had undiagnosed isoniazid resistance at the start or who developed isoniazid resistance later while on first-line regimen treatment. In such cases, rapid molecular testing for rifampicin resistance must be done (or repeated). Once rifampicin resistance is excluded, a full 6-month course of (H)REZ-Lfx is given. The duration is driven by the need to give levofloxacin for 6 months, which usually implies that the companion first-line medicines are taken for longer than this.
3. If rifampicin resistance is detected, the patient needs to be started on a recommended MDRTB treatment regimen.

It is imperative to perform Xpert in all mono and PDR cases before enrolling them on treatment. This excludes cases with R, RZ, RZE resistance as such cases require full MDR TB treatment. Likewise, it is essential to always use Xpert MTB/RIF at month 0, 2, and 3 and if rifampicin resistance is found switch to full MDR-TB treatment.

6.2.16 **Drug dosages for Hr-TB regimen**

Table 7: Drug dosages for Hr-TB regimen with 4-drug FD C (RHZE) - Adults

Weight bands in adults	4-drug adult FDC RHZE-150/75/400/275*	Levofloxacin 250mg
35-49 kg	3 tablets	3 tablets
50-64 kg	4 tablets	4 tablets
65-75 kg	5 tablets	4 tablets

*patients <35 kg may receive 3 tablets/day and patients >75 kg may receive 6 tablets/day if they tolerate this dose

Table 8: Drug dosages for Hr-TB regimen with 3-drug FDC (RHZ) - Children

Weight bands in children*	3-drug paediatric FDC RHZ-	Ethambutol 100mg	Levofloxacin 100mg
4-7 kg	75/50/150 1 tablet	1 tablet	1 tablet
8-11 kg	2 tablets	2 tablets	2 tablets
12-15 kg	3 tablets	3 tablets	3 tablets
16-24 kg	4 tablets	4 tablets	4 tablets

*In children weighing 25 kg or more the adult schedule shown in the previous section is followed.

If levofloxacin 100mg dispersible tablet is not available, the 250mg tablet can be used with 6(H)REZ in children aged 0-14 years, based on a slightly different weight band from the above:

Weight	Levofloxacin 250mg
5 - 6 kg	½ tablet / day
7 - 9 kg	¾ tablet / day
10 – 15 kg	1 tablet / day
16 – 23 kg	1.5 tablets / day
24 – 30 kg	2 tablets / day
31 kg +	Follow adult schedule (up to 1g / day)

6.2.17 Organization of DR-Treatment services and methods to ensure patient adherence

6.2.17.1 *Education of patients and their families*

All patients and their families should receive education about MDR-TB, its treatment, potential adverse drug reactions and the need for adherence with therapy. Educational interventions should commence at the start of therapy and continue throughout the course of treatment. Education can be provided by the attending doctors, nurses, lay and community health workers, and other health care workers. Materials need to be appropriate to the literacy levels of the population and should be culturally sensitive.

The key in the management of MDR-TB is the assurance of a steady supply of medications provided to the patients free of charge through a reliable network of trained providers. Care should be delivered by a multidisciplinary team of providers, including physicians, nurses, social workers, and community health workers or volunteers.

6.2.17.2 *Initial in-patient care*

When an MDR-TB presumptive is confirmed to have MDR-TB, the respective DTC who referred the patient for investigation, will be informed of the DST result by the PMDT Unit of the National hospital. The DTC will confirm the address of the patient and will arrange for the patient's transportation to the PMDT Unit in the National Hospital. The PMDT Unit will decide upon DR-TB treatment for the patient and refer the patient to Klibur Domin (in-patient facility), with their DST result and the "DR-TB referral for treatment form". The patient is counselled, a PMDT treatment card opened, a PMDT patient Identity Card issued to the patient, and DR-TB treatment initiated. The patient will be admitted to the DR-TB in-patient facility for a period of 4 weeks for pre-treatment evaluation and to monitor for early ADRs. Those who are severely ill or with co-morbidities can be admitted for a longer duration as per the physician's judgement. Patients will be discharged subsequently and will continue treatment on ambulatory basis. The program will establish mechanisms for follow up of patients at the referral hospitals in the municipalities and ensure the availability of necessary investigations and trained staff to monitor, manage, record and report ADRs appropriately. In the interim, until these facilities are secured, patients will be admitted for a longer duration (3-6 months) at the DR-TB in-patient facility (Klibur Domin).

6.2.17.3 *Ambulatory care*

Following completion of the above, the patient is discharged from the PMDT in-patient facility to the municipality that they reside in, with one week's supply of drugs, and a copy of the treatment card and referral form. The respective DTC must be informed by the attending physician of the patient's planned discharge one week prior to the actual date of discharge, by means of the "PMDT referral for treatment form". The respective DTC should co-ordinate with the PMDT facility for the transfer of drugs and patient records. The DTC should send a copy of the treatment card to the PMDT facility at the end of every quarter for updating of the MDR-TB Register. The patient should be provided DOT through the nearest DOT centre. Community based DOT may be an alternative option. Community based DOT requires very close daily monitoring. The patient's family must be well informed and motivated to collaborate, a reliable DOT provider must be appointed, and regular supervision is essential. The DOT provider should be a person whom the patient is comfortable with. This may be a health worker trained to deliver second-line anti-TB medicines. The DOT provider should have the appropriate training and skills. Every month patients treated in an ambulatory setting must go to the nearest PMDT facility (CHC/Referral Hospital) where the required monthly follow-up investigations can be performed. The DOT provider and the treatment supporter must make certain that the patient does not miss these monthly appointments. Every 3 months the patient should have follow-up from the National Hospital/Klibur Domin by the DR-TB Committee.

A DR-TB patient on ambulatory treatment may be contagious, particularly during the early weeks or months of treatment. It is therefore extremely important that proper infection control measures are observed, not only in the PMDT facility but also at the patient's home and by the patients themselves.

This will require a lot of discipline by the patients, but they need to understand their responsibility and social duty to protect the community from exposure to drug resistant germs.

6.2.17.4 *Drug Intake*

Many of the second-line drugs cause gastro-intestinal upset, which is an important cause of non-adherence to treatment: many patients refuse to take certain medications or even the full treatment. In order to improve adherence, not all drugs have to be taken together, some may be administered in split doses and some may be given together with food. The only drugs that should never be given with food are H and Cs, while other drugs (Cfz, Bdq and Dlm) have to be taken with food to improve absorption.

6.2.17.5 *Adherence Support*

Patients with MDR-TB may be more likely to have had problems with non-adherence in the past. In addition, adherence with MDR-TB therapy is made more difficult by its prolonged treatment regimens, with larger numbers of drugs that have more serious adverse effect profiles. Thus, MDR-TB patients are at risk of not being able to appropriately adhere with treatment, an essential element to prevent the generation of pan-resistant strains with the potential for community-wide spread and virtually no chance of cure for the patient.

MDR-TB treatment can be successful with high overall rates of adherence when adequate support measures are provided. These measures include enablers and incentives for delivery of DOT to ensure adherence to treatment and may include the following: reimbursement of travel expenses to patient and attendants for visits to CHC and the PMDT in-patient facility; emotional/psychological support; patient, family and peer education on MDR-TB treatment; early and effective management of adverse drug reactions; and incentives to the DOT providers. The patients will be provided a monthly incentive for nutritional support and transport allowance for coming to the PMDT facility for monthly follow ups.

6.2.17.5.1 Socioeconomic interventions

Socio-economic problems should, as far as possible, be addressed to enable patients and their families to adhere to the MDR-TB treatment. The program, wherever available, will avail the services of professional social workers that can assess the need for the appropriate socioeconomic interventions, and monitor their delivery.

6.2.17.5.2 Social and emotional/ psychological support

Having MDR-TB can be an emotionally devastating experience for patients and their families; there may be stigma attached to the disease and this may interfere with adherence to therapy. In addition, the long nature of MDR-TB therapy combined with the medications' adverse effects may contribute to depression, anxiety and further difficulty with treatment adherence. The provision of emotional support to patients may improve chances of adhering with therapy. This support may be provided formally in the form of support groups or one-on-one counselling with trained providers. Informal support can also be provided by physicians, nurses, community workers or volunteers, and family members. Ideally a multidisciplinary team, comprising of a social worker, nurse, health educators, companions, and doctors, should be set up to act as a "support to adherence" team to the patient.

6.2.17.6 *Follow-up of the non-adherent patient*

When patients discontinue treatment, visits should be made to their houses by the health staff or community volunteer and the patients should be brought back to treatment. This should be done within one day of interruption.

All efforts should be made to prevent drop out of patients before it happens. It will be more difficult to motivate patients if drop out has already happened. However, if patients drop out, it should be recognized as early as possible. The important steps to prevent drop out are the following:

1. Recording of full addresses: Complete address of the patient should be recorded in the laboratory register, treatment card and the tuberculosis register. If available, the phone

number of the patient or a contact person should also be recorded. If the health staff feels that the patient is likely to drop out, then the health staff must collect more information about patient's residence and the details of a contact person.

2. Counselling and motivating the patient: At the beginning of treatment, the patient should be told about the important aspects of DR-TB and that DR-TB is curable only if treatment is taken regularly for the entire course. The patient should also be told about the need for follow up smear examination at regular intervals and its schedule.
3. Initial home visit: A visit to the patient's house should be made in order to confirm the address and to enquire whether any of the household contacts have symptoms of tuberculosis who should then be advised to have smear examination done.
4. Organization of the treatment cards: Treatment cards need to be kept in such a way that they can be easily found when patients come for DOT. Every day, the cards of those patients who have come for DOT should be kept as a different lot so that the cards of the patients who have not come for DOT will be easily visible.
5. Home visit to retrieve patients who discontinue treatment: If patients drop out from treatment, home visits should be made by the health staff or community volunteer to motivate and bring the patient back to treatment within one day of interruption in the intensive phase, and at least within a week in the continuation phase. The DOT provider should find out from the patient why he/she did not come for DOT and what can be done to ensure that he/she does not drop out in future. Health staff or community volunteer should never blame patients; instead, efforts should be made to understand the difficulties of the patient and to further motivate them to receive treatment regularly.

6.2.18 **Monitoring during DR-TB treatment**

6.2.18.1 ***Clinical monitoring***

Until sputum conversion, patients will be hospitalized at the Klibur Domin facility.

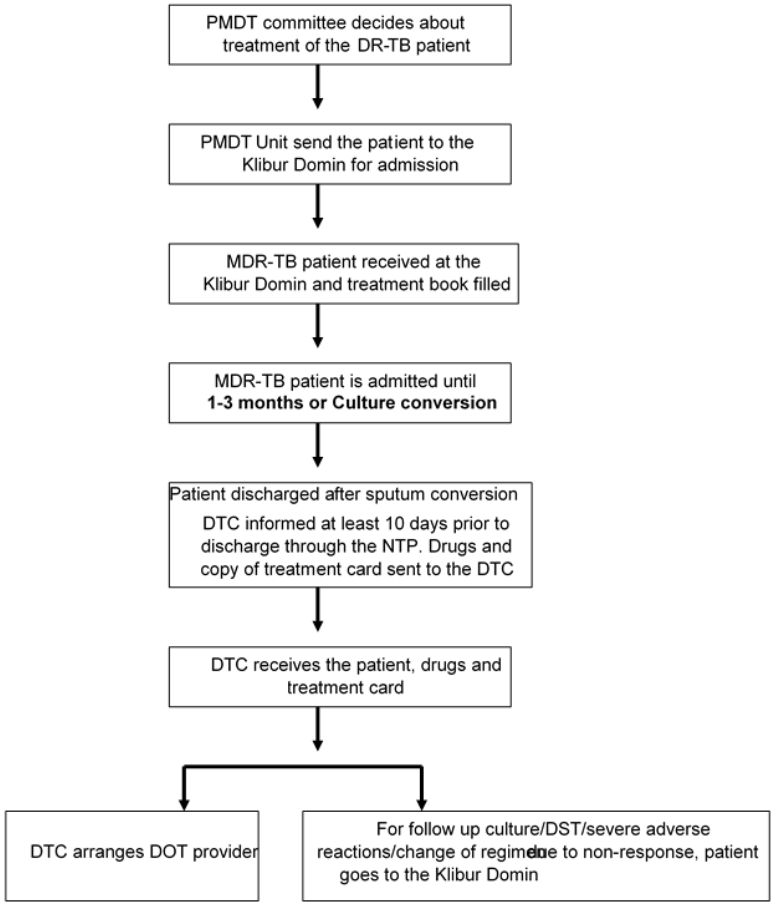
Patients will be hospitalized at the Klibur Domin facility for 4 weeks for pre-treatment evaluation and to monitor for early ADRs. Those who are severely ill or with co-morbidities can be admitted for a longer duration as per the physician's judgement. Patients will be discharged subsequently and will continue treatment on ambulatory basis. The program will establish mechanisms for follow up of patients at the referral hospitals in the districts and ensure availability of necessary investigations and trained staff to monitor, manage and record and report ADRs appropriately. In the interim, until these facilities are secured, patients will be admitted for a longer duration at the DR-TB in-patient facility (Klibur Domin).

During ambulatory treatment patients should visit the nearest PMDT facility (at the referral hospital) and will be seen by a doctor and follow up investigations will be done. Every 3 months the patient should visit Klibur Domin/National Hospital for assessment by the DR-TB Committee. The responsible doctor should assess clinical, microbiologic, and radiologic responses to treatment, measure weight, assess possible adverse reactions, and encourage the patient to continue treatment. The follow-up visit should result in updating of treatment cards. Patient flow and monitoring are summarized below.

Close monitoring of patients is necessary to ensure that the adverse effects are recognized early by the DOT provider. DOT makes it possible to closely monitor patients. Patients should be encouraged to volunteer if they experience any adverse effects, though they should not be asked any leading question to elicit any adverse reaction. However, if the patient makes any complaint, s/he should be interrogated in detail and the necessary action taken. The DOT provider should be trained to recognize adverse reactions like nausea, vomiting, diarrhoea, skin rash, loss of hearing, reduced sensation, psychiatric symptoms and jaundice. Training should also be provided on the management of minor reactions and when the patients should be referred to the medical officer. Severe adverse reactions should be referred to the PMDT unit. Patients may need to be hospitalized during CP for medical or psychosocial reasons.

Severe adverse reactions should be referred to the PMDT unit. Patients may need to be hospitalized during CP for medical or psychosocial reasons.

Figure 2: Patient flow and monitoring during DR-TB treatment



6.2.18.2 ***Follow-up investigations during treatment***

The most important objective evidence of response to MDR treatment is the conversion of sputum culture to negative. Smear conversion is less reliable than culture conversion, which reflects the viability of tubercle bacilli and is a more accurate reflection of response to treatment. Good quality sputum is essential to get proper results.

- Patients will be considered **culture converted** after having two consecutive negative cultures taken at least one month apart.
- Time to culture conversion is calculated as the interval between the date of MDR-TB treatment initiation and the date of the first of these two negative consecutive cultures (the date that the sputum specimens are collected for culture should be used).
- Patients will be considered **smear converted** after having two consecutive negative smears taken at least one month apart.

The table below summarises all required follow-up examinations during DR-TB treatment: The cultures should be done monthly from 3-6 months and then quarterly until the end of treatment

Table 9: Follow-up examinations during DR-TB treatment

	Baseline Visit	Week 2	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	While on injectable*	Until end of treatment	End of treatment	Post-treatment month 6
Clinical evaluation												
Vital signs	X		X	X	X	X	X	X	Monthly			
Performance status	X			X							X	
Brief peripheral neuropathy screen	X		X	X	X	X	X	X	Monthly		X	X
Visual acuity and colour-blindness screen	X		X	X	X	X	X	X	Monthly		X	X
Assessment and follow-up of adverse events	X	X	X	X	X	X	X	X	At each scheduled /unscheduled visit		X	X
Weight	X	X	X	X	X	X	X	X	Monthly		X	
Bacteriological testing												
Smear	X		X	X	X	X	X	X	Monthly		X	X
Culture	X				X	X	X	X	Quarterly		X	X
Xpert MTB/RIF	X											
Culture-based first-line DST	X			If smear- or culture-positive								
Laboratory testing												
ECG	X	X	X	X	X	X	X	X			X	X
Full Blood Count	X	X	X	X	X	X	X	X	Monthly		X	
Urea, creatinine	X		X	X	X	X	X	X	Monthly		X	
Serum electrolytes (potassium)	X		X	X	X	X	X	X	Monthly		X	
Liver function tests (AST, ALT)	X		X	X	X	X	X	X	Monthly		X	
TSH	X				X				every 3 months			
Chest X-Ray	X							X			X	

6.2.19 Management of contacts of MDR-TB patients

A close contact of a MDR-TB patient is someone who has been exposed to infection with drug resistant *M. tuberculosis* by sharing air space with a patient who has confirmed MDR-TB. Close contacts are defined as people living in the same household or spending multiple hours a day together with the patient in the same indoor living space. They can be family members, colleagues, friends, roommates and neighbours.

All close contacts of MDR-TB cases should be identified through contact tracing and those who are symptomatic will be evaluated for active TB. Special attention needs to be paid to children. The TB screening will include a complete clinical examination, an Xpert MTB/Rif test of a sputum sample or other relevant specimen and a chest X-ray. If the Xpert MTB/Rif result is RR, the patient must be sent to the nearest MDR Unit.

Screening of contacts of MDR-TB patients should be an ongoing process. Asymptomatic contacts need to be screened at diagnosis, at the end of the intensive phase and at the end of treatment. Contacts should also receive appropriate health information and education regarding TB and MDR-TB.

Preventive therapy is recommended for contacts of MDR-TB patients

6.2.20 Palliative care

If a patient presents a treatment failure and an alternative treatment regimen is not possible, treatment will have to be suspended. Suspension of therapy should be carefully planned. It should start with discussions among the clinical team, including all physicians, nurses and DOT workers involved in the patient's care. Once the clinical team decides that treatment should be suspended, a clear plan should be prepared for approaching the patient and the family. This process usually requires a number of visits and takes place over several weeks. Home visits during the process offer an excellent opportunity to talk with family members and the patient in a familiar environment. It is not recommended to suspend therapy before the patient understands and accepts the reasons to do so and agrees with the supportive care offered.

A number of supportive measures can be used once the therapy has been suspended. It is very important that medical visits continue and that the patient is not abandoned. Supportive care for MDR-TB treatment failure includes:

- Pain control and symptom relief: Codeine with paracetamol gives relief from moderate pain but also helps control cough. Other cough suppressants can be added. If possible, stronger analgesics, including morphine, should be used to keep the patient adequately comfortable.
- Relief of respiratory insufficiency. Oxygen can be used to alleviate shortness of breath. Morphine also provides significant relief from respiratory insufficiency and should be offered if available.
- Nutritional support. Small and frequent meals are often best for a person at the end of life.
- Regular medical visits. When therapy stops, regular visits by the treating physician and support team should not be discontinued.
- Continuation of ancillary medicines. All necessary ancillary medications should be continued as needed to treat symptoms such as nausea, vomiting, depression, anxiety.
- Psychological support to the patient and family caregivers to assist in the planning of decisions related with the end of life and provision of emotional support.
- Respect for patient's beliefs and values. The patient and family caregivers may seek and find comfort in spiritual and religious practices. The health-care providers should respect this.

- Inpatient-care or home-care. Home-based care should be offered to patients and families who want to keep the patient at home, whenever appropriate infection control practices can be followed. Institutionally based end-of-life care should be available to those for whom home care is not feasible or desirable.
- Preventive measures. Oral care, prevention of bedsores, bathing and prevention of muscle contractures are indicated in all patients. Regular scheduled movement of the bedridden patient is very important.
- Infection control measures should be continued as the patient often remains infectious for long periods of time.

7 TB CO-MORBIDITIES AND SPECIAL SITUATIONS

7.1 TB TREATMENT IN PEOPLE LIVING WITH HIV

Among treated TB patients, death rates are higher in HIV-positive than in HIV-negative patients. Case-fatality is higher in people living with HIV with smear-negative pulmonary and extrapulmonary TB, as these patients are generally more immunosuppressed than those with smear-positive TB. The case-fatality rate is reduced in patients who receive concurrent ART (see section 7.1.4.4 below).

The first priority for HIV-positive TB patients is to initiate TB treatment, followed by co-trimoxazole and ART. For TB diagnosed in a person already taking ART, see section 7.1.3.1.

New TB patients living with HIV should be treated with the same regimen used for non-HIV patients.

Rifampicin induces the activity of hepatic enzymes, leading to sub-therapeutic concentrations of some antiretroviral drugs. This is discussed in Annex 2: Essential information on first-line anti-tuberculosis drugs.

7.1.1 Goal and objectives of TB-HIV activities

The HIV pandemic presents a significant challenge to global TB control. TB is a leading preventable cause of death among PLHIV. NTP will engage in a set of collaborative activities with the HIV/AIDS programme at the CDC department to mitigate the dual burden of TB/HIV in populations at risk of/or affected by both diseases. The goal of collaborative TB/HIV activities is to decrease the burden of TB and HIV in people at risk of/or affected by both diseases. The objectives are:

- To establish and strengthen the mechanisms of collaboration and joint management between the HIV programme and the NTP for delivering integrated TB and HIV services through the primary health care services
- To reduce the burden of TB in PLHIV, their families and communities by ensuring the delivery of the Three Is for HIV/TB (see below) and the early initiation of ART
- To reduce the burden of HIV in patients with presumptive and diagnosed TB, their families and communities by providing HIV prevention, diagnosis and treatment.

7.1.2 Mechanism for delivering integrated TB and HIV services

1. Establishment of a national coordinating body for collaborative TB/HIV activities

The HIV program and the NTP, together with partners from the private-for-profit sector and civil society organizations will work together to provide access to integrated services for the prevention, diagnosis, treatment and care of TB/HIV. A national coordinating body for collaborative TB/HIV activities will be set up with the following areas of responsibility:

• governance and coordination at national and sub-national levels

• resource mobilization

• provision of general policy and program direction for the management of activities

• capacity-building including training

• ensuring coherence of communications about TB and HIV

• ensuring the involvement of civil society, nongovernmental and community organizations, and individuals

2. Determination of HIV prevalence among TB patients and TB prevalence among PLHIV

Surveillance is essential to inform programme planning and implementation. There are three key methods for surveillance of HIV among TB patients: a) periodic surveys (cross-sectional HIV seroprevalence surveys among a small representative group of TB patients within a country); b) sentinel surveys (using TB patients as a sentinel group within the general HIV sentinel surveillance system); and c) data from the routine HIV testing and counselling of patients with presumptive or diagnosed TB. The national coordinating body should chose a method taking into account the underlying HIV epidemic state, the overall TB situation, and the availability of resources and experience. Incorporating HIV testing with future TB prevalence surveys and anti-TB drug resistance surveillance will offer an opportunity to expand HIV testing and improve knowledge on the relationship between HIV and DR-TB at the population level. It also provides critically important individual benefits to PLHIV, including better access to testing, early case detection and rapid initiation of treatment. Rates of TB among people newly enrolled in HIV care and/or among those initiating ART should be monitored based on analysis of routine programme data.

3. Joint TB/HIV planning to integrate the delivery of TB and HIV services

Medium and long-term joint strategic planning to successfully and systematically scale up collaborative TB/HIV activities nationwide and deliver integrated TB and HIV services should be developed. The HIV programme and the NTP will include TB/HIV components in their national plans for prevention, diagnosis, treatment and care. The roles and responsibilities of each programme in implementing specific TB/HIV activities at all levels should be clearly defined. Joint planning should be harmonized with Timor-Leste's national health strategic plans and health-system strengthening agenda.

Crucial elements for joint TB/HIV planning include the activities detailed in this chapter of the NTP manual, as well as resource mobilization, capacity-building and training, TB/HIV advocacy, programme communication, the involvement of CSOs, including NGOs, PLHIVs, people who have been diagnosed with TB (including people who have completed anti-TB treatment) and communities, engagement of private for-profit and operational research. The HIV programme and the NTP should also plan and coordinate reviews of joint programmes as well as routine monitoring and evaluation of integrated services.

4. Monitoring and evaluation of collaborative TB/HIV activities

M&E provides the means to assess the quality, effectiveness, coverage and delivery of collaborative TB/HIV activities. It promotes a learning culture within and across programmes and ensures continuous improvement of individual and joint programme performance. M&E involves collaboration between the HIV programme, the NTP and the general health system, the development of referral linkages between different services and organizations, and joint supervision. These activities should be integrated with existing M&E systems.

7.1.3 Reducing the burden of TB among people living with HIV and initiating early antiretroviral therapy (the Three I's for HIV/TB)

7.1.3.1 *Intensified TB case-finding and assurance of high-quality anti-tuberculosis treatment*

All people living with HIV should be regularly screened for TB using a clinical symptom-based algorithm consisting of current cough, fever, weight loss or night sweats at the time of initial presentation for HIV care and at every visit to a health facility or contact with a health-care worker afterwards. Adults and adolescents living with HIV who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases. Screening for TB is important regardless of whether they have received or are receiving TPT or ART. Similarly, children living with HIV who have any one of the following symptoms – poor weight gain, fever or current cough or contact history with a TB case – may have TB and should be evaluated for TB and other conditions.

In people with a positive screen, the diagnostic workup for TB should be done in accordance with the diagnostic algorithms (Figure 6 & 7) of this Manual to identify either active TB or an alternative

diagnosis. Smear-negative pulmonary and extrapulmonary TB are common among people living with HIV and are associated with poor treatment outcomes and excessive early mortality. The Xpert MTB/RIF assay will be the primary diagnostic test for TB in people living with HIV. Among seriously ill patients in HIV-prevalent settings, empirical anti-tuberculosis treatment should be initiated in case of negative investigations and no improvement to parenteral antibiotics. New TB patients living with HIV should receive the standard regimen described in section 6.1.3 of this Manual and should be started on ART regardless of CD4 count as soon as possible within the first 8 weeks of anti-tuberculosis treatment.

Summary of recommendations

1. Adults and adolescents living with HIV should be screened for TB with a clinical algorithm; those who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases
2. Children living with HIV who have any of the following symptoms – poor weight gain, fever or current cough or contact history with a TB case – may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, children should be offered TPT regardless of their age
3. The Xpert MTB/RIF assay will be the primary diagnostic test for TB in people living with HIV. Urine Lateral flow urine lipoarabinomannan assay (LF-LAM) can also be used for confirming TB among PLHIV in the eligible population as per the 2019 WHO Policy Update on LF-LAM for the diagnosis of active tuberculosis in people living with HIV.
4. TB patients with known positive HIV status should receive the standard TB treatment regimen described in section 6.1.3 of this Manual.

7.1.3.2 *Tuberculosis Preventive Therapy (TPT) and early antiretroviral therapy*

TPT is given to individuals with latent infection with *Mycobacterium tuberculosis* in order to prevent progression to active disease *(Refer to Section 6.1: Management of LTB*I). Exclusion of active TB is critically important before TPT is started. The absence of all of current cough, night sweats, fever, or weight loss can identify a subset of adolescents and adults living with HIV who have a very low probability of having TB disease that can reliably be initiated on TPT. In children, the absence of poor weight gain, fever and current cough can identify children who are unlikely to have TB. TPT is given as part of a comprehensive package of HIV care for all eligible PLHIV irrespective of degree of immunosuppression, ART use, previous TB treatment and pregnancy. Information about TPT should be made available to all PLHIV. Providing TPT as a core component of HIV preventive care should be the responsibility of the HIV program and HIV service providers. Evidence has shown that TPT is as efficacious but safer than rifampicin and pyrazinamide containing regimens used for prevention of TB disease in those latently infected. Tuberculin skin testing (TST) should not be a requirement for initiating TPT among PLHIV.

ART is a powerful strategy to reduce TB incidence among PLHIV across a broad range of CD4 cell counts. ART reduces the individual risk of TB by 54% to 92% and the population-based risk by 27% to 80% among PLHIV. ART also reduces TB recurrence rates by 50%. The most profound reduction in incidence of HIV-related TB is seen when ART is initiated as soon after people test HIV-positive. Timor-Leste's national TB/HIV coordinating recommends initiating ART for all HIV-positive patients regardless of CD4 count.

Summary of recommendations

1. Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered TPT
2. Adults and adolescents who are living with HIV, have unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive TPT as part of a comprehensive package of HIV care. TPT should be given to such individuals irrespective of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB, and pregnant women

3. Tuberculin skin test (TST) is not a requirement for initiating TPT in PLHIV. PLHIV who have a positive TST benefit more from TPT; TST can be used where feasible to identify such individuals
4. Providing TPT to PLHIV does not increase the risk of developing isoniazid-resistant TB. Therefore, concerns regarding the development of INH resistance should not be a barrier to providing TPT
5. Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB
6. Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive TPT as part of a comprehensive package of HIV prevention and care services
7. In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive TPT if the evaluation shows no TB disease
8. All people living with HIV irrespective of the WHO clinical stage should start ART

7.1.4 Interventions to Reduce the burden of HIV in TB presumptive and patients with diagnosed TB

7.1.4.1 *HIV testing and counselling for TB patients*

HIV testing and counselling for TB patients offers an entry point for a continuum of prevention, care, support and treatment for HIV and for TB. Evidence from observational studies shows that testing TB patients and their contacts for HIV yields a high number of new diagnoses of HIV infection, as prevalence of HIV is higher than among the general adult population. Routine HIV testing and counselling should be offered to all TB patients as benefits of testing accrue to the patient, their partner, the family and the community at large. The testing should be readily available and voluntary, informed consent should be obtained and confidentiality should be protected. Moreover, TB patients with a new potential HIV exposure or who are at higher risk of HIV exposure and with an HIV-negative test result should be re-tested after 4 weeks from the time of initial testing.

Summary of recommendations

1. Routine HIV testing should be offered to all TB patients
2. Partners of known HIV-positive TB patients should be offered voluntary HIV testing and counselling with mutual disclosure

7.1.4.2 *HIV prevention interventions for patients with presumptive and diagnosed TB*

Prevention of HIV includes interventions to: a) prevent sexual transmission through male and female condoms, male circumcision, HIV testing and counselling including couple's counselling and testing, early ART; b) prevent transmission through sharing contaminated injecting equipment among injecting drug users; and c) behavioural interventions and brief interventions to prevent hazardous alcohol use and use of other psychostimulants.

HIV prevention services also include prevention of vertical transmission of HIV. All HIV-infected women should start lifelong ART, which is also safe and effective in reducing vertical transmission.

In health-care settings, transmission of HIV can be prevented through primary prevention measures such as standard precautions, injection safety, blood safety and safe waste disposal, as well as secondary prevention measures such as occupational post-exposure prophylaxis. Among people who inject drugs, comprehensive harm reduction programming such as wide access to sterile injecting equipment, opioid substitution therapy and outreach services to reduce the risk of HIV transmission and other negative health effects of injecting drug use should be implemented.

Summary of recommendations

1. All health care facilities should implement comprehensive HIV prevention strategies for their patients and their partners, targeting sexual, parenteral or vertical transmission or should establish a referral linkage with the HIV program to do so.

2. Procedures for voluntary, acceptable and confidential HIV counselling and testing for health-care providers and for reduction of occupational and nosocomial exposure to HIV infection should be in place at all health care facilities.
3. All personnel working with presumptive and confirmed TB cases, PLHIV and people who use drugs should be able to assess risk factors for HIV infection and transmission and should provide comprehensive information and services to their clients to minimise their risks.
4. Access to comprehensive TB and HIV prevention, diagnosis, treatment and care as well as drug treatment services, including opioid substitution therapy, should be ensured for people who use drugs
5. Vertical transmission of HIV should be prevented by referring all HIV-positive pregnant women attending TB services to providers of services for prevention of vertical transmission of HIV for ART or prophylaxis as needed.

7.1.4.3 *Co-trimoxazole preventive therapy for TB patients living with HIV*

Co-trimoxazole is a broad-spectrum antimicrobial agent that prevents a range of secondary bacterial and parasitic infections in eligible adults and children living with HIV. TB patients living with HIV should receive Co-trimoxazole preventive therapy (CPT) and it should be implemented as an integral component of the HIV chronic care package. CPT is a simple, well-tolerated and cost-effective intervention for PLHIV and can be administered concomitantly to ART. Evidence from randomized controlled trials, including areas of high levels of antibiotic resistance, has shown reduced mortality, morbidity and hospitalization with no significant increase in adverse events among smear-positive TB patients with HIV regardless of their CD4 counts. CPT does not select for sulfadoxine–pyrimethamine-resistant malaria parasites among HIV-uninfected household members of PLHIV receiving the medicine, and also reduces the number of malaria episodes among household members. Routine CPT should be administered in all HIV-infected patients with active TB disease regardless of their CD4 cell count.

Summary of recommendations

- Routine co-trimoxazole preventive therapy should be administered in all HIV-infected patients with active TB disease regardless of their CD4 counts

7.1.4.4 *HIV prevention interventions, treatment and care for TB patients living with HIV*

A comprehensive package of prevention, diagnosis, treatment and care interventions (continuum of care) should be provided to all PLHIVs, ideally starting well before the need for ART. Pre-ART care includes regular assessment of the clinical and immunological stages of infection, prevention of illness, care for OIs, preparation for adherence to ART, nutritional support, provision of safe water, sanitation and hygiene, psychosocial support, and prevention and management of mental health disorders, including alcohol and other substance use. It is also essential to provide HIV prevention methods for PLHIV to prevent inadvertent HIV transmission ("positive prevention" or "prevention for positives").

A continuum of care should also be provided to PLHIVs who are receiving, or who have completed their anti-TB treatment through integrated services or strengthened referral systems. Particular attention should be paid to seriously ill patients (e.g., patients with MDR-TB and XDR-TB). Palliative care, both chronic and terminal as needed, should be offered to ensure that patients and their families live out their lives with minimal suffering and loss of dignity, even when all available curative treatments have been exhausted.

Summary of recommendations

1. All PLHIV who are diagnosed with TB should receive integrated services for prevention, diagnosis, treatment and care of TB and HIV.
2. HIV programmes and TB-control programmes should ensure access to a continuum of comprehensive and integrated services for prevention, care and treatment for PLHIVs who are receiving, or who have completed their anti-TB treatment.

7.1.4.5 *Provision of ART for TB patients living with HIV*

ART greatly improves the survival and the quality of life of TB patients living with HIV, prevents HIV transmission, and should be considered part of HIV and TB treatment and prevention. The availability of ART can also encourage people to be tested for HIV. All health care facilities should ensure that TB patients diagnosed with HIV infection are offered ART as early as possible.

ART should be started as a matter of emergency (within 2 weeks after the onset of anti-TB treatment) in TB patients with a CD4 count less than 50 cells/mm^3 and as early as possible in the remaining cases. Caution is needed in PLHIVs with TB meningitis, as immediate ART is significantly associated with more severe adverse events when compared with initiation of ART 2 months after the start of anti-TB treatment.

Patients should be closely followed up to assess the occurrence of side-effects related to cotreatment and of TB-associated immune reconstitution inflammatory syndrome (IRIS), which is common in patients with TB started on ART, but usually self-limited.

Early use of ART is also recommended for TB patients living with HIV who also receive medication with second-line anti-TB regimens for DR-TB. Rifampicin reduces drug levels of both non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors through induction of the cytochrome P450 liver enzyme system. Efavirenz should be used in preference to nevirapine when rifampicin is needed for treatment of TB. When rifampicin is given with protease inhibitors, highly variable and mainly subtherapeutic plasma concentrations of the protease inhibitor are observed, even in the presence of boosted doses of ritonavir. Rifabutin, listed in WHO Model List of Essential Medicines, is a less potent inducer of the cytochrome P450 system, which can be used in patients on ART regimens that include a protease inhibitor.

Summary of recommendations

1. ART should be started in all TB patients living with HIV irrespective of their CD4 counts
2. Anti-tuberculosis treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment. Those HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells cells/mm3) should receive ART immediately within the first 2 weeks of initiating TB treatment.
3. Efavirenz should be used as the preferred NNRTI in patients starting ART while on anti-TB treatment (strong recommendation, high quality of evidence)
4. Rifabutin can be used instead of rifampicin in patients on ART regimens that include a protease inhibitor

7.1.4.6 *Treatment of MDR-TB IN PEOPLE LIVING WITH HIV*

The presentation of MDR-TB in the HIV-infected patient does not differ from that of drug-sensitive tuberculosis in the HIV-infected patient. However, the diagnosis of TB in HIV-positive persons can be more difficult and may be confused with other pulmonary or systemic infections. As the HIV disease progresses and the individual becomes more immunocompromised, the clinical presentation is proportionately more likely to be extrapulmonary or smear-negative than in HIV-uninfected TB patients. This can result in misdiagnosis or delays in diagnosis, and in turn, higher morbidity and mortality. The treatment of HIV positive individuals with MDR-TB is the same as for HIV negative patients. However, treatment is more difficult and adverse events more common. Deaths during treatment, partly due to TB itself and partly due to other HIV-related diseases, are more frequent in HIV-infected patients, particularly in the advanced stages of immunodeficiency. Due to the increased frequency of adverse drug events, rigorous monitoring in this particular group of patients is required in order to ensure adherence to treatment, early identification and treatment of adverse events and to reduce default.

7.1.4.6.1 Initiating ART in patients with MDR- TB

The use of ART in HIV infected patients with TB improves survival for both drug resistant and susceptible disease. However, HIV infected MDR patients without the benefit of ART may experience mortality rates exceeding 90%. The likelihood of adverse effects could compromise the treatment of HIV or MDR-TB if both treatments are started simultaneously. On the other hand, undue delay in starting ART could result in significant risk of HIV-related death amongst MDR patients. ART should be initiated as soon as possible in all HIV/TB co-infected patients with active TB (within 8 weeks after the start of TB treatment).

Patients who are already on ART at the time of MDR-TB diagnosis should be continued on ART when MDR-TB therapy is initiated. Occasionally, patients with HIV-related TB may experience a temporary exacerbation of symptoms, signs or radiographic manifestations of TB after beginning TB treatment. This paradoxical reaction occurs in HIV-infected patients with active TB and is thought to be a result of immune restitution due to the simultaneous administration of ARV and tuberculosis medication (IRIS Syndrome). Symptoms and signs may include high fever, lymphadenopathy, expanding intra-thoracic lesions and worsening of chest radiographic findings. The diagnosis of a paradoxical reaction should be made only after a thorough evaluation has excluded other aetiologies, particularly TB treatment failure. For severe paradoxical reactions prednisone (1-2 mg/kg for 1-2 weeks, then gradually decreasing doses) may be used. Both anti-TB treatment and Anti-Retroviral Treatment should be continued even there is an exacerbation of symptoms.

7.2 CHILDHOOD TB (2019 TB MTR)

Diagnosis of childhood TB: The diagnostic algorithm of TB in children has been available in the 2017 National Guideline for the Management of Tuberculosis in Children. The algorithm flow is clear but does not give detailed information on how to diagnose TB in children clinically. In addition, with the current algorithm the diagnosis of TB tends to be centralized at the National Hospital. Observation at the CHCs documented that the doctors at the CHCs never diagnosed TB in children but were giving treatment after the child was diagnosed by a paediatrician at the hospital. Meanwhile, as per the information from the paediatricians at the National Hospital, most childhood TB treated in the National Hospital were with EPTB, of which some were in late condition. This may indicate low awareness of childhood TB in the community, as well as the problem of early detection of TB in children by health workers at the CHCs.

The number of malnourished children in Timor-Leste is high. Nevertheless, they were hardly ever been screened for TB. Integration between the Department of Nutrition of MoH and NTP in this issue has not been established. Similarly, most health workers in Timor-Leste have been trained in integrated management of childhood illnesses (IMCI) by the Department of Maternal and Child Health of MoH; however there has been no coordination or integration between MCH and NTP. In fact, recently IMCI has listed TB as one possibility in children with cough > 2 weeks, fever and malnourished.

Treatment of TB in children: The current recommendation for treatment is using FDC drug, with a dosage of 50H/75R/150Z (Table 13).

Children with suspected or confirmed PTB or TB peripheral lymphadenitis who live in settings with low HIV prevalence and/or low prevalence of isoniazid resistance, and children who are HIV-negative, can be treated with a three-drug regimen (HRZ) for 2 months followed by a two-drug regimen (HR) for 4 months *(Source: Rapid advice: treatment of tuberculosis in children. Geneva, World Health Organization, 2010 (WHO/HTM/TB/2010.13)*. The number of FDC tablets for different weight categories of children is given in Table 14.

Table 13: The dosages of anti-TB medicines to be used daily for the treatment of TB in children:

Anti-TB drug	Dose and range (mg/kg body weight)	Maximum dose (mg)
Isoniazid	10 (7-15)	300
Rifampicin	15 (10-20)	600
Pyrazinamide	35 (30-40)	–

Table 14: Number of fixed-dose combination tablets for different weight categories

Weight	Numbers of tablets	
Band	Intensive phase:	Continuation phase:
	RHZ 75/50/150	RH 75/50
4-7 kg	1	1
8-11 kg	2	2
12-15 kg	3	3
16-24 kg	4	4
25+ kg	*Adult dosages recommended*	

Contact investigation: Screening of child household contacts of source cases with bacteriologically confirmed TB is recommended. The national guideline suggests the use of symptom-based screening, which is appropriate for a limited resource setting like most areas in Timor-Leste. Nevertheless, this recommendation has not been routinely implemented, and if implemented, no systematic recording and reporting is available.

Recommendations

- Improve commitment and political will by:
  - Designating a dedicated person to serve as a childhood TB focal point in the NTP.
  - Form a child TB working group in the NTP involving persons from the NTP, Department of MCH in MoH, Department of Nutrition of MCH, clinicians (paediatricians and general physicians), and partners.
  - Strengthening advocacy, communication and social mobilization for childhood TB
- Improving community awareness of TB (including childhood TB). Community campaign for TB should be conducted. Walk for talk forum is a good opportunity to start.
- Improving case-finding with simple algorithm to diagnose TB in children and to improve the preventive treatment coverage. Paediatric TB for Timor-Leste algorithm is as follows:

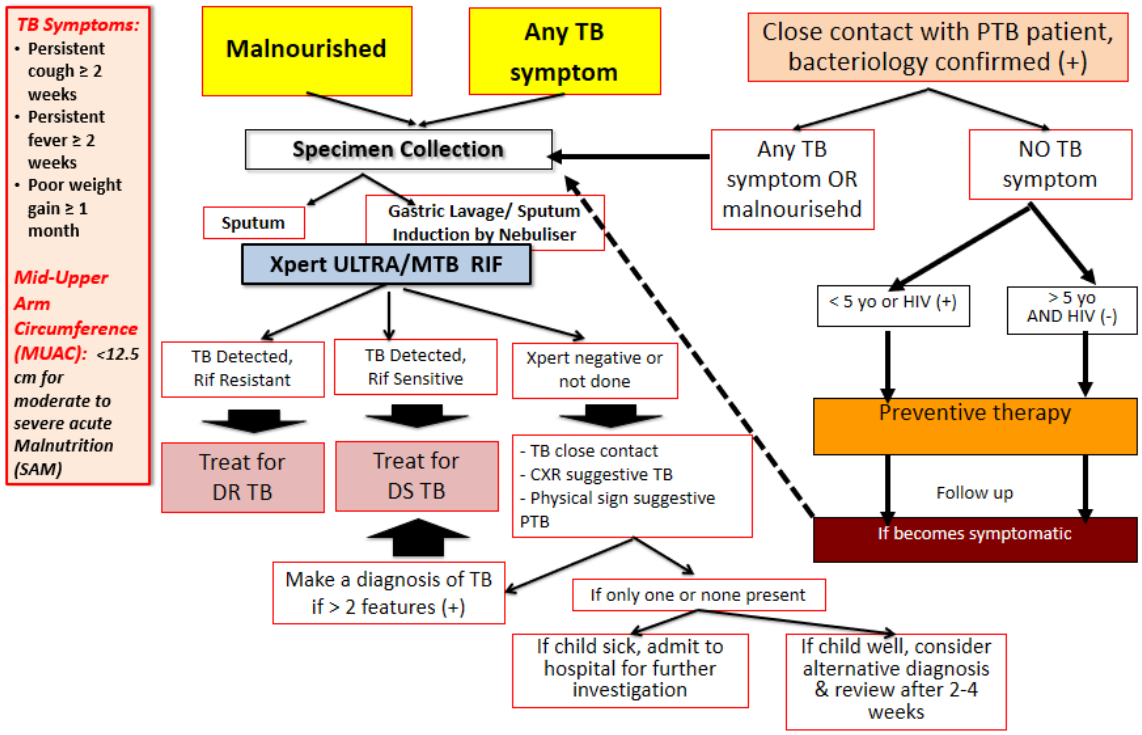


FIGURE 11. ALGORITHM FOR CHILD TB DIAGNOSIS AND PREVENTIVE TREATMENT

The entry point for finding TB in children can be either from children with malnutrition, any symptom of TB or those who had a close contact with a pulmonary TB patient (bacteriologically confirmed). All of these children should be screened for the possibility of TB. Collecting sputum in children has been thought to be challenging with low yield of positive bacteriology confirmation. However, with the increasing number of DR-TB cases in TL, we should initiate this as the first step to diagnose TB in children. Clinical diagnosis will be more likely in children, and this should be a competency for doctors at the CHCs to establish the diagnosis.

7.3 TREATMENT OF TB IN SPECIAL CONDITIONS

Although TB most commonly affects the lungs, any organ or tissue can be involved. Of specific forms of EPTB, lymphatic, pleural, and bone or joint disease are the most common, while pericardial, meningeal and disseminated (miliary) forms are more likely to result in a fatal outcome.

Provider-initiated HIV testing is recommended as part of the evaluation of all TB patients and patients in whom the disease is suspected. HIV testing is especially important in persons with or suspected of having EPTB because of the increased frequency of extrapulmonary involvement in persons with immunosuppression. Extrapulmonary TB is considered to be WHO clinical stage 4 HIV disease. (More details on the treatment of TB in persons living with HIV are provided in section 7.1)

Pulmonary and extrapulmonary disease should be treated with the same regimens. However, in individual cases 9–12 months of treatment for TB meningitis (given the serious risk of disability and mortality), and 9 months of treatment for TB of bones or joints (because of the difficulties of assessing response) can be considered by the treating physician. Unless drug resistance is suspected, adjuvant corticosteroid treatment is recommended for TB meningitis and pericarditis. In patients with tuberculous meningitis, an initial adjuvant corticosteroid therapy with dexamethasone or prednisolone tapered over 6-8 weeks should be used. In patients with tuberculous pericarditis, an initial adjuvant corticosteroid therapy may be used. The drug most frequently used is prednisolone, in a dosage of 2 mg/kg daily, increased up to 4 mg/kg daily in the case of the most seriously ill patients, with a maximum dosage of 60 mg/day. The dose should then be gradually reduced (tapered) over 1–2 weeks before stopping.

Although sometimes required for diagnosis, surgery plays little role in the treatment of extrapulmonary TB. It is reserved for management of late complications of disease such as hydrocephalus, obstructive uropathy, constrictive pericarditis and neurological involvement from Pott's disease (spinal TB). For large, fluctuant lymph nodes that appear to be about to drain spontaneously, aspiration or incision and drainage appear beneficial.

7.3.1 Pregnant women and women of childbearing age

7.3.1.1 *DS-TB in Pregnant women and women of childbearing age*

Women of childbearing age should be asked about current or planned pregnancy before starting TB treatment. A pregnant woman should be advised that successful treatment of TB with the standard regimen is important for successful outcome of pregnancy. The first line anti-TB drugs are safe for use in pregnancy.

A breastfeeding woman who has TB should receive a full course of TB treatment. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to the baby. Mother and baby should stay together, and the baby should continue to breastfeed. After active TB in the baby is ruled out, the baby should be given 6 months of isoniazid preventive therapy, followed by BCG vaccination.

Pyridoxine supplementation is recommended for all pregnant or breastfeeding women taking isoniazid.

7.3.1.2 *DR-TB in pregnant women and women of childbearing age*

- Pregnancy is not a contraindication to treatment.
- The decision whether or not to treat should be based on an assessment of the risks and benefits for the mother and the fœtus.
- If treatment is deferred: high risk of serious worsening of the mother's general condition during pregnancy, increased risk of abortion, low birth weight and risk of disseminated TB for the baby.

- Inform patient of the risk of Am-related secondary ototoxicity and potential teratogenic risk for the foetus. Consider replacing Am by Dlm or Bdq if Dlm is not available. Lzd is effective but more toxic.

RR-TB in pregnant women

- Risks:
    - For the mother:
        - Death, in case of no treatment.
        - Severe vomiting in the first trimester of pregnancy (Pto/Eto).
    - For the fœtus: potential teratogenic risk, ototoxicity (Am).
- Steps to take: Immediate treatment initiation.
        - Start short-course regimen. Consider replacing Am by Dlm or Bdq if Dlm is not available. Lzd is effective but more toxic.

RR-TB in women of childbearing age

- Do pregnancy test before treatment initiation.
- Advise against pregnancy during RR-TB treatment:
        - Encourage the use of contraceptives.
- During treatment follow-up visits:
        - Always enquire about amenorrhea.
        - Perform pregnancy test if needed.

7.4 PATIENTS WITH DIABETES

Diabetic patients with drug-resistant TB may have worse treatment outcomes. Furthermore, the presence of diabetes may enhance adverse reactions to anti-tuberculosis drugs, particularly renal impairment and peripheral neuropathies. Diabetes should be closely monitored and treated throughout the duration of anti-tuberculosis treatment.

Diabetes mellitus: A study in 2015[22] has estimated the prevalence of diabetes mellitus among adults in Timor to be around 15%. Diabetes has a strong association with TB and increases its risk by 3 times. TB patients with poor glycaemic control are at higher risk of unfavourable outcomes such as failure, relapse and amplification of resistance. The country currently does not have a formal NCD program and there are no guidelines on prevention and care of diabetes. Therefore, it is essential to screen all TB patients for diabetes and manage them appropriately. Also, diabetes patients must be screened for TB regularly (algorithms on TB-Diabetes bi-directional screening are attached). Testing for diabetes for all TB patients and ensuring adequate glycaemic control by drugs and lifestyle modification. Provide treatment (drugs and life-style modification) and follow up facilities for diabetes patients.

[22] An estimation of the prevalence of diabetes mellitus and diabetic retinopathy in adults in Timor-Leste; Rosie Claire Hewitt Dawkins et al; BMC Research Note Volume 8, Article number: 249 (2015)

Figure 12: Algorithm of TB screening among DM patients (Source: Adopted from Cambodia NTP Guidelines)

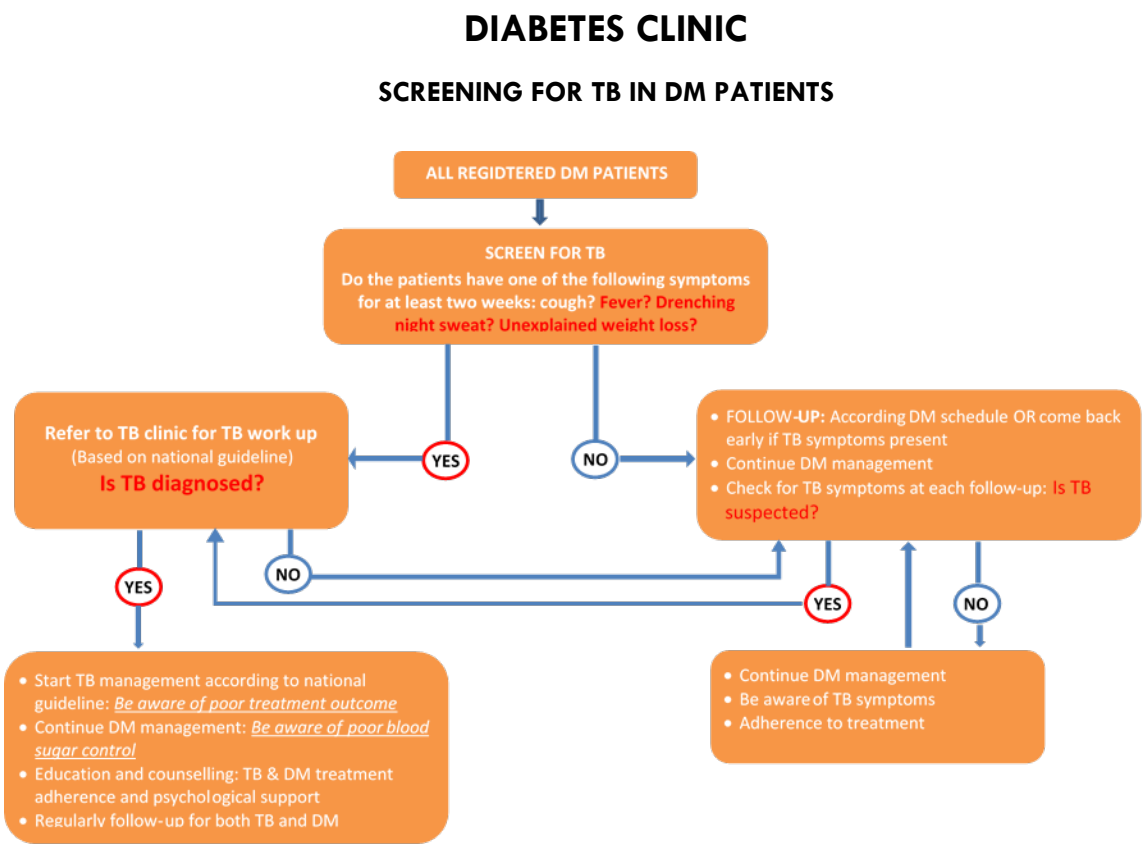
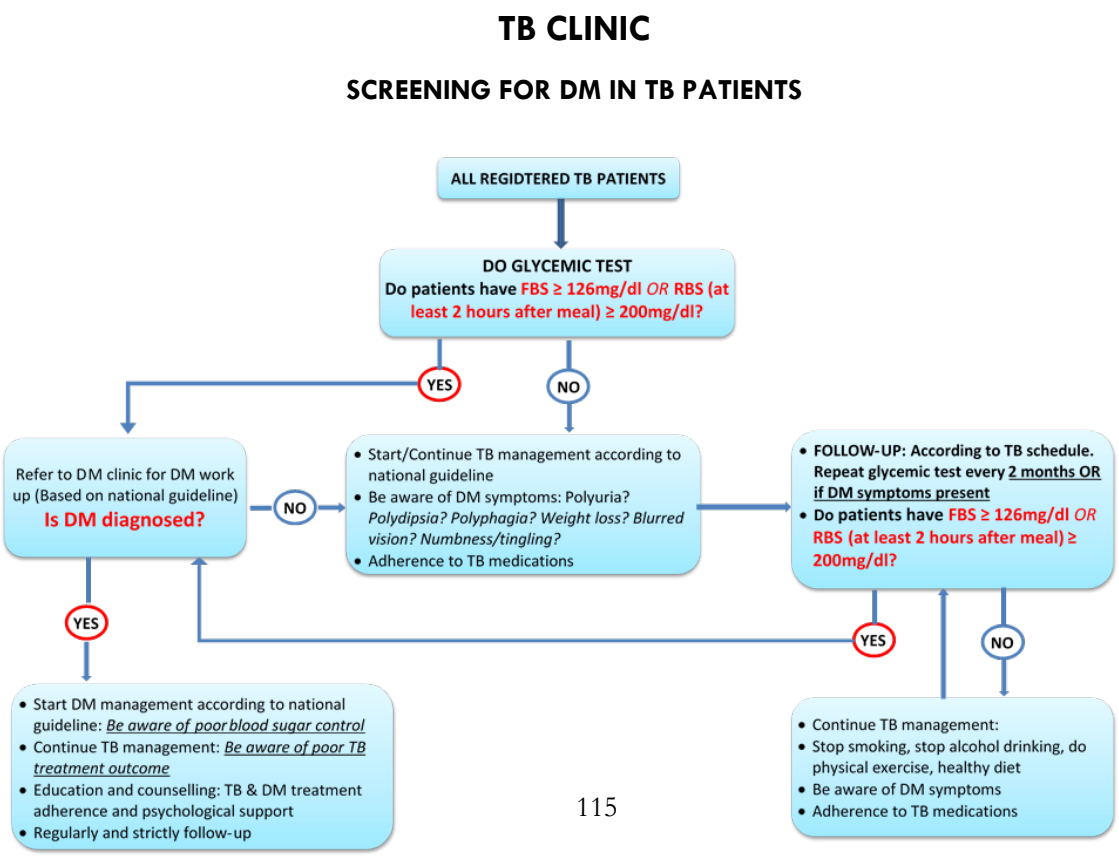


Figure 13: Algorithm on DM screening among TB patients (Source: Adopted from Cambodia NTP Guidelines)



FORMAT: Referral form for TB-DM Screening

Patient's Name: ……..…Sex: …… Age: ……
Current disease: ☐ TB ☐ Diabetes (ID in registration book: ……..……)
Name of Health Facility: ……..……
Refer from: …… To: ……

REFERRAL (To completed by referrer)

Reason for referral: ☐ TB suspicion (☐ Cough ☐ Fever ☐ Night sweats ☐ Weight loss
☐ Other: ……)
☐ DM suspicion (☐ FBS: ……..mg/dl ☐ RBS:…….…. …mg/dl
☐ Other: ……)

Refer to: ☐ TB department ☐ DM department

Treatment given: ……

Date:……/……/…… Name of referrer: …… Signature: ……, Tel: ……

DIAGNOSIS (To completed by receiver)

Diagnosis: ☐ TB (☐ Sputum smear (+) ☐ GeneXpert ☐ Clinical evaluation
☐ Other: ……..)
☐ DM: (☐ FBS …… ☐ RBS: …… ☐ Other: ……)
☐ Other:

……

Date of diagnosis: ……

Treatment given: ……

Date:……/……/…… Name of physician: …….…… Signature: ……., Tel: ……

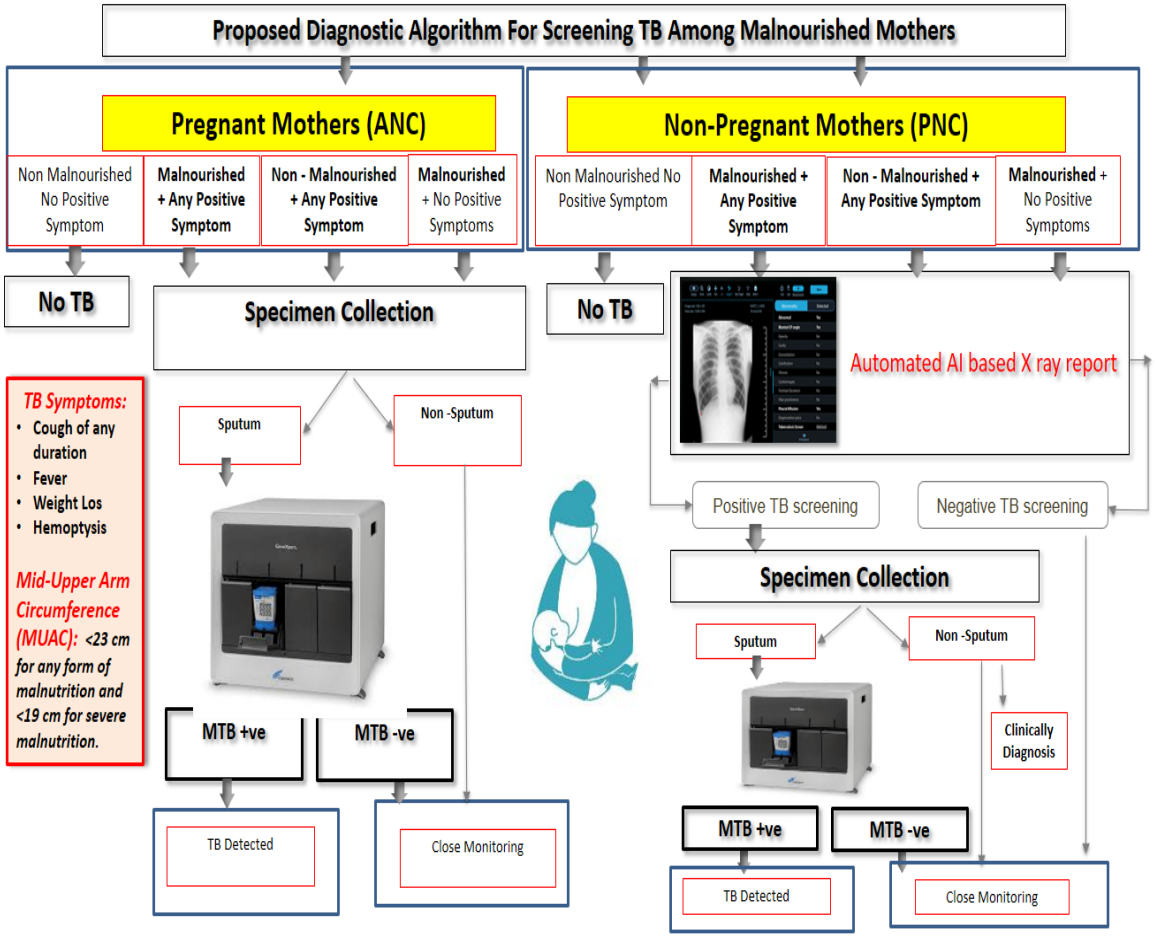
Please ask patient to brink this form back to original health department

7.5 PATIENTS WITH MALNUTRITION

Malnutrition is an important risk factor for TB. Studies have shown that malnourished TB patients, have higher risk of loss to follow-up and poor outcomes. Timor-Leste has one of the highest rates of malnutrition in the world, with 46 per cent of children under five suffering from chronic malnutrition. The number of undernourished people in Timor-Leste has remained constant around 300,000.

Malnourished children and adults to be screened for TB under active and passive case-finding efforts and linked with nutritional support program. The nutritional status of all notified TB patients should be assessed (by measuring MUAC or BMI) and those with malnourishment should be provided nutritional support. Advocate for extending the existing nutritional support program (for mothers and children) to TB patients also.

Figure 14: Algorithm for Screening TB among Malnourished Mothers



7.6 PATIENTS WITH SMOKING

Tobacco use in Timor-Leste is high with an estimated 33% of the population smoking daily and an estimated 61% of Timorese men using tobacco products regularly. Smoking could be one of the reasons for the high incidence of TB in the country. Tobacco use could be one of the reasons for the high incidence of TB in Timor.

Linkages can be established with the tobacco control program and to provide necessary tobacco cessation services to TB patients and help them quit. Smokers should be screened for TB on regular

basis. An association between tobacco smoke and tuberculosis (TB) has been debated for nearly 100 years. There is now considerable evidence confirming the presence, strength and consistency of this association. Three independent systematic reviews and meta-analyses have synthesized a large body of evidence on tobacco and TB, summarizing evidence of the association between active smoking and three TB outcomes: TB infection (detected using tuberculin skin testing), active TB disease and mortality due to TB. The South-East Asia Regional Response Plan for Integration of TB and Tobacco 2017–2021) provides an overview of the outcome-specific pooled RR estimates from three independent meta-analyses. These analyses indicate the following associations between TB and tobacco :

- Smokers are almost twice as likely to be infected with TB and progress to active disease.
- Smoking interferes with TB at every stage of the disease. It increases the risk of latent TB infection, culture conversion, sputum smear positivity, cavitary disease, treatment delay, treatment default, poor treatment outcomes and transmission of the disease. Some of these effects are mediated by a higher bacillary load among smokers.
- Smokers are also twice as likely to die from TB. However, there is limited to no evidence of the association between smokeless tobacco and TB

The South-East Asia Regional Response Plan for Integration of TB and Tobacco 2017–2021 envisions the following Goals, Objectives and Strategies:

Goal

To reduce the burden of TB and tobacco in the WHO South-East Asia Region.

Objectives

The objectives of TB/tobacco integration are:

1. Reduce tobacco-related TB incidence and mortality
2. Improve TB treatment outcomes
3. Provide universal access to counselling and tobacco cessation services for all people with TB and presumptive TB
4. Encourage tobacco cessation in the health system
5. Promote tobacco-free environments

Strategies

The interventions and activities to reach the overall goal and objectives are grouped under the following three strategies:

(1) Joint TB-tobacco actions-policy development, planning, training and monitoring
(2) Integrated patient-centred care and prevention
(3) Research and innovation

Strategy 1: Joint TB-tobacco actions-policy development, planning, training and monitoring

Joint strategic policy development, planning and monitoring is essential for ensuring that TB/tobacco activities are effectively implemented and monitored at all levels of the health-care delivery system. Monitoring and supervision of joint TB and tobacco control activities should be included in the supervisory checklist of both TB and tobacco control programs at the district managerial level and at all health units delivering diagnostic and treatment services to TB patients and tobacco users.

1. Ensure that TB/tobacco operational plans are part and parcel of the national strategic plans and that adequate resources allocated for the same;

2. Establish a Joint Working Group with representatives of relevant entities such as the Technical Advisory Groups of the TB and Tobacco control programs;
3. Involve NGOs, CBOs and communities: The perspective of the civil society is essential and must be incorporated into any planning and implementation process;
4. Frame national TB/tobacco collaborative plan incorporating the latest global recommendations;
5. Develop technical and operational policies and frameworks for implementation for TB-tobacco integration in primary health care settings;
6. Establish guidelines for joint planning and monitoring;
7. Build the institutional capacity necessary to ensure sustainability of the joint activities of the NTP and the National Tobacco Control Program;
8. Integrate tobacco cessation in NTP modules and TB diagnosis and management in tobacco control modules
9. Integrate training: Training on joint activities of the NTP and the National Tobacco Control Program should be established, integrating reciprocal elements in training curriculum and training materials, thereby facilitating capacity-building of health-care professionals;
10. Integrate supervision and monitoring: put systems in place for supportive supervision, regular monitoring and reporting in accordance with recommended indicators on joint activities in TB and tobacco programs.

Strategy 2: Integrated patient-centred care and prevention interventions

1. Improve awareness among patients and communities: generating awareness on TB/tobacco linkage should be part of the overall information education and communication efforts of both TB and tobacco programs;
2. Advocate and strongly enforce a policy of smoke (tobacco)-free environments for all places where services are delivered to TB suspects and TB patients;
3. Ensure tobacco use screening of all patients with TB and presumptive TB using standard screening tools;
4. Ensure access to tobacco cessation services for patients with TB and presumptive TB who need them;
5. Offer brief advice ("5As approach") routinely through the health staff managing TB patients in primary health care facilities. Institutionalize '5Rs' approach for patients who are unwilling to quit. Alternatively, use the ABC (Ask, Brief advice, Cessation support) approach. Pharmacotherapy can be instituted by trained medical staff as needed; and
6. Refer support for patients needing intensive behavioural intervention or other pharmacological medications by specialized health professionals.

Strategy 3: Research and innovation

1. Develop prioritized research agenda for TB/tobacco, including association between TB and smokeless tobacco use;
2. Promote TB/tobacco research with a focus on operational research; and
3. Support innovations in models of integration, tobacco cessation services, diagnosis and management.

7.7 LIVER DISORDERS

This section covers TB treatment in patients with pre-existing liver disease; for detection and management of hepatitis induced by anti-TB drugs, see section 8.1.1..

Patients with the following conditions can receive the usual TB regimens provided that there is no clinical evidence of chronic liver disease, hepatitis virus carriage, a past history of acute hepatitis, or current excessive alcohol consumption. However, hepatotoxic reactions to anti-TB drugs may be more common among these patients and should therefore be anticipated.

In patients with unstable or advanced liver disease, liver function tests should be done at the start of treatment. If the serum alanine aminotransferase level is more than 3 times normal before the initiation of treatment,[23] the following regimens should be considered.[24] The more unstable or severe the liver disease is, the fewer hepatotoxic drugs should be used.

Possible regimens include:

- Two hepatotoxic drugs (rather than the three in the standard regimen):
  — 9 months of isoniazid and rifampicin, plus ethambutol (until or unless isoniazid susceptibility is documented);
  — 6–9 months of rifampicin, pyrazinamide and ethambutol.

Expert consultation is advisable in treating patients with advanced or unstable liver disease. Clinical monitoring (and liver function tests, if possible) of all patients with pre-existing liver disease should be performed during treatment.

7.8 RENAL FAILURE AND SEVERE RENAL INSUFFICIENCY

7.8.1 DS-TB in patients with renal failure

The recommended initial TB treatment regimen for patients with renal failure or severe renal insufficiency is 2 months of isoniazid, rifampicin, pyrazinamide and ethambutol, followed by 4 months of isoniazid and rifampicin. Isoniazid and rifampicin are eliminated by biliary excretion, so no change in dosing is necessary. There is significant renal excretion of ethambutol and metabolites of pyrazinamide, and doses should therefore be adjusted. Three times per week administration of these two drugs at the following doses is recommended: pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg). These are the same mg/kg doses as those listed under Daily in Table 1.

While receiving isoniazid, patients with severe renal insufficiency or failure should also be given pyridoxine in order to prevent peripheral neuropathy.

7.8.2 DR-TB in patients with renal failure

Caution should be used in the administration of SLIs to patients with renal impairment.
If creatinine clearance <90 ml/min, Am should be prescribed 2–3 times per week at 12–15 mg/kg; E and Z should be given three times per week. In case of creatinine clearance <60 ml/min despite dose reduction to 2-3 times/week, stop the injectable drug and replace it with Dlm or Lzd and continue E and Z three times per week. Consider Bdq if Dlm is not available or if Lzd is contraindicated (severe anaemia, neuropathies etc.).

7.8.3 Patients with initial hearing loss

In patients with initial hearing loss, consider replacing Am by Dlm or Lzd if Dlm is not available, to prevent worsening of the hearing loss. The duration of the intensive phase remains unchanged. Consider Bdq.

[23] Note that TB itself may involve the liver and cause abnormal liver function.
[24] In some cases of concurrent acute (i.e. viral) hepatitis not related to TB or TB treatment, it may be possible to defer TB treatment until the acute hepatitis has resolved.

8 ACTIVE DRUG SAFETY MONITORING AND MANAGEMENT (ADSM)

8.1.1 ADSM

Health programs that systematically monitor patient safety are in a better position to prevent and manage adverse drug reactions (ADRs), relieve patient suffering and improve treatment outcomes. Likewise, TB programs that actively pursue drug-safety monitoring and management are better prepared to introduce new anti-TB drugs and novel regimens.

Active TB drug-safety monitoring and management (ADSM) is a method of detecting, recording, and reporting adverse event using systematic clinical and laboratory assessment of patients on TB treatment. ADSM applies to patients on treatment with: (i) new anti-TB drugs; (ii) novel MDR-TB regimens; or (iii) extensively drug-resistant TB (XDR-TB) regimens, in order to detect, manage and report suspected or confirmed drug toxicities. The recording and reporting activities of ADSM primarily target the serious adverse events (SAEs) as a basic requirement. The appropriate and timely management of ADRs is an integral component of ADSM and patient care.

Key activities of ADSM are:

- **Active and systematic clinical and laboratory assessment during treatment** to detect drug toxicity and AEs
- All **AEs detected should be managed in a timely manner** in order to deliver the best possible patient care
- Standardized **data should be systematically collected and reported for any detected SAE** to be used in the future

Doing ADSM is of paramount importance especially because it ensures patient safety. ADSM is also useful in helping health programs to prevent and manage adverse drug reactions and improve patient's quality of life. National tuberculosis programs (NTPs) that actively pursue drug safety monitoring and management are also better prepared to introduce new tuberculosis (TB) drugs and novel regimens.

Implementing ADSM may require a lot of effort involving various sectors. ADSM is best to be initiated using a top-down approach, starting at the national level and progressing down to the health facilities treating the patient.

Suggested key steps to implement ADSM are:

1. Create a national coordinating mechanism for ADSM
2. Develop a plan for ADSM
3. Define management and supervision roles and responsibilities
4. Create standard data collection materials
5. Train staff for collection of data
6. Define schedules and routes for data collection and reporting
7. Consolidate ADSM data electronically
8. Develop (or use existing) capacity for signal detection and causality assessment

Identification and management of adverse events:

An adverse event, as per the International Conference on Harmonization (ICH), is defined as any untoward medical occurrence in a subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal finding), symptom

or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product. This includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition or abnormal results of diagnostic procedures including laboratory test abnormalities.

A serious adverse event (SAE) is any untoward medical occurrence that:

- results in death;
- life-threatening;
- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect;
- is a suspected transmission of any infectious agent via a medicinal product;
- is medically important

Adverse drug reaction (ADR) is any untoward medical occurrence considered associated with use of a specific drug/s. It can be serious (as defined above) or non-serious (does not fulfil the criteria for serious ADR).

Attribution definitions

Attribution is defined as the relationship between the AE and the therapy (drug/s). It is established by 'Causality assessment' which is done by the DR-TB Committee. The causality assessment can have the following results:

Not related: An AE that is not related to the use of the drug.

Doubtful: An AE for which an alternative explanation is more likely, e.g. concomitant drug(s), concomitant disease(s) or the relationship in time suggests that a causal relationship is unlikely.

Possible: An AE that might be due to the use of the drug. An alternative explanation, e.g. concomitant drug (s) or concomitant disease(s) is inconclusive. The relationship in time is reasonable; therefore, the causal relationship cannot be excluded.

Certain (Very likely): An AE that is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation, e.g. concomitant drug(s), concomitant disease(s). The relationship in time is suggestive, e.g. confirmed by de-challenge and re-challenge.

The treatment provider will monitor and record all adverse events routinely. Laboratory screening tests will be done routinely as per the MDR guidelines. The tests conducted during the pre-treatment evaluation (ECG, liver function tests, kidney function tests etc.) will give a baseline for all parameters and help identify patients who are at increased risk for adverse effects or poor outcomes. Health staff should be trained to ensure that adverse effects of drugs are recognized quickly and managed appropriately.

For minor adverse events (AE) the treatment providers refer the patient to the physician at the CHC and for serious adverse events, which may require hospitalization, to the referral hospital/National Hospital/Klibur Domin. For management of serious adverse events (SAE) the National DR-TB Committee should be consulted.

The broad principles of management of adverse events are:

- If adverse effect is mild continuing the treatment regimen and manage with ancillary drugs if needed.
- In case of serious adverse events the offending drug/s should be stopped and then can be reintroduced at a lower dose or withdrawn permanently.
- An essential component of the management is psychosocial support which can be provided through patient education by treatment provider and patient support groups.

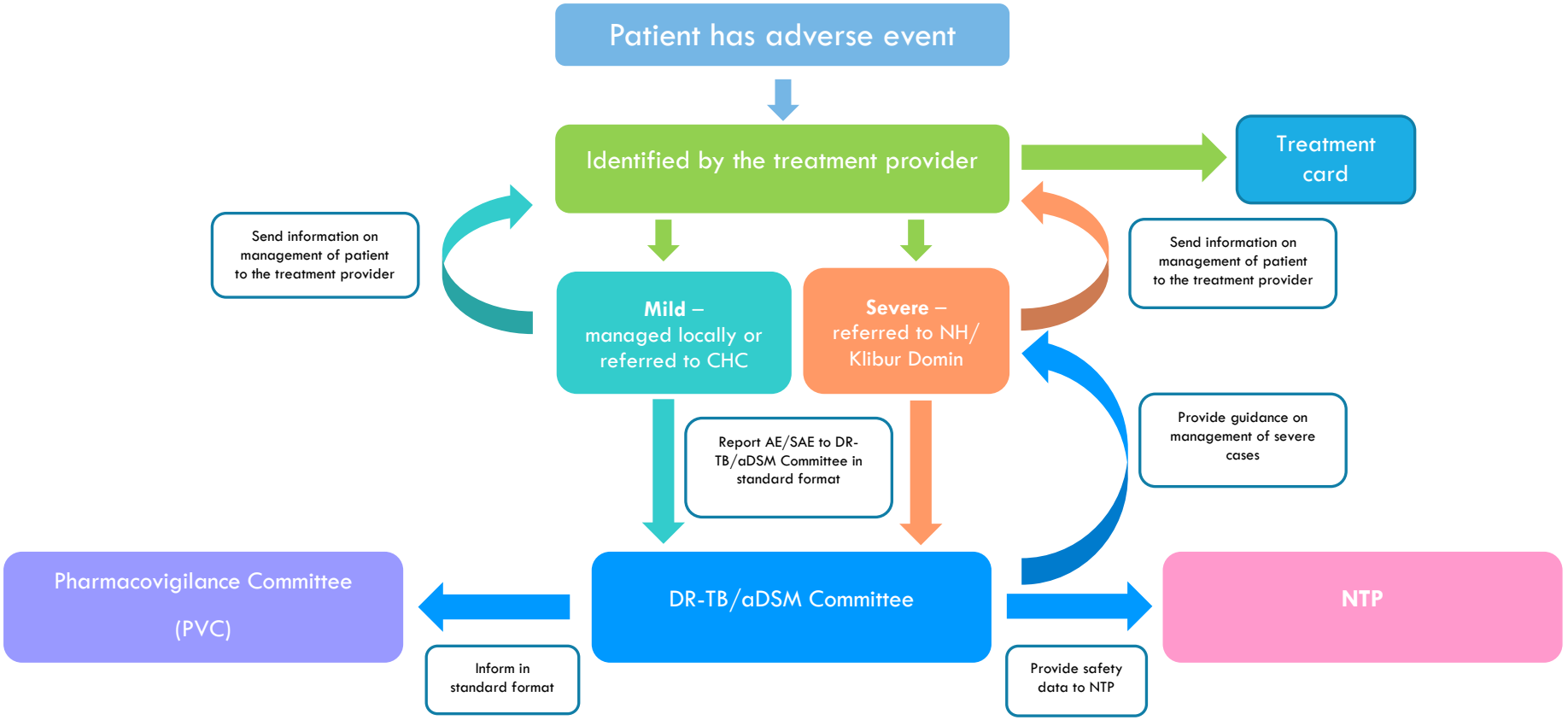
Timely, accurate and complete reporting and analysis of adverse events are required to be reported under the program. This is crucial for the protection of patients.

Monitoring of Adverse Events:

The ADSM/DR-TB Committee will be responsible for monitoring the adverse events (AE) and serious adverse events (SAE) of patients while on regimens containing new or repurposed drugs. The Committee will provide necessary guidance to the TB program on their safety and efficacy.

The adverse events will be reported by the treatment providers, treating physicians at CHC/National Referral Hospitals, National Hospital (Dili) and Klibur Domin using the ADSM formats (Annex 1). Simultaneously the AEs will be recorded in the treatment card by the treatment provider and the treating physician. The AEs will also be reported to the Pharmacovigilance Committee of Timor Leste which will be established shortly.

Flow chart for ADSM



Adverse event reporting format
(Annex 1)

Patient's Name:	**Age:** _ _	**Sex:**	**PMDT No:**	**Date:** _ _/_ _/_ _ _ _
Address:			**Height (cm):**	**Weight (Kg):**

Type of TB:	**Type of Drug Resistance:**
Pulmonary ☐	RR/MDR-TB ☐ RR/MDR + FQ/SLI ☐ XDR ☐
Extrapulmonary ☐	H mono/poly

Current regimen:	**Date of start of regimen:**

Drug	**Dose**	**Date/Month/Year since the drug was started**
Rifampicin		
INH		
Pyrazinamide		
Ethambutol		
Bedaquiline		
Linezolid		
Moxifloxacin		
Levofloxacin		
Clofazimine		
Capreomycin		
Cycloserine		
Ethionamide		
PAS		
Delamanid		
Streptomycin		

Details of the event:

Date of onset: __/__/____ Time of onset: __:__

(Describe the details related to the event)

Type of Serious Adverse Event:
Death ☐ Life threatening ☐ Hospitalisation ☐ Permanent Disability ☐ Congenital anomaly ☐

Outcome of the event	**Date of outcome**
Recovered/resolved ☐	__/__/____
Recovered/resolved with sequelae ☐	__/__/____
Fatal ☐	__/__/____
Recovering/resolving ☐	__/__/____
Not recovering ☐	__/__/____
Unknown ☐	__/__/____

Causality Assessment (to be done by ADSM Committee)

Drug	Certain	Probable	Possible	Unlikely	Not assessable
Rifampicin					
INH					
Pyrazinamide					
Ethambutol					
Bedaquiline					
Linezolid					
Moxifloxacin					
Levofloxacin					
Clofazimine					
Capreomycin					
Cycloserine					
Ethionamide					
PAS					
Delamanid					
Streptomycin					

Results of other lab tests done					
Test	**Date**	**Result**	**Test**	**Date**	**Result**
Sputum Smear			ALT		
Sputum Culture			AST		
Xpert MTB/RIF			Lactic acid	`	
LPA			Lipase		
HIV			Bilirubin		
CD4			ESR		
Hb			WBC		
Creatinine			B.Urea		
B. Glucose			HbA1c		
TSH			S. Potassium		
S Calcium			S. Magnesium		
CXR			ECG		

Table 10: Symptom-based approach to managing side-effects of anti-TB drugs

Side-effects	Drug(s) responsible	Management
Major		*Stop responsible drug(s) and refer to clinician urgently*
Skin rash with or without itching	Streptomycin, isoniazid, rifampicin, pyrazinamide	Stop anti-TB drugs
Jaundice (other causes excluded), hepatitis	isoniazid, pyrazinamide, rifampicin	Stop anti-TB drugs
confusion (suspect drug induced acute liver failure if there is jaundice)	most anti-TB drugs	Stop anti-TB drugs
Visual impairment (other causes excluded)	ethambutol	Stop Ethambutol
Shock, purpura, acute renal failure	Rifampicin	Stop rifampicin
Minor		*Continue anti-TB drugs, check drug doses*
Anorexia, nausea, abdominal pain	pyrazinamide, rifampicin, isoniazid	give drugs with small meals or just before bedtime and advise patient to swallow pills slowly with small sips of water. if symptoms persist or worsen, or there is protracted vomiting or any sign of bleeding, consider the side-effect to be major and refer to clinician urgently.
Joint pains	pyrazinamide	Aspirin or non-steroidal anti-inflammatory drug, or paracetamol
Burning, numbness or tingling sensation in the hands or feet	Isoniazid	pyridoxine 50–75 mg daily (*3*)
Drowsiness	Isoniazid	reassurance. give drugs before bedtime
Orange/red urine	Rifampicin	reassurance. patients should be told when starting treatment that this may happen and is normal
Flu syndrome (fever, chills, malaise, headache, bone pain)	intermittent dosing of rifampicin	change from intermittent to daily rifampicin administration (*3*)

8.1.2 Symptom-based approach to managing side-effects of anti-TB drugs during treatment of DR-TB

i. Identification and grading of adverse events

Adverse events (AEs) are more frequent in patients on second-line TB treatment than with first-line drugs and are the main cause of treatment interruption. Good counselling at the beginning of the treatment and careful monitoring and management are the basis of patient adherence. During the first baseline visit, co-morbidities that are associated with a high risk of AEs, such as diabetes, kidney and liver failure, malnutrition, HIV infection, excessive alcohol and drug use, etc., should be identified and recorded. The underlying causes of AEs should be identified and treated. AEs are classified according to their severity.

Table 11: Grading of the severity of adverse events during DR-TB treatment

Grade	*Description*
Grade 1: Mild	Mild or transient discomfort without limitation of normal daily activities; no medical intervention or corrective treatment required.
Grade 2: Moderate	Mild to moderate limitation of normal daily activities; minimal medical intervention or corrective treatment required.
Grade 3: Severe	Marked limitation of normal daily activities; medical intervention and corrective treatment required; possible hospitalization.
Grade 4: Life-threatening or permanent injury	Extreme limitation of normal daily activities; medical intervention and corrective treatment required, almost always in a hospital setting.

Ref: 2008 ANRS* scale for the gradation of the severity of adverse events in adults.

**Agence Nationale pour la Recherche sur le SIDA et les hépatites* (National AIDS and Hepatitis Research Agency), Paris, France.

Reference values for testing for more frequent AEs and the classification of laboratory test results by AE severity for short treatment regimen and new drugs are described in detail in the Annex.

Grade 1 AEs need only be noted in the patient's card, whereas Grade 2 AEs require medical intervention with ancillary drugs, of which the most frequently used are detailed in the table below:

Table 12: Frequently used ancillary drugs during DR-TB treatment

Therapeutic class	*Drugs*
Antidepressants	Amitriptyline
Antidiarrhoeals	Loperamide
Antiemetics	Metoclopramide (or metopimazine) and ondansetron
Antihistamines	Cetirizine (or diphenhydramine)
Antiulcer drugs	Cimetidine (or ranitidine) and omeprazole
Corticosteroids	Prednisolone, hydrocortisone
Non-steroidal anti-inflammatory drugs (NSAIDs)	Acetylsalicylic acid and ibuprofen
Vitamins and mineral supplements	Pyridoxine (vitamin B6). Potassium and magnesium.

These drugs should be stocked and be available at all times in TB treatment units where patients with drug-resistant TB are being treated.

Serious AEs (SAEs), which are either life-threatening or could cause permanent damage (degrees 3 and 4), should be managed by an experienced clinician who will identify the drug suspected, reduce dosage or discontinue its use and replace it with an equivalent drug if the drug needs to be definitively discontinued.

Changing a regimen drug should be considered only as a last resort after any attempt to manage AEs with ancillary drugs has failed.

ii. Contraindications and Drug Interactions of anti-TB drugs during treatment of DR-TB

The table below summarises contraindications and precautions for drugs used in the standardized DR-TB regimen:

Table 13: Contraindications and Precautions with Bdq, Dlm and Lzd

Drug Name	Relative contraindication	Precautions
Bdq, Dlm	History of syncopal episodes, ventricular arrhythmias or severe coronary artery disease Baseline ECG with QTcF >500ms (repeated)	Use with caution if QTcF >450/470ms in male/female patients. Weekly ECG monitoring and serum electrolyte screening should be performed if Bdq or Dlm is being used despite a cardiac contraindication. Dlm is less cardiotoxic than Bdq (new data has shown that QTC-F prolongation with combined use of Ddq and Dlm is clinically modest and safe)
Bdq, Lzd, Dlm	Severe renal failure	Usually no dose adjustment is required in mild to moderate renal failure; with precaution in severe renal failure/impairment
Bdq	Severe hepatic failure	Try not to use if patient has severe liver function impairment
Lzd	Pre-existing mild to moderate peripheral neuropathy (based on Basic Peripheral Neuropathy Screening (BPNS), subjective sensory neuropathy scoring, Severe Myelosuppression and Anaemia, moderate neutropenia	Special precautions when used in combination with Cs, high dose INH and diabetics. In mild to moderate Myelosuppression and Anaemia Lzd can be used with lower doses, 300 mg daily or 600 mg alternative days with close monitoring

1. Drug Interactions and Overlapping Toxicities with Bdq, Dlm and Lzd

It is essential to consider the drug-drug interactions with Bdq, Dlm and Lzd as use in concomitant treatment with many routinely prescribed drugs may have various levels of impact, including having either decreased or increased absorption, toxicity and adverse events. It may be necessary

that patients should be given a card mentioning the name of drugs that should not prescribed by any GP/doctor while the patient is in ambulatory care in the community. Therefore, treating physicians should review all the medicines patients are taking while enrolling on MDR TB Treatment.

2. Drug Interactions with Bedaquiline

Use of the following drugs should be avoided in conjunction with Bdq:
Strong/moderate inducers of cytochrome P450: These may decrease blood levels of Bdq: Efavirenz, Rifamycins, Phenytoin, Carbamazepine, Phenobarbital, Ritonavir-boosted PIs

Oral azole antifungals (can be used up to two weeks): Itraconazole, Fluconazole

Macrolide antibiotics other than azithromycin

3. Drug Interactions with Delaminid

First line Anti-TB Therapy (HRZE), as these drugs appear to reduce the level of Dlm

4. Overlapping Toxicity with Bedaquiline and Delaminid

Antipsychotic drugs (Haloperidone, Risperidone), many anti-nausea drugs (Ondansetrone, Granisetron, Domperidone, Chlorpromazine), methadone, cardiac drugs that may affect the heart rhythm (Amiodarone, Beta-blockers, Digoxin, Quinidine)
Linezolid and concomitant medicines that increase serotonin levels; Serotonin re-uptake inhibitors (SSRIs): fluoxetine, paroxetine; Tricyclic antidepressants: amitriptyline, nortriptyline Serotonin 5-HT1 receptor agonists, MAO inhibitors: phenelzine, isocarboxazid Other serotoninergic agents: meperidine, bupropion, or buspirone, quetiapine

iii. Gastro-intestinal disorders

Nausea and vomiting

Suspected drugs: Pto/Eto, PAS, H, E, Z, Cfz, Bdq.

- Toxicity of the Pto/Eto on the gastric mucosa.
- Possible risk of hypokalaemia.

Treatment:

1 Rehydration using oral rehydration solution (ORS).

2 Recommend taking a light meal before medication.

3 Prescribe metoclopramide 10-20 mg 30 minutes before drug intake.

4 If vomiting persists, prescribe ondansetron 2–8 mg 30 minutes before drug intake.

5 Divide Pto/Eto dose into morning and evening provided DOT is ensured (dose dependent effect; higher doses better tolerated by most patients in the evening).

6 For patients concerned about possible nausea, prescribe diazepam 5 mg 30 minutes before medication.

Gastritis

Suspected drugs: Pto/Eto, PAS.

Treatment:

1. Recommend taking a light meal before medication.
2. Absorption of FQs is reduced by drugs containing cations, such as magnesium and aluminium (and sucralfate) (high reduction); iron (moderate reduction); calcium, zinc (and multivitamins) (low reduction).
3. Prescribe omeprazole 20-40 mg in the evening (2 hours before or 3 hours after medication).

Diarrhoea

Suspected drugs: PAS, Pto/Eto.

Treatment:

1. Encourage patient to tolerate mild diarrhoea.
2. Encourage fluid intake.
3. Treat diarrhoea with no complications (no blood in the stools, no fever) with loperamide 4 mg, followed by 2 mg after each bowel movement up to a maximum of 10 mg in 24 hours.
4. Check potassium levels and hydration status in case of severe diarrhoea.

Hepatotoxicity

Suspected drugs: Z, H, Pto/Eto, Bdq, PAS, Lzd, FQ (very rarely).

- Symptoms: nausea, vomiting, abdominal pain, jaundice.

Management:

1. Pay attention to medical history (viral hepatitis, HIV infection, alcohol use, etc).
2. If ALT, AST ≤5 times the upper limit of normal and there is no jaundice, continue treatment and treat nausea and vomiting.
3. If ALT, AST >5 times the upper limit of normal and/or jaundice (bilirubin>3 mg/ dl), stop all drugs and assess the transaminases every week; if they return to 2 times the upper limit of normal, reintroduce the least hepatotoxic drugs (Am, E, Mfx, Cfz) and check transaminase levels. Then, reintroduce hepatotoxic drugs in the following order: Pto/Eto, H and Z and monitor transaminase levels every 3 days. Check transaminase values after introducing each drug.
4. If drug reintroduction leads to the return of hepatotoxicity, remove the culprit drug from the treatment and replace it by another if this is an essential drug. Do not replace H and Z.
5. Monitor transaminase levels monthly.

i. Kidney disorders

Nephrotoxicity

Suspected drugs: Km, Am, Cm, E, Z, Cs.

- Higher risk if intensive phase is prolonged.

Treatment:

1 Close monitoring of creatinine (and potassium) every week or every 2 weeks.

2 Adequate hydration.

3 If creatinine clearance <90 ml/min, prescribe Am 2-3 times per week at 12-15 mg/kg; give E and Z, 3 times/week. If creatinine clearance remains <60 ml/min despite dose reduction to 2-3 times/week, stop the injectable drug and replace it with Dlm or Lzd. Give E and Z, 3 times/week.

4 If Dlm is not available or if Lzd is contraindicated, consider Bdq.

NB: in case of increase in creatinine levels, severe malnutrition or advanced age, renal functions are determined by calculating creatinine clearance using the Cockroft-Gault formula:

$$Cl\ Cr = \frac{(140\text{-age}) \times \text{Weight} \times k}{Cr}$$

- Cl Cr: estimation of the creatinine clearance in ml/min;
- Cr: creatinine levels in µmol/l;
- Age: age in years;
- Weight: in kg; • k: coefficient (1.23 for men and 1.04 for women).

Note: Creatinine conversion from µmol/l to mg/dl: mg/dl = µmol/l / 88.4.

Table 14: Stages of kidney disease according to creatinine clearance levels

Stage of chronic kidney disease	*Creatinine clearance (ml/min)*	*Action on TB drugs*
Stage 1 Normal	≥90	
Stage 2 Mild	60–89	2-3 times per week
Stage 3 Moderate	30–59	Stop the injectable and switch to Dlm or Lzd or Bdq
Stage 4 Severe	15–29	
Stage 5 Terminal	<15	

Electrolyte imbalance

Suspected drugs: Cm, Km, Am.

- Hypokalaemia: $K^+ < 3.5$ mEq/l.
- Hypomagnesaemia: $Mg^{2+} < 1.5$ mEq/l.
- Hypokalaemia may be refractory if the concurrent hypomagnesaemia is not corrected.
- Higher risk if intensive phase is prolonged.
- Vomiting, diarrhoea and diuretics may cause electrolyte imbalance.
- Risk of QTc prolongation (check ECG).
- Electrolyte imbalances are reversible upon discontinuation of the injectable drug (however, this might take weeks or months!).
- Hypokalaemia and hypomagnesaemia are often asymptomatic.
- Symptoms of moderate intensity: fatigue, myalgia, cramps, weakness of the lower limbs, somnolence, confusion.
- Symptoms associated with severe electrolyte loss: tetany, paralysis and severe arrhythmias.

Treatment:

1. Encourage dietary intake of potassium (bananas, oranges, tomatoes, chocolate …).
2. Check for signs of dehydration among patients with vomiting and diarrhoea. Start oral or IV rehydration.
3. Consider potassium supplementation: oral slow-release tablets of potassium chloride 1,200–3,600 mg daily in 2–3 divided doses (600 mg = 8 mEq).
4. In case of severe hypokalaemia: KCl IV: 10 mEq/h (10 mEq KCl will raise serum potassium by 0.1 mEq/l).
5. If potassium levels are low, check magnesium levels (if this is not possible, consider empirical treatment with magnesium in all cases of hypokalaemia with magnesium gluconate at 1,000 mg twice a day).
6. Prescribe spironolactone 25 mg/day in refractory cases.
7. Check ECG for QTc prolongation.

ii. Neurological disorders

Peripheral neuropathy

Suspected drugs: Lzd, Cs, H, FQs, SLIs, Pto/Eto, E.

- Check for possible comorbidities: diabetes, HIV, alcohol abuse, hypothyroidism, malnutrition.
- No formal contraindications to anti-TB treatment in case of comorbidities.

Treatment:

1. Pyridoxine 100-200 mg/day (maximum dose 100 mg/day in pregnant women).
2. Amitriptyline 25-50 mg in the evening (maximum dose 150 mg/day in three doses).
3. Carbamazepine 100-400 mg x 2/day (follow-up and monitoring of transaminases).

Optic neuritis

Suspected drugs: Lzd, E.

- Serious, irreversible if medication is not immediately discontinued.
- Loss of colour vision (green colour first). Perform Ishihara test (table of colour discrimination). Ishihara tables are available on the web.

Treatment:

1. Immediate discontinuation of Lzd and/or E.

Seizures

Suspected drugs: Cs, H, FQs.

Treatment:

1 Discontinue Cs, the drug likeliest to be responsible.

2 Always check creatinine levels in patients with sudden onset of seizures. Compromised renal function may cause increased serum concentrations of Cs.

3 Begin anti-convulsive treatment (carbamazepine, phenytoin or valproic acid).

4 Replace Cs by Pto/Eto (or PAS) if not previously used in a failed regimen.

iii. Osteoarticular disorders

Arthralgia

Suspected drugs: Z, FQs, Bdq.

Treatment:

- Prescribe NSAIDs: ibuprofen 600 mg 3 times/day.
- Rest the joint.
- Symptoms generally diminish with time and without any intervention.

Tendinitis (Achilles' tendon)

Suspected drugs: FQs (all).

Treatment:

1 Prescribe NSAIDs: ibuprofen 600 mg 2-3 times a day.

2 Rest the joint.

3 Tendon rupture is more probable among patients with diabetes and among the elderly, but rare among patients with MDR-TB.

4 If significant inflammation persists, discontinue FQ use and replace with Bdq.

iv. Dermatological disorders

Itchiness, skin rashes and allergic reactions

Suspected drugs: all.

Steps to take:

1 Symptoms generally resolve spontaneously in the first few weeks.

2 In case of dryness of the skin, use moisturizing cream.

3 Prescribe antihistamines (diphenhydramine 25–50 mg or cetirizine 5–10 mg before medication).

4 Prescribe corticosteroid ointments.

5 Prescribe oral prednisolone in low doses (10–20 mg/day) if there is no improvement.

6 Identify and discontinue the drug in question only in case of serious AEs (e.g., Stevens Johnson syndrome and Lyell's syndrome).

v. Thyroid disorders

Hypothyroidism

Suspected drugs: Pto/Eto+PAS, Pto/Eto, PAS.

- Reversible at the end of the treatment.
- If thyroid stimulating hormone (TSH) levels increase, assess symptoms of hypothyroidism.
- If TSH >1.5–2 times upper limit of normal, initiate treatment.

Treatment:

- Levothyroxine 100–150 µg/day in adults; 75–100 µg/day in young adults; 50 µg/day in elderly people (> 65 y); 25 µg in case of serious cardiovascular disease.
- Reassess TSH levels after 1–2 months and adjust levothyroxine dosage accordingly.

vi. Metabolic disorders

Hypoglycaemia and hyperglycaemia

Suspected drugs: Gfx, Mfx.

- Reversible at the end of treatment.
- Good glucose control is important during treatment.
- Higher risk with Gfx than with Mfx.

Treatment:

1 Treat hypoglycaemia and hyperglycaemia as needed.

2 Stop Gfx, replace with Mfx and monitor glycaemia.

Lactic acidosis

Suspected drug: Lzd.

- Build-up of lactates in the body, which results in an excessively low pH in the blood.
- Consequence of mitochondrial toxicity.
- Monitor with blood test (arterial or venous).
- Symptoms: abdominal pain, nausea, vomiting, rapid deep breathing, general weakness.

Treatment:

1 Stop Lzd and replace with another drug with similar characteristics (e.g., imipenem or meropenem + clavulanic acid).

vii. Haematological disorders

Bone marrow aplasia

Suspected drug: Lzd.

Treatment:

1 Discontinue Lzd immediately in case of severe medullar aplasia (Grade 3) of the white or red blood cells, or platelets.

2 Consider blood transfusion in case of severe anaemia.

3 Consider possible causes of haematological disorders unrelated to Lzd.

4 Reduce Lzd dosage (300 mg/day or 600 mg thrice a week instead of 600 mg/day) if the aplasia resolves and check complete blood count.

viii. Psychiatric disorders

Depression

Suspected drugs and conditions: psychological and socio-economic conditions, Cs, H, FQs.

Treatment:

1 Assess psychological and socio-economic conditions.

2 Discontinue Cs, which is the drug most likely to cause depression.

3 Always check creatinine levels in patients with sudden onset of depression. Impaired renal functions can raise Cs serum concentrations.

4 If moderate or severe symptoms persist, initiate anti-depressant treatment with fluoxetine, amitriptyline or similar drugs. Do not administer these in conjunction with Lzd (risk of serotonin syndrome).

5 Replace Cs with Pto/Eto (or PAS) if not previously used in a failed drug regimen.

Psychosis

Suspected drugs: Cs, H, FQs.

Treatment:

1 Discontinue Cs, which is the drug most likely to be responsible.

2 Always check creatinine levels in patients with sudden onset of psychosis. Impaired renal function can raise Cs serum concentrations.

3 If moderate or severe symptoms persist, initiate antipsychotic treatment with haloperidol.

4 Replace Cs with Pto/Eto (or PAS) if not previously used in a failed regimen.

ix. Cardiac disorders

QTc interval prolongation

Suspected drugs: FQs, Bdq, Dlm, Cfz, Mfx prolongs QTc more than Lfx and Gfx.

Treatment:

1 Repeat ECG and confirm QTc prolongation.

2 Take note of conditions such as diarrhoea, vomiting, use of diuretics, alcohol and ancillary drugs (ondansetron at high dose).

3 Check potassium, magnesium and calcium levels and maintain normal electrolyte levels (refer to electrolyte loss in the section on renal disorders).

4 If QTc <500 ms, continue Mfx or Bdq or Dlm and perform ECG once a week.

5 If QTc ≥500 ms, temporarily hold all drugs prolonging QT and replace Mfx with Gfx or high-dose Lfx (if Gfx is not available) after normalization.

6 If QTc still ≥500 ms, consider discontinuing Cfz and refer to cardiologist wherever possible.

7 If QTc still ≥500 ms, consider discontinuing Bdq and/or Dlm.

NB: Refer to the Annex for the definition, measurement and clinical implications of the QT interval.

x. Role of the PMDT unit in the management of adverse reactions

Whenever a patient has serious adverse reactions to any of the second-line anti-TB drugs, he/she should be admitted at the PMDT unit and the committee decides on further management of the patient. This may require withholding or discontinuing the offending drug in the treatment regimen. The committee will be responsible for arranging the drugs to be given for managing these reactions.

Timely and intensive monitoring for identifying and management of adverse reactions are essential components of the MDR-TB services. This will help to improve patient adherence to treatment, reduce mortality and obtain better treatment outcomes. Ancillary drugs for the management of adverse reaction should be made available to the patient free of cost. Proper training of staff and support to the patient are other important activities that are required.

9 TUBERCULOSIS LABORATORY QUALITY CONTROL AND SUPERVISION

The following steps will ensure the quality control of sputum smear microscopy. The laboratory technician at every DDC should keep all the sputum smears for at least one month and the regional supervisor collects the smears for crosschecking at the national laboratory. The regional supervisor will collect all smear-positive and 10% of smear-negative slides, which will be crosschecked at the national laboratory. The TB laboratory supervisor (TLS) from the national laboratory during his/her visit to DMCs will cross check a random sample of slides (5 positive and 5 negative slides). The supervisor will indicate his/her reading and comments in the laboratory register and will record the number of slides examined and the discrepancies in his/her diary. The district level laboratory technician at the CHC will supervise the CHCs at the sub-district level and ensure the quality of microscopy. The director, doctors and clinical nurses of the CHC should be supervising laboratory services. These staff should be appropriately trained in supervision of TB microscopy.

A field visit is an ideal way to obtain a realistic assessment of the conditions and skills practiced in the laboratory. On-site evaluation of NTRL and Municipal Laboratory Senior Technician to all the microscopic centres is therefore an essential component of a meaningful Quality Assurance (QA) program. Ideally, on-site evaluation should be performed at least once a year by personnel from a higher-level laboratory (NTRL) in order to evaluate the overall operational conditions in the microscopy centres. On-site visits by experienced laboratory personnel from a higher-level laboratory provides an opportunity for immediate problem solving, corrective action and on-site retraining. Three different types of field visits can be used as part of an ongoing QA process, depending on the resources available and the performance capability of the laboratory being visited.

- At least once a month visit by Senior Technician to the Microscopic Centre, is required.
- At least once a year visit by laboratory supervisors is recommended for NTRL by SNRLs and for Municipal TB Centres by NTRL.
- When poor performance has been identified through on-site evaluation, blinded rechecking or panel testing, additional visits by trained laboratory personnel from a higher-level laboratory (the NTRL or SNRL Laboratory Supervisor) are mandatory to perform a comprehensive evaluation of all laboratory procedures, implement corrective action, and provide training.

On-site visits include a comprehensive assessment of laboratory safety including infection control measures; conditions of equipment, adequacy of supplies as well as the technical components of AFB smear microscopy. Sufficient time must be allotted for the visit to include observation of all the work associated with AFB smear microscopy, including preparing smears, staining and reading of smears. On-site evaluation should also include examining a few stained positive and negative smears to observe the quality of smearing and staining as well as the condition of the microscope.

Laboratory Supervisors must be knowledgeable in all operational and technical elements of AFB smear microscopy, and also have sufficient expertise to observe technicians performing routine tasks. They should also facilitate quality improvement through on the spot problem solving and suggestions for corrective action wherever needed.

On-Site Evaluation by Municipal Senior Laboratory Technician

Monthly visits to the Microscopy Centres by the district / sub-district Lab supervisors are required. On-site evaluation by Senior Laboratory Technicians is generally limited to ensuring the following NTP/NTRL requirements: recording and reporting of results; assessing operational conditions, safety, supplies, equipment and total workload.

Supervisors should make sure that Standard Operating Procedures (SOPs) are in place and that SOPs are displayed in all microscopy centres, internal QC as per NTP/NTRL is performed, and a functional

binocular microscope is available. Since the ability to identify AFB and report the same is considered essential for anyone working in a TB control program where diagnosis and follow-up are largely based on AFB-microscopy, reading 5 positive and 5 negative smears are a necessary part of the routine monthly visit. Visits by senior technicians are also useful to collect data on TB laboratory workload, smear positivity rate for suspects and follow up examinations.

These are important for several reasons. Heavy workload may contribute to poor performance. A low workload may not be adequate to maintain proficiency in reading AFB smears. At microscopy centres, where smear microscopy is only a part of the LT's activity, a workload of less than 10 a week or more than 20-25 AFB smears a day may interfere with the quality of smear microscopy.

Monitoring slide positivity rates is necessary to determine appropriate sample sizes for a random blinded rechecking program. Any significant changes in the indicators may indicate performance problems and for calculation of necessary laboratory supplies. For example, a change in positivity rate outside the expected range may signal a problem in over-reading or under-reading, especially if a new technician has been posted.

The visit should involve a comprehensive assessment of laboratory safety including IC measures; conditions of equipment, adequacy of supplies as well as the technical components of AFB smear microscopy. Sufficient time must be allotted for the visit to include observation of all the work associated with AFB smear microscopy, including preparing smears, staining and reading of smears.

On-site evaluation should also include examining a few stained positive and negative smears to observe the quality of smearing and staining as well as the condition of the microscope. Some of the activities at microscopy centres that need to be observed during supervision visits include proper disinfection of all specimens using disinfectants such as 5% phenol, 5% hypochlorite or freshly prepared 10% bleach solution; availability of reagents within expiry date etc. Care should be taken to ensure that newly prepared batches of reagents are not being mixed with old batches of reagents.

Checklists

Any simple checklist will require well-established standards of acceptability and extensive training for consistent application and recording of what is observed to be unacceptable.

On-site visits by both adequately trained laboratory or non-laboratory personnel should ensure the availability and practice of the following:

i) Written standard operating procedures (TB Laboratory Manuals and Modules, display of charts on smear preparation, staining and reading etc.)

ii) Adequate supply of reagents within expiry date.

iii) Proper, well-functioning equipment and an adequate supply of consumables

iv) Internal QC such as the use of unstained positive and negative smears for every new batch of stains / reagents - ensuring that positive and negative control slides are used with all newly made batches of stains.

v) Laboratory safety practices including infection control measures.

vi) Accurate record keeping consistent with the requirements of NTP/NTRL (for example "triangulation" between laboratory register, TB register and treatment cards).

vii) Prompt reporting of results to treatment centres or physicians.

viii) Availability of a functional binocular microscope. At a minimum, district supervisors must be familiar with simple microscope function, and be able to visualize a clear image through the microscope lens. In addition, all facilities should have annual maintenance contracts for the binocular microscopes.

ix) Proper storage of patient's slides for EQA including rechecking to enable the supervisors to collect appropriate number of slides to be sent to reference laboratory.

x) Staff with adequate training with refresher courses with a capability of undertaking corrective action when appropriate.

xi) Evaluation of workload and proportion of positive smears to be examined.

xii) All chest symptomatic who are smear positive in the laboratory register are recorded in the TB register. Registers other than standard NTP/NTRL registers are not to be maintained. Also, laboratories should not do "pre-screening before testing" of cases.

xiii) The findings and need for corrective action or additional resources that are required.

On-site evaluation of the technical practices in the laboratory performed by properly trained laboratory staff from a higher-level laboratory includes all of the operational elements listed above, as well as:

i) Evaluating sputum collection procedures.

ii) Observing and evaluating procedures for smear preparation, staining, and reading.

iii) Rechecking several positive and negative smears to evaluate staining, smear thickness, smear size, and results.

iv) Reviewing results of panel testing and/or rechecking. Providing suggestions for corrective action or implementing corrective action as needed.

10 PROCUREMENT SUPPLY CHAIN MANAGEMENT FOR TB DIAGNOSTICS AND DRUGS

First line anti-TB drugs (4FDC) and all second line anti-TB drugs are centrally procured through the GDF. The Serviço Autonomo Medicamento Equipamento Saúde (SAMES) is an autonomous agency for procurement and logistics relating to drugs etc. with responsibility for clearance, storage and distribution of diagnostics was well as TB medicines including SLDs using QanTB software. MDR drugs are stored in a temperature-controlled room within the larger SAMES storage facility in Dili. The diagrams below illustrate the NTP management procedures with respect to diagnostics and drugs.

Figure 3: Management cycle for NTP diagnostics

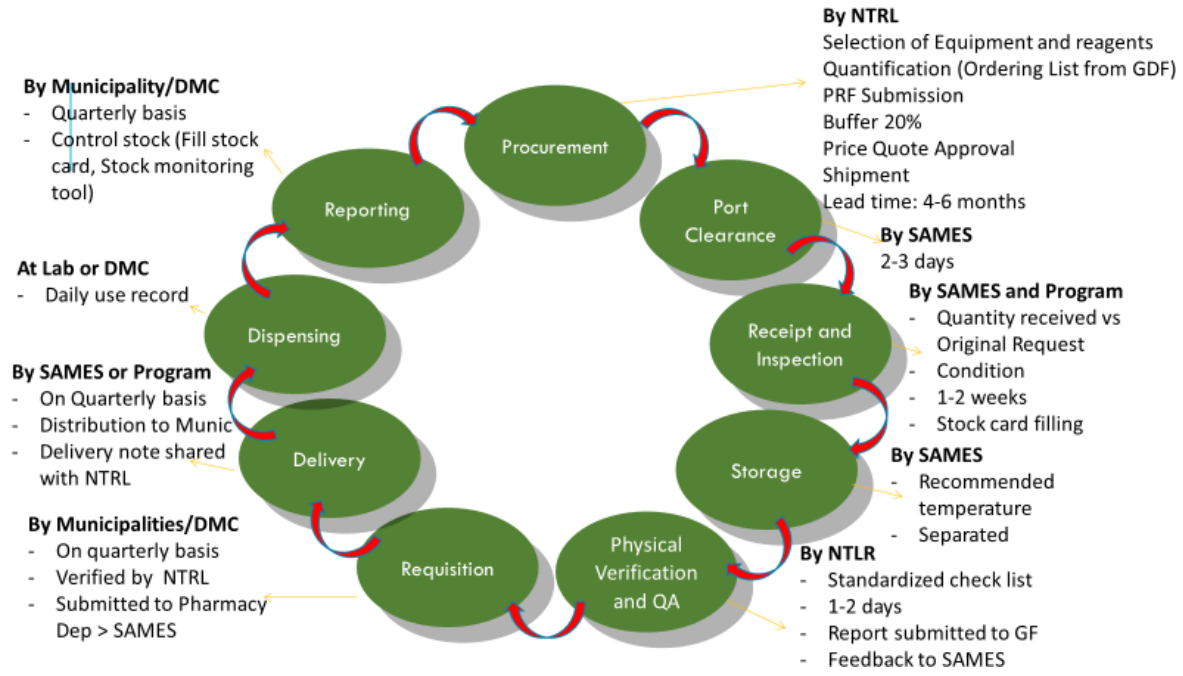
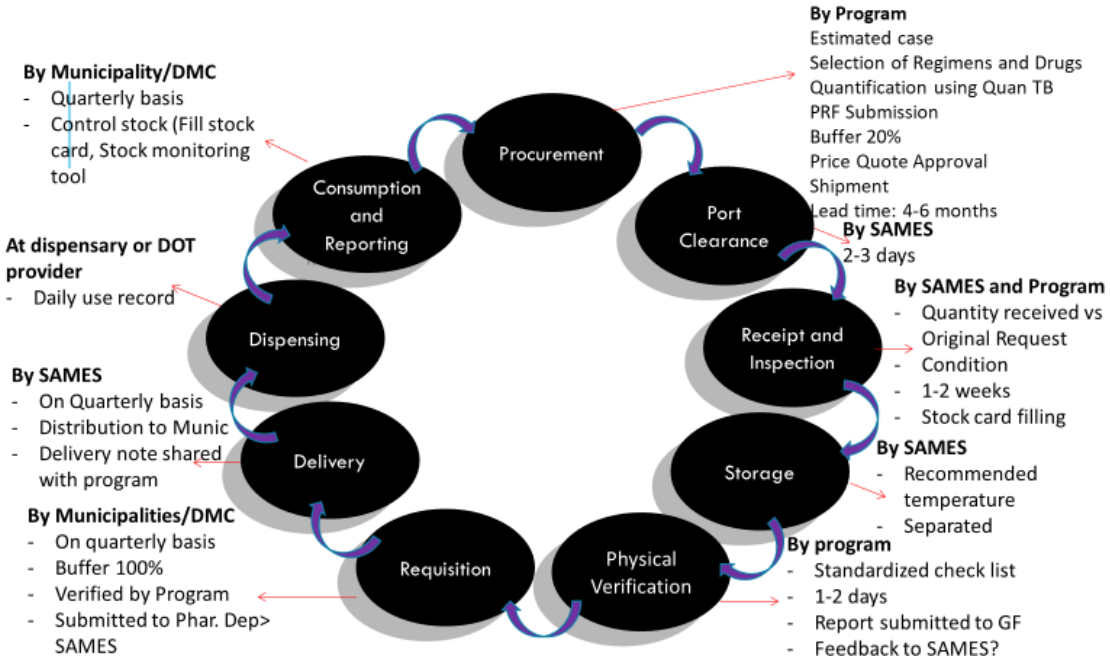
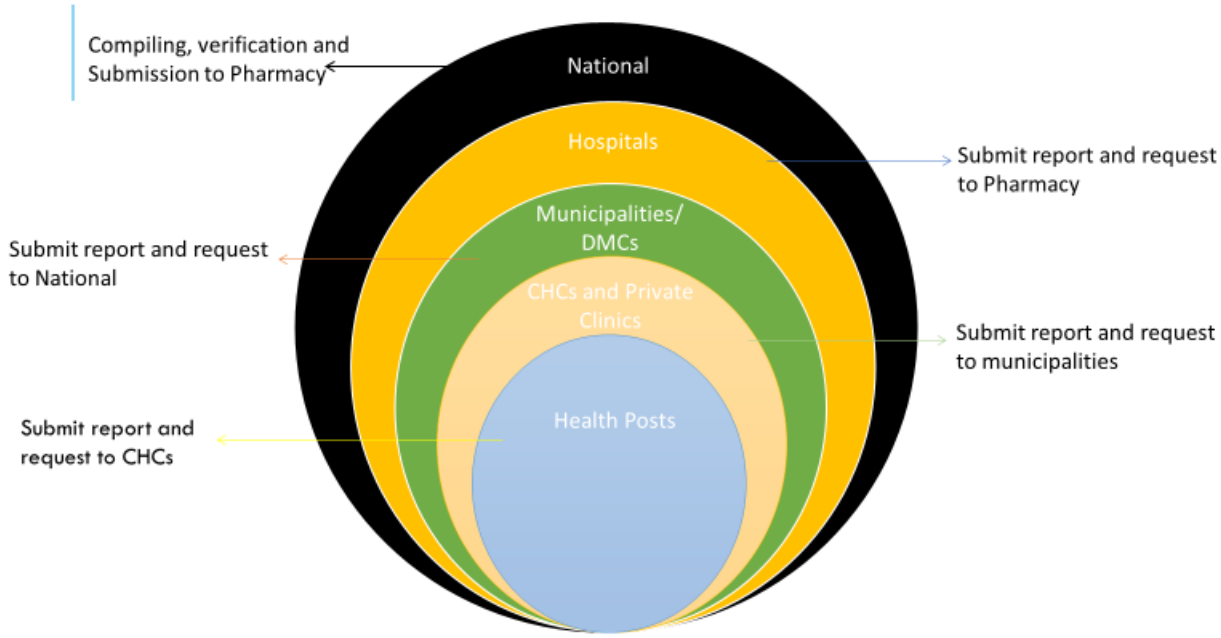


Figure 4: Management cycle for NTP drugs



The NTP will organise quarterly meetings between the NTRL, NTP, Pharmacy Department and SAMES. Collective requests for both diagnostics and drugs are prepared by the different levels of health care services according to the responsibilities illustrated in the figure below. Distribution of both diagnostics and drugs is organized by SAMES.

Figure 5: Quarterly diagnostic and drugs reports and requests prepared at different levels of health facilities

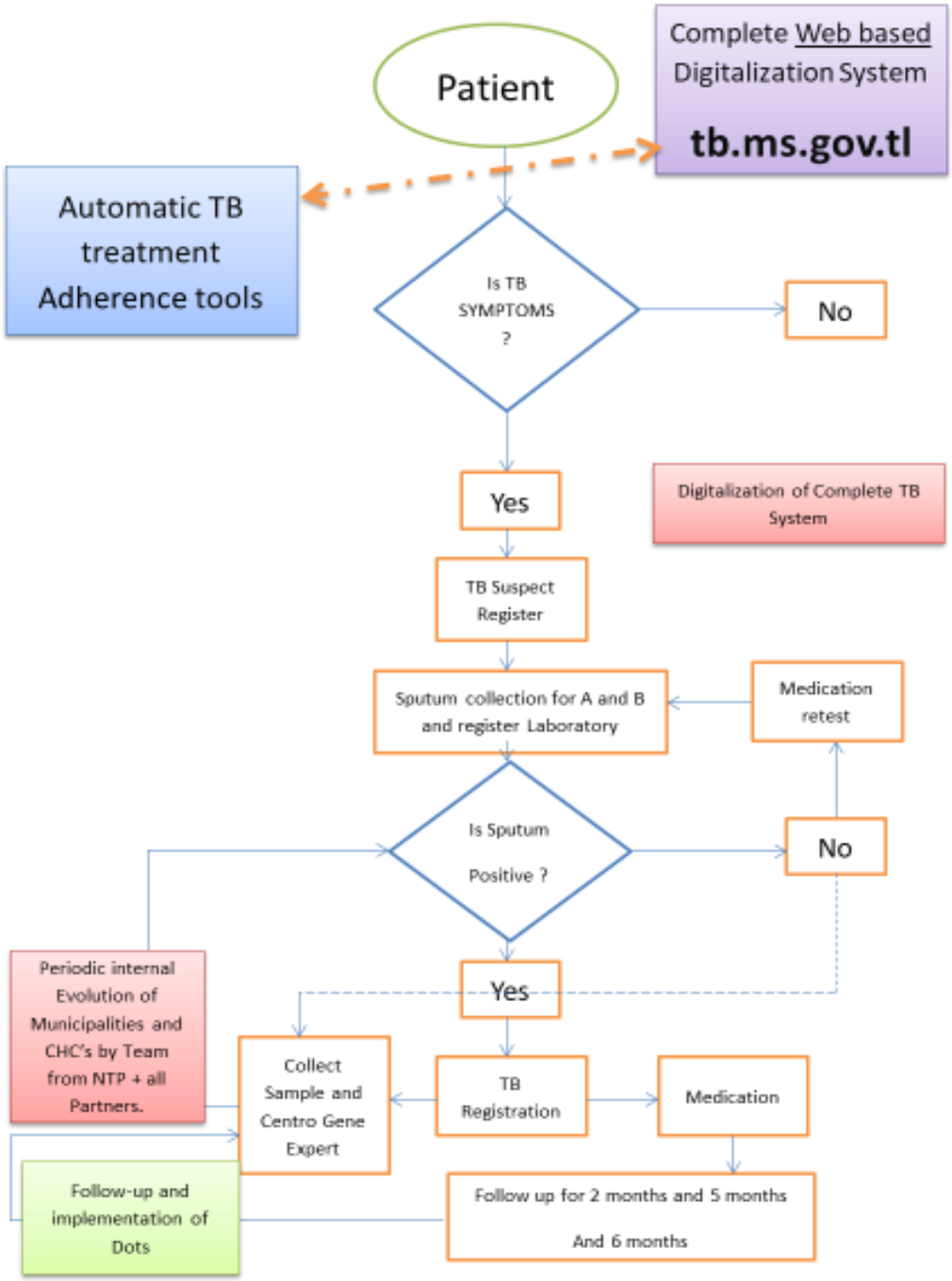


11 RECORDING AND REPORTING

11.1 APPLICATION OF DIGITAL TECHNOLOGY FOR CASE-BASED SURVEILLANCE

The NTP is currently developing an electronic recording and reporting system which will enable case-based surveillance through a digital database for TB. The NTP plans to implement an Automatic TB Electronic Observation of Therapy and Monitoring System, which is summarized in the diagram below.

Figure 6: Automatic TB Electronic Observation of Therapy and Monitoring System



Until this system becomes available, the NTP will continue to use a paper-based recording and reporting system. A further plan for migration to District Health Information System – 2 (DHIS2) is envisioned by the NTP from 2020.

11.2 RECORDING FORMS

Samples of all NTP forms and registers are shown in Annex 3 of this Manual.

Recording & Reporting

Maintenance of accurate records and registers of patients and program activities; and reporting data to the municipality/central unit, is essential for proper monitoring and management of the National Tuberculosis Control Program (NTP). NTP records and reports are standardized and provide the required information for managing the program effectively.

The following standardized records are to be used in the NTP:

Forms	Registers
Referral Slip	Tuberculosis Laboratory Register
Laboratory Request Form for Specimen Examination	Tuberculosis Register
Contact Tracing and TPT Forms	LTBI Register
Tuberculosis Treatment Card	Presumptive TB Register
DR-TB Treatment Card	Vulnerability assessment register with scoring
Patient's TB Identity Card	Referral & Feedback TB Register
DR-TB Patient Identity Card	Stock Register
Referral/ Transfer form for treatment	Culture and DST Laboratory Register
Referral/ Transfer form for treatment of DR-TB	Second-line TB treatment register
TB-HIV Forms	
TB-Diabetes Screening Forms	

Referral/Transfer form for treatment

The Referral / Transfer form for treatment is kept at all health facilities. The medical officer of the diagnostic health facility which refers patients for treatment (both DS-TB & DR-TB) to other peripheral health facilities must complete the top half of the form which includes the patient characteristics. Once the patient arrives, the receiving unit fills in the bottom half of the form and sends it back to the referring unit. Information regarding referral of patients should also be noted in the TB notification register.

The Referral / Transfer form is to be used when transferring registered patients currently under treatment from one reporting unit to another. If a patient is being 'Transferred Out', a Referral / Transfer Form and a copy of the Tuberculosis Treatment Card will be sent from the "transferring unit", i.e. referring health facility / TU to the "receiving unit", i.e. health facility/ TU where the patient will receive further treatment. The first part of the form contains information about the patient, her/his disease, treatment details and address of the transferring unit. This information should be used to complete a new Tuberculosis Treatment Card for the patient, who should be reregistered as a "transfer in" case in the receiving unit. When the patient has reported to the receiving unit, the bottom part of the form is completed by the receiving unit and returned to the transferring unit. This is to communicate patients' follow up examination results at the end of the intensive phase and the treatment outcome to the transferring unit.

All NTP Forms and Registers with a focus on strengthening municipality and sub-district level reporting are Annexed (Transition Plan to DHIS 2 TOOL):

Drug Sensitive (DS) - TB

QUARTERLY REPORTS

1. Quarterly Reports from Municipality Level, including quarterly reports on contacts & vulnerability assessment - CF, TO, PMR, DLS – TB & DR TB Drugs, TB-HIV, TB-Diabetes
2. Quarterly Reports from CHC Level, including quarterly reports on contacts & vulnerability assessment - CF, TO, PMR, DLS – TB & DR TB Drugs, TB-HIV, TB-Diabetes

REGISTERS

1. Municipality Level – 2 Registers: TB & LTBI Registers
2. Sub-Municipality Level – 5 Registers: 1) Duplicate TB & 2) LTBI Registers; 3) Lab Register; 4) Presumptive TB Register; 5) Vulnerability Assessment Register
3. Referral Feedback Register: HNGV & Maubisse Referral Hospital

Treatment Card & Transfer Form

Integrated Municipality & Referral Hospital TB Centres: Baucau, Maliana, Oecusse and Suai

Drug Resistant (DR) - TB

QUARTERLY REPORTS

1. Quarterly Reports from Municipality Level,
2. Quarterly Reports from CHC Level

REGISTER: DR-TB Register & PMDT Treatment Card

TB Presumptive Register

This register is used in those health facilities that identify tuberculosis presumptives, collect sputum and make smear fixation, or collect Xpert MTB/RIF samples. The smears or Xpert MTB/RIF samples are sent to the designated microscopy or diagnostic centre (DMC/DDC) for smear microscopy or Xpert MTB/RIF testing. It is important to note down the complete address of all tuberculosis presumptives in the TB presumptive register.

Request for examination of biological specimen for TB

This is the standard form that accompanies a biological sample sent to a laboratory for smear microscopy, culture, Xpert MTB/RIF or DST. The form includes culture and DST as the NTP will make these services available at the national level in the future.

If analyses of several types of specimen (e.g. sputum and other fluids) are requested a separate request form should be used for each specimen.

If multiple analyses (e.g. culture and DST on the same sputum sample) are requested the results should be sent from the laboratory to the requestor as they become available, rather than waiting until all test results are confirmed.

The requestor completes the upper portion of the form including basic demographic and contact details of the patient being tested. Depending on the type of analysis required, the requestor also fills in the date of sample collection in the lower part of the form.

The lower part of the form is used to communicate results back to the facility that requested the tests using a standardized notation. The person responsible for the test result must be clearly identified.

Laboratory register for smear microscopy and Xpert MTB/RIF

This register can be used for both sputum-smear microscopy and Xpert MTB/RIF examinations.

If more than one specimen is being tested in the course of investigation of the same patient, as is commonly the case when serial sputa are tested using by microscopy, the results **are recorded on the same line**. This also applies if both direct sputum smear microscopy and Xpert MTB/RIF examinations are carried out for the same patient with presumptive TB. If a patient is tested again during another diagnostic episode (e.g. if a patient with presumptive TB has a negative initial test and presents again with symptoms after a few months), the test results are registered in a new row. Results of tests undertaken for monitoring of patients on treatment are likewise entered in separate rows.

Laboratory register for culture, Xpert MTB/RIF and drug susceptibility testing

This register will used for the national reference laboratory. The method of diagnostic testing (culture or Xpert MTB/RIF) is indicated in the first two columns under "Type of examination".

If more than one specimen is being tested in the course of the investigation of the same patient, as is commonly the case when serial sputa are tested using microscopy, the results **are recorded on the same line**. This also applies if both direct sputum smear microscopy and Xpert MTB/RIF examinations are carried out for the same patient with presumptive TB. If a patient is tested again during another diagnostic episode (e.g. if a patient with presumptive TB has a negative initial test and presents again with symptoms after a few months), the test results are registered in a new row. Results of tests undertaken for monitoring of patients on treatment are likewise entered in separate rows.

District TB register

The district TB register is intended primarily for recording the data needed to monitor district performance, using indicators and reports about TB patients. It is also commonly used to summarise testing results and treatment decisions in order to determine whether basic diagnostic and treatment guidelines are correctly implemented. No information that is beyond this monitoring scope should be included in the register.

The register should contain the records of all patients diagnosed with TB and eligible for TB treatment, including those diagnosed with RR-TB or MDR-TB, regardless of whether treatment was actually started. All of these cases are notifiable and should be included in the summary case notification reports sent to higher levels. The registration date is the date on which the BMU decides that a patient has TB and is eligible for treatment.

Bacteriological examination before the start of treatment ("month 0") now allows for the registration of results from an Xpert MTB/RIF test. Space is provided for recording whether the case is RR-TB or MDR-TB. Both smear and culture results can be recorded.

Second-line TB treatment register

The second-line TB treatment register is intended primarily to keep a record of those data that are important for generating indicators and reports of patients on second-line regimens for RR-TB or MDR-TB. In contrast to the district register it is restricted to patients who have actually started on a second-line TB treatment regimen. This register is also commonly used to follow, at a glance, the adequacy of testing and treatment decisions.

The second-line TB treatment register should be updated regularly from the individual second-line TB treatment cards and from laboratory registers. Patients are recorded in the register consecutively by *date of registration*. A patient's date of registration is the day when health staff enter him or her in the register; however, in some countries it may be the date when the review panel decided to register the patient for second-line treatment.

Bacteriological examination before the start of treatment ("month 0") allows for the registration of results from an Xpert MTB/RIF test.

Tuberculosis Treatment Card

The tuberculosis treatment card is filled as soon as the diagnosis of TB is made and when the treatment is initiated. It is kept at the health facilities where the patient receives treatment (either at the TB clinic, district hospital, CHC, PHC, Health post, etc.). For patients who have to be given treatment at the sub-centre or village level by a multi-purpose worker, a duplicate card is made and given to the most peripheral health staff directly supervising drug administration of the patient. In case a duplicate is used, the information is periodically transferred on to the main card. The 'TB-responsible staff' at the health facility transfers the relevant data, particularly the results of bacteriological examinations, from the treatment card to the TB register.

Tuberculosis Patient Identity Card

This card is completed as soon as the diagnosis of TB is made and while treatment is initiated. This card is kept by the patient. The most important information in this card is the date of starting treatment, the regimen being used, and the drugs to be consumed under direct observation of the health worker, and the information on observation and collection of drugs at the health facility during the continuation phase. Appointment dates for collection of drugs during the continuation phase and follow-up examinations are entered on the reverse side of the card.

PMDT Treatment Card

This card is a key instrument for the DOT Provider administering the drugs daily to the patient. When a patient starts a Category IV treatment, the DOT Provider should fill in the treatment card. The card should be updated daily, ticking off the administration of drugs. The card is the source from which to complete and periodically update the Category IV register. When or if the patient moves (for example from a specialized hospital to his/her district of origin for follow-up) the card, or a copy of the card, must follow the patient. A copy of this card may be used as a notification form and to inform about final outcome of treatment.

11.3 REPORT FORMS

Quarterly report on TB case registration in the district

This is the standard aggregated report of cases as recorded in the district register and of laboratory activity as recorded in the laboratory register.

The categories of cases in the report are stratified by whether they are bacteriologically confirmed or clinically diagnosed, by site of disease and by previous history of treatment. For all incident cases (new and relapses), a breakdown by age group and sex is requested. The form also captures the yield of bacteriological tests among patients with presumptive TB tested, and the yield of HIV testing among TB cases tested.

Among HIV-infected cases, the numbers on ART and CPT during the quarter are recorded.

Quarterly report on TB treatment outcomes in the district

This is the standard quarterly report used to monitor treatment outcomes for all TB cases that have not been started on second-line treatment.

The report enumerates the treatment outcomes of patients registered (i.e. recorded in the district register) in the quarter that ended 12 months previously. For example, if this report is completed at the

close of the second quarter data are compiled on patients registered in the second quarter of the previous calendar year.

This report **excludes**:

- Patients who were transferred in from another BMU;
- Patients who were found to have RR-TB or MDR-TB and who were started on a full MDR-TB treatment regimen (i.e. were moved to the second-line treatment register).

The report **includes** TB/HIV activities as this allows the NTP to update the data it has previously collected in the quarterly report on TB case registration in the basic management unit.

Quarterly report on PMDT TB case finding

This is the standard aggregated report of DR-TB cases as recorded in the PMDT register. The report is provided in two parts, one for all patients diagnosed and a second for all patients put on treatment.

Interim Report for MDR treatment

Each quarterly cohort defined by the date of the start of PMDT registration should have an interim or preliminary outcome report after the initial months of treatment depending on the treatment regimen. This report should be prepared by the PMDT treatment coordinator based on the PMDT treatment register. Since reporting at the end of treatment is very late (after two or even three years), preliminary results are desirable for all cohorts.

Quarterly PMDT Treatment Outcome Report

This is the standard quarterly report used to monitor treatment outcomes for all TB cases that have been started on second-line treatment. Reporting periods vary depending on the type of treatment regimen.

Quarterly Report on Program Management

This is completed at the district level by the DTC and sent to the national level. This report indicates the status of program performance and the stock of drugs and logistics in the district.

Reports are completed by the staff at the district level on the first week of each quarter and sent to the national level. The data has to be analysed at the district level. Remedial actions must be initiated immediately at the district level where the technical and managerial indicators have not been achieved. Reports and district wide analysis must be sent to the central level NTP.

11.4 TRANSMISSION OF REPORTS

All sub districts have to submit reports on case-finding, smear conversion, results of treatment and program management to the DTC. The DTC will compile the sub-district reports to generate the district level reports. The reports are:

- Quarterly report on Case Finding
- Quarterly Report on Sputum Conversion:
- Quarterly Report on Treatment Outcome registered 12-15 months earlier
- Quarterly Report on Program Management

These reports are to be completed in duplicate by each district TB coordinator; one copy will be sent to the central TB unit and the other retained for their records. The dates for analysing the results of the treatment (treatment outcomes) of patients who started treatment during a particular quarter are as shown in the example below.

Start of treatment	**Date of analysis**
1st January to 31st March 2020	1st week April 2021
1st April to 30th June 2020	1st week July 2021
1st July to 30th September 2020	1st week October 2021
1st October to 31st December 2020	1st week January 2021

11.5 PROCESS OF RECORDING AND REPORTING

When a tuberculosis presumptive is identified at a health facility, his/her name will be entered in the TB presumptive register. Then the laboratory form for sputum examination and Xpert MTB/RIF is completed to refer the patient for bacteriological investigation. In the designated microscopy or diagnostic centre, the name of the patient is entered in the laboratory register. When the physician decides the category of treatment for a patient who is diagnosed as having TB, the treatment card and patient identity card are prepared.

If the patient is diagnosed at the district CHC, the particulars are entered in the TB Register on the same day and the TB number is allotted. If the patient is diagnosed in the sub-district, the address is verified, the patient is put on treatment at the CHC/HP and the registration is done during the supervisory visit of the DTC.

The treatment Card is maintained at the CHC or health post where the patient is diagnosed. If the patient is to be treated in a health post or by a community volunteer, a duplicate card will be prepared and given to the DOT provider to record the DOT.

Treatment cards are organized at drug distribution centres according to the day of scheduled observation and the phase of treatment (intensive phase or continuation phase). When the patient swallows the medication under direct observation in this manner, the cards of patients who do not present for treatment will be apparent on the same day, and appropriate action for their retrieval can be taken. The health staff records the drug administration at the time of intake by the patient.

In cities (Dili and Baucau) diagnosis is also made in hospitals, where microscopy and treatment administration is done by hospital staff. After the doctor decides on the category of the patient, the treatment card and patient identity card are prepared, and the patient is registered in the TB Register

(by the visiting district TB coordinator) and allotted a TB number. The doctor explains the treatment schedule and refers the patient to the district CHC near his/her residence for DOT. When the DOT provider is a community volunteer, he/she will be given a duplicate Treatment Card together with the patient's drugs.

12 TRAINING, SUPERVISION, MONITORING AND EVALUATION

12.1 TRAINING

The NTP involves many activities, such as case finding by sputum smear microscopy, directly observed treatment with standardized short-course chemotherapy, use of an improved recording and reporting system, etc. High quality training is critical to the successful implementation of the NTP. It is imperative to conduct quality training of all levels of personnel who have TB-related responsibilities. Training of relevant staff according to the new guidelines is an important aspect of the NTP. It is essential to ensure that, by careful planning, all types of personnel who are to perform TB-related activities are adequately trained prior to implementation of NTP. The entire training process at the district has to be closely monitored by the District TB Coordinator.

Development of a schedule for training

The personnel at each level support and supervise the level directly below them.

Generally, staff at the district level should be trained before the staff at the sub-district level, and the staff at the sub-district level should be trained before the staff at the peripheral levels. In order to ensure that the appropriate persons are trained at the correct time, training schedules for the staff of the health facilities and the staff of laboratory staff services must be developed.

12.2 SUPERVISION

How and why supervision is to be conducted

Supervision should be a systematic process for increasing the efficiency of health staff by developing their knowledge, perfecting their skills, improving their attitudes towards their work and increasing their motivation. It is thus an extension of training. Supervision is carried out in direct contact with the health worker. In simple terms, managers supervise health workers and other people involved in NTP activities. Supervision should be performed at all levels of health infrastructure. All health workers need help to solve problems and overcome difficulties. They also need feedback on their performance and encouragement in their work.

Good supervision is the process of helping health workers improve their performance. During supervisory visits, one should observe and reinforce stipulated practices in the various components of the NTP as well as identify and correct inadequate performance and recording discrepancies, if any, before these become a major problem. The crux of supervisory visits should be education, coordination, motivation, facilitation and guidance with the overall objective of implementing corrective action. The regional TB supervisor at the central level is primarily responsible for the supervisory activities in the allotted districts, while the district TB coordinators are responsible to supervise their respective district. Though they may go individually for supervisory activity, some of the visits should be done as a team for better coordination. The key indicators and frequency of supervisory visits should be as indicated under the job description of each category of staff.

Some health units will need more supervision than others, the important guiding criteria for which are:

1. The sputum smear conversion rate is below 85% at 3 months
2. There is no regular supply of drugs by the health unit to patients during the continuation phase of treatment. This can be supervised by:
    a. Observing the patients to see whether they bring the empty blister packs when they come to collect weekly blister packs.

b. Tallying the marking on the tuberculosis treatment cards and comparing with the information given by the patient

3. Monitoring of treatment of pulmonary tuberculosis cases by sputum smear examination at appropriate intervals is inadequate
4. Cure rate less than 85% or default rate is more than 10%

There should be emphasis on sputum examination as a method of diagnosis. The proportion of new smear-positive cases should be roughly equal to that of new smear-negative patients. Districts and sub-districts with a high proportion of smear-negative cases require more frequent supervision.

Frequent visits need to be planned to health units, which require close supervision. The health units should be sent prior information about the supervisory visits. However, some surprise visits to the health units must also be undertaken. The activities of the health workers under the NTP can be used as a guideline for preparing the checklist.

12.3 NTP CHECKLIST FOR HEALTH FACILITIES PROVIDING TREATMENT

Checklist for Supervisory Visits to Health Facilities Providing TB-Control Services		
Health facility ..... District TB Coordinator.....		
Health worker responsible for TB activities ..... Date		
Review *Tuberculosis Treatment Cards* for all current TB patients and those who recently completed treatment. Register all newly detected cases in the *District TB Register*. Update the register for other patients. **Then select issues from this checklist to examine or follow up on during this visit, based on previous performance, problems, any recent changes in areas such as procedures or staffing, or training needed or completed**		
Check *Tuberculosis Treatment Cards*	***YES****	***NO****
1. Is each patient on the correct treatment regimen? 2. Have sputum examination results been recorded correctly? 3. Do treatment cards indicate that all patients are receiving directly observed treatment? Is treatment regular and correctly recorded? 4. Have all TB patients been tested for HIV? 5. Are all HIV-positive patients receiving ART and CPT? 6. Are contacts of TB patients listed on the treatment card? Was each contact who is younger than 5 years and other contacts who have cough examined as a suspected TB case (indicated by results recorded on the card)? 7. Are contacts of TB patients younger than 5 years who do not have TB put on TPT? 8. Are patients undergoing smear examination at 2 months (at 3 months if on retreatment regimen)? 9. Are patients undergoing smear examination at 5 months and during the last month of treatment? 10. Are patients who are smear-positive at 2 months undergoing smear examination after 1 more month? 11. Are previously treated patients and HIV-positive patients getting Xpert MTB/RIF at the start of treatment? 12. Are patients who are smear-positive at 3 months, 5 months, or in the last month of treatment getting Xpert MTB/RIF? 13. Are patients who are suspected MDR-TB cases referred appropriately 14. For each patient who has completed treatment, is the information on the treatment card sufficient to determine treatment outcome?		
	YES	***NO***

Review *Register of TB Presumptives* and/or *Tuberculosis Laboratory Register* (if available)		
1. Does the facility have a *Register of TB Presumptives*?		
2. If yes, are the results of sputum smear microscopy written in the *Register of TB Presumptives*?		
3. Is there only a reasonable delay between sending sputum and receiving microscopy results?		
4. If the facility has both a *Register of TB Presumptives* and a *Tuberculosis Laboratory Register* in the facility, do the microscopy results recorded in them match?		
5. Do results in the *Register of TB Presumptives* match the results recorded on the *Tuberculosis Treatment Card*?		
6. Have all smear-positive patients started treatment for TB?		

* Tick YES or NO for each question. Any NO answer indicates a problem that should be addressed. For each problem, investigate to determine the causes of the problem and possible solutions.

Look at the work environment. Follow and observe the general flow of patients through the facility.	***YES***	***NO***
1. At the entrance, are there signs asking adults with cough to inform the nurse or doctor?		
2. Is there a system to identify patients with cough (irrespective of reason for attending) and refer them for sputum collection?		
3. Is there good ventilation (open windows, exhaust fans) in the waiting area, in patient-care areas, and where treatment of TB patients is directly observed?		
4. Do patients with a cough wait outside or in an area separate from other patients?		
5. Is the patient flow arranged to minimise the time that suspected TB cases and TB patients are with or pass by other patients?		
	YES	***NO***

Examine and ask about supplies. Is there:		
1. An adequate supply of anti-TB medicines? Are anti-TB medicines well maintained, not expired? Note quantities in stock:		
2. An adequate supply of needles, syringes and diluent for injections?		
3. A system for the safe disposal of needles and syringes?		
4. An adequate supply of TPT (for children exposed to TB and other contacts according to NTP policy)?		
5. An adequate supply of co-trimoxazole for CPT for TB/HIV patients?		
6. An adequate supply of sputum containers? Number in stock: …….		
7. An adequate supply of:		
– *Tuberculosis Treatment Cards*?		
– *Request for Sputum Examination*?		
– *Tuberculosis Referral/Transfer*?		
8. Cough hygiene poster on display?		
9. A procedure to dispose of unwanted or expired medicines safely?		
Ask and, if possible, observe health workers with patients. Do they:	***YES***	***NO***
1. Ask all adult outpatients about cough, and correctly identify suspected TB cases?		
2. Teach patients to cover their mouth and nose when they cough?		
3. Send suspected TB cases to the laboratory or collect sputum samples for examination?		
4. Collect sputum outdoors or in a well-ventilated area?		
5. Recommend HIV testing to TB patients? Provide or refer patients to HIV testing services?		
6. Administer the correct medicines for the treatment regimen?		
7. Watch patients swallow the tablets?		
8. Mark the treatment card **after** watching the patient swallow the tablets?		
9. Correctly give a streptomycin injection **after** the tablets have been swallowed? (if applicable)		
10. Give each injection with a **sterile** syringe and needle? (if applicable)		
11. Inform TB patients and suspected cases about TB in a considerate and appropriate manner?		
12. Ask TB patients about their contacts and record their names on the treatment card?		
13. Ask TB patients to bring any contacts younger than 5 years or other contacts who cough to the health facility for assessment?		
14. Screen contacts of TB cases?		
15. Give IPT to young children and other contacts as appropriate?		

Ask whether health workers have any questions or problems. *Notes:*		
Were there changes in staff responsible for TB activities? Fill in the chart, *Staff Positions and Training for TB-Related Activities,* every 6 months.	*Update the chart when there are changes.*	
Talk to TB patients, if possible. Do patients know: 1. What disease they have? 2. The number of tablets to take each day? 3. When to come back for the next appointment? 4. The duration of treatment? 5. What to do when they experience problems (side-effects)? 6. Why sputum examinations are needed? 7. How to prevent the spread of TB? 8. To cover their mouth and nose when coughing? 9. Who else in their household should be examined or tested for TB? **Ask whether patients have any problems that may prevent them from completing treatment.**	**P1**	**P2**
Talk to DOT Providers. Ask: 1. How many TB patients do you support? 2. May I examine your patients' *Tuberculosis Treatment Cards?* Determine whether it is marked correctly. 3. Did you receive sufficient training to prepare you to be a TB treatment supporter? 4. How often does a supervisor from the health facility check your work and your patients' treatment cards? 5. Have you ever run out of medicines? 6. What do you do when a TB patient interrupts (stops coming for) TB treatment? **Answer any questions that the TB treatment supporter has.**	**DP1**	**DP2**

Quarterly **Ask the health worker responsible for TB control about recent monitoring results. Has the health worker calculated the following for appropriate quarters? If so, what are the results?**	***Write the figures below***	
1. The total number of TB cases currently on treatment. 2. The proportion of outpatients aged 15 years and older who were identified as suspected TB cases. 3. The proportion of suspected TB cases tested who were sputum smear-positive. 4. The proportion of new sputum smear-positive cases that – was cured – completed treatment. 5. The proportion of TB patients tested for HIV. 6. The proportion of HIV-positive patients on CPT.		
If there is a microscopy unit, observe and ask the staff:	***YES***	***NO***
1. Does it have good air flow? 2. Are the work areas, slides and supplies well organized and cleaned regularly? 3. Are used sputum containers and other used supplies managed according to appropriate biosafety and safe hazardous-waste disposal procedures? 4. Are slides sent for external quality control according to national guidelines? 5. Is the microscopy register complete, and the information used for monitoring?		

Observations from this supervisory visit
Describe problems identified during this visit
Possible causes of the problems
Actions and recommendations

12.4 General principles for monitoring and evaluation

Monitoring

Monitoring is the process of observing whether an activity or service is occurring as planned. It is the continuous oversight of the implementation of an activity, seeking to ensure that input deliveries, work schedules, targeted outputs, and other required actions are proceeding according to plan. Monitoring aims to identify evidence of any diversion from a planned course of action, thus identifying the need for a more formal evaluation of the activities and allowing timely solutions to problems to be sought. The monitoring of NTP is a continuous process of surveillance on the implementation and outcomes of program activities and informs operational decision-making.

Evaluation

Evaluation is determining as systematically and objectively as possible the relevance, effectiveness and impact of activities in the light of their objectives.

Indicators

Indicators are the variables that are measured to assess to what extent the plans are implemented, and the objectives achieved. The main indicators in the NTP are shown below.

12.5 Monitoring NTP output and outcome indicators

Table 15 below provides a list of key programmatic indicators that are grouped under the respective components of the NTP's strategy. Most of these indicators measure the quality of performance at the service delivery level.

Table 15: NTP output and outcome indicators

NTP strategy component	**Indicator** Definition	**Source**
High-quality DOTS	**Notification rate of all forms of TB cases** TB cases (all forms) notified to the NTP during a specified period (number)	TB register, Quarterly reports
	Notification rate of bacteriologically confirmed cases TB cases (bacteriologically confirmed) notified to the NTP during a specified period (number)	TB register, Quarterly reports
	Treatment success rate, bacteriologically confirmed TB cases Cases successfully treated (cured plus completed treatment) among the bacteriologically confirmed TB cases registered during a specified period (number and percentage)	TB register, Quarterly reports
Improving diagnosis	**Quality assurance for smear microscopy** Laboratories showing adequate	External quality assurance

	performance in external quality assurance for smear microscopy among the total number of laboratories that undertake smear microscopy during the reporting period (number and percentage)	
	Adequate use of Xpert MTB/RIF Percentage of TB presumptives qualifying for Xpert MTB/RIF for which Xpert MTB/RIF was used	Presumptive register, Laboratory register
Drug supply management	**Stock-outs of first-line anti-TB drugs** Reporting districts reporting no stock-out of first-line anti-TB drugs on the last day of the quarter (number and percentage)	Quarterly report on drug orders or remaining stock on the last day of the quarter in district
	Stock-outs of second-line anti-TB drugs Reporting districts reporting no stock-out of first-line anti-TB drugs on the last day of the quarter (number and percentage)	Quarterly report on drug orders or remaining stock on the last day of the quarter in district
Monitoring and evaluation	**Timeliness of routine reporting** Reporting units submitting timely reports according to NTP guidelines (number and percentage)	Quarterly report on TB case registration / TB treatment outcome in districts
TB/HIV	**Proportion of TB patients with known HIV status** TB patients registered during the reporting period who had an HIV test result recorded in the TB register among the total number of TB patients registered during the reporting period (number and percentage)	TB register, Quarterly reports
	Proportion of HIV-positive TB patients who receive co-trimoxazole preventive therapy (CPT) HIV-positive TB patients, registered over the reporting period, starting or continuing CPT treatment during their TB treatment among all HIV-positive TB patients registered during the reporting period (number and percentage)	TB register, Quarterly reports
	Proportion of HIV-positive registered TB patients given	TB register, Quarterly reports

	antiretroviral therapy during TB treatment HIV-positive TB patients who are started on or continue previously initiated antiretroviral therapy, during TB treatment, among all HIV-positive TB patients registered during the reporting period (number and percentage)	
Tuberculosis Preventive Therapy (TPT)	**Number (and proportion) of household contacts of index patients** initiated on TPT (disaggregated into <5 years and ≥ 5 year) **Of those initiated on TPT the number (and proportion) who completed TPT** (disaggregated into <5 years and ≥ 5 years) **Number (and proportion) of PLHIV patients** initiated on TPT	TB Register; Contact and LTBI Treatment Register; Quarterly report on Contact Tracing and LTBI From TB-HIV monthly report
MDR-TB	**MDR presumptives with Xpert MTB/RIF result** Presumptives with Xpert MTB/RIF results among those eligible for Xpert MTB/RIF testing according to NTP manual during the specified period of assessment (number and percentage)	Format for monitoring testing of presumptive MDR TB patients, laboratory register
	Confirmed MDR-TB cases enrolled on treatment Laboratory-confirmed MDR-TB cases enrolled on second-line anti-TB treatment during the specified period of assessment (number)	Laboratory register, MDR TB treatment register
	Treatment success rate, laboratory confirmed MDR-TB Laboratory-confirmed MDR-TB cases successfully treated (cured plus completed treatment) among those enrolled in second-line anti-TB treatment during the year of assessment (number and percentage)	MDR TB treatment register
Infection control	**Infection control in health facilities** Health care facilities that have infection control practices in place that include airborne infection control for TB control among the total number of facilities (number and percentage)	Data for the numerator of this indicator should be obtained from yearly survey or routine reporting. Data for the denominator are reported routinely
	Ratio of TB notification rate	Data for the numerator of this

	(all forms) in health care staff (all staff) over the TB notification rate in general population, adjusted for age and sex.	indicator should be obtained from yearly survey or routine reporting. Data for the denominator are reported routinely

12.6 MONITORING NTP IMPACT INDICATORS

12.6.1 Prevalence

The prevalence of TB is the number of cases of TB in a population at a given point in time (expressed as number of cases per 100,000 population). The prevalence of TB determines the risk of TB infection in a community, that is, how much transmission is occurring. The prevalence of TB is approximately the incidence of TB multiplied by the average duration of disease. Improved case-finding and treatment both shorten the duration of disease, so prevalence responds more rapidly than incidence to changes in TB control. Periodic assessment of the prevalence of TB disease can therefore be more useful for measuring the short-term impact of TB control (for example, within five to ten years) than efforts to measure changes in TB incidence. Changes in TB prevalence over time are best measured by implementing at least two surveys at sufficient intervals.

There are two methods for estimating the TB prevalence. Direct measurement uses a cross-sectional population-based survey. TB prevalence surveys typically require sample sizes of 50,000 to 100,000 people in high TB burden countries, and implementation is expensive and logistically challenging. Indirect estimation of TB prevalence is derived from estimated TB incidence multiplied by the average duration of disease. However, neither incidence nor disease duration is typically measured directly, and indirect estimates of prevalence have a high level of uncertainty.

Indirect estimates of TB prevalence (estimates not obtained from a population-based survey) should not be used for targeting or program evaluation purposes. Only direct measurements from population-based surveys are suitable for program monitoring and evaluation purposes.

A TB prevalence study should be carefully designed with experts' consultations. If a study or survey is planned the NTP will refer to the general guidance found in the WHO policy and recommendations for measuring progress in global TB control.[25] A typical survey is designed to detect 70 to 100 smear-positive cases, using X-ray as a screening tool. Culture examinations are also essential for confirmation of diagnosis.

12.6.2 Incidence

The incidence of TB is the number of new cases of TB (including recurrent episodes of disease in patients who had previously been declared cured of a prior episode of TB) that occur each year. Incidence (cases arising in a given time period) gives an indication of the burden of TB in a population, and of the size of the task faced by a national TB control program. Incidence can change as the result of changes in transmission (the rate at which people become infected with *Mycobacterium tuberculosis*), or changes in the rate at which people infected with *Mycobacterium tuberculosis* develop TB disease (for example, as a result of changes in nutritional status or of HIV infection). Because TB can develop in people who became infected many years previously the effect of TB control on incidence is less rapid than the effect on prevalence or mortality.

There are three practical methods of measuring or estimating TB incidence in a given year:

- Direct measurement from TB notification data when TB surveillance meet high standards of coverage and quality
- Estimation by assessing the completeness of TB notification data through inventory studies using record-linkage and capture-recapture modelling;
- Estimation from expert opinion using the "onion model" framework.

[25] World Health Organization. Tuberculosis prevalence surveys: A handbook. WHO; 2011.

Other methods for measuring incidence are impractical and resource-intensive (for example, nationwide cohort studies of TB incidence) or they rely on difficult-to-validate assumptions and poorly performing tests (for example nationwide tuberculin surveys in children). Indirect estimates of incidence derived from measurements of prevalence or mortality have wide confidence intervals and are not used by WHO because of the absence of reliable measurements of average disease duration or TB case fatality rates at the country level.

12.7 EVALUATION OF CASE FINDING AND TREATMENT RESULTS

12.7.1.1 ***Evaluation of case finding***

The central unit of the NTP will tabulate, check the quality, analyse the quarterly reports of case finding, and produce explanatory remarks about all districts. In the report covering all four quarters, rates (per 100,000) will be calculated. The figures of the districts will be compared with that of the previous year. The reports will be distributed to all districts to provide feedback of case-finding activities, which will be important background information for supervisory visits.

1. Indicators

1. Notification rate of bacteriologically confirmed tuberculosis cases

The numbers and rates (per 100,000 population) should be compared between districts over time. A low rate of notified cases may be the result of insufficient case finding (not enough TB presumptives referred or examined), improper bacteriological diagnosis, many tuberculosis presumptives not reporting to the health services, or a combination of all of these. It should be ensured that all TB presumptives attending general health services are being examined according to the guidelines with the recommended number of sputum samples. Efforts should be made to educate the doctors, nurses and other health care providers to identify and to investigate all tuberculosis presumptives. Active case finding is not recommended except in rare situations. On the other hand, efforts should be made to improve diagnosis of tuberculosis among patients attending health facilities by ensuring that all persons with cough for 2 weeks or more are subjected to bacteriological investigation by smear microscopy and/or Xpert MTB/RIF.

2. Proportion of pulmonary smear-positive cases out of all pulmonary cases (%)

If the proportion of the smear-positive cases is less than 50%, either smear examinations are not requested for all TB presumptives by doctors, the quality of microscopy is not adequate, and there is over-diagnosis based only on clinical symptoms and radiology. Although HIV increases the probability of smear-negative disease, this does not happen in a large enough proportion to be noticeable in this type of analysis.

3. Proportion of extrapulmonary cases

Normally extrapulmonary cases should account for about 10% of the total pulmonary cases. If the proportion of extrapulmonary cases reported is very high, there is probably over diagnosis, and if the proportion is very low, there is probably under diagnosis. Both these situations need technical monitoring. In places where prevalence of TB-HIV co-infection is high the proportion of extrapulmonary cases can be higher.

4. Proportion of paediatric cases:

If this proportion is very high, doctors may be over diagnosing tuberculosis and if the proportion is too low, there may be under diagnosis.

12.7.1.2 ***Evaluation of treatment***

The Quarterly report on smear conversion rate for smear-positive patients at 2 and 3 months gives an indication about the efficacy of the treatment regimen and the degree of supervision during the intensive phase.

The Quarterly Report on results of treatment gives information on new smear-positive cases, smear-positive relapses and other retreatment cases in each district. The most important indicator is the cure rate (and treatment completion rate) in new smear-positive cases. It is expected that in Timor-Leste, with the regiments used, the success rate (the cure plus completion rates) should be at least 85%.

An important step, before data analysis, is to check that the cohorts are complete, e.g. all the cases notified for that period have been included in the report on treatment results and any exclusion explained in detail. The most important items to analyse are:

1. Proportion of patients who are cured or completed treatment

Cure is the main indicator for evaluation of the performance of the NTP. The trend of cure rates should be followed in time, and once it has reached optimum levels (above or near 85% for new cases and relapses) it should be maintained. A small proportion of smear-positive cases completing treatment but without bacteriological evidence of negative smear ("treatment completed") is acceptable as they can be patients in whom productive cough has disappeared and smear examination on sputum could not be done. However, even in all such cases, efforts such as irritation of posterior pharyngeal wall, steam inhalation, warm saline gargles, etc. should be made to bring out the sputum. Even after these efforts, if sputum is not available and only a saliva sample is obtained then this sample should be examined during follow-up examinations. The achieved cure rate should be compared with the desired cure rate of more than 85%. If the achievement is less than that stipulated, then reasons for the shortcomings need to be analysed and immediate remedial measures planned and executed.

2. Proportion of patients lost to follow-up

The proportion of defaulters should be less than 5% in a well-functioning program. A high rate of default is the most common cause of low cure rates. Common causes are poor communication, information, health education and motivation to the patients. The reasons for default also include poor accessibility to treatment services, especially direct observation of treatment, in respect of geographical, financial, social factors and long waiting time in the health unit. Indifferent staff behaviour may also lead to the services being inaccessible or underutilized. Patient migration due to various reasons is also an important reason for default. A second component is the lack of or poor defaulter retrieval action. Many health service providers consider that their responsibility is limited to the door of the health centre and that it is up to the patient to complete the treatment indicated. An important philosophy and characteristic of a public health program like the NTP is that, in order to protect the community, the health system is responsible for its effective implementation.

3. Proportion of patients transferred out

This indicator will present variations from one region to another depending on the stability of the population. In a poorly functioning program, "transfer" is used as a way of disguising patients lost from supervision. In fact, for a gross evaluation, transfers in which there is no information on the patient afterwards may be treated as defaults. In well-organized programs, transferred outpatients who complete their treatment in a different district may be traced and their results obtained. In any case, the proportion of transfers should be considered in view of the characteristics of the population, and if high, special actions should be taken to ensure that the transfer includes adequate information to the recipient service (both directly and through the patient), and that the patient has access to continuation of treatment and that the treatment is completed without interruption.

4. Proportion of failures

Failure of treatment is related to irregular drug intake and to drug resistance. An early indicator of failure is the sputum smear conversion rate at 2 and 3 months after the start of treatment. When low

conversion rates are observed, the supervisors should ensure that every dose of medication in the intensive phase of treatment and at least one dose per week in the continuation phase are given under direct observation, that the regimens are prescribed correctly and in particular that patients are properly categorized. Special care should be observed in categorizing a case as a "new case" i.e. only if they have received treatment for less than a month or no treatment at all in the past. Failure of retreatment cases strongly indicates MDR-TB.

5. Proportion of retreatment cases

Retreatment cases are the result of poorly organized programs in the past. When a more effective strategy is implemented, the proportion of retreatment cases (including failures, relapses and treatment after default) is usually high in comparison with the new cases. One of the challenges of a good treatment program is to reduce retreatment cases and chronic cases (patients who have failed retreatment) by curing them with appropriate regimens and by curing new cases thereby preventing failures, relapses and treatment after default cases. With a good performing NTP in place, in a few years, the proportion of retreatment cases will diminish and stabilize.

6. Proportion of deaths

The most common cause for high mortality due to TB was previously due to the delay in diagnosis, which would result in poor clinical condition of the patient. This situation was primarily a result of poor coverage of health services and difficult access of patients to bacteriological diagnostic facilities and treatment centres. The increase in TB-HIV co-infection increases the proportion of TB cases that dies, partly due to TB and also due to other HIV-related diseases.

12.7.1.3 *Evaluation of program management and logistics*

The report on program management and logistics provides indications about the NTP's program management. The indicators include the proportion of staff in position against the planned number, the proportion of staff trained in the NTP, the proportion of health facilities supervised by the supervisory staff, the percentage of referral of outpatients for smear microscopy (TB presumptives), percentage of positive cases among the TB presumptives examined (smear positivity), the percentage of smear positive patients registered out of such patients diagnosed (treatment initiation), the proportion of patients put on DOTS within a week of diagnosis (quality of DOT), the management of drugs and other logistics etc. The Quarterly Report on drug supply helps in calculating the drug and logistic requirements at the District Levels.

13 HEALTH EDUCATION, ADVOCACY, COMMUNICATION, SOCIAL MOBILIZATION

Nations around the world have come to realize that advocacy, communication and social mobilization (ACSM) increase the value of and can make substantial inroads towards Tuberculosis control.

There is growing evidence that ACSM is a valuable set of principles to help address the four key challenges to TB control at the country level, including in Timor-Leste:

- Improving case detection and treatment adherence;
- Combating stigma and discrimination;
- Empowering people affected by TB; and
- Mobilizing political commitment and resources for TB

The NTP has developed a Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019, which also makes use of ACSM principles to mobilize political support and leadership for TB control strategies in Timor-Leste at all levels; to empower people affected by TB; to improve case detection and boost treatment adherence; and to tackle stigma.

13.1 STRATEGIC OBJECTIVES OF COMMUNICATION ACTIVITIES (SOCA)

The strategic objectives of the communication activities (SOCA) of the MoH's Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste until the end of 2019 are specific, measurable, achievable, realistic and timely and contextualized to the Timor-Leste experience and context.

Each SOCA contributes towards supporting the achievement of the objectives of the National Strategic Plan for Tuberculosis Control for Timor-Leste 2018 – 2022 and at the same time help address the four key challenges to TB control at the country level, including in Timor-Leste.

SOCA 1: To achieve high level stewardship and policy commitment to zero deaths, zero disease and zero suffering due to tuberculosis in Timor-Leste by 2035.

SOCA 2: To encourage and promote a Ministry of Health with health facilities and services delivery fit-for-purpose in active case finding, early case detection, treatment and cure of Tuberculosis across Timor-Leste.

SOCA 3: To empower the community to actively support cutting the chain of transmission of tuberculosis by knowing how to recognise the symptoms of tuberculosis infection and what actions to take to protect one-self, the family, and the community from tuberculosis.

SOCA 4: To ensure that TB sufferers seek treatment and commit to the full course of prescribed treatment until cured from the disease.

SOCA 5: To promote through TB champions, that is, people who are respected and can guide others to seek early diagnosis and treatment, that TB is curable and to reduce the social and cultural stigma attached to tuberculosis in Timor-Leste.

13.2 AUDIENCES, MESSAGES, CHANNELS, EXPECTED RESULTS

The **key audiences** of this Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019 are segmented to be in line with the strategic aims outlined above.

The **key messages** of this Strategic Plan to Communicate TB are also aligned to the specific aims outlined above and that will be strategically socialized to the key audiences. The key messages of this plan will motivate and inspire key audiences to know more, to think and to act around the outlined objectives to halt the transmission of TB and illness and death caused by TB in Timor-Leste.

Different audiences acquire their information and knowledge differently so the **key channels** of this Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019 are aligned also to the segmented audiences for each of the objectives. Several channels of communication may be employed when reaching out to a segmented key audience using the **Media** (community, national, international, print, broadcast, web, social), **Lobbying** (community, municipal and national government, development partners, special interest groups), **Marketing** (advertising, posters, brochures, video, radio spots), and **Events** (workshops and conferences, public meetings, events).

Targeting key strategic and segmented audiences (who) with key messages (what and why) using key channels (how) will allow the implementers of this Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019 to know upfront the expected results of the various interventions contained in the subsequent communication plans to be implemented.

What follows then is a breakdown of the strategic aims, the audiences, messages, channels, and expected results for each of the aims outlined above and how these in turn help address the key challenges to TB control in Timor-Leste and their alignment with the overarching objectives of the National Strategic Plan for Tuberculosis Control for Timor-Leste 2018 - 2022.

SOCA 1: To achieve high level stewardship and policy commitment to zero deaths, zero disease and zero suffering due to tuberculosis in Timor-Leste by 2035.

TB Challenge: Mobilizing political commitment and resources for TB

Improving Case Detection and Treatment Adherence

Combating Stigma and Discrimination

TB NSP Alignment: Objective 5, and Objective 6

The **key audiences** for SOCA 1 are:

The Senior Leadership, Policy Makers and Development Partners:

- President
- Prime Minister
- Health Minister and Vice Ministers
- Relevant Line Ministers
- President of the National Parliament
- Parliamentarians from Commission F
- Development Partners

The **key messages** for the key audiences of SOCA 1 are:

- Leaders of the nation (President, Prime Minister, Government Ministers, Parliamentarians) must create policies, legislation, regulations, and directives that prevent all Timorese from becoming infected with TB, that enable all Timorese with TB to be treated for the illness until cured, and that avoid the death of Timorese people caused by TB.

- The Government of Timor-Leste must substantially escalate advocacy and socialization for prevention and cure of TB to an actionable national priority level.

- The government must commit to increasing domestic funding for the National TB Program given that the Timor-Leste National TB Program is being supported by the Global Fund, and this is not a sustainable solution.

- The Ministry of Health must lead and work together with health development partners implementing TB programs in ensuring adequate and effective programs that follow the National TB Program including also the effective allocation of funds to avoid duplication of efforts and wastage of resources.

The **key channels** for the key messages of SOCA 1 are:

- Government of Timor-Leste with WHO to co-host National Conference on TB in 2019
- Workshops on TB towards establishing TB Alliance/Commission for Timor-Leste
- Regular meetings with Commission F of the National Parliament on TB
- Ministry of Health Directive instructing health professionals nationally to undertake active case finding, early diagnosis, for treatment, for continuation of treatment until completion, and to cure TB infection.
- IEC materials developed for Policy Makers on what they can do about TB
- Message to the nation from President, Prime Minister and Senior Ministers on TB
- Review TB supporting legislation, regulations and guidelines
- Workshop on state funding allocation for TB
- Direct media to interview key Ministers and Parliament on TB (Press Conference and Briefings)
- Participation at high level event marking 24 March World TB Day (including March for TB)

The **key expected results** for SOCA 1 are:

- High level stewardship and commitment to combat the epidemic of TB in Timor-Leste
- Escalation of elimination of TB as a national priority
- Increase state funding for National TB program annually
- Stronger leadership of Health Development Partners on TB
- National TB Alliance/Commission created for Timor-Leste
- Several TB supportive legislation, guidelines and directives passed

SOCA 2: To encourage and promote a Ministry of Health with health facilities and services delivery fit-for-purpose in active case finding, early case detection, treatment and cure of Tuberculosis across Timor-Leste.

TB Challenge: Improving Case Detection and Treatment Adherence

TB NSP Alignment: Objective 1, Objective 2, Objective 3, Objective 4, Objective 5, and Objective 6.

The **key audiences** for Strategic Aim 2 are:

Front-Line Health Professionals and other Allied Health Professionals from both the Ministry of Health and from Health Programs for TB supported by external donors:

- Doctors
- Nurses
- Midwives
- Chemists
- TB workers
- Health Promoters

The **key messages** for they key audiences of SOCA 2 are:

- Go out to the community to actively find cases of TB and refer patients to a health facility for early diagnosis, for treatment, for continuation of treatment until completion, and to cure TB infection.
- Health professionals have the training, tools and knowledge to advise, diagnose, treat and cure TB infection.
- TB can be cured by a well-trained health professional at a well-equipped health care facility.
- You must give out correct information and advice on TB.

The **key channels** for the key messages of SOCA 2 are:

- National Workshop for Front-Line Health Professionals and other Allied Health Professionals on TB.
- Municipal Workshop for Front-Line Health Professionals and other Allied Health Professionals on TB.
- IEC Materials on TB for Front-Line Health Professionals and other Allied Health Professionals (TB kit with poster, brochure, fact sheets, USB with TB video, banners to be placed at strategic locations i.e. markets, churches, community centre, local government).
- Organization of World TB Day 24 March 2019 to be developed by Department of Health Promotion of MoH.
- Calendar of Advocacy Events on TB for 2019 to be developed by Department of Health Promotion of MoH.
- Performance-based checklist on TB for Front-Line Health Professionals and other Allied Health Professionals on TB, prepared by Human Resources of MoH.

The **key expected results** for SOCA 2 are:

- Health professionals actively engaged in TB case finding.
- Front Line health professionals trained and confident with skills to advise, diagnose, treat and cure TB infection.
- Community confident in going to health facilities for diagnosis of TB and treatment
- Community and TB patients and families better informed on TB.
- Effective IEC materials developed and established in strategic locations around the country to reinforce recall of TB messaging.
- Front-Line Health Professionals and other Allied Health Professionals on TB aware of their duty on TB.

SOCA 3: To empower the community to actively support cutting the chain of transmission of tuberculosis by knowing how to recognise symptoms of tuberculosis infection and what actions to take to protect one-self, the family, and the community from tuberculosis.

TB Challenges: Improving case detection and treatment adherence

Combatting stigma and discrimination

Empowering people affected with TB

TB NSP Alignment: Objective 1, Objective 2, and Objective 3

The **key audiences** for SOCA 3 are:

Local Leaders, civil society, the media, households and individuals:

- Community Leaders
- Religious Leaders
- Traditional Leaders
- Media representatives
- NGOs
- CBOs
- Youth Groups
- Households
- Individuals

The **key messages** for the key audiences of SOCA 3 are:

- A persistent cough may be TB and it needs to be checked by a health professional at a health facility.
- If your cough persists, get yourself to a health facility for early diagnosis.
- If someone in your community/group/family has a persistent cough, get her/him to be checked by a health professional at a health facility.

- Recognise the symptoms of TB, including a bad cough that lasts 2 weeks or longer, pain in the chest, coughing up blood or sputum (mucus from deep inside the lungs), weakness or fatigue, weight loss, no appetite, chills, fever, sweating at night.

- A bad cough might be nothing, it might be TB, the only way to know is to get checked at a health facility.

- When *Saúde na Família* (SnF) teams come to your house, and if you or anyone in your family has a bad cough ask for a TB test.

The **key channels** for the key messages of SOCA 3 are:

- IEC Materials on TB for Community (TB kit with poster, brochure, fact sheets, USB with TB video and social media posts on TB, banners to be placed at strategic locations i.e. markets, churches, community centre, local government).
- National Workshops (2 times in 2019) with Presidents of Municipalities, Administrative Post Chiefs, and Suco Chiefs co-hosted by STAE and the MoH on recognizing TB in the community.
- Media workshop on reporting on TB.
- Socialization activities with NGOs and CBOs on TB at National and Municipal level
- Special monthly radio show on MoH's *Hora da Saúde* dedicated to TB awareness, prevention and treatment (12 radio shows) with a health panel from MoH and partners, to be broadcast in all 20+ community radio stations nationwide.
- Three TV debates (TVTL, GMN and TVed) on TB in Timor-Leste.
- Billboard to be placed in front of health facilities motivating people to come get tested for TB.

The **key expected results** for SOCA 3 are:

- Developed knowledge and awareness of TB symptoms and what to do, where to go.
- Municipal and local leadership socialized on importance of keeping vigilance on TB in the community.
- Greater coverage of TB issues and messages on national and local media.
- TB IEC materials strategically placed reinforcing recall of TB messaging.
- Increase motivation in the community to get tested for TB because TB is preventable, treatable and curable.

SOCA 4: To ensure that TB sufferers seek treatment and commit to the full course of prescribed treatment until cured from the disease.

TB Challenge: Improving Case Detection and Treatment Adherence

Empowering People Affected by TB

TB NSP Alignment: Objective 1, Objective 2, and Objective 3

The **key audiences** for SOCA 4 are:

The TB patient and the household family:

- TB patients
- Household family members (grandmother, grandfather, mother, father, wife, husband, daughter, son, aunt, uncle, cousin, other extended family)
- TB Key Affected Population (TB-HIV, TB-Diabetes, TB-Smoke, TB-Alcohol, I have TB-Prisoner, I have TB-Orphan, others).

The **key messages** for the key audiences of SOCA 4 are:

- If I stick to my TB treatment I will be totally cured, I won't spread TB and I won't die of TB
- The best way to protect myself and my family from TB is to stick to my TB treatment until completion
- I have been diagnosed with TB, now I must make sure everyone in my household gets tested for TB as well.
- I have TB-HIV, TB-Diabetes, TB-Smoke, TB-Alcohol, I have TB-Prisoner, I have TB-Orphan, I must attend a dedicated TB screener at the Hospital/health facility.
- I must make sure my grandmother, grandfather, mother, father, wife, husband, daughter, son, aunt, uncle, cousin, other extended family, sticks to the TB treatment until completion.

The **key channels** for they key messages of SOCA 4 are:

- IEC Materials for TB Patients (TB kit with poster, brochure, fact sheets, USB with TB video and social media posts on TB).
- Regular domiciliary visits by PSF's and SnF team to socialize on TB and gather data from TB patients.
- Special monthly radio show on MoH's *Hora da Saúde* dedicated to TB awareness, prevention and treatment (12 radio shows) with a health panel from MoH and partners, to be broadcast in all 20+ community radio stations nationwide.
- Three TV debates (TVTL, GMN and TVed) on TB in Timor-Leste.
- Dedicate part of regular SnF Community Consultative Meetings to discuss TB in the community and in the households, mapping of status of TB in the community, and collective community solutions for adherence to TB treatment.
- Health Professionals to conduct special information sessions for TB Key Affected Populations (KAP)

The **key expected results** for SOCA 4 are:

- Uptake of TB patients completing their TB treatment and being cured.
- Increased family engagement with patients of TB towards completing TB treatment.
- Uptake in diagnosis for TB of families of TB patients.
- Community empowered to come up with solutions for TB in their own community.
- Key affected population with TB empowered to get tested for TB infection, seek treatment and adhered to full treatment.

SOCA 5: To promote through TB champions, that is, people who are respected and can guide others to seek early diagnosis and treatment, that TB is curable and to reduce the social and cultural stigma attached to tuberculosis in Timor-Leste.

TB Challenge: Combating Stigma and Discrimination

Improving Case Detection and Treatment Adherence

Empowering People Affected by TB

Mobilizing Political Commitment and Resources for TB

TB NSP Alignment: Objective 1, Objective 2, Objective 3, Objective 4, Objective 5, and Objective 6.

The **key audiences** for SOCA 5 are:

The society at large who will be socialized by strategic TB champions.

Society at large

The TB champions (President, Prime Minister, Vice-Minister of Health, Mana Lourdes, Dr Dan Murphy, Dr Rui Araújo, Dr Rajesh Pandav)

The **key messages** for the key audiences of SOCA 5 are:

- TB can be totally cured.
- I used to have TB, but I am still alive today because I trusted my health professional and my health facility.
- Early diagnosis by a health professional and commitment to full treatment of TB through a health facility will cure you.
- When you find out you have TB from a health professional, you discover your TB can be cured.
- There is no shame in having TB because it can be cured by timely and adequate treatment.
- I chose not to be ashamed or embarrassed by TB, I chose to get treated and cured instead.

The **key channels** for the key messages of SOCA 5 are:

- Activity with TB Champions to socialize them of their role and introduce them to the media through a Press Conference.
- IEC Materials on TB for TB Champions (TB kit with poster, brochure, fact sheets, USB with TB video and social media posts on TB).
- Video message and/or PSA for TV, YouTube and other social media posts with TB messages promoted by TB champions.
- Calendar of activities for TB Champions for 2019 to be developed by MoH.

The **key expected results** for SOCA 5 are:

- Timorese aware TB is preventable, treatable and curable.
- Uptake in Timorese going to a health facility to get tested for TB.
- Developed trust in Health System, health professionals and health facility to be able to treat TB infection.
- Reduction of TB stigma.
- Reduction in number of TB deaths.

13.3 TIMETABLE OF DATES WITH KEY ACTIVITIES

It is crucial for the implementation of this Strategic Plan to Communicate TB in Timor-Leste that interventions are planned, realistic and timely according to an agreed timetable of key activities to be achieved.

For instance, on 8-9 November 2018, a National Workshop on TB will be conducted. This represents an opportunity to deliver on some of the key points of this Strategic Plan to Communicate TB.

Every year also, Timor-Leste celebrates 24 March to mark World TB Day. This day, and days and months preceding and following it, offer important windows of opportunity to schedule activities related to TB in Timor-Leste.

Once this Strategic Plan to Communicate TB in Timor-Leste is approved and signed-off, an exercise should be conducted to translate the contents of this strategic plan into a work plan with a timetable of dates around key activities for implementation in 2018-2019.

13.4 RESOURCES

This Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019 will be owned and implemented by the Ministry of Health, Department of Contagious Diseases, TB Unit, and by the Department of Health Promotion.

Implementation of this plan will be supported technically by the Medical Officer for Tuberculosis of the World Health Organization (WHO) in Timor-Leste and by a committee composed by MoH, WHO and other partners working on TB in Timor-Leste.

Funding for the implementation of this Strategic Plan to Communicate TB for Timor-Leste will be coordinated between MoH though funds from the Global Fund, and with WHO and the health development partners.

13.5 RISKS AND MITIGATION

There are several risks that might pose challenges and threaten the successful implementation of this Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019. Below the key risks are identified with activities for mitigation of risks proposed, which once implemented will increase the likelihood of this Strategic Plan to Communicate TB realizing its vision, mission and strategic objectives.

Risk 1	Community – lack of awareness of symptoms, infection, what to do and where to go.
Mitigation	Ministry of Health, Department of Health Promotion, with support from health development partners committed to undertaking socialization and outreach activities in the community on TB.
Risk 2	Institutional – no outreach system as TB not seen as a priority at municipal and suco levels.
Mitigation	Government of Timor-Leste and Ministry of Health institutionalize outreach for TB as a national, municipal and suco public health priority.
Risk 3	Active case detection – this is not happening adequately and effectively and there are funding limitations for this to happen.
Mitigation	Ministry of Health directive to all health professionals that a key performance indicator attached to their TOR includes TB active case detection.
Risk 4	Treatment compliance - if TB patients do not commit to undertaking their complete TB treatment, the cycle of transmission will not be interrupted.
Mitigation	Through SnF Aden Care e-health surveillance system map active cases of TB in community to inform outreach activities to ensure TB patients commit to undertaking full course of TB treatment until cured with support from health professionals and a health facility.
Risk 5	Transport and geographical conditions and other social determinants.
Mitigation	Coordinate and collaborate with other line ministries and development partners to support transport, outreach activities, and other support including accommodation and subsidies to rural, remote and very isolated patients/families with and affected by TB.

13.6 EVALUATION

To be able to determine whether this Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019 has yielded the expected results, routine assessment of the impacts of the implementation of plans generated by this strategy will need to be conducted.

The cognitive information about the impact and coverage of communication interventions on TB on key audiences through key messages and using strategic channels of communications will be sourced through both quantitative and qualitative methodologies.

Several **Quantitative Evaluation** activities will be undertaken to source numerical information on the following points of evaluation:

- Proportion of Case Finding Interventions
- Proportion of new TB Cases found
- Proportion of TB Cases treated
- Proportion of TB patients cured
- Proportion of TB deaths
- Proportion of Workshops and other Engagements with Key Stakeholders
- Proportion of new IEC materials on TB produced and reach
- Proportion of TB trainings/workshops conducted
- Proportion of Media Coverage of TB issues
- Proportion of new TB policies, guidelines, directives approved
- Proportion of Timorese according to segmented categories attending TB activities

Several **Qualitative Evaluation** interventions will be undertaken to determine cognitive or behavioural change in key audiences on the following points of evaluation:

- Increased knowledge of TB symptoms
- Increased knowledge of where to go and what to do after TB infection
- Increased ability of community to refer patients for TB screening and support for sticking to treatment until cured
- Increased ability of Health Professionals to detect and report TB cases early
- Increased recognition that TB is curable in general population
- Increased quality of TB reporting by the media

13.7 Plan for Implementing Communication Activities for Tuberculosis in Timor-Leste for 2018 – 2019 (Summary)

SOCA 1: To achieve high level stewardship and policy commitment to zero deaths, zero disease and zero suffering due to tuberculosis in Timor-Leste by 2035.

**SOCA – Strategic Objective of Communication Activity*

Key Audiences	Key Messages	Key Channels	Key Expected Results	TB Challenge	NSP Align
• President • Prime Minister • Health Minister and Vice Ministers • Relevant Line Ministers • President of the National Parliament • Parliamentarians from Commission F • Development Partners	• Leaders of the nation (President, Prime Minister, Government Ministers, Parliamentarians) must create policies, legislation, regulations, directives that prevent all Timorese from getting infected with TB, that enable all Timorese with TB to be treated for the illness until cured, and avoid the death of Timorese caused by TB. • The Government of Timor-Leste must substantially escalate advocacy and socialization for prevention and cure of TB to an actionable national priority level. • The government must commit to increasing domestic funding for the	• Government of Timor-Leste with WHO to co-host National Conference on TB in 2019. • Workshops on TB towards establishing TB Alliance / Commission for Timor-Leste. • Regular meetings with Commission F of the National Parliament on TB. • Ministry of Health Directive instructing health professionals nationally to undertake active case finding, early diagnosis, for treatment, for continuation of treatment until completion, and to	• High level stewardship and commitment to combat the epidemic of TB in Timor-Leste. • Escalation of elimination of TB as a national priority. • Increase state funding for National TB program annually. • Stronger leadership of Health Development Partners on TB. • National TB Alliance/Commission created for Timor-Leste. • Several TB supportive legislation, guidelines and directives passed.	• Mobilizing political commitment and resources for TB • Improving Case Detection and Treatment Adherence	Objective 5 Objective 6

	National TB Program given that the Timor-Leste National TB Program is being supported by the Global Fund, and this is not a sustainable solution. • The Ministry of Health must lead and work together with health development partners implementing TB programs in ensuring adequate and effective programs that follow the National TB Program including also the effective allocation of funds to avoid duplication of efforts and wastage of resources.	cure TB infection. • IEC materials developed for Policy Makers on what they can do on TB. • Message to the nation from President, Prime Minister and Senior Ministers on TB. • Review TB supporting legislation, regulations and guidelines. • Workshop on state funding allocation for TB. • Direct media to interview key Ministers and Parliament on TB (Press Conference and Briefings). • Participation at high level event marking 24 March World TB Day (including March for TB).			

SOCA 2: To encourage and promote a ministry of health with health facilities and services delivery fit-for-purpose in active case finding, early case detection, treatment and cure of Tuberculosis across Timor-Leste.

Key audiences	Key messages	Key channels	Key Expected Results	TB Challenge	NSP Align
• Doctors • Nurses • Midwives • Chemists • TB workers • Health Promoters	• Go out to the community to actively find cases of TB and refer patients to a health facility for early diagnosis, for treatment, for continuation of treatment until completion, and to cure TB infection. • Health professionals have the training, tools and knowledge to advise, diagnose, treat and cure TB infection. • TB can be cured by a well-trained health professional at a well-equipped health care facility. • You must give out correct information and advice on TB.	• National Workshop for Front-Line Health Professionals and other Allied Health Professionals on TB. • Municipal Workshop for Front-Line Health Professionals and other Allied Health Professionals on TB. • IEC Materials on TB for Front-Line Health Professionals and other Allied Health Professionals (TB kit with poster, brochure, fact sheets, USB with TB video, banners to be placed at strategic locations i.e. markets, churches, community centre, local government). • Organization of World TB Day 24 March 2019 to be developed by Department of Health Promotion of MoH.	• Health professionals actively engage in TB case finding. • Front Line health professional trained and confident with skills to advise, diagnose, treat and cure TB infection. • Community confident in going to health facilities for diagnosis of TB and treatment • Community and TB patients and families better informed on TB. • Effective IEC materials developed and established in strategic locations around the country to reinforce recall of TB messaging. • Front-Line Health Professionals and other Allied Health Professionals on TB	• Improving Case Detection and Treatment Adherence	Objective 1 Objective 2 Objective 3 Objective 4 Objective 5 Objective 6

		• Calendar of Advocacy Events on TB for 2019 to be developed by Department of Health Promotion of MoH. • Performance-based checklist on TB for Front-Line Health Professionals and other Allied Health Professionals on TB, prepared by Human Resources of MoH.	aware of their duty on TB.		

SOCA 3: To empower the community to actively support cutting the chain of transmission of tuberculosis by knowing how to recognise symptoms of tuberculosis infection and what actions to take to protect one-self, the family, and the community from tuberculosis.

Key Audiences	Key Messages	Key Channels	Key Expected Results	TB Challenge	NSP Align
• Community Leaders • Religious Leaders • Traditional Leaders • Media representatives • NGOs • CBOs • Youth Groups • Households • Individuals	• A persistent cough may be TB and it needs to be checked by a health professional at a health facility. • If your cough persists, get yourself to a health facility for early diagnosis. • If someone in your community/group/family has a persistent cough, get her/him to be checked by a health professional at a health facility. • Recognise the symptoms of TB, including a bad cough that lasts 2 weeks or longer, pain in the chest, coughing up blood or sputum (mucus from deep inside the lungs), weakness or fatigue, weight loss, no appetite, chills, fever, sweating at night. • A bad cough might be nothing, it might be TB, only way to know is to get checked at a health facility.	• IEC Materials on TB for Community (TB kit with poster, brochure, fact sheets, USB with TB video and social media posts on TB, banners to be placed at strategic locations i.e. markets, churches, community centre, local government). • National Workshops (2 times in 2019) with Presidents of Municipalities, Administrative Post Chiefs, and Suco Chiefs co-hosted by STAE and MoH on recognizing TB in the community. • Media workshop on reporting on TB. • Socialization activities with NGOs and CBOs on TB at National and Municipal level.	• Developed knowledge and awareness of TB symptoms and what to do, where to go. • Municipal and local leadership socialized on importance of keeping vigilance on TB in the community. • Greater coverage of TB issues and messages on national and local media. • TB IEC materials strategically placed reinforcing recall of TB messaging. • Increase motivation in community to get tested for TB because TB is preventable, treatable and curable.	• Improving case detection and treatment adherence • Combatting stigma and discriminatio n • Empowering people affected with TB	Objective 1 Objective 2 Objective 3

	• When *Saúde na Família* (SnF) teams come to your house, and if you or anyone in your family has a bad cough ask for a TB test.	• Special monthly radio show on MoH's *Hora da Saúde* dedicated to TB awareness, prevention and treatment (12 radio shows) with a health panel from MoH and partners, to be broadcast in all 20+ community radio stations nationwide. • Three TV debates (TVTL, GMN and TVed) on TB in Timor-Leste. • Billboard to be placed in front of health facilities motivating people to come get tested for TB.			

SOCA 4: To ensure that TB sufferers, including key affected populations, seek treatment and commit to the full course of prescribed treatment until cured from the disease.

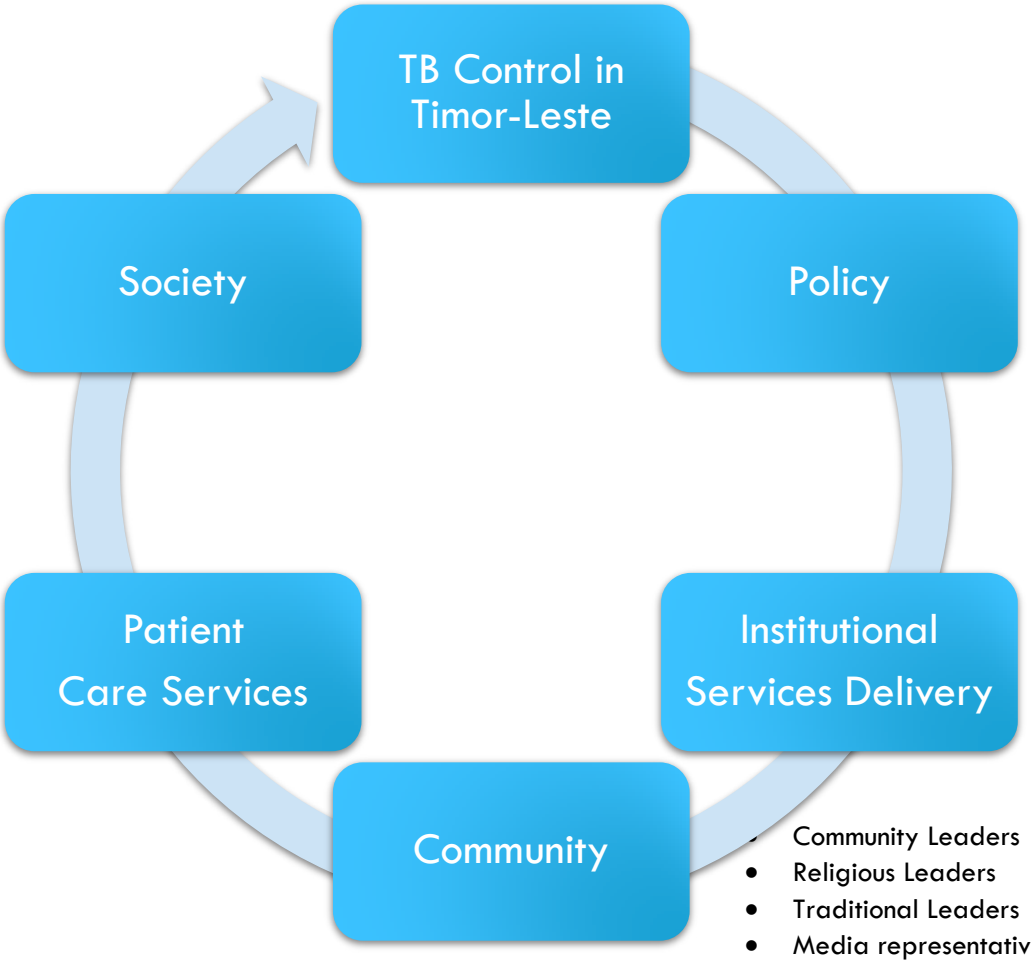
Key Audiences	Key Messages	Key Channels	Key Expected Results	TB Challenge	NSP Align
• TB patients • Household family members (grandmother, grandfather, mother, father, wife, husband, daughter, son, aunt, uncle, cousin, other extended family) • TB Key Affected Populations (KAP)	• If I stick to my TB treatment I will be totally cured, I won't spread TB and I won't die of TB • The best way to protect myself and my family from TB is to be stick to my TB treatment until completion • I have been diagnosed with TB, I must make sure everyone in my household gets tested for TB as well. • I have TB-HIV, TB-Diabetes, TB-Smoke, TB-Alcohol, I have TB-Prisoner, I have TB-Orphan, I must attend a dedicated TB screener at the Hospital/health facility. • I must make sure my grandmother, grandfather, mother, father, wife, husband, daughter, son, aunt, uncle, cousin, other extended family, sticks to the TB treatment until completion.	• IEC Materials for TB Patients (TB kit with poster, brochure, fact sheets, USB with TB video and social media posts on TB). • Regular domiciliary visits by PSFs and SnF team to socialize on TB and gather data from TB patients. • Health Professionals to conduct special information sessions for TB Key Affected Populations (KAP) • Special monthly radio show on MoH's *Hora da Saúde* dedicated to TB awareness, prevention and treatment (12 radio shows) with a health panel from MoH and partners, to be broadcast in all 20+ community radio stations nationwide.	• Increased uptake of TB patients completing their TB treatment and being cured. • Increased family engagement with patients of TB towards completing TB treatment. • Uptake in diagnosis for TB of families of TB patients. • Community empowered to come up with solutions for TB in their own community. • Key affected population with TB empowered to get tested for TB infection, seek treatment and adhered to full treatment.	• Improving Case Detection and Treatment Adherence • Empowering People Affected by TB	Objective 1 Objective 2 Objective 3

		• Three TV debates (TVTL, GMN and TVed) on TB in Timor-Leste. • Dedicate part of regular SnF Community Consultative Meetings to discuss TB in the community and in the households, mapping of status of TB in the community, and collective community solutions for adherence to TB treatment.			

SOCA 5: To promote through TB champions, that is, people who are respected and can guide others to seek early diagnosis and treatment, that TB is curable and to reduce the social and cultural stigma attached to tuberculosis in Timor-Leste.

Key Audiences	Key Messages	Key Channels	Key Expected Results	TB Challenge	NSP Align
• Society at large • The TB champions: – President – Prime Minister – Vice-Minister of Health – Mana Lourdes – Dr Dan Murphy – Dr Rui Araújo – Dr Rajesh Pandav	• TB can be totally cured. • I used to have TB but I am still alive today because I trusted my health professional and my health facility. • Early diagnosis by a health professional and commitment to full treatment of TB through a health facility will cure you. • When you find out you have TB from a health professional, you discover your TB can be cured. • There is no shame in having TB because it can be cured by timely and adequate treatment. • I chose not to be ashamed or embarrassed by TB, I chose to get treated and cured instead.	• Activity with TB Champions to socialize them of their role and introduce them to the media through a Press Conference. • IEC Materials on TB for TB Champions (TB kit with poster, brochure, fact sheets, USB with TB video and social media posts on TB). • Video message and/or PSA for TV, YouTube and other social media posts with TB messages promoted by TB champions. • Calendar of activities for TB Champions for 2019 to be developed by MoH.	• Timorese aware TB is preventable, treatable and curable. • Uptake in Timorese going to a health facility to test tested for TB. • Developed trust in Health System, health professionals and health facility to be able to treat TB infection. • Reduction of TB stigma. • Reduction in number of TB deaths.	• Combating Stigma and Discrimination • Improving Case Detection and Treatment Adherence • Empowering People Affected by TB • Mobilizing Political Commitment and Resources for TB	Objective 1 Objective 2 Objective 3 Objective 4 Objective 5 Objective 6

Communication Levels / Audience Segmentation



- President
- Prime Minister
- Health Minister and Vice Ministers
- Relevant Line Ministers
- President of the National Parliament
- Parliamentarians from Commission F
- Development Partners

- Doctors
- Nurses
- Midwives
- Chemists
- TB workers
- Health Promoters

- Community Leaders
- Religious Leaders
- Traditional Leaders
- Media representatives
- NGO's
- CBO's
- Youth Groups
- Households
- Individuals

- TB patients
- Household family members (grandmother, grandfather, mother, father, wife, husband, daughter, son, aunty, uncle, cousin, other extended family)

- Society at large
- The TB champions

14 OPERATIONAL RESEARCH

In order to achieve the goal of the NTP requiring the scale up of current efforts to implement interventions of proven effectiveness, the program needs to undertake research to determine how to implement these interventions and monitor their impact, and also develop improved and new strategies and interventions. Key staff working in TB program should be encouraged to involve themselves and engage in research activities to improve their knowledge and analytical skills. This will allow them to utilize research findings as the basis (evidence-based information) to guide and improve TB program activities in their areas of work.

Key operational researches arise from the current limitations faced by NTP such as:

- Delay in diagnosis and treatment and the access to health services
- Different and innovative strategies to implement DOT
- Low patient compliance (reasons for default)
- Issues involved in diagnosis and treatment of MDR-TB
- Coordination between TB and HIV/AIDS programs
- Community involvement and participation in tuberculosis control

ANNEXES

ANNEX 1: FORMAT FOR ADVERSE EVENT REPORTING

Patient's name:	**Age:** _ _		**PMDT No:**	**Date:** _ _/_ _/_ _ _ _
Address:			**Height (cm):**	**Weight (Kg):**
Type of TB: Pulmonary ☐ ☐ Extrapulmonary		**Type of drug resistance:** RR/MDR-TB ☐ RR/MDR + FQ/SLI ☐ XDR ☐ H mono/poly		

Current regimen:		**Date of start of regimen:**
Drug	**Dose**	**Date/Month/Year since the drug was started**
Rifampicin		
INH		
Pyrazinamide		
Ethambutol		
Bedaquiline		
Linezolid		
Moxifloxacin		
Levofloxacin		
Clofazimine		
Capreomycin		
Cycloserine		
Ethionamide		
PAS		
Delamanid		
Streptomycin		

Details of the event:

Date of onset: __/__/____ Time of onset: __:__

(Describe the details related to the event)

Type of serious adverse event:
Death ☐ Life threatening ☐ Hospitalisation ☐ Permanent Disability ☐ Congenital anomaly ☐

Outcome of the event		**Date of outcome**
Recovered/resolved	☐	__/__/____
Recovered/resolved with sequelae	☐	__/__/____
Fatal	☐	__/__/____
Recovering/resolving	☐	__/__/____
Not recovering	☐	__/__/____
Unknown	☐	__/__/____

Isoniazid

General information

Isoniazid, the hydrazide of isonicotinic acid, is highly bactericidal against replicating tubercle bacilli.

It is rapidly absorbed and diffuses readily into all fluids and tissues. The plasma half-life, which is genetically determined, varies from less than 1 hour in fast acetylators to more than 3 hours in slow acetylators. Isoniazid is largely excreted in the urine within 24 hours, mostly as inactive metabolites.

Clinical information

Administration and dosage

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

Adults:

5 mg/kg (4–6 mg/kg) daily, maximum 300 mg
10 mg/kg (8–12 mg/kg) three times weekly, maximum 900 mg.

Children:

10-15 mg/kg daily, maximum 300 mg

Contraindications

- Known hypersensitivity.
- Active, unstable hepatic disease (with jaundice)

Precautions

Clinical monitoring (and liver function tests, if possible) should be performed during treatment of patients with pre-existing liver disease. Patients at risk of peripheral neuropathy, as a result of malnutrition, chronic alcohol dependence, HIV infection, pregnancy, breastfeeding, renal failure or diabetes, should additionally receive pyridoxine, 10 mg daily. Where the standard of health in the community is low, pyridoxine should be offered routinely. For established peripheral neuropathy, pyridoxine should be given at a larger dose of 50–75 mg daily.

Since isoniazid interacts with anticonvulsants used for epilepsy, it may be necessary to reduce the dosage of these drugs during treatment with isoniazid. If possible, serum concentrations of phenytoin and carbamazepine should be measured in patients receiving isoniazid with or without rifampicin.

Use in pregnancy

Isoniazid is not known to be harmful in pregnancy. Pyridoxine supplementation is recommended for all pregnant (or breastfeeding) women taking isoniazid.

Adverse effects

Isoniazid is generally well tolerated at recommended doses.

Systemic or cutaneous hypersensitivity reactions occasionally occur during the first weeks of treatment.

Sleepiness or lethargy can be managed by reassurance or adjustment of the timing of administration.

The risk of peripheral neuropathy is excluded if vulnerable patients receive daily supplements of pyridoxine. Other less common forms of neurological disturbance, including optic neuritis, toxic psychosis and generalized convulsions, can develop in susceptible individuals, particularly in the later stages of treatment, and occasionally necessitate the withdrawal of isoniazid.

Symptomatic hepatitis is an uncommon but potentially serious reaction that can usually be averted by prompt withdrawal of treatment. More often, however, an asymptomatic rise in serum concentrations of hepatic transaminases at the outset of treatment is of no clinical significance and usually resolves spontaneously as treatment continues.

A lupus-like syndrome, pellagra, anaemia, and arthralgias are other rare adverse effects. Monoamine poisoning has been reported to occur after ingestion of foods and beverages with high monoamine content, but this is also rare.

Drug interactions

Isoniazid inhibits the metabolism of certain drugs, which can increase their plasma concentration to the point of toxicity. Rifampicin, however, has the opposite effect for many of these drugs. For example, the available data indicate that administering both rifampicin and isoniazid causes a reduction in plasma levels of phenytoin and diazepam.

Isoniazid may increase the toxicity of carbamazepine, benzodiazepines metabolized by oxidation (such as triazolam), acetaminophen, valproate, serotonergic antidepressants, disulfiram, warfarin and theophylline.

Overdosage

Nausea, vomiting, dizziness, blurred vision and slurring of speech occur within 30 minutes to 3 hours of overdosage. Massive poisoning results in coma preceded by respiratory depression and stupor. Severe intractable seizures may occur. Emesis and gastric lavage, activated charcoal, antiepileptics and IV sodium bicarbonate can be of value if instituted within a few hours of ingestion. Subsequently, haemodialysis may be of value. High doses of pyridoxine must be administered to prevent seizures.

Storage

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

Rifampicin

General information

A semisynthetic derivative of rifamycin, rifampicin is a complex macrocyclic antibiotic that inhibits ribonucleic acid synthesis in a broad range of microbial pathogens. It has bactericidal action and a potent sterilizing effect against tubercle bacilli in both cellular and extracellular locations.

Rifampicin is lipid-soluble. Following oral administration, it is rapidly absorbed and distributed throughout the cellular tissues and body fluids; if the meninges are inflamed, significant amounts enter the cerebrospinal fluid. A single dose of 600 mg produces a peak serum concentration of about 10 µg/ml in 2–4 hours, which subsequently decays with a half-life of 2–3 hours. It is extensively recycled in the enterohepatic circulation, and metabolites formed by deacetylation in the liver are eventually excreted in the faeces.

Since resistance readily develops, rifampicin must always be administered in combination with other effective antimycobacterial agents.

Clinical information

Administration and dosage

Rifampicin should preferably be given at least 30 minutes before meals, since absorption is reduced when it is taken with food. However, this may not be clinically significant, and food can reduce intolerance to drugs. Rifampicin should always be given in combination with other effective antimycobacterial agents. It is also available for intravenous administration in critically ill patients.

Adults:

10 mg/kg (8–12 mg/kg) daily or 3 times weekly, maximum 600 mg.

Children:
10-20 mg/kg daily, maximum 600 mg

Contraindications

- Known hypersensitivity to rifamycins.
- Active, unstable hepatic disease (with jaundice)

Precautions

Serious immunological reactions resulting in renal impairment, haemolysis or thrombocytopenia are on record in patients who resume taking rifampicin after a prolonged lapse of treatment. In this rare situation, rifampicin should be immediately and permanently withdrawn.

Clinical monitoring (and liver function tests, if possible) should be performed during treatment of all patients with pre-existing liver disease, who are at increased risk of further liver damage.

Patients should be warned that treatment may cause reddish coloration of all body secretions (urine, tears, saliva, sweat, semen and sputum), and that contact lenses and clothing may be irreversibly stained.

Use in pregnancy

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

Adverse effects

Rifampicin is well tolerated by most patients at currently recommended doses but may cause gastrointestinal reactions (abdominal pain, nausea, vomiting) and pruritus with or without rash.

Other adverse effects (fever, influenza-like syndrome and thrombocytopenia) are more likely to occur with intermittent administration.

Exfoliative dermatitis is more frequent in HIV-positive TB patients.

Temporary oliguria, dyspnoea and haemolytic anaemia have also been reported in patients taking the drug 3 times weekly; these reactions usually subside if the regimen is changed to daily dosage.

Moderate rises in serum concentrations of bilirubin and transaminases, which are common at the outset of treatment, are often transient and without clinical significance. However, dose-related hepatitis can occur and is potentially fatal: it is therefore important not to exceed the maximum recommended daily dose of 600 mg.

Drug interactions

Rifampicin induces hepatic enzymes, and may increase the dosage requirements of drugs metabolized in the liver, including:

- anti-infectives (including certain antiretroviral drugs discussed below, mefloquine, azole antifungal agents, clarithromycin, erythromycin, doxycycline, atovaquone, chloramphenicol);
- hormone therapy, including ethinylestradiol, norethindrone, tamoxifen, levothyroxine;
- methadone;
- warfarin;
- cyclosporine;
- corticosteroids;
- anticonvulsants (including phenytoin);
- cardiovascular agents including digoxin (in patients with renal insufficiency), digitoxin, verapamil, nifedipine, diltiazem, propranolol, metoprorol, enalapril, losartan, quinidine, mexiletine, tocainide, propafenone;
- theophylline;
- sulfonylurea hypoglycaemics;
- hypolipidaemics including simvastatin and fluvastatin;
- nortriptyline, haloperidol, quetiapine, benzodiazepines (including diazepam, triazolam), zolpidem, buspirone.

Since rifampicin reduces the effectiveness of oral contraceptives, women should be advised to choose between one of two options for contraception. Following consultation with a clinician, the patient may use an oral contraceptive pill containing a higher dose of estrogen (50 µ g); alternatively, a nonhormonal method of contraception may be used throughout rifampicin treatment and for at least one month subsequently.

Current antiretroviral drugs (non-nucleoside reverse transcriptase inhibitors and protease inhibitors) interact with rifampicin. This may result in ineffectiveness of antiretroviral drugs, ineffective treatment of TB or an increased risk of drug toxicity.

Biliary excretion of radiocontrast media and sulfobromophthalein sodium may be reduced and microbiological assays for folic acid and vitamin B_{12} disturbed.

Overdosage

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

Storage

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

Pyrazinamide

General information

Pyrazinamide is a synthetic analogue of nicotinamide that is only weakly bactericidal against *M. tuberculosis* but has potent sterilizing activity, particularly in the relatively acidic intracellular environment of macrophages and in areas of acute inflammation. It is highly effective during the first 2 months of treatment while acute inflammatory changes persist. Its use has enabled treatment regimens to be shortened and the risk of relapse to be reduced.

It is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout all tissues and fluids. Peak plasma concentrations are attained in 2 hours and the plasma half-life is about 10 hours. It is metabolized mainly in the liver and excreted largely in the urine.

Clinical information

Administration and dosage

Pyrazinamide is administered orally.

Adults (usually for the first 2 or 3 months of TB treatment):

25 mg/kg (20–30 mg/kg) daily

35 mg/kg (30–40 mg/kg) 3 times weekly.

Children:

30-40 mg/kg daily, maximum 2000 mg

Contraindications

- Known hypersensitivity.
- Active, unstable hepatic disease (with jaundice)
- Porphyria.

Precautions

Patients with diabetes should be carefully monitored since blood glucose concentrations may become labile. Gout may be exacerbated. Clinical monitoring (and liver function tests, if possible) should be performed during treatment of patients with pre-existing liver disease. In patients with renal failure, pyrazinamide should be administered three times per week, rather than daily. *Use in pregnancy*

The 6-month regimen based upon isoniazid, rifampicin and pyrazinamide should be used whenever possible. Although detailed teratogenicity data are not available, pyrazinamide can probably be used safely during pregnancy.

Adverse effects

Pyrazinamide may cause gastrointestinal intolerance.

Hypersensitivity reactions are rare, but some patients complain of slight flushing of the skin.

Moderate rises in serum transaminase concentrations are common during the early phases of treatment. Severe hepatotoxicity is rare.

As a result of inhibition of renal tubular secretion, a degree of hyperuricaemia usually occurs, but this is often asymptomatic. Gout requiring treatment with allopurinol occasionally develops. Arthralgia, particularly of the shoulders, may occur and is responsive to simple analgesics (especially aspirin). Both hyperuricaemia and arthralgia may be reduced by prescribing regimens with intermittent administration of pyrazinamide.

Rare adverse events include sideroblastic anaemia and photosensitive dermatitis.

Overdosage

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

Storage

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

Ethambutol

General information

A synthetic congener of 1,2-ethanediamine, ethambutol is active against *M. tuberculosis*, *M. bovis* and some nonspecific mycobacteria. It is used in combination with other anti-TB drugs to prevent or delay the emergence of resistant strains.

It is readily absorbed from the gastrointestinal tract. Plasma concentrations peak in 2–4 hours and decay with a half-life of 3–4 hours. Ethambutol is excreted in the urine both unchanged and as inactive hepatic metabolites. About 20% is excreted unchanged in the faeces.

Clinical information

Administration and dosage

Ethambutol is administered orally.

Adults:

15 mg/kg (15–20 mg/kg) daily

30 mg/kg (25–35 mg/kg) 3 times weekly.

Children:

15-25 mg/kg daily, maximum 1200 mg

Dosage must always be carefully calculated on a weight basis to avoid toxicity, and the dose or the dosing interval should be adjusted in patients with impaired renal function (creatinine clearance <70 ml/min). If creatinine clearance is less than 30 ml/ minute, ethambutol should be administered 3 times per week.

Contraindications

- Known hypersensitivity.
- Pre-existing optic neuritis from any cause.

Precautions

Patients should be advised to discontinue treatment immediately and to report to a clinician if their sight or perception of colour deteriorates. Ocular examination is recommended before and during treatment. Whenever possible, renal function should be assessed before treatment. Plasma ethambutol concentration should be monitored if creatinine clearance is less than 30 ml/min.

Use in pregnancy

Ethambutol is not known to be harmful in pregnancy.

Adverse effects

Dose-dependent optic neuritis can result in impairment of visual acuity and colour vision in one or both eyes. Early changes are usually reversible, but blindness can occur if treatment is not discontinued promptly. Ocular toxicity is rare when ethambutol is used for 2–3 months at recommended doses. Signs of peripheral neuritis occasionally develop in the legs. Other rare adverse events include generalized cutaneous reaction, arthralgia and, very rarely, hepatitis.

Overdosage

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

Storage

Tablets should be stored in tightly closed containers.

ANNEX 3 NTP RECORDING AND REPORTING FORMS

1) Referral Slip

SR No. _____

REFERRAL SLIP

Date: ……Lab referred to:……..

Name of referring PSF/ NGO/ Health Worker:
……. Name of Patient:
…… Age: …… years
Sex: M / F / TG
Address of patient (with landmarks)

……..

……

……
Patient's / Contact person's Mobile number:
_____
Kindly tick

- ☐ Cough……..days
- ☐ Fever……..days
- ☐ Loss of weight ……kgs
- ☐ Night sweat ……..days
- ☐ Blood in sputum/ cough ……days
- ☐ Contact of TB / MDR TB

Referred by (Name & Sign)

2) Patient Identity Card- TB

MINISTRY OF HEALTH
COMUNICABLE DESEASES DEPARTMENT
NATIONAL TUBERCULOSIS CONTROL PROGRAMME

TB FORM 5

TB PATIENT IDENTITY CARD

TB. Register No and Year _____

Complete Name _____

Complete Address _____

Sex ☐ Male ☐ Female Age _____

Name of Treatment Unit _____ Treatment Start Date _____

Clasification of Disease ☐ Pulmonary ☐ Extra Pulmonary

Type of Examination and Result		
Sputum Smear Microscopy	Xpert MTB/RIF	Chest X-Ray

Type of Patient

☐ New ☐ T. After loss to Follow up

☐ Relapse ☐ Other

☐ T. After Failure

TREATMENT REGIMEN tick (✓)one

	NEW CASE (2RHZE/4RH)	
	RHZE (150mg/75mg/400mg/275mg) + 4 RH (150mg/75mg)	RH (150mg/75mg)

	PEDIATRIC (2RHZE/4RH)			
	RHZ(60/30/150)		E100	RH(60/30)

TREATMENT OUTCOME AND DATE tick (✓) one

Date of Decision _____

☐ CURE ☐ LOSS TO FOLLOW UP

☐ TREAMENT COMPLETED ☐ DIED

☐ FAILURE ☐ NOT EVALUATED

3) Presumptive TB Register

MINISTRY OF HEALTH

COMMUNICABLE DISEASES DEPARTMENT

NATIONAL TUBERCULOSIS CONTROL PROGRAMME

PRESUMPTIVE TUBERCULOSIS REGISTER

Sl. No	Date of Registration	Complete Name	Age/Sex		Complete Address	HIV Status (R/NR/UK/CS)①	Diabetes Status ②	MDR-TB Risk(Yes/No)③	Classification (P/EP)	Refer by④ HF/PSF/SISCa/ PC/ PP/NGO/ TH/HTC/ DM Clinic	Date Sputum Sent to Laboratory	Date Results Received	Result (Microscopy or Xpert Ultra)		Date of treatment Initiation	TB No/ Year
			Male	Female									Microscope (Neg, Scanty, 1+, 2+ or 3+) ⑤	Xpert Ultra (T, RR, TI, N, I) ⑥		

Note::

① HIV Status (R = Reactive, NR = Non-Reactive, UK = Unknown, CS = Clinical Sign);

② MDR-TB Risk: suspect TB who with close contact with confirmed MDR-TB Case, Previously treated with bacteriologically confirmed and coinfected TB/HIV;

③ Refer by: HF = Health facility (write the name of the health facility), PSF = Volunteer, SISCa, PC = Private clinic, PP = Private practitioner, NGO = NGO staff, TH = Traditional healer and HTC = HIV testing and counselling;

④ Write the actual result or highest grade

⑤ Xpert Result: *T* = MTB detected and rifampicin resistance not detected; *RR* = MTB detected and rifampicin detected; *TI* = MTB detected and rifampicin resistance indeterminate; *N* = MTB not detected; *I* = Invalid or error or no result

⑥ If Xpert Result *TI* or *I* appear, please do the test again till final results (T or RR or N).

4) Referral Feedback TB Register

MINISTRY OF HEALTH

COMMUNICABLE DISEASES DEPARTMENT

NATIONAL TUBERCULOSIS CONTROL PROGRAMME

REFERRAL FEEDBACK TUBERCULOSIS REGISTER

Sl. No	Date of Refferal	Complete Name	Age/Sex		Complete Address (With municipality, post- administrative, Suko & Aldea name)	Mobile No. (Of Patient & One Family Member)	P/ EP	New/ DR-TB	Laboratory Serial No.	Date of Laboratory Result (Microscope/	Result (Microscopy or Xpert Ultra)		Referred to (Municipality/ CHC)	Date of Feedback/ Date of starting treatment	TB No/ Year (For Transferred Out Patient)
			Male	Female							Microscope (Neg, Scanty, 1+, 2+ or 3+)	Xpert Ultra (T, RR, TI, N, I)			

Note::

① HIV status (R = Reactive, NR = Non-Reactive, UK = Unknown, CS = Clinical Sign)

② MDR-TB risk: suspect TB who with close contact with confirmed MDR-TB Case, Previously treated with bacteriologically confirmed and coinfected TB/HIV

③ Refer by: HF = Health facility (write the name of the health facility), PSF = Volunteer, SISCa, PC = Private Clinic, PP = Private practitioner, NGO = NGO staff, TH = Traditional healer and HTC = HIV testing and Counselling

④ Write the actual result or highest grade

⑤ Xpert Result: *T* = MTB detected and rifampicin resistance not detected; *RR* = MTB detected and rifampicin detected; *TI* = MTB detected and rifampicin resistance indeterminate; *N* = MTB not detected; *I* = Invalid or error or no result

⑥ If Xpert Result *TI* or *I* appear, please do the test again till final results (T or RR or N).

5) TB Laboratory Register

MINISTRY OF HEALTH

COMMUNICABLE DISEASES DEPARTMENT
NATIONAL TUBERCULOSIS CONTROL PROGRAMME

Tuberculosis Laboratory Register

Lab Serial No.	Registration date	Complete Name	Age / Sex		Complete address	Name of CHC	HIV Status (R/NR/UK/CS) ①	MDR-TB Risk (Yes/No) ②	Refer by ③	Reason for examination			Result of examination ⑤				Remarks
			Male	Female					HF/PSF/ SISCa/PC/PP/ NGO/ TH/VCCT	Diagnose New ④	If follow up: Month of treatment (2, 6)	If follow up: TB Reg. No. & Year	Microscope (Neg, Scanty, 1+, 2+, or 3+) 1	Microscope (Neg, Scanty, 1+, 2+, or 3+) 2	Xpert Ultra MTB/Rif (T, RR, TI, N, or I)	Diabetes status (If MTB+ve):	

① HIV status (R=Reactive, NR=Non Reactive, UK=Unknown, CS=Clinical sign)

② MDR-TB risk: suspect TB who with close contact with confirmed MDR-TB case, Re-treatment with bacteriologically confirmed and coinfected TB/HIV

③ Refer by: HF = Health facility (write the name of the health facility), PSF = Volunteer, SISCa, PC = Private clinic, PP = Private practitioner, NGO = NGO staff, TH = Traditional healer and HTC = HIV testing and counselling

④ Put tick mark (✓) for diagnosis reason and write REPEAT if repeat examination

⑤ Diabetes criteria: FBS>=126 mg/ dL or 7 mmol/ RBS, at least 2 hours after meal, >=200 mg/dL or 11 mmol)

⑤ Notation method for recording smear microscopy and GeneXpert test

Microscopy result record		Xpert result record		
No AFB	Neg	MTB detected, RR not detected		T
1--9 AFB/100 HPF	Scanty (and report No. of AFB)	MTB detected, RR detected		RR
1--99 AFB/HPF	1+	MTB detected, RR indeterminate		TI
1--10 AFB/HPF	2+	MTB not detected		N
> 10 AFB/HPF	3+	Invalid /No result/Error		I

RR = Rifamficin Resistance

6) Referral /Transfer Form for Treatment

NATIONAL TUBERCULOSIS PROGRAMME
Referral / Transfer form for treatment Serial Number

To be filled in triplicate. One copy to be sent to the Municipality TB Coordinator receiving the patient, one copy to the health facility where the patient is referred to, and one copy to the patient

Name and address of referring health facility _____

Contact Number and e-mail address of referring health facility: _____

Name and address of health facility to which patient is referred _____

_____

Name of patient_____ **Age**_____ **Sex M ☐ F☐ TG☐**

Complete

Address_____

_____ **Contact no.**_____

Patient detail	
Site of disease ☐ Pulmonary ☐ Extra Pulmonary, Site _____ **Type of Patient** ☐ New ☐ Recurrent ☐ Transferred in ☐ Treatment After Failure ☐ Treatment After Lost to Follow-up ☐ Others, previously treated (Specify)_____ **Case Definition** ☐ Microbiologically confirmed ☐ Clinically diagnosed **H/O of ATT:** ___ months of treatment ___ months since end of last episode	**Diagnosis details** Date of diagnosis: __/__/___ Name of laboratory/ CHC: Type of test: ZN / Xpert Ultra / Culture Result : TB number (For Transferred In/ Out patient): HIV Status: ☐ R ☐ NR ☐ Unknown DST Status: ☐ Rif Sensitive ☐ Rif Resistant ☐ Unknown, if unknown **Sample sent for DST to** _____ Date: __/__/__ **Treatment regimen:** ☐ New **Date of treatment initiation: __/__/__** **Number of doses:**_____

Referred for:
- ☐ Initiation of treatment
- ☐ Treatment continuation (If initiated from the hospital)
- ☐ Adverse drug reaction (give details) _____
- ☐ Transfer out (give details)_____
- ☐ Any other (give details) _____

Name and designation of the referring doctor_____

Date referred

----------✂----------✂----------

Serial Number_____

For use by the health facility where the patient has been referred

Name of receiving health facility_____ Name of CHC and Municipality_____

Name of patient _____ TB No (if available) _____

Age_____ Sex M F TG ☐ Date of receipt of patient_____

Date of initiation of treatment _____ Treatment regimen _____

Result of End IP specimen examination _____ Date of end IP specimen examination _____

Treatment outcome _____ Date of treatment outcome _____

Signature_____ Designation_____

Date_____

This portion of the form has to be sent back to the referring unit as soon as the patient has been initiated on NTP treatment

7) Referral Form for TB-DM Screening

Referral Form for TB-DM Screening

Patient's name: .....Sex: ..... Age: .....
Current disease: ☐ TB ☐ Diabetes (ID in registration book: .....)
Name of health facility: .....
Refer from: ..... To: .....

REFERRAL (To completed by referrer)	
Reason for referral:	☐ TB suspicion (☐ Cough ☐ Fever ☐ Night sweats ☐ Weight loss ☐ Other: .....)
	☐ DM suspicion (☐ FBS: .....mg/dL ☐ RBS:..... ...mg/dL ☐ Other: .....)
Refer to:	☐ TB department ☐ DM department
Treatment given:	.....
Date:...../...../..... Name of referrer: ..... Signature: ....., Tel:	
DIAGNOSIS (To completed by receiver)	
Diagnosis:	☐ TB (☐ Sputum smear (+) ☐ GeneXpert ☐ Clinical evaluation ☐ Other: .....)
	☐ DM: (☐ FBS ..... ☐ RBS: ..... ☐ Other: .....)
	☐ Other: .....
Date of diagnosis:	
Treatment given:	
Date:...../...../..... Name of physician: ..... Signature: …......, Tel:	
Please ask patient to brink this form back to original health department	

8) Referral Form from TB Program to HIV Testing and Counselling (HTC)

Referral Form from TB programe to

HIV Testing and Counselling (HTC)

Name of referring health facility: _____
Muncipality:_____

Name of referring person: _____ Referral date: _____

Referred to (nearest VCT): _____

Name of patient: _____ Age:_____ Sex: _____

TB No. : _____Registration Year:_____ Type of TB case: _____

.....

Services provided by HTC (filled by HTC Staff)

Name of health facility who received referral and municipality: _____

Pre-test Counselling and informed consent: _____ Date: _____

HIV Test: _____ Date: _____

Post-test Counselling and Result given: _____ Date _____

Name and signature HTC staff _____

.....
.....

9) HIV--TB Line List (Referred/Presumptive TB cases)

HIV--TB Line List (Referred/Presumptive TB cases)

Recording Month and Year:

Sl. No.	Date	HIV Care Registration No. (Pre-ART)	Name	Age	Sex (M/F/TG)	Contact No.	Address – Municipality/ District	Status at the time of TB referral (Pre-ART/ART)	Type/ Name of the facility where referred to *(provide code and name of the facility)*[1]	Type of test[2]	Is the patient diagnosed with TB (Yes/NO)	**If diagnosed with TB**					**If Diagnosed with DR-TB**		
												Drug Resistance status (Yes/No)	Type of TB diagnosed[3]	Date of TB diagnosis (dd/mm/yyyy)	TB No.	Date of starting ATT (dd/mm/yyyy	Date of referral to DR-TB centre? (dd/mm/yyyy)	Name of DR-TB centre referred for treatment **	Date of starting DR-TB treatment (to be provided by STS)

***Note*:**

1. (A) DMC, (B) XpertUltra, (C) Radiology, (D) Histopathology, (E) Others
2. (A) XpertUltra, (B) Smear, (C) Culture, (D) TST (for children under 5 years of age), (E) Others
3. Definition: Microbiological diagnosis through Culture, GeneXpert, Smear, TST and histopathology, & Clinical diagnosis through X-ray, USG, etc. Pick the relevant code: (i) Pulmonary TB (Microbiologically confirmed), (ii) Pulmonary TB (Clinically diagnosed), (iii) Extrapulmonary TB (Microbiologically confirmed), (iv) Extrapulmonary TB (Clinically diagnosed)

* In case of invalid/error/no result/indeterminate result, wait for final diagnosis and update the status as and when the results become available

** Refer the patient to the DR TB centre with the referral form and inform the TB Coordinator/ Responsible

10) HIV-TB Register (Confirmed TB Cases)

HIV TB Register (Confirmed TB Cases)

Recording 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
S.NO.	Date	HIV Care Registration Number (Pre-ART)	Name	Age	Sex (M/F/TG)	Contact Number	Address - Block, District, State	From where the patient has been referred? (Pick appropiate code and provide name of the facility)[1]	Drug Resistance status (Yes/No)	Type of TB diagnosed[2]	Date of TB diagnosis (dd/mm/yyyy)	TB Number	Patient category[3]	Date of starting ATT (dd/mm/yyyy)	If not initiated on ATT , reason for the same[4]	Type/Name of facility from where the patient is receiving TB treatment *(provide code and name of the*	Type of treatment (Category I/IV)	Date of treatment completion	Treatment outcome[6]	Is the patient on CPT? (Yes/No)	Date of ART initiation	ART Registration Number	If not initiated on ART, reason for the same[7]	Remarks

Note:

1. (A) Referred by ART center for TB diagnosis, (B) Referred by ICTC for TB diagnosis, (C) K/C/O TB referred by NTP to ICTC, (D) Referred from private practitioner/Other.
2. **Definition: Microbiological** diagnosis through Culture, GeneXpert, Smear, TST and histopathology, & **Clinical** diagnosis through X-Ray, USG etc. **Pick the relevant code:** (i) Pulmonary TB (Microbiologically confirmed), (ii) Pulmonary TB (Clinically diagnosed), (iii) Extra-Pulmonary TB (Microbiologically confirmed), (iv) Extra Pulmonary TB (Clinically d
3. (A) New, (B) Relapse, (C) Treatment after default, (D) Failure, (E) Retreatment, (F) Others: Specify
4. (A) Patient transferred-out to other ART center, (B) Patient not reporting for treatment/LFU, (C) Patient died before ATT initiation, (D) Patient taking treatment in the private sector, (E) Others: Specify
5. (A) ART center, (B) NTP, (C) Private institution, (D) DRTB, (E) Others: Specify
6. (A) Cured, (B) Treatment completed, (C) Died, (D) Treatment failure, (E) Defaulted, (F) Transfer out, (G) Switched over to MDR TB treatment, (H) Others: Specify
7. (A) Patient transferred-out to other ART center, (B) Patient not reporting for treatment/LFU, (C) Patient died before ART initiation, (D) Patient taking treatment in the private sector, (E) Others: Specify

11) HIV/TB Monthly Report (Intensified TB Case Finding and Diagnosis)

HIV/TB					Date Source
Intensified TB Case Finding and Diagnosis					
(From Patient Visit Register and HIV/TB Line-List- 1 month prior to reporting month)					
3b.1) Number of PLHIV attending ART Centre during the month (Pre ART and ART)					Patient vist register
3b.2) Out of the above, number of PLHIV screened for 4 symptoms					Patient vist register/MLL
3b.3) Out of the above, number of PLHIV with presumptive TB (those with anyone/more 4s symptom/s)					MLL
3b.4) Out of the above, number of PLHIV with presumptive TB referred from ART centre for TB diagnosis					HIV/TB linelist
3b.5) Out of the above, number of PLHIV with presumptive TB, tested for TB diagnosis					HIV/TB linelist
3b.6) Out of the above, number of PLHIV diagnosed as having TB:	**In Pre ART Care at the time of TB diagnosis**	**On ART at the time of TB diagnosis**	**Total**		HIV/TB linelist
(i) Pulmonary TB (Microbiologically confirmed)			0		HIV/TB linelist
(ii) Pulmonary TB (Clinically diagnosed)			0		HIV/TB linelist
(iii) Extra-Pulmonary TB (Microbiologically confirmed)			0		HIV/TB linelist
(iv) Extra Pulmonary (Clinically diagnosed)			0		HIV/TB linelist
3b.7) Total PLHIV Diagnosed with TB	0	0	0		HIV/TB linelist
3b.8) Out of **(3b.7)**, number of TB patients with RRTB (Rif Resistant TB)					
3 c. Treatment for TB and HIV in Co-Infected PLHIV					
(From the HIV- TB register -1 months prior to reporting month)					
3c.1) Total PLHIV Diagnosed with TB of the total refered from ART center ***(same a***					
3c.2) Patients who reported to the ART center with already diagnosed TB status					
3c.3) Total number of TB patients enrolled in HIV/TB register 2 months prior to reporting month ***(3c.1+3c.2)***					
3c.1) Total number of Co-infected patients enrolled in HIV/TB register 1 months prior to reporting month					
3c.2) Out of **(3c.1),** number of Co-infected patients receiving TB treatment	**Government (NTP)**	**Private**	**Total**		
			0		
3c.3) Out of **(3c.2),** number of TB patients with RRTB (Rif Resistant TB) receiving Cat IV treatment					
3c.4) Out of **(3c.1),** number of Co-infected patients initiated on CPT					
3c.5) Out of **(3c.1),** number of Co-infected patients initiated on ART					
3 d. TPT Status (3HP)					
(From Master Line List- 1 months prior to reporting month)					
3d.1) Number of PLHIV newly initiated on TPT during the month					
3d.2) Number of PLHIV completed TPT during the month					

12) Vulnerability Screening Tool/Vulnerability Assessment Register

Vulnerability Screening Tool/Vulnerability Assessment Register

Address of the household (HH):

House No/Name: No. of HH Members: No. of Children < 5 years: BCG Vaccination Status (Yes/ No): BCG Scar Status (Yes/ No): Distance from the Health Post/CHC:	Phone No: 1 2 3	**Reg. Number:** XXXX2020/ Name of the village……/ House No…….. Or XXXX2020/ Name of the hospital/ Health facility……..…….. Name of the nearest CHC: Name of the village: Name of the interviewer: Interviewer occupation (PSF/TB Responsible/ Nurse/ KP/ Other):

Name *Naran*	Sex M/F/TG	Age	1. a Slum	1.b Past H/o TB **(3 Yr)**/ Present TB	1.c Health worker	2a. PLHIV status	3a. Malnutrition status (MUAC)	3b. Migrant labour (Cross border/ Intl. Migrants)/ Prisoner	(In Health facility/ Hospital) 3c. Diabetes	(In Health facility/ Hospital) 3d. COPD /asthma	(In Health facility/ Hospital) 3e. Liver/ kidney disease	(In Health facility/ Hospital) 3f. Bed ridden/palliative care	3g. Smoking/ Use of solid Fuels in HH: Firewood	3h. Alcohol	4a. Symptoms present: -Cough -Fever -Weight Loss -Hemoptysis	4b Sputum collected and sputum examination form filled	Asymptomatic, but identified vulnerable requiring X-ray *(For example, Asymptomatic contacts with Bac+ve, malnourished, smoker, alcohol use, etc.)*	**SCORE**

Note on SCORING: *Vulnerability factors (with their weighted scores in brackets) are: Household contact (5), Immunosuppressive therapy (4), Malnutrition (4), Health care worker (3), Diabetes (3), Organ dysfunction (3), Worked/lived in districts/sub-districts (CHCs) with TB notification rates ≥200/100 000 (3), Street dweller (3), Migrant labour (Cross border migrants) (2), Chronic lung disease(2), Smoking/ Use of solid Fuels in HH: Firewood (2), Alcoholism (2), Prison inmate (2) Age above 60 (1), Slum dweller (1). If the total score is 5 or above, the person is classified as highly vulnerable and requires symptom screening in every 3 months. If the total score is 1 to 5, the person is moderately vulnerable and to be screened for symptoms once every year.*

[Ref: https://www.who.int/tb/features_archive/action-plan-launched-72-regional-committee/en/]

13) Quarterly Report Form on Vulnerability Assessment

National TB Programme Level **Municipality**

Quarterly Report Form on Vulnerability Assessment

Date of the Report:

Name of the Municipality:

Name of the Municipality TB Coordinator:

Total Population of the Municipality:

Name of the CHCs	Total population *Total populasaun*	Total No. of HH covered Numeru total uma kain ne'ebe kobre	Number of vulnerable individuals mapped Numeru ema vulnarabel sira ne'ebe iha mapa*				Presumptive TB identified, and sputum samples collected Identifika Presumtive TB no kolekta sample sputum	Presumptive TB identified, and CXR done (including asymptomatic) Presumptive TB ne'ebé identifika tiha ona, no Chest X-Ray ne'ebé halo
			Mal	Smo	Alc	Migrants		

Note: *Mal: Malnourished; Smo: Smoker (Yes/ No); Alc: Daily alcohol consumption (Yes/ No); Migrant worker

14) Quarterly Report Form on Quarterly Monitoring of Mapped Vulnerable Individuals

National TB Programme
Municipality Level

Quarterly Report Form on Quarterly Monitoring of Mapped Vulnerable Individuals

Date of the Report:

Name of the Municipality:

Name of the Municipality TB Coordinator:

Total Population of the Municipality:

Name of CHC	Total population *Total populasaun*	Number of vulnerable individuals mapped (Baseline) Numeru ema vulnarabel sira ne'ebe iha mapa				Presumptive TB identified, and sputum samples collected Identifika Presumtive TB no kolekta sample sputum	Presumptive TB identified, and CXR done (including asymptomatic) Presumptive TB ne ' ebé identifika tiha ona, no Chest X-ray ne ' ebé halo (inklui asymptomatic)
		Mal	Smo	Alc	Migra nts		

Note: *Mal: Malnourished; Smo: Smoker (Yes/ No); Alc: Daily alcohol consumption (Yes/ No); Migrant worker

15) Contact Tracing and LTBI Treatment Register

Contact Tracing and LTBI Treatment Register

Sl. No.	Index cases		Contact's progressive No.	Contact's Complete Names	Age	Sex	Date seen	Result (1)	LTBI treatment initiation		1st month	2nd month	3rd month	4th month	5th month	6th month	Treatment outcome	Remarks/ Reason for not completion
	Name	TB No.							Date	Regimen (2)	Date and result (3)	Date and result (3)	Date and result (3)	Date and result (3)	Date and result (3)	Date and result (3)		

Note:
1) NE: Not evaluated; No-TB: evaluated and active TB disease excluded; TB: evaluated and active disease suspected
2) H: Isoniazid daily for 6 months; 3HP: 3RH: isoniazid and rifampicin daily for 3 months
3) F: Continue treatment and follow up; I: treatment interrupted (includes lost to follow up); C: treatment completed; D: treatment failed
4) To be filled in at the time of treatment completion – i.e., after 3 or 6 months of treatment; C: treatment completed; NC: treatment not completed.

16) National Quarterly Reporting Form for TB Registration – Household Contacts

National Quarterly Reporting Form for TB Registration No. of people who are household close contacts of contagious TB or child TB cases						
	Identified	Checked for active disease	TB identified	TB treatment initiated	Eligible for preventive treatment	Initiated preventive treatment
Total No. of contacts						
Among them: No. of children under 5 years						

17) TB Treatment Card (KARTAUN TRATAMENTU TUBERCULOZU)

TB FORM 4

PROGRAMA NACIONAL KONTROLA TUBERCULOZU
KARTAUN TRATAMENTU TUBERCULOZU

Naran Kumpletu
Sexu ☐ Mane ☐ Feto Idade
Hela Fatin kumpletu no numeru telefone

Naran, hela fatin kumpletu no numeru telefone kontaktu pessoal

Visita uma inisia husi no data:

Istoria tratamentu TB iha tempu uluk & Durasaun (se Sim, Numeru Rej. TB):

Numeru Rejistu TB / Tinan

Naran fasulidade sa úde ne'ebe halo tratamentu

Naran & No. telefone fornecedor DOT -

Pozisaun fornecedor DOT:	☐ Pessoal saude ☐ Matan Do'ok	☐ Staff NGO ☐ Klinka Privadu	☐ PSF ☐ Family

Fulan	Mear Tasak Mikroskopiu			XpertUltra MTB/RIF			Todan Isin (kg)
	Data	No. Lab	Resultadu	Data	No. Lab	Resultadu	
Inisiu							
Fulan 2							
Fim tratamentu							

Kor matak aplika deit ba follow up ezaminasaun mear tasak mikroskopiu positivu

Klasifikasaun Moras
☐ Pulmaun
☐ Ekstra Pulmaun
Site:

Tipu pasiente
☐ Foun
☐ Rekaida
☐ T. Hafoin Falla
☐ T. Depois lakon husi FU
☐ Seluk

Ray-X iha Inisiu
Data:
(-) Normal
(+) Abnormalidade Lae (La halo)

TB / HIV		
	Data	Resultadu
Teste HIV		
Hahu CPT		
Hahu ART		
Resultadu CD4		
No. Rej ART & Data		

I. *FASE INTENSIVU* (Data)

REGIMENTU NO DOSAGEM *(Circlu ho apropriadu ba kategoria iha kraik)*

Kazu Foun (lor-loron) ba fulan rua
RHZE (150/75/400/275)

Kazu Pediaria (lor-loron) ba fulan rua
50H/75R/150Z

Diabetes Status	
FBS	**RBS**
>=126 mg/ dl or >=7 mmol	At least 2 hrs after meal, >=200mg/ dl or >=11 mmol

R= Rifampicin H= Isoniazide Z= Pyrazinamide E= Ethambutol

Tau marka (✓) iha loron ne'ebe pasiente hemu aimoruk ho observasaun directa, Tau marka (-) iha loron ne'ebe pasiente hemu aimoruk la ho obeservasaun directa, Tau marka (O) se pasiente la hemu aimoruk

Fulan / Tinan	Data																											Total Dosis ne'ebe fo ona	
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Fulan Ne'e	Kumulativu

II. *FASE KONTINUASAUN*

Circlu ho apropriadu ba kategoria iha kraik

Kazu Foun (Lor-loron) ba fulan 4

Kazu Pediatria (Lor-loron) ba fulan 4	

Tau marka (✓) iha loron ne'ebe pasiente hemu aimoruk ho observasaun directa, Tau marka (-) iha loron ne'ebe pasiente hemu aimoruk la ho obeservasaun directa, Tau marka (O) se pasiente la hemu aimoruk

Fulan / Tinan	Data																											Total Dosis ne'ebe fo ona	
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Fulan Ne'e	Kumulativu

Resultadu Tratamentu (marka ✔ida)		**Data Deside**
	Kura	
	Tratamentu Kumpletu	
	Mate	
	Falla Tratamentu	
	Lakoh husi Follow up	
	La Avalia	

Observasaun

Asaun Buka Tuir Pasiente ne'ebe lakon no Resultadu

Data	Husi	Razaun La hemu Aimoruk	Resultadu husi aktividade ne'e

Sreening ba kontaktu Besik (Children, Adults and PLHIV contacts)

No	Naran Kumpletu	Idade	Relasaun ho Pasiente	Data Hare	Resultadu	TPT	Tratamentu TB (S/L)
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							

18) Quarterly Report on TB Case Finding (Municipality Level)

QUARTERLY REPORT ON TUBERCULOSIS CASE - FINDING (MUNICIPALITY LEVEL)

DISTRICT	NAME OF DOT CENTER	YEAR	SIGNATURE AND DATE OF COMPLETION THIS FORM
NAME OF HEALTH FACILITY	DTC OR TB RESPONSIBLE	QUARTER[a]	

Block 1 : All TB cases registered during the quarter[b]

	New	Relapse	Previously treated excluiding relapse	Other	Total
Pulmonary, bacteriologically confirmed					
Pulmonary, clinically diagnosed					
Extrapulmonary, bacteriologically confirmed					
Extrapulmonary, clinically diagnosed					

Block 2: All Pulmonary and Extra Pulmonary new and previously treated for TB (bacteriologically confirmed or clinically diagnosed) registered during the quarter by age group and sex

	0 - 4		5 - 14		15 - 24		25 - 34		35 - 44		45 - 54		55 - 64		65 +		Total
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
Pulmonary, bacteriologically confirmed (new and Relapse)																	
Pulmonary, clinically diagnosed (new and relapse)																	

Extrapulmonary, bacteriologically confirmed (new and Relapse)																	
Extrapulmonary, clinically diagnosed (new and Relapse)																	
Others																	

Block 3: Laboratory diagnostic activity[c]

Patient with presumptive TB undergoing bacteriological examination	Patient with presumptive TB with positive bacteriological examination result

Block 4: TB/HIV activities (all TB cases registered during the quarter)

Patients tested for HIV at the time of TB diagnosis or during the course of treatment OR with known HIV status[d] at the time of TB diagnosis	HIV-positive TB patients	HIV-positive TB patients on ART	HIV-positive TB patients on CPT

Block 5: TB & Diabetes Activities

TB Patients undergoing FBS examination by Glucometer	TB Patients with DM

Block 6: LTBI Management

No. of children (>2 years to 14 years) contacts provided with 3HP	No. of adult contacts provided with 3HP	No. of PLHIV provided with 3HP

b "Transferred in" cases are excluded

c Data aggregated from the TB laboratory register based on Date specimen received, and excluding patients examined for follow-up.

d Include all TB patients previously known to be HIV-positive (e.g. documented evidence of enrolment in HIV care such as enrolment in the pre-ART register or in the ART register once started on ART) or with a documented negative HIV test conducted at the time of TB diagnosis.

19) Quarterly Report on TB Case Finding (CHC Level)

MINISTRY OF HEALTH

NATIONAL TUBERCULOSIS CONTROL PROGRAMME

QUARTERLY REPORT ON TUBERCULOSIS CASE - FINDING (CHC LEVEL)

DISTRICT	NAME OF DOT CENTER	YEAR	SIGNATURE AND DATE OF COMPLETION THIS FORM
NAME OF HEALTH FACILITY	DTC OR TB RESPONSIBLE	QUARTER[a]	

Block 1 : All TB cases registered during the quarter[b]

	New	Relapse	Previously treated excluiding relapse	Other	Total
Pulmonary, bacteriologically confirmed					
Pulmonary, clinically diagnosed					
Extrapulmonary, bacteriologically confirmed					
Extrapulmonary, clinically diagnosed					

Block 2: All Pulmonary and Extra Pulmonary new and previously treated for TB (bacteriologically confirmed or clinically diagnosed) registered during the quarter by age group and sex

	0 - 4		5 - 14		15 - 24		25 - 34							35 - 44		45 - 54		55 - 64		65 +		Total
	M	F	M	F	M	F	M						F	M	F	M	F	M	F	M	F	
Pulmonary, bacteriologically confirmed (new and Relapse)																						
Pulmonary, clinically diagnosed (new and relapse)																						

Extrapulmonary, bacteriologically confirmed (new and Relapse)																					
Extrapulmonary, clinically diagnosed (new and Relapse)																					
Others																					

Block 3: Laboratory diagnostic[c]

Patient with presumptive TB undergoing bacteriological examination	Patient with presumptive TB with positive bacteriological examination result

Block 4: TB/HIV (all TB cases registered during the quarter)

Patients tested for HIV at the time of TB diagnosis or during the course of treatment OR with known HIV status[d] at the time of TB diagnosis	HIV-positive TB patients	HIV-positive TB patients on ART	HIV-positive TB patients on CPT

Block 5: TB & Diabetes

TB Patients undergoing FBS examination by Glucometer	TB Patients with DM

Block 6: LTBI Management

No. of children (>2 years to 14 years) contacts provided with 3HP	No. of adult contacts provided with 3HP	No. of PLHIV provided with 3HP

b "Transferred in" cases are excluded

c Data aggregated from the TB laboratory register based on Date specimen received, and excluding patients examined for follow-up.

d Include all TB patients previously known to be HIV-positive (e.g. documented evidence of enrolment in HIV care such as enrolment in the pre-ART register or in the ART register once started on ART) or with a documented negative HIV test conducted at the time of TB diagnosis.

20) Treatment Outcome Report for TBCases Registered 6—8 Months Earlier

MINISTRY OF HEALTH

NATIONAL TUBERCULOSIS CONTROL PROGRAMME

TREATMENT OUTCOME REPORT FOR TUBERCULOSIS CASES REGISTERRED 6 - 8 MONTHS EARLIER (MUNICIPALITY LEVEL)

DISTRICT	NAME OF DOT CENTER	YEAR	SIGNATURE AND DATE OF COMPLETION THIS FORM
NAME OF HEALTH FACILITY	DTC OR TB RESPONSIBLE	QUARTER[a]	

Block 1: All TB cases registered during the quarter (except for TB cases moved to the second-line treatment register)

Type of TB patient	Number of cases registered	Treatment outcomes						Move to Second line Treatment	Total Evaluated
		Cured	Treatment Completed	Treatment Failed	Died	Loss to Follow up	Not Evaluated		
Bacteriologically confirmed, new and relapse (Pulmonary & Extra Pulmonary)									
Clinically diagnosed, new and relapse (Pulmonary & Extra Pulmonary)									
HIV-positive, all type									

* Retreatment Cases (exlcluding Relapse) and other Previous treatment

Block 2: TB/HIV activities (all TB cases registered during the quarter)

HIV-positive TB patients	HIV-positive TB patients on ART	HIV-positive TB patients on CPT

[a]Registration period is based on date of registration of cases in the TB register, following the start of treatment. Q1: 1 January – 31 March; Q2:1 April – 30 June; Q3: 1 July –30 September; Q4:1 October – 31 December

Block 3: Treatment Observation by DOT Provider's

Directly Observed Treatment (DOT)								
Tipu kazu TB	**DOT (by)**						**Not DOT**	**Total**
	Health Staff	**NGO Staff**	**Private Clinic**	**Traditional Healer**	**Volunteer/PSF**	**Family DOT**		
Bacteriologically confirmed, new and relapse (Pulmonary & Extra Pulmonary)								
Clinically diagnosed, new and relapse (Pulmonary & Extra Pulmonary)								

Block 4: Treatment Outcome by Volunteer (PSF=Family Health Promoter)[b]

Type of TB case	Number of cases registered	Treatment outcomes					
		Cured	Treatment Completed	Treatment Failed	Died	Loss to Follow up	Not Evaluated
New Pulmonary Bacteriologically confirmed							
New Pulmonary Clinically diagnosed							
New Extra Pulmonary Bacteriologically and clinically Diagnosed							

Aproved by

[b] Total Number of TB cases should same as Block 4 column DOT by volunteer/PSF

21) Treatment Outcome Report for TB Cases Registered 12—15 Months Earlier (Age Disaggregated)

MINISTÉRIO DA SAÚDE

PROGRAMA NACIONAL KONTROLA TUBERCULOZO

TREATMENT OUTCOME OF TUBERCULOSIS CASES REGISTERED IN THE LAST 12-15 MONTHS

MUNICIPALITY	NAME OF DOR CENTER	YEAR	SIGNATURE AND DATE OF FORM COMPLETION
NAME OF HEALTH FACILITY	TB RESPONSIBLE	QUARTER	

Block 1: Number of TB case registered during this quarter

	Type of patient	Total number of TB case registered			Outcome of treatment															Total Evaluated		
					Cured			Completed			Failure			Death			Loss to follow up		Not evaluated				
		Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
1.1	Bacteriologically confirmed, new and relaps (Pulmonary and extra-pulmonary)< **14 ys of age**																					
1.2	Bacteriologically confirmed, new and relaps (Pulmonary and extra-pulmonary) **15 ys and above**																					
2.1	Clinically diagnosed, new and relaps (Pulmonary and extra-pulmonary) < 14 ys																					
2.2	Clinically diagnosed, new and relaps (Pulmonary and extra-pulmonary) 15 ys and above																					
3.1	Re-treatment (Relaps not included)* **<14**																					
3.2	Re-treatment (Relaps not included)* 15 ys and above																					
4.1	HV positive, all type																					

Block 2: HIV/TB Collaboration activity (All forms of TB registered during this quarter with with HIV negative)

Total number of all forms of TB registered	Treatment outcome						Total Evaluated
	Cured	Completed	Failure	Death	Loss to follow up	Not evaluated	

Block 3: HIV/TB Collaboration activity (All forms of TB registered during this quarter with HIV test not done)

Total number of all forms of TB registered	Treatment outcome						Total Evaluated
	Cured	Completed	Failure	Death	Loss to follow up	Not evaluated	

Block 4: HIV/TB Collaboration activity (All TB cases registered during this quarter)

HIV positive TB patients	HIV positive TB patients put on ART	HIV positive TB patients given CPT

*Period of registration based on date of registraon recorded in TB register, following date of treatment. Q1: 1 January-31 March, Q2: 1 April-30 June, Q3: 1 July-30 September, Q4: 1 October-31 Desembre

Block 5:Treatment Observation from DOT provider

Type of TB case	Directly Observed Treatment (DOT)						
	DOT (husi)						Total
	Health staffs	NGO staff	Private clinic	Traditional	Volunteers/PSF	Not DOT	
Bacteriologically confirmed, new and relaps (Pulmonary and extra-pulmonary)							
Clinically diagnosed, new and relaps (Pulmonary and extra-pulmonary)							
Retreatment (Relaps not included)*							

Block 6: Treatment outcome of patients whose treatment was observed by volunteers/ PSF[b]

Type of TB case	Total TB case whose treatment observed by volunteers/PSF	Treatment outcome						Total of TB patient evaluated
		Cured	Treatment completed	Positive (failures)	Death	Loss to follow up	Not evaluated	
Bacteriologically confirmed, new and relaps (Pulmonary and extra-pulmonary)								
Clinically diagnosed, new and relaps (Pulmonary and extra-pulmonary)								
Retreatment (Relaps not included)*								

Approved by

22) Order Form for Anti TB Treatment

DEMOCRATIC REPUBLIC OF TIMOR-LESTE

MINISTRY OF HEALTH

DISTRICT HEALTH SERVICES OF .....

ORDER FORM FOR ANTI-TB TREATMENT

Quarter Year Date:

DOTS Centre:

Enter the No. of TB cases enrolled in the previous quarter from Quarterly Report on Case Finding

Drugs	***2RHZE/4RH***			***2SRHZE/1RHZE/5RHE***			***2RHZE/4RH***		**Total (C)**	**D = A + B + C**
	Cases	**Factor**	**Total (A)**	**Cases**	**Factor**	**Total (B)**	**Cases**	**Factor**		
R.150/H.75/Z.400/E.400 mg		168			252					
R. 150/H.75 mg		336			420					
E.400 mg					280					
S. 1 gr					56					
Spuit/Seringe 5 cc					56					
Aquabidest 5 mL					56					
R. 60 / H.30 / Z.150 mg								112		
R.60 / H.60 mg								168		
R.60 / H.30 mg								224		
E. 100								112		
H. 100 mg								336		

Drugs	Running requirements	Reserve requirements	Currently in stock		Currently in stock with expiry date		
	E (=D)	F (=E)	G		Date of Expiry Quantity	Date of Expiry Quanti ty	Date of expiry Quantity
R.150/H.75/Z.400/E.400 mg				Tablets			
R. 150/H.75 mg				Tablets			
E.400 mg				Tablets			
S. 1gr				Vial			
Spuit/Seringe 5 cc				Unit			
Aquabidest 5 mL				Ampoules			
R. 60/H.30/Z.150 mg				Tablets			
R.60/H.60 mg				Tablets			
R.60/H.30 mg				Tablets			
E. 100				Tablets			
H. 100 mg				Tablets			

23) Order Form for Laboratory Supplies

REPÚBLICA DEMOCRÁTICA DE TIMOR LESTE

MINISTÉRIO DA SAÚDE

PROGRAMA TUBERCULOZO

ORDER FORM FOR LABORATORY SUPPLIES

Name of DMC		Quarter		Year	
		Date:			

Enter the No. of cases AFB positive enrolled in the previous quarter (From the Quarterly Report on Case Finding)

Material	Total TB cases	Factor	Running requirement	Reserve requirement	Current stock	Total order
	A	B	C = A x B	D = C	E	F = C + D - E
Carbol fuchsin		130				
Methylene blue		130				
Acid alcohol 3%		182				
Xylol		23				
Filter paper @100/box		2.6				
Lens paper @ 50/box		5.2				
Wire loop		0.2				
Imersion oil		2.6				
Disinfektan/*Disinfectant*		130				

Methylene spirit		65				
Lysol 5%		7.8				
Masker/*disposable mask*		23				
Tissue		0.06				

Calculation needed for sputum container and microscope slide		Total TB cases treated in the previous quarter	Microscope slide	Sputum container
a	Total pulmonary bacteriologically confirmed TB cases (new and re-treatment)….x 26 (from TB case finding report)			
b	Total pulmonary clinicaly diagnosed adult …x2 (form TB case finding)			
c	Running requirements (A+B)			
d	Reserve requirements 100% (=C)			
e	Current stock (closing balance)			
f	Total order (C+D-E)			

Prepared by: Approved by:

24) Second-line (RR-TB/ MDR) TB register

RR-TB / MDR-TB REGISTER

Unique second-line TB treatment register no	Date entered in second-line TB treatment register	Name	Sex (M/F)	Age	Address	TB Register Number / Date entered in TB register	Site of disease (P/EP)	Registration group	Second-line drugs received previously (Y/N/UK)	Date sample taken for DST	Result of drug susceptibility testing (R=Resistance, S=Susceptible, C=Contaminated)										Reasons for entering in second-line TB treatment register		Regimen (in drug initials) / Start date
											H	R	E	S	Amk / Km	Cm	FQ	Other	Other	Other	RR-TB / MDR-TB confirmed	Presumptive RR-TB/MDR-TB	

Smear (S), culture (C) or Xpert MTB/RIF (X) results											Smear (S) and culture (C) results during treatment (continued)																Smear (S) and culture (C) results during treatment (continued)																							
Start of treatment Month 0			Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 7		Month 8		Month 9		Month 10		Month 11		Month 12		Month 13		Month 14		Month 15		Month 16		Month 17		Month 18		Month 19		Month 20		Month 21		Month 22		Month 23		Month 24	
S	C	X	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C
Date			Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date		Date	

Smear (S) and culture (C) results during treatment (continued)								Final outcome (Cured, Treatment completed, Treatment failed, Lost to follow-up, Died, Not Evaluated)	TB/HIV activities			Remarks
Month 25		Month 26		Month 27		Month 28			HIV Status (R/NR/UK/CS)	On ART (Y/N)	On CPT (Y/N)	
S	C	S	C	S	C	S	C					
Date		Date		Date		Date		Date		Date	Date	

25) Quarterly Report on Presumptive MDR-TB Patients

National TB Programme

Quarterly Report on Presumptive MDR-TB Patients

Format for monitoring testing of presumptive MDR-TB patients

Name of Municipality:			Quarter and Year:		
Type of presumptive MDR/RR patients	**No. eligible for DST (a)**	**No. Tested (b)**	**Percentage (a/b X100) (c)**	**No. diagnosed as MDR/RR**	**No. enrolled on treatment**
Re-treatment cases					
Sputum positive during follow up					
Contacts of MDR/RR patients					
TB-HIV					

SIX-MONTHLY REPORT ON ENROLLEMNT RR MDR XDR TB IN SECOND-LINE TREATMENT

District _____ Health facility_____	20 _____ year _____quarter
Name of reporting person _____Signature_____	Date of the completion of form _____

BLOCK 1. Number of RR/MDR-TB patients detected during the period of assessment and enrolled into second-line treatment

TB patient type	**Identified during the assessment period**	**Number of patients enrolled into second-line treatment during the assessment period**
All patients eligible for treatment*		
Including: < 15 years		
females		
Confirmed RR-TB or MDR-TB		
Confirmed RR/MDR-TB, HIV+		

* **Presumptive or confirmed RR-TB or MDR-TB**

BLOCK 2. Delay in start of second-line treatment

Number of detected cases	**Number of cases that started the treatment**	**Interval between DST results and start of treatment (in days)**			**Reasons for not enrolling into treatment**					
		Mean	Minimum	Maximum	Died before the start of treatment	Stock-out of second-line drugs	Type of resistance is not eligible for treatment	Refused from treatment	Advanced stage of disease	Other

SIX-MONTHLY REPORT ON RR-TB DETECTION

District _____ Health facility_____ Name of reporting person _____Signature_____	20 _____ year _____quarter Date of the completion of form _____

BLOCK 1. Surveillance of drug resistance

Risk category	Tested by Gene Xpert Ultra	Confirmed MTB	Confirmed RR-TB
New TB cases			
Retreated cases			
Unknown treatment history			
TOTAL			
Among them:			
HIV positive cases on ART			
HIV positive not on ART			
Children <15 years			
Females			
Contact of confirmed RR cases			
Treatment failure using first-line drugs			

BLOCK 2. Delay in detection

Number of RR cases with information on interval	Interval between presumption of RR-TB and Gene-Xpert results (in days)		
	Mean	Minimum	Maximum

28) Annual Report of Final Outcome of TB Cases with RR/MDR-TB on Second-line Treatment

ANNUAL REPORT OF FINAL OUTCOME OF TB CASES WITH RR/MDR-TB ON SECOND-LINE TREATMENT

District _____ Health facility_____ Name of reporting person _____Signature_____	Year of treatment start_____ Date of the completion of form _____

TB patient type	Number of TB cases						
	Started on treatment	Cured	Treatment completed	Treatment Failed	Died	Lost to Follow-up	Not evaluated
All confirmed RR-TB and MDR-TB cases							

29) Quarterly Report on Interim Results of TB Cases with RR/MDR-TB on Second-line Treatment

QUARTERLY REPORT ON INTERIM RESULST OF TB CASES WITH RR/MDR-TB ON SECOND-LINE TREATMENT

District _____ Health facility_____ Name of reporting person _____Signature_____	20 _____ year _____quarter Date of the completion of form _____

Number of confirmed RR-TB and MDR-TB cases started on second lint treatment	**Culture negative at six months**	**Died by sixth months**	**Lost to follow-up by six months**

Number of cases started on second-line treatment found not to have RR-TB or MDR-TB

30) Second-line TB Treatment Card

SECOND-LINE TB TREATMENT CARD

Second line registration Number ☐☐☐ ☐☐ ☐☐☐ (Code of district / Year / Consecutive number)

Health facility _____ **Year** _____

Date of registration of RR/MDR-TB ___/_____/___ **Treatment cohort**_____

I. DEMOGRAPHIC DATA

Name _____	Date of birth ___/_____/___	Sex ❒ M ❒F
Address and phone		
Contact person name and phone		

II. PREVIOUS TUBERCULOSIS TREATMENT EPISODES

№	Date of registration	District TB registration number	Start date (if unknown put year)	Registration group	Regimen (write regimen in drug abbreviations)	Outcome

Previously treated with secondline drugs?
❒ Yes
❒ No
❒ Unknown

Abbreviations of II line TB drugs: Amk = Amikacin, Km = Kanamycin, Cm = Capreomycin, Ofx = Ofloxacin, Lfx = Levofloxacin, Mfx = Moxifloxacin, Gfx = Gatifloxacin, Pto = Prothionamide, Eto = Ethionamide, Cs = Cycloserine, PAS = para-aminosalycilic acid, Bdq=Bedaquiline, Clr=Clarithromycin, Cfz=Clofazimine, Ipm=Imipenem, Lzd=Linezolid. Amx/Clv=Amoxicillin/clavulanate, T=Thiacetazone

III. REGISTRATION GROUP

❒ New	❒ Failure after first treatment regimen with FLD
❒ Relapse	❒ Failure after treatment regimen with SLD
❒ After loss to follow-up	❒ Previously treated with unknown outcome
Transfer in (from another second-line treatment program. If yes, name of center _____	Yes / No

IV. DRUG-RESISTANCE

❒ RR-TB	❒ XDR-TB
❒ MDR-TB	❒ PDR-TB

RR-TB – Rifampicin resistant TB;
MDR TB multidrug resistant TB;
*XDR TB extensively resistant tuberculosis;
PDR TB (without RR) – any polydrug resistance without resistance to R

V. LOCATION (circle one of both)

❒ Pulmonary	
❒ Extrapulmonary	_____ (specify site)

VI. TB/HIV INFORMAION

VII. MEETINGS OF MDR REVIEW PANEL

	Date	Results*
HIV test		
CPT start		
ART start		

*(Pos) Positive; (Neg) Negative; (I) Indeterminate; (ND) Not Done/Unknown

Date	Decision	Date of next meeting of review panel

VIII. LABORATORY MONITORING

	Microscopy			X-pert	Culture		
Treatment month	**Date**	**Laboratory number of specimen**	**Result**	**Result**	**Date of inoculation**	**Specimen number**	**Result**
Diagnostic	__/__/__				__/__/__		
0	__/__/__				__/__/__		
1	__/__/__				__/__/__		
2	__/__/__				__/__/__		
3	__/__/__				__/__/__		
4	__/__/__				__/__/__		
5	__/__/__				__/__/__		
6	__/__/__				__/__/__		
7	__/__/__				__/__/__		
8	__/__/__				__/__/__		
9	__/__/__				__/__/__		
10	__/__/__				__/__/__		
11	__/__/__				__/__/__		
12	__/__/__				__/__/__		
13	__/__/__				__/__/__		
14	__/__/__				__/__/__		
15	__/__/__				__/__/__		
16	__/__/__				__/__/__		
17	__/__/__				__/__/__		

IX. RESULTS OF EXAMINATIONS

Drug Sensitivity Test (DST) results R- resistant S- sensitive																		**X-ray**		
Date of specimen collection for DST	**Date of DST result**	**H**	**R**	**S**	**E**	**Z**	**Km**	**Amk**	**Cm**	**Pto**	**Eto**	**Ofx**	**Lfx**	**Mfx**	**PAS**	**Other**	**Other**	**Date**	**Result**	
																			Progress (+) / (-)	**Destruction Yes/No**
__/__/__	__/__/__																	__/__/__		
__/__/__	__/__/__																	__/__/__		
__/__/__	__/__/__																	__/__/__		

X. MONITORING OF Adverse events during the treatment with second-line TB drugs

Suspected Drug(s)	Date of registration	Type of Adverse Event	Severity*	Actions taken**	Date of interruption/change of regimen/dosage	Outcome of adverse event*** *(record the date)*	Facility

* **Degree of severity: 1 –** mild, **2** – moderate, **3** –severe/ life-threatening, **4** – Unknown
** **Actions taken**: **1-** Medicine withdrawn, **2-** Dose increased, **3-** Dose reduced, **4-**Dose not changed, **5-** Unknown
*** **Outcome of Adverse Event (AE) : 1 –** Recovered/ Resolved, **2** – Recovering / Resolving, **3-** Resolved with sequelae **4** – Not Recovered /Resolved, **5** –Unkown

XI. Results of labortory examinations and conclusionS of specialists during the treatment

Date	Blood test								Urine test				CD4	Visual Acuity	Consultation of ENT specialist	Audio-gramma	ECG
	Hemoglobin	Serum Creatinine	ALT/AST	Bilirubin	TSH	Urea	Potassium	Sugar	Protein	Leucocytes	RBC	Pregnancy test					

XII. TREATMENT OUTCOME

❒ Cure	❒ Died	
❒ Treatment completed	❒ Lost to follow up	
❒ Treatment failure	❒ Not evaluated	Date_____

XIII. REMARKS

_____

_____

_____

_____

_____

_____

_____

XIV. ADMINISTRATION OF DRUGS DURING THE INTENSIVE AND CONTINUATION PHASE OF TREATMNET

MDR ID												Month		Treatment month		

Health facility	Weight (kg)

Prescription date	Drug	Dose (mg)	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	Prescribed	Received

Health facility	Month		Weight (kg)		Treatment month		

Prescription date	Drug	Dose (mg)	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	Prescribed	Received

Mark in the boxes: ✓=Directly Observed

N= Not supervised

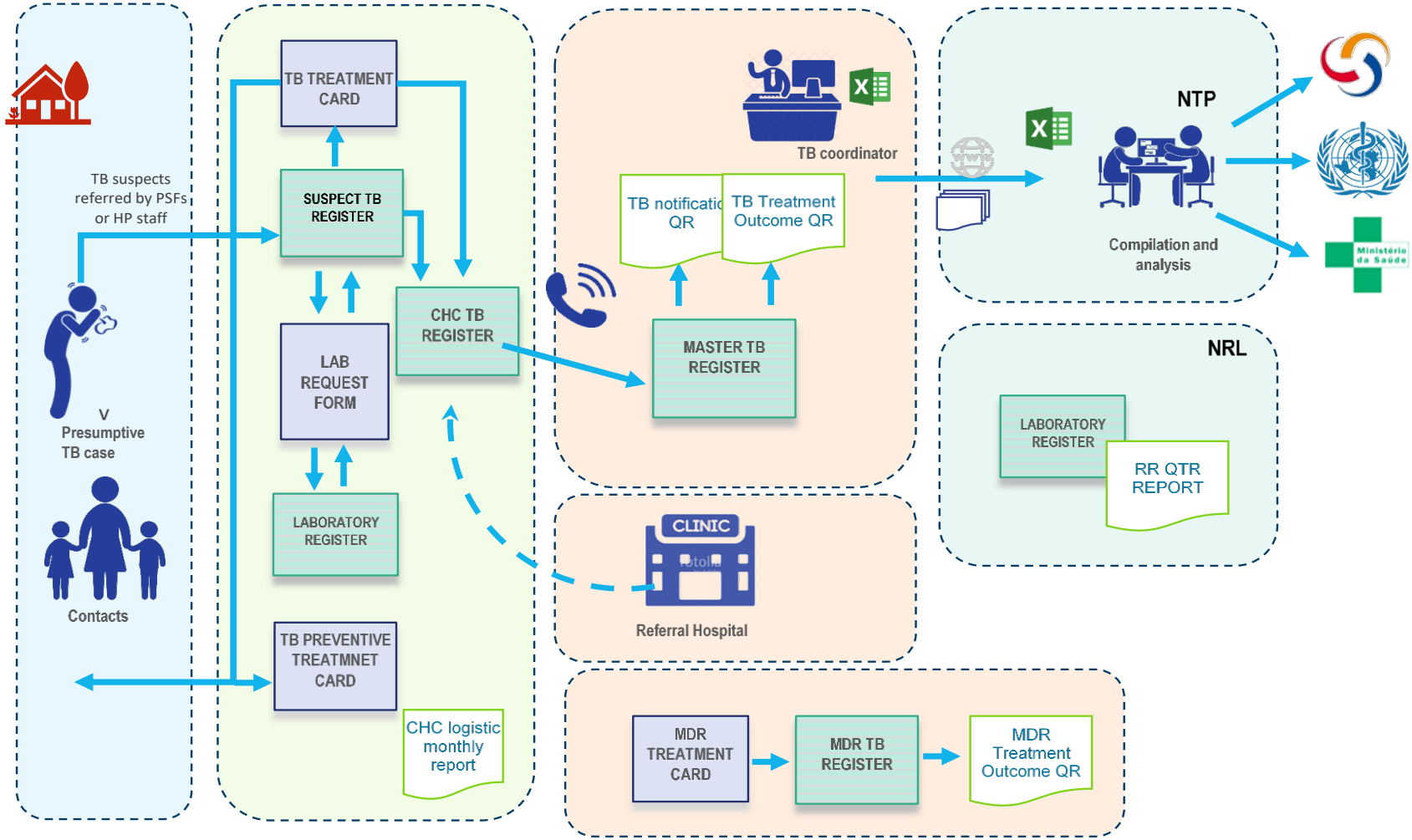
Ø= Drugs Not Taken

Split cell diagonally to record two administrations in one day

if split doses are used mark the upper left half for the Morning dose and the lower right for the Evening dose

ANNEX 4: DIAGRAM OF TB INFORMATION FLOW

. Diagram of TB information flow



ANNEX 5: PREPARATION, TRANSPORT AND PROCESSING OF SPUTUM SAMPLES

a) For tests with dead bacilli (molecular tests)

- **Principle**

When preparing a sample from a patient with presumptive RR-TB, the health worker should preserve the smear-positive sample in ethanol for dispatch to a laboratory equipped with Xpert or LPA (GenoType® MTBDRPlus or MTBDRsl) equipment.

In order to ensure inactivation of the TB bacilli, the final concentration of ethanol should be approximately 70%. This can be attained by adding 1 volume of sputum to 2 volumes of commonly available, industrial-quality ethanol at about 95%.

- **Equipment**

Option 1:

A 50 ml conical tube with hermetically closing screwcap (Falcon®-type) containing 10 ml of 95% ethanol.

Or

Option 2:

- 50 ml tube (Falcon®-type)
- 95% ethanol (denatured alcohol)
- **Preparation**
- Leave sputum in pot on the bench overnight to allow it to liquefy;
- The following day, shake the sample slowly and gently in circular movements for several seconds with the cap closed; • Let stand for 15–30 min before opening;
- Assess the volume of the sample.

Option 1:

If the volume of the sputum sample is <5 ml, reduce the volume of ethanol in the 50 ml Falcon® tube until the quantity of ethanol is approximately two times that of the sputum. If sample volume is >5 ml, add ethanol from another 50 ml tube to ensure that the volume of the ethanol is approximately double that of sputum volume.

Option 2:

- Pour two volumes of 95% ethanol for each volume of sputum into a 50 ml tube, pour the sample into the 50 ml tube containing the 95% ethanol, allowing it to flow down the sides of the tube;
- Hermetically seal the 50 ml tube and shake the test tube by inverting it about 20 times;
- Write the name of the patient and that of the BMU on the test tube with an indelible marker pen;
- Keep the test tube at room temperature until the following day to ensure that the bacilli are dead;
- Fill out the Xpert Test Request Form.

- **Transport**

No security packaging is necessary to transport the test tubes, as the bacilli are dead. Ensure that the tubes are properly closed and place them in a thick, flame-sealed plastic bag for transportation.

If air transport is used, the total volume of ethanol should not exceed 30 ml per tube or 300 ml per package of x number of test tubes (Inflammable, Dangerous Goods Class A according to International Air Transport Association regulations).

Laboratory procedures for Xpert testing:

- Transfer a minimum of 2 ml of the sputum-ethanol mixture into the cartridge without using the Cepheid reagent.

Laboratory procedures for LPA:

- Centrifuge the test tube at 3,000g for 15 min;
- Remove the supernatant;
- Put the sediment back into suspension in 50 ml of sterile distilled water;
- Carry out a second centrifugation at 3,000g for 15 min;
- Remove the supernatant and use the sediment.

b) For culture on solid egg-based medium

- **Principle**

This form of transportation uses antiseptic CPC, which enables live TB bacilli to be conserved at room temperature for a month.

- **Materials required**
- 50 ml (Falcon®) tubes that are sterile, conical, plastic, graduated (do not re-use tubes).
- 1% CPC solution: dissolve 20 g of salt (NaCl) and 10 g of CPC powder in 1,000 ml of distilled water and place the mixture in an autoclave; keep the mixture at room temperature to avoid precipitation and inactivation (the lifespan of the solution is 1–2 years); fill each 50 ml tube aseptically with 5 ml of the solution.
- Sanitary paper, cotton, labels, adhesive/duct tape, plastic bags, plasticized envelopes, cardboard cartons.
- **Preparation**
- Discontinue all anti-tuberculosis drugs for 1–2 days.
- Provide the patient with two 50 ml Falcon® tubes containing 5 ml of CPC solution (see below for details) and ask him to collect a sputum sample in the morning.
- Ensure that the tubes are hermetically sealed without using excessive force to avoid cracking the cap.
- Shake slowly and gently to mix the sputum with the CPC solution.
- Label the tube and give a unique number to each label (leukoplast-type adhesive label or coated paper covered by transparent adhesive tapes); do not write on the tube with an indelible marker pen as writings may come off with the chemicals used in the laboratory.

- Record data in a register with the sample identification number and details about the patient; to create an ID number for each sample, the code of the town (e.g., RAB), the year (e.g., 17) and the sequential number of the laboratory register (e.g., 001) could be used, with the extension "A" or "B" to indicate samples from the same patient collected on 2 successive days. These numbers should never be used again; if other samples are later collected from the same patient, they should have different ID numbers.

- Always preserve the tubes with the CPC solution, regardless of whether with or without sputum, at room temperature (CPC crystallizes at low temperatures).

- **Packaging**

- Wrap each tube separately in absorbent paper (tissue paper).

- Completely wrap the tubes in cotton.

- Place the tubes in a strong plastic envelope and hermetically flame-seal it; Ziploc bags may also be used.

- Place the envelope in a strong cardboard box and add absorbent material.

- Attach a list of samples (each with a unique ID number and the full name of the patient) to the package after having first placed the samples in a plastic bag.

- Hermetically seal the box with adhesive tape and stick the address label on the box.

- **Transport**

- Samples should ideally be delivered within a maximum period of 10 days after collection; avoid exceeding 4 weeks since then few or no viable acid-fast bacilli (AFB) will remain.

- The most rapid means of transport should be used to send the tubes.

- **c) For culture in liquid medium or agar**

CPC or other detergent-type antiseptic substances are not suitable for transporting sputum if culture is performed in liquid medium (7H9 medium, as in the case of automated MGIT™) or on agar-based solid medium (Middlebrook media). The product remains active and bacilli growth is inhibited. It should be noted that Ziehl-Neelsen and auramine staining of sputum transported in CPC often yields false-negative results. Smear microscopy of such samples on arrival at the reference laboratory is of little or no use and should never be used for diagnosis if a site laboratory result obtained directly from sputum is available.

Samples intended for liquid or agar culture should be transported and processed rapidly and refrigerated (cold chain). Optimal results are only possible with samples that are processed immediately after collection in the laboratory. The longer the period required for transportation and the lower the number of bacilli at the beginning, the poorer the results are likely to be – either due to the excessively high rate of soft decontamination (for example, when the standard 1% NaCl-NaOH is used) or due to the large number of false-negatives in case of hard decontamination (for example, when Petroff's method is used for a long time). A double dose of the PANTA™ antibiotic mix (polymyxin B, amphotericin B, nalidixic acid, trimethoprim, azlocillin; BD, Sparks, MD, USA) or Selectatabs™ (Mitchison's method) if added to the medium may help reduce contamination without excessively affecting the decontamination technique.

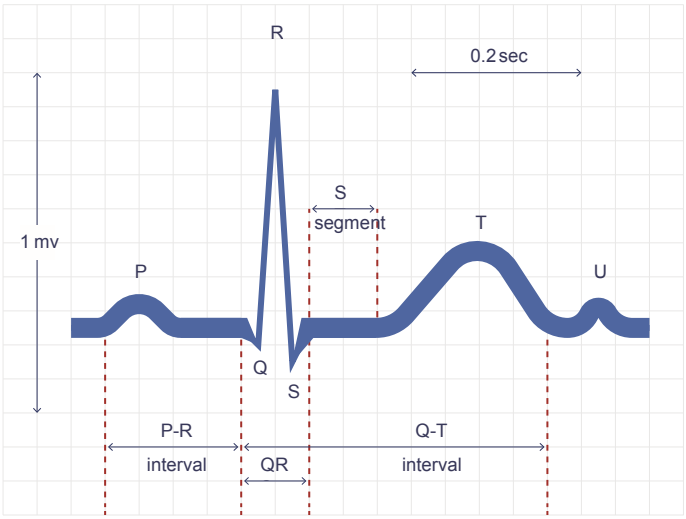
ANNEX 6: QT INTERVAL AND QTC: DEFINITION, MEASUREMENT AND CLINICAL IMPLICATIONS

- **QT interval**

- The QT interval is the ECG trace which begins at the start of the Q wave and terminates at the end of the T wave.

- The QT interval measures the time necessary for the ventricle to depolarise and repolarise.

- It is measured in seconds (s).



- **Characteristics and features of the QT interval**

- The QT interval varies in duration from one lead to another and may last up to 50 ms in healthy individuals. It is longer in V2 and V3 precordial leads.

- The QT interval can vary in the same individual by up to 75 ms on the same day.

- Several physiological conditions may affect the duration of the QT interval:

sleep, the prone position, standing upright or orthostasis, etc.

- **Risk factors for QT lengthening**

- Female sex.

- Elderly people.

- Cardiac pathologies (hypertrophy, heart failure, ischaemia etc.).

- Hypothyroidism.

- **Hypokalaemia,** hypomagnesaemia, hypocalcaemia.

- **Drugs that prolong and extend the QT interval (anti-tuberculosis drugs and drugs used to manage AEs: Mfx, Bdq, Dlm, Cfz and ondansetron at high dose).**
- Bradycardia.
- Use of diuretics (furosemide and thiazides).
- Medical history of congenital long QT syndrome.
- HIV.

The QT interval is inversely proportional to heart rate.

- The QT interval becomes shorter in case of rapid heart rate.
- The QT interval lengthens in case of slow heart rate.

Why should the QT interval be corrected?

- The corrected QT interval (QTc) estimates the QT value at a heart rate of 60 beats per minute (bpm).
- This enables the comparison of QT values at different heart rates and improves the detection of patients with an increased risk of cardiac arrhythmias.

What is the importance of the QTc?

A prolongation of the QTc signifies that the heart muscle takes longer than normal to repolarise between contractions.

- Increased risk of arrhythmia (torsade de pointe) = syncope, sudden death.

What does QTc prolongation signify?

- Normal QTc is <450 ms in men and <470 ms in women.
- QTc is said to be prolonged when it reaches >500 ms in both men and women.

A prolonged QTc does not always indicate heart failure/cardiac disorder but is a risk factor for arrhythmia (torsade de pointe) and may lead to syncope and sudden death. This is why some anti-tuberculosis drugs (Mfx, Cfz, Bdq, Dlm) are contraindicated in case of prolonged QTc.

- **Measurement of the QTc**

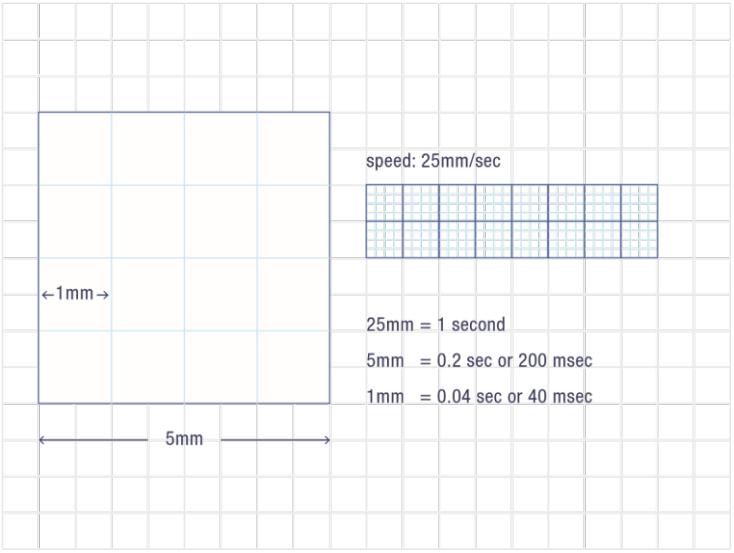
Most ECG machines automatically measure the QT interval and the corrected QT (QTc). However, these measurements are not always reliable due to several reasons: algorithms used for the calculation differ among manufacturers; it is difficult to interpret the T and U waves; and the formula used is not always specified (Bazett's formula is widely used. It may over-correct or under-correct QTc according to heart rates).

This is why it is important to know how to measure and calculate QTc manually.

- **Step 1: measuring the QT interval**
- Measure the QT interval in lead II, V5 or V6, as these show more clearly the end of the T wave.
- Several intervals (3–5) should be measured. The longest space should be taken into consideration.
- Measurement of the QT interval (in seconds): count the number of small squares from the beginning of the QRS complex up to the end of the T wave. Each square represents 0.04 s, if we assume the scroll speed to be 25 mm/s as usual.

· 1 small square = 1 mm = 0.04 s (or 40 ms)

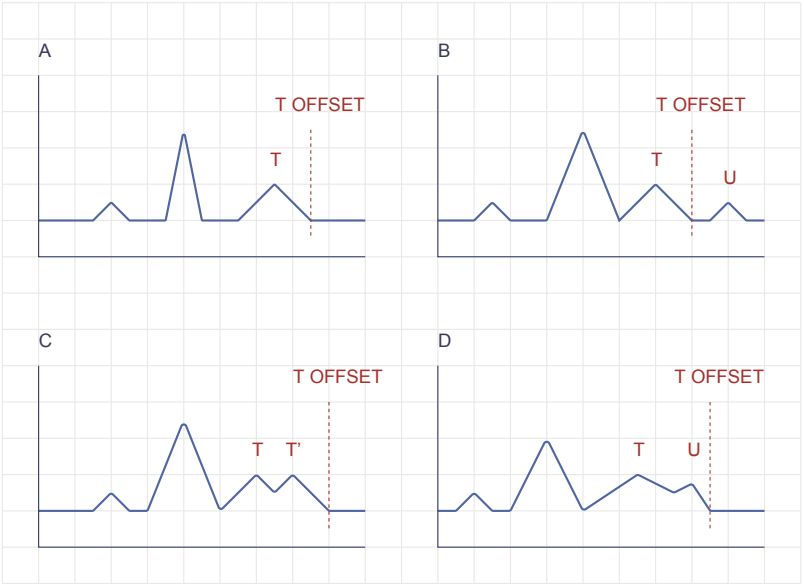
· QT (s) = number of squares x 0.04



- **U waves**

- Small U waves that are distinct from the T wave should not be measured; large U waves (>1 mm) that are merged with the T wave should be included in the QT measurement.

- Hypokalaemia causes an apparent lengthening of the QT interval due to the merging of T and U waves, with the U waves evident in precordial leads.



A) T wave: measure QT interval at the end of the T wave.

B) Small U wave distinct from the T wave: measure the QT interval at the end of the T wave C) Dysphasic T wave (same morphology): measure QT interval at the end of the T' wave.

D) U wave merged with the T wave: measure QT interval at the end of the U wave.

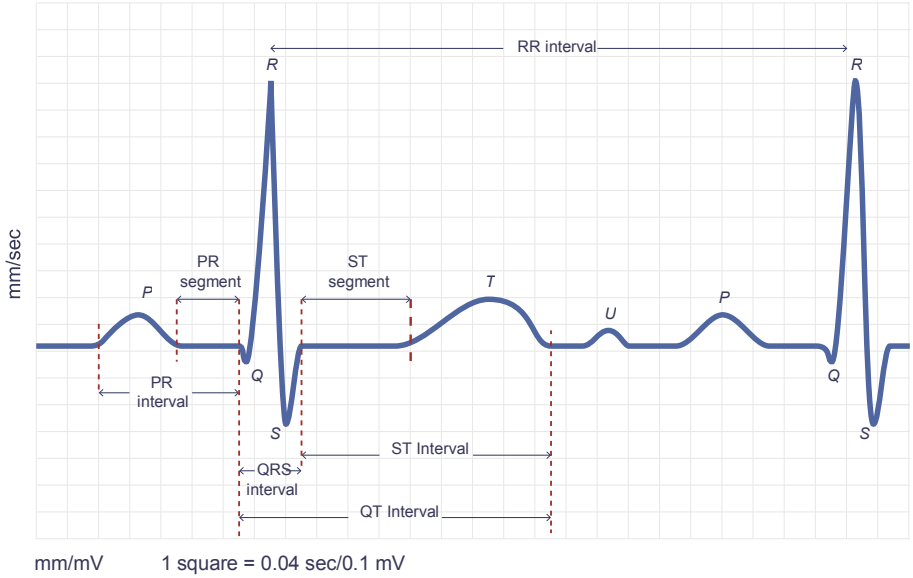
- **Step 2: how to measure the R-R interval**

- The R-R interval corresponds to the time elapsed between an R wave and the following one (duration of the R-R cycle).

- The R-R interval measures the time elapsed between one depolarization and another.

- It is measured in seconds (s).

- Several successive cycles (3 to 5) should be measured. The shortest interval should be taken into consideration.



- Measurement of the R-R interval (in seconds): count the number of small squares between the first R wave and the following one. Each square represents 0.04 seconds, assuming the chart scroll speed to be 25 mm/sec as usual.

· 1 small square = 1 mm = 0.04 s (or 40 ms)

· R-R (s) = number of small squares x 0.04

- **Step 3: How to calculate QTc**

The Framingham formula is reliable and used to calculate QT interval correction.

$QT_{cFra}(s) = QT + 0.154\ [1\text{-}RR(s)]$

- QT interval: distance between the start of the QRS complex and the end of the T wave in seconds (number of small squares x 0.04).

- R-R: distance between two R waves: R et R' in seconds (number of small squares x 0.04).

- $QT_{cFra}(s)$ x 1,000 = $QT_{cFra}(ms)$.

The Fridericia formula is also reliable and used to calculate QT interval correction.

$QT_{cF}(s) = QT/\sqrt[3]{RR}$

ANNEX 7: AUDIOMETRY: DESCRIPTION, MEASUREMENT AND CLINICAL IMPLICATIONS

Monitoring of hearing loss is important for two reasons:

- With early detection, it is possible to reduce the dose or discontinue use of the drug responsible, thus preventing further hearing loss.
- If hearing loss is significant, hearing aids should be provided for the patients.

There are three types of hearing loss:

- Conductive hearing loss: damage to the external ear (usually a blocked canal, for example, earwax blockage), or damage to the middle ear (otitis, ossicle damage, etc.).
- Neurosensorial hearing loss: dysfunction of the internal ear (cochlea), which generally results in damage to hair cells or the auditory nerve. **In MDR-TB treatment, the use of second-line injectable drugs can cause this type of hearing loss**.
- Mixed hearing loss: a combination of conductive hearing loss and neurosensorial loss.

The first step in the detection of auditory disorders is to eliminate the possibility of conductive hearing loss by examining the ear canal with an otoscope.

The second step consists of carrying out an audiometry.

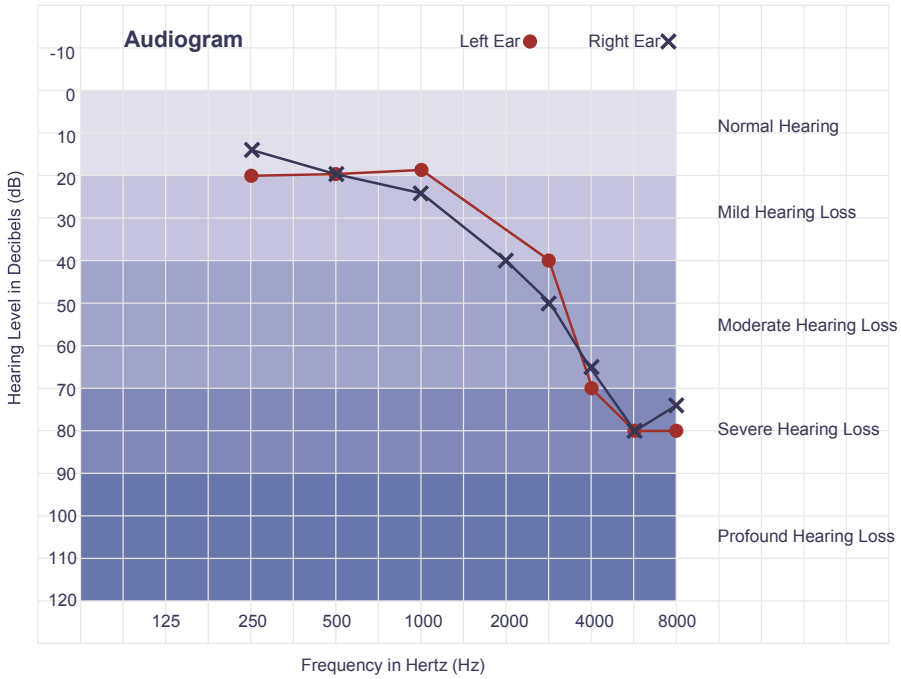
Audiometry:

- This test involves playing a pure frequency sound (measured in Hertz, Hz) at an intensity (measured in decibels, dB) with increasing loudness to determine at which intensity the patient is able to hear.
- An audiometry is carried out by using an electronic device called an audiometer.

Desirable characteristics and features of the audiometer:

- Frequencies between 125 and 8,000 Hz.
- Powered by (A/C) mains electricity and by batteries.
- Clear tone of sounds to avoid the need for a soundproof booth. An ordinary silent room should suffice.

- Easy for both the patient and the health care worker to use, so training can be kept to a minimum.



- An audiogram is a graph on which the audiometry results are plotted.
- It shows the lowest sound that an individual can hear at specific frequencies from the lowest to the highest.

- **Measurement of hearing loss**

- Average hearing loss (AHL) is calculated for each ear at frequencies of 500, 1,000, 2,000 and 4,000 Hz.

$$AHL = \frac{HL500Hz+HL1,000HZ+HL2,000Hz+HL4,000Hz}{4}$$

- Round up the AHL to the upper bound.
- Consider the worst hearing ear to grade the loss.
- Determine the degree of AHL according to the rating scale for AEs.

Grade 1: Mild	*Grade 2: Moderate*	*Grade 3: Severe*	*Grade 4: Profound*
Mild deficit: 21–40 dB	Moderate deficit: 40–70 dB 1st degree: 41–55 dB 2nd degree: 56–70 dB	Severe deficit: 70–90 dB 1st degree: 71–80 dB 2nd degree: 81–90 dB	Profound deficit: >90 dB 1st degree: 91–100 dB 2nd degree: 101–110 dB 3rd degree: 111–120 dB
Speech perceived if the voice is normal. Difficulty in perceiving low intensity sounds and soft voices.	Difficulty in perceiving even loud sounds and loud voices. Provide hearing aids.	Words only heard when shouted in the ear. Provide hearing aids.	Words cannot be understood at all. Only very loud noises are heard.

-

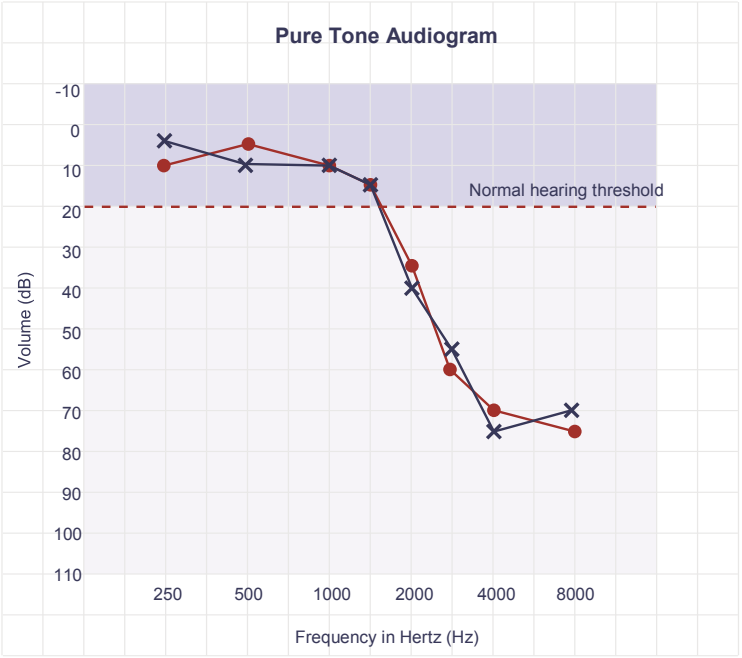
- **Practical example:** Hearing loss

Frequency (Hz)	*Right ear (dB)*	*Left ear (dB)*
500	30	55
1,000	50	65
2,000	65	70
4,000	65	75
Average hearing loss	53*	67°

*52.5 dB rounded to 53

°66.25 dB rounded to 67

- AHL in the ear with poorer hearing: 67 dB (left ear)
- Degree of loss: D2 (second band).



Sample audiogram

Ministério da Saúde

END TB

World Health Organization

Timor-Leste