Republic of Namibia
Ministry of Health and Social Services

National Guidelines for the Management of Tuberculosis

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Division: Health Sector Response
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Third Edition

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Vision[1]:

A Namibia where tuberculosis and leprosy are no longer a public health threat.

Mission statement

Provision of high quality tuberculosis and leprosy prevention, diagnosis, treatment and care services with focus on universal access, equity for all those at risk and responsiveness to emerging challenges in the context of the Namibia Ministry of Health and Social Services Strategic Plan 2009-2013 and the Millennium Development Goals.

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[1] Second Medium-term Strategic Plan for Tuberculosis and Leprosy, 2010-2015

TABLE OF CONTENTS

TABLE OF FIGURES

LIST OF TABLES

LIST OF APPENDICES

LIST OF RECORDING AND REPORTING TOOLS FOR TUBERCULOSIS

PREFACE

Among all infectious and curable diseases worldwide, tuberculosis (TB) is the commonest cause of death. Despite recent decreases in the number of notified cases, Namibia still has an alarmingly high TB burden, reporting 12,625 TB patients in 2010. This is equivalent to a case notification rate (CNR) of 589 cases per 100,000 population, one of the highest in the world. In 2009 alone 1,044 people were reported to have died while on TB treatment.

Despite a significant progress in ensuring that TB patients successfully complete treatment, an increasing number of patients are becoming difficult to cure on standard treatment because they have developed multidrug-resistant tuberculosis (MDR-TB). This form of TB has become the greatest threat to the achievement of global and national TB control targets.

In 1995, the Ministry of Health and Social Services released the first *National Guidelines for the Management of Tuberculosis,* which was followed by the second edition published in 2006. There have since been numerous developments in the TB epidemic in the country as well as in approaches to TB control, necessitating revision of the guidelines to address peculiarities of the country's TB epidemic.

This third edition of the guidelines provides updates based on new knowledge and lessons learnt during nationwide implementation of TB control initiatives. The areas that have received particular attention include TB infection control, programmatic management of drug-resistant TB (PMDT), TB diagnostics, paediatric TB and advocacy, communication and social mobilisation (ACSM) for TB control. There has been a revision of the TB/HIV section to reflect the latest WHO guidelines on TB/HIV co-management as well as to be in line with the 2010 edition of the *National Guidelines for Antiretroviral Therapy*. Consequently, the monitoring and evaluation tools were also revised.

The *National Guidelines for the Management of Tuberculosis* include information gathered from various stakeholders as well as various international publications, in particular the WHO's fourth edition of the *Tuberculosis Treatment Guidelines*. They are intended for use by all health care workers involved in the management of TB suspects and patients. The technical staff at the national and regional levels will be responsible for ensuring adherence to these guidelines through orientation, training and supervision. It is my sincere hope that the guidelines will provide the needed guidance in management and control of TB in Namibia.

I wish to thank all those who contributed to the revision of this document, in particular Dr Farai Mavhunga; Ms Getrude Platt; Dr Nunurai Ruswa, Ms Naita Nashilongo, Ms Helena Mungunda, Ms Hilma Ipinge, Ms Penny Uukunde and Ms Benetha Bayer; Dr Panganai Dhliwayo, Dr Omer Ahmed Omer and Dr Abbas Zezai, Ms Rosalia Indongo, Dr Laura Brandt, Dr Edwin Sithole, Ms Miriam Kasanda, Dr Desta Tiruneh, Mr Souleymane Sawadogo, Ms Selma Shiyamba, Mr Qamar Niaz, Mr Christopher Ntege, Mr Robert Chana Chipchet, Ms Dawn Pereko, and Mr Francis Kalemeera, as well as all the health care workers who contributed to the revision. Lastly I would like to express my appreciation for the financial support from United States Agency for International Development (USAID) for supporting the printing of these guidelines.

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Mr K. K. Kahuure

Permanent Secretary

LIST OF ABBREVIATIONS

ACSM	advocacy, communication and social mobilisation
AFB	acid-fast bacilli
AIDS	acquired immune-deficiency syndrome
Am	amikacin
Amx/Clv	amoxicillin/clavulanate
ART	antiretroviral therapy
ARV	antiretroviral (medicine)
BCC	behaviour-change communication
CB-DOT	community-based directly observed treatment
CCRC	Central Clinical Review Council of the NTLP
CDC	United States Centres for Disease Control and Prevention
Cfx	ciprofloxacin
Cfz	clofazimine
CHPA	Chief Health Programme Administrator
Clr	clarithromycin
Cm	capreomycin
CMO	Chief Medical Officer
CMS	central medical stores
CPT	co-trimoxazole preventive therapy
CrCl	(renal) creatinine clearance
Cs	cycloserine
DCC	District Coordination Committee
DM	direct microscopy
DOT	directly-observed treatment
DOTS	directly observed treatment - short course (WHO strategy)
DSP	Directorate of Special Programmes
DST	drug susceptibility testing
DTLC	District Tuberculosis and Leprosy Coordinator
E	ethambutol
ESR	erythrocyte sedimentation rate
Eto	ethionamide
FDC	fixed-dose combination
FLD	first line (anti-TB) drugs (or medicines)
GFATM	Global Fund to fight AIDS, TB and Malaria
GLC	Green Light Committee
GRN	Government of the Republic of Namibia
H	isoniazid
HAART	highly active anti-retroviral therapy
HCT	HIV counselling and testing
HIV	human immunodeficiency virus
IEC	information, education and communication
Ipm/Cln	imipenem/cilastatin
IPT	isoniazid preventive therapy
ITECH	International Training and Education Centre for Health
IUATLD	International Union against Tuberculosis and Lung Disease (The Union)

KAP	knowledge, attitude, practices
Km	kanamycin
KNCV	*Koninklijke Nederlandse Centrale Vereniging* (Royal Dutch Tuberculosis Association)
Lfx	levofloxacin
Lzd	linezolid
MDR-TB	multi-drug-resistant tuberculosis
Mfx	moxifloxacin
MOTT	mycobacteria other than tuberculosis
MTP-I	First Medium Term Plan (for TB)
MTP-II	Second Medium Term Plan (for TB and leprosy)
MoHSS	Ministry of Health and Social Services
NGO	non-governmental organisation
NIP	Namibia Institute of Pathology
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NTLP	National Tuberculosis and Leprosy Programme
Ofx	ofloxacin
OR	operational research
PAS	para-aminosalicylic acid
PHC	primary health care
PLHIV	People Living with HIV
PCP	pneumocystis pneumonia
PTB	pulmonary tuberculosis
R	rifampicin
RACOC	Regional Aids Coordinating Committee
RMT	Regional Management Team
RTLC	Regional Tuberculosis and Leprosy Coordinator
S	streptomycin
SAT	self-administered treatment
SLD	second line (anti-TB) drugs/medicines
STI	sexually transmitted infection
TB	tuberculosis
TIPC	Therapeutics Information and Pharmaco-Vigilance Centre
UNAM	University of Namibia
USAID	United States Agency for International Development
VCT	voluntary counselling and testing (for HIV)
WHO	World Health Organisation
Z	pyrazinamide

1 INTRODUCTION

1.1 The National Tuberculosis and Leprosy Programme (NTLP)

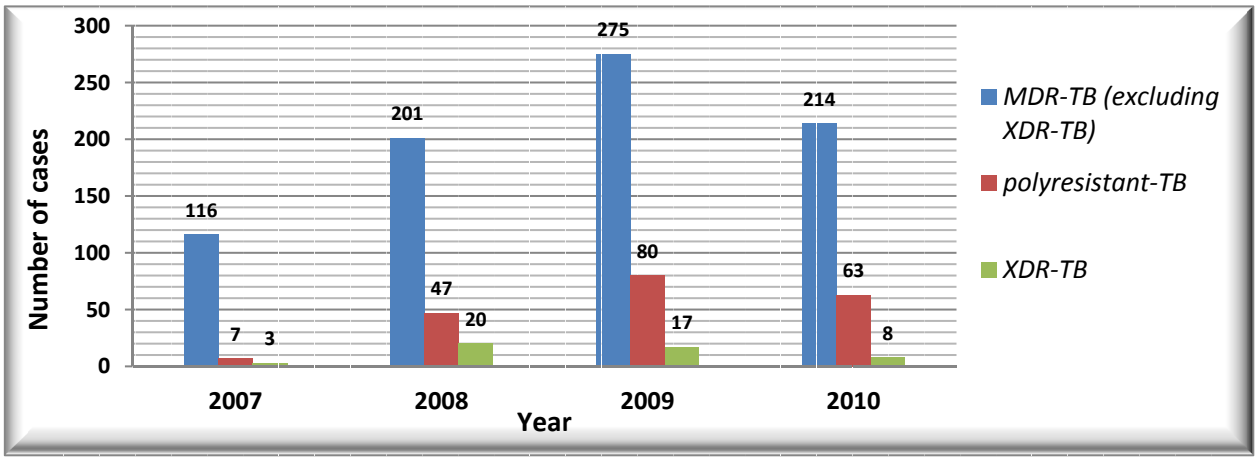
A national programme for the control of tuberculosis (TB) and leprosy was established in 1991 under the Primary Health Care (PHC) directorate, and was moved to the Directorate of Special Programmes (DSP) upon the latter's formation in 2004. The first edition of the *National Guidelines for the Management of Tuberculosis* was published in 1995, followed by the second edition in 2006. An evaluation of the implementation of the first medium-term plan for tuberculosis (TB MTP-I) was conducted in 2009, leading to the development of the second medium-term plan for TB and leprosy (TBL MTP-II, 2010-2015). These guidelines will therefore be implemented within the framework of TBL MTP-II.

1.2 Burden of tuberculosis

Namibia has one of the highest case notification rates (CNR) of TB in the world ((WHO Report 2009). 12,625 cases of TB were notified in 2010, equivalent to a CNR of 589/100,000 population. The high case load is attributed mainly to the HIV epidemic as reflected by an HIV prevalence of 18.8% among ante-natal clinic attendees (MoHSS, 2010) and an HIV prevalence rate of 56% among TB patients (MoHSS, 2011). The distribution of the TB burden varies by region, with the most affected regions as of 2010 being Khomas and Kavango (MoHSS, 2011).

An increase in the number of notified cases of drug-resistant TB (DR-TB) has been noted since 2007 when the country began to systematically record and report these cases as shown in *Figure 1* below.

Figure 1: Drug-resistant TB in Namibia 2007-2010



1.3 TB and HIV

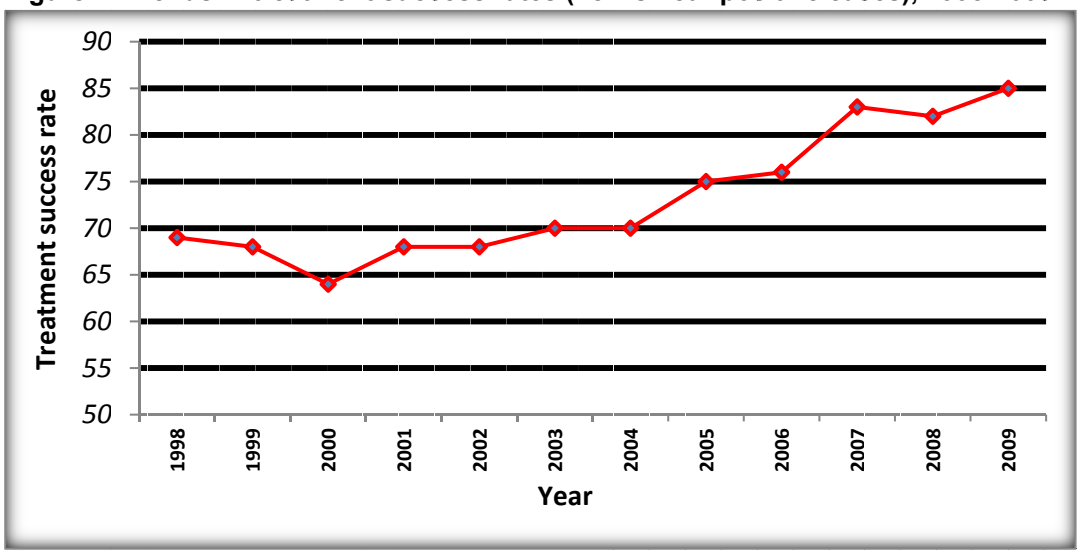
TB is a leading killer of people living with HIV (PLHIV) (WHO, 2006), and 56% of TB patients notified in Namibia in 2010 were co-infected with HIV (MoHSS, 2011). HIV and TB care therefore need to be integrated especially at the service provision level to ensure comprehensive care for co-infected patients. All TB patients should know their HIV status and should receive appropriate HIV care and treatment, including antiretroviral therapy (ART). Conversely all PLHIV should be routinely screened for TB.

1.4 Treatment outcomes

A treatment success rate of 85% of the detected infectious cases is an important yardstick adopted for TB control by the World Health Assembly in 1993. The target has however since been revised to 90%. The treatment success rate for new smear positive cases in Namibia has been on the increase since 2005 (Figure 2) and was 85% for the patients commenced on treatment in 2008. There is

therefore need to intensify efforts to ensure that the country surpasses the 90% target by minimising unfavourable treatment outcomes such as treatment default and "transfer out".

Figure 2: Trends in treatment success rates (new smear positive cases), 1998-2009.



2 ORGANISATION AND PROGRAMME MANAGEMENT

2.1 Structure of the National Tuberculosis and Leprosy Programme (NTLP)

The health sector reforms implemented since Namibia's independence in 1991 have led to increased decentralisation and integration of public health services. At the service level, TB and leprosy programme activities are fully integrated as nurses and doctors undertake the core functions of diagnosis and treatment. Structurally, NTLP activities are implemented through a decentralised system at national, regional, district and community levels.

2.1.1 National level

The MoHSS through the Directorate of Special Programmes (DSP) is responsible for the overall coordination, implementation, monitoring and evaluation of TB and leprosy control. The directorate is headed by a director and its two divisions (Health Sector Response and National AIDS Coordination Programme Secretariat) are each headed by a deputy director. The Health Sector Response division comprises three sub-divisions: National HIV/AIDS and STI Programme, National Tuberculosis and Leprosy Programme and National Vector-borne Disease Control Programme. Each of these sub-divisions is headed by a Chief Medical Officer (CMO) assisted by a Chief Health Programme Administrator (CHPA) and varying numbers of Senior Health Programme Administrators (SHPA).

2.1.2 Regional Level

The Regional Management Team (RMT) is responsible for the coordination of TB control at regional level, and for supporting and overseeing TB control activities at district level. In each of the thirteen regions a CHPA and SHPA are appointed in the Special Disease Programmes division to provide support to the regional CMO in the implementation of the major communicable public health diseases. The SHPA assigned to TB and leprosy activities is functionally referred to as the Regional TB and Leprosy Coordinator (RTLC).

Medical doctors are responsible for diagnosis of complicated forms of TB, including sputum-smear negative and extra-pulmonary TB. They should also provide leadership to the clinical team in case management as well as providing technical support to the District TB and Leprosy Coordinator (DTLC). All regions should designate a facility for the management of drug-resistant TB (DR-TB) and other complicated TB cases to ensure coordinated case management as well as adequate capacity building. Since management of DR-TB is very complicated and demanding, these facilities should preferably be staffed with health workers whose main responsibility is the management of these cases.

2.1.3 District level

2.1.3.1 District Coordinating Committee (DCC)

The District Coordinating Committee (DCC) is responsible for overall health planning, coordination, management and implementation in each district, including TB control activities in both the public and private sector. The coordination and implementation of TB control activities is overseen by the Principal Medical Officer (PMO) with the support of the Primary Health Care (PHC) supervisor and the District TB and Leprosy Coordinator.

2.1.3.2 District hospitals

Medical doctors and nurses at district hospitals diagnose, treat and admit TB patients where necessary. These officers should routinely undergo training in management of TB, including TB/HIV co-infection.

2.1.3.3 Health centres and clinics

Health centres and clinics are managed by registered or enrolled nurses and serve as the primary gateway to health care. Doctors from the district hospitals conduct clinics on specific days, and patients with complicated TB should also be reviewed during these clinics. Nurses at this level should receive training on TB since most TB suspects will be identified and managed at this level.

2.1.3.4 Outreach teams

Outreach teams should be trained and competent in the identification and management of uncomplicated TB. The teams should screen patients who visit the mobile clinic with signs and symptoms of TB. Patients already on treatment should be followed up as appropriate. Treatment interrupters and defaulters should be traced and managed accordingly. Health education should be given during these outreach visits.

2.1.3.5 School health services

School health teams provide essential health services and should be competent in identification of TB suspects among school children. Children already on treatment can be followed up by the school health team in collaboration with teachers. The school health teams are also responsible for health education on TB, among other health conditions, and should sensitise teachers and learners on the importance of early diagnosis and treatment.

2.1.3.6 Environmental health staff

The environmental health officers and assistants as well as health inspectors should be an integral component of the TB programme in every district. They should take the lead in contact and defaulter tracing as well as in the implementation of household infection control measures.

2.1.3.7 Local authorities and Regional Councils

The regional councils and local authorities have established various structures and activities for HIV that could be very beneficial to TB patients by providing community health education. The inclusion of community based DOT in existing home based care programmes will enhance treatment adherence. Advocacy, education and treatment of TB can therefore be delivered by various stakeholders who are RACOC members with an expansion of their terms of reference to include TB activities.

2.1.3.8 Non-governmental Organisations (NGOs)

NGOs will complement the role of the MoHSS in providing the continuum of care required for bringing a patient to cure or treatment completion. Their activities will mainly focus on providing treatment support, including directly-observed treatment (DOT) as well as providing other supportive measures to facilitate patients' treatment and rehabilitation. The NTLP should play a central role in the coordination of community tuberculosis care.

2.1.3.9 Private sector

The private sector offers health services at various levels. Currently the notification of cases of TB by the private sector is variable. There is, therefore need to strengthen public-private collaboration in diagnosis, treatment and notification of TB based on the NTLP treatment guidelines, as well as to enforce the existing regulations regarding notifiable diseases in the country.

2.1.4 Community level

The community plays an important role in TB control by identifying and referring symptomatic patients. Community-based organisations, especially home-based care organisations, should play an important role as they care for PLHIV and their families, who are at high risk of developing TB. The expansion of

community TB care has contributed to the decrease in default rates from 17% in 2000 to 4% in 2009. Critical to this success is the recruitment of field promoters who complement the role of nurses and ensure a continuum of care from TB diagnosis to cure or treatment completion.

Traditional healers should be engaged and trained to identify and refer patients with TB signs and symptoms, as well as to provide support to TB patients.

2.2 Collaboration and coordination

2.2.1 Inter-programme, inter-divisional and coordination within the health sector

The NTLP and the HIV/AIDS and STI Programme acknowledge the necessity to collaborate closely at all levels in providing care to PLHIV and patients with TB, as in many instances the two diseases affect the same patient. The mainstreaming of TB activities in HIV planning and management and that of HIV in TB planning and implementation are reflected in the *National Strategic Framework for HIV and AIDS Response in Namibia 2010/11-2015/16* and the *Second Medium Term Strategic Plan (MTP-II) for Tuberculosis and Leprosy 2010-2015,* respectively. The NTLP collaborates closely with NGOs and other sectors already active in HIV prevention, care and support activities in the implementation of TB/HIV collaborative activities.

Additionally the NTLP collaborates with:

- Namibia Institute of Pathology (NIP) in order to ensure well-coordinated, accessible and quality-assured TB laboratory services.
- Division Pharmaceutical Services in the MoHSS to ensure an uninterrupted supply of quality assured anti-TB medicines

2.2.2 Multi-sectoral Collaboration

TB disproportionately affects sectors such as prisons and fishing, farming and mining industries, among others. These sectors have crowded living or working conditions which favour the transmission of TB. Productivity of the workforce may be hampered by long absences from work by those with TB disease. In order to facilitate the coordination and mainstreaming of TB in the health policy of above-mentioned sectors, terms of reference for TB should be added to the existing multi-sectoral coordinating structures in place for HIV.

2.2.3 International Collaboration

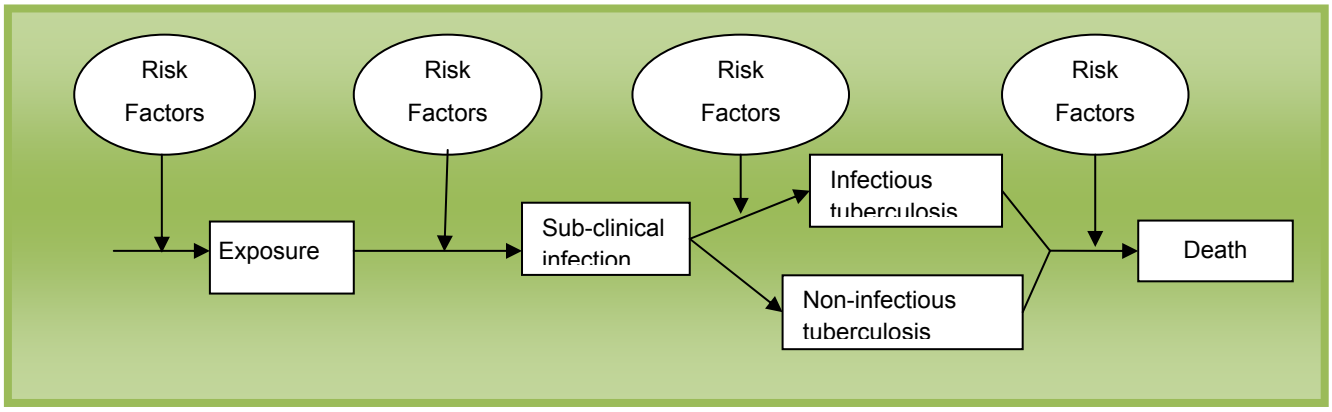
The NTLP collaborates with various international technical and funding agencies including WHO, KNCV Tuberculosis Foundation, USAID, CDC, ITECH, GLC and The Union. The NTLP shall continue to engage these partners and seek new partnerships whenever necessary.

3 PRINCIPLES OF TUBERCULOSIS CONTROL

3.1 Drivers of the TB epidemic

Risk factors for the transmission of TB at population level include poor living and working conditions, and factors that impair the host's immune system, such as HIV infection, malnutrition, smoking, diabetes, alcohol abuse and indoor air pollution. Addressing these factors in their totality is therefore crucial to achieving the goal of eliminating TB as a public health problem in Namibia. Figure 3 below outlines the model of TB epidemiology, taking into account the risk factors at the various stages of the infection-to-disease continuum.

Figure 3: Model for tuberculosis epidemiology



The most important risk factors for TB transmission are summarised in *Table 1* below.

Table 1: Main risk factors for the spread and burden of TB

RISKS RELATED TO:	RISK FACTORS
1. Exposure	• Population density • Family size • Differences in climatic conditions • Age of sources of infection
2. Sub-clinical infection	• Airborne transmission through infectious droplet nuclei • Characteristics of the infectious patients • Air circulation and ventilation • Reducing expulsion of infectious material from source cases • Host immune response • Other modes of transmission: *M.bovis*
3. TB disease	• HIV infection • Age • Genetic factors • Environmental factors • Medical conditions (diabetes mellitus) • Pregnancy • Re-infection
4. Death	• Site of TB • Type of TB • Timeliness of diagnosis • HIV co-infection, AIDS

3.2 The DOTS strategy

Namibia has adopted the WHO's Directly Observed Treatment Short Course (DOTS) strategy which is the most cost-effective public health approach to fight TB. The five elements of the DOTS Strategy are summarised in Box 1 below.

Box 1: Elements of the DOTS Strategy

1	Sustained political commitment to TB control, expressed in terms of adequate human and financial resources;
2	Access to quality-assured network of sputum smear microscopy
3	Standardised short-course chemotherapy for all cases of TB under proper case management conditions, including directly observed treatment
4	Uninterrupted supply of quality-assured anti-TB medicines;
5	Recording and reporting system enabling treatment outcome assessment of all patients and assessment of overall programme performance

Key features of a successful DOTS programme are:

- A strong and competent central (or national level) unit
- Documents on policy and treatment guidelines available and implemented at each health unit
- A reporting and recording system using standardised registers
- A human resource development programme
- A nationwide network of laboratory diagnostics services, including sputum smear microscopy accessible to patients in the primary health care services and subject to regular quality control
- Regular supply of medicines and diagnostic materials
- Supervision for TB control at all levels in the health system
- A long-term programme development plan with budget details, funding sources and responsibilities.

3.2.1 Directly Observed Treatment (DOT)

The most reliable measure to ensure that patients take their medicines as prescribed is DOT. DOT means that TB patients swallow their TB medicines in the presence of another person observing them swallowing the medicines. The person who is the observer is called a DOT supporter because psychological support is crucial for DOT. The DOT supporter can be a health care worker or any other person who has assumed co-responsibility for the TB treatment of the patient for the entire treatment period. DOT must be provided in a patient-friendly and supportive manner, preferably by the same person throughout treatment.

Frequent rotation of health care workers in the health facilities and TB clinics is *not* good practice for ensuring proper case management and implementation of TB infection control. Health care workers trained and interested in working with TB patients should be encouraged to continue working in the TB clinic for prolonged periods of time. This will enhance patient adherence, reduce treatment interruption and improve treatment success rates. Provision of TB services requires a compassionate attitude, very good personal communication skills, and a thorough knowledge of TB treatment issues.

3.3 Beyond DOTS - The Stop TB strategy

In 2006, at the World Economic Forum in Switzerland, the Global Plan to Stop Tuberculosis was launched. The plan sets forth a roadmap for treating 50 million people for TB and enrolling 3 million patients who have both TB and HIV on antiretroviral therapy by 2015. It aims to halve TB prevalence and deaths compared with 1990 levels by 2015. The treatment success rate target set in this plan is 90%. *Box 2* highlights the components of the Stop TB Strategy

Box 2: Components of the Stop TB Strategy

1. Pursue high-quality DOTS expansion and enhancement

a. Secure political commitment, with adequate and sustained financing
b. Ensure early case detection, and diagnosis through quality-assured bacteriology
c. Provide standardised treatment with supervision, and patient support
d. Ensure effective medicine supply and management
e. Monitor and evaluate performance and impact

2. Address TB-HIV, MDR-TB, and the needs of poor and vulnerable populations

- Scale-up collaborative TB/HIV activities
- Scale-up prevention and management of multidrug-resistant TB (MDR-TB)
- Address the needs of TB contacts, and of poor and vulnerable populations

3. Contribute to health system strengthening based on primary health care

- Help improve health policies, human resource development, financing, supplies, service delivery and information
- Strengthen infection control in health services, other congregate settings and households
- Upgrade laboratory networks, and implement the Practical Approach to Lung Health (PAL)
- Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health

4. Engage all care providers

- Involve all public, voluntary, corporate and private providers through Public-Private Mix (PPM) approaches
- Promote use of the International Standards for Tuberculosis Care (ISTC)

5. Empower people with TB, and communities through partnership

- Pursue advocacy, communication and social mobilisation
- Foster community participation in TB care
- Promote use of the Patients' Charter for Tuberculosis Care

6. Enable and promote research

- Conduct programme-based operational research, and introduce new tools into practice
- Advocate for and participate in research to develop new diagnostics, medicines and vaccines

3.4 NTLP supportive strategies

The core-strategies of TB control can only be achieved if supported by the following strategies:

3.4.1 Training

Health care workers need to be trained on NTLP technical guidelines. This training should include orientation for newly recruited health-care workers, as well as pre-and in-service training.

3.4.2 Patient education and information

Patients who fully understand their disease and its treatment are more likely to complete their treatment. Prior to starting treatment, the health care worker should always take some time and discuss with the patient the diagnosis and treatment.

3.4.3 Supervision

Supervision is a two-way process which aims to improve work performance through joint problem solving and positive reinforcement. Supervision is essential in maintaining quality services and also motivates the workforce. However, it is effective only when those receiving supervision stay long enough in their respective positions to implement the recommendations made during supervision.

3.4.4 Advocacy, communication and social mobilisation (ACSM)

Advocacy is the process of ensuring that adequate financial and material resources are available for TB control; and that TB is accorded its status among the country's priorities. Behaviour-change *communication* aims to change knowledge, attitudes and practices among various groups of people. It informs the public of the services that exist for diagnosis and treatment and relays a series of messages about the disease – such as "*get tested for TB if you have a cough for more than two weeks*", or "*if you are on TB treatment, complete it*". *Social mobilisation* brings together community members and other stakeholders to strengthen community participation for sustainability and self-reliance. Social mobilisation generates dialogue, negotiation and consensus among a range of players that includes decision-makers, the media, NGOs, opinion leaders, policy-makers, the private sector, professional associations, TB-patient networks and religious groups. Empowering TB patients and the affected communities helps to achieve timely diagnosis and treatment completion, especially among families of TB patients.

3.4.5 Planning

All staff working at national, regional and district level must be competent in planning in order to prioritise activities and mobilise funds available for programme activities. Planning should take into account the unique situations in different districts and regions; and should include review of the TB data in each locality so that plans are responsive to the challenges and needs of the local TB programme.

3.4.6 Collaboration and networking

Since its determinants are diverse, TB can therefore not be tackled by the MoHSS alone. TB control activities are fully integrated at the service delivery level, and because of the close association between TB and HIV, the MoHSS structures at all levels must always look for opportunities to mobilise all sectors and organisations working on health promotion and care in the communities and workplace.

3.4.7 Operational research

Operational research (OR) aims to establish how well a programme is performing, and compares the (cost-) effectiveness of different operational approaches. It exploits the benefits of a well-functioning routine recording and reporting system, or can include ad-hoc or complementary data collection for research purposes. OR can help the programme to decide on better (more effective or efficient) technical policies; more likely to achieve the programme's goals and objectives.

4 DIAGNOSIS OF TUBERCULOSIS

4.1 Introduction

Diagnosis of TB is usually simple when the person has pulmonary tuberculosis (PTB) and sputum smear microscopy is positive, or when culture for *M.tb* is positive. Bacteriological examination is the only reliable confirmation of presence of bacilli causing TB. In cases of extra-pulmonary TB and/or when sputum smears are negative, more investigations are needed to confirm TB disease. Adherence to TB medication is a heavy burden for the patient and his family in terms of costs, potential side-effects and stigma, hence the need to make an accurate diagnosis to avoid subjecting the patient to unnecessary treatment.

4.2 Mechanism of TB transmission and pathogenesis

In Namibia TB is almost always caused by *mycobacterium tuberculosis (M.tb);* infections caused by other mycobacteria are rare. *M.tb* is transmitted from an infectious patient primarily through coughing and is inhaled by the contact *(droplet transmission)*. The inhaled bacilli settle in the lung, and cause infection *(primary infection)*. In most cases, the bacilli are contained by the body's immune system and remain dormant for the rest of the person's life without any further consequences. The majority of infected people with intact immunity (90-95%) will never develop TB disease. Individuals with compromised immune systems (HIV infection, diabetes, malnutrition, *etc*) may develop TB disease at any point in their life.

Pulmonary tuberculosis (PTB) is the most frequent form (80%) of TB disease. This is also the most important form in public health due to its infectiousness. Patients with untreated sputum smear-positive PTB are highly infectious while those who present with smear negative PTB are less infectious. Sputum smear-positive TB is uncommon in younger children and, therefore small children are less infectious. Adult patients with sputum-smear positive PTB are thus the main sources of infection. Curing such patients is therefore the highest public health priority.

The tubercle bacilli can inhabit any organ of the body including the pleural cavity, lymph nodes, kidney, bladder, bone, meninges, skin, eyes, ovaries as well as skeletal, spinal and gastro-intestinal systems. TB presenting in other organs is mostly non-infectious and is referred to as extra-pulmonary tuberculosis (EPTB). Additionally, TB can be found in more than one organ in the same patient, including a combination of PTB and EPTB.

4.3 Pulmonary tuberculosis (PTB)

4.3.1 Medical History

The most common signs and symptoms of PTB are:

- Persistent cough for 2 weeks or more
- Haemoptysis (coughing up blood)
- Chest pain
- Night sweats
- Dyspnoea (shortness of breath)
- Loss of appetite
- Loss of weight

TB disease is much more likely in patients with these symptoms and who have a positive TB contact. The first step to diagnosis is taking a careful medical history when a patient presents with any of the above signs and symptoms. *Table 2* lists some of the important questions that each health worker should ask the patient.

Table 2: Important questions in history taking in a TB suspect

SIGN / SYMPTOM	QUESTIONS TO ASK	CONSIDERATIONS
Cough	How long have you been coughing?	All patients with a productive cough for 2 weeks or more are PTB suspects and must have their sputum examined for TB bacilli.
	Is the cough productive or dry?	Both are possible in TB, but usually it is productive.
	What is the colour of the sputum?	The colour is whitish, unless there is a secondary infection, or there is blood in the sputum.
Blood in the sputum	Is there blood in the sputum?	This is usually observed by the patient and causes a lot of anxiety.
Chest pain	Does it hurt only when you breathe?	This may point to inflammation of the pleura (pleurisy), lung infarction, or trauma.
	Where is the pain or where else does it hurt?	When it is not well defined, it is usually caused by inflammation and infiltration of the lung
Shortness of breath	How long have you had this?	If it is a long-standing problem, it might point to asthma, chronic obstructive pulmonary disease, anaemia etc. If it is of shorter duration, it may be caused by lung fibrosis, pleural effusion, pneumothorax, all possibly caused by TB.
	Does it occur when you exert yourself, climb stairs/hill?	If it is associated with exertion, it might be due to heart failure, or pericardial effusion. The latter is common in TB patients who are HIV positive.
Profuse sweating mostly at night	Since when have you had this?	Recurrent fever in TB occurs mostly at night, waking up the patient in a state of profuse sweating.
Loss of weight	When did you first notice this?	Usually for some weeks, and caused by the general malaise associated with TB disease leading to loss of appetite and increased metabolism.
Loss of appetite	When did you first notice this?	Usually for some weeks, and related to the general malaise associated with TB disease
Tiredness, weakness	When did you first notice this?	Usually long standing problem, associated with the general malaise of TB disease

4.3.2 Investigations

4.3.2.1 Sputum Smear Examination

The most specific and reliable evidence of TB disease is a positive culture of *M.tb*. Culture is expensive and the mycobacteria may take up to six weeks to grow and should therefore only be used according to the algorithms in ***Error! Not a valid bookmark self-reference.***, *Figure 5* and *Figure 6*. Direct microscopy is less expensive, quick, and highly specific and provides reliable evidence of mycobacteria in the lungs. Sputum smear microscopy is therefore an important investigation in the diagnosis of PTB and is the cornerstone of the DOTS strategy. All

adults and older children suspected of having PTB must provide sputum for smear examination. Young children are often unable to produce sputum because they cannot cough it up on request.

Collection of sputum sample

Whenever PTB is suspected, two sputum specimens must be collected for examination, within 24 hours (see *Box 3*). The healthcare worker attending to the patient should complete the sputum-smear request form for every sputum specimen. Similar details should be recorded in the *Sputum Examination Register* for monitoring purposes. The patient should be advised to come back to the health facility after a few days depending on how long the results usually take to be available at the health facility. The laboratory should communicate the results to the requesting clinician or health facility as soon as they are ready. This is especially urgent for positive smear results.

Box 3: Sputum sample collection in the ambulatory patient

Spot specimen

The patient is asked to produce a sputum specimen during the initial consultation; this is referred as a "*spot"* collection**.** The patient should be advised to rinse his/her mouth with water to prevent food particles from mixing with the sputum. Specimen collection should be carried out in a well-ventilated place, preferably outdoors. The health care worker should verify that the sample contains sputum and not saliva. The patient is then given a second sputum container to take home for collection of the *early morning* specimen.

Early morning specimen

As directed, immediately on waking up, the patient should cough up a specimen of sputum into the container and take it to the health facility. This is usually the specimen with the highest yield of TB bacilli.

Whenever PTB is suspected in an *in-patient*, sputum must be collected using the same spot-morning system as described above. The earlier the diagnosis is made the better the outcome for the patient and the less the transmission of TB in the health facility.

Box 4: The role of the health care worker in obtaining a good sputum specimen

A well instructed patient is the basis for a good sputum sample and sputum smear result

It is very important that health care workers instruct the patient on how to produce a deep cough for the purpose of getting real sputum from the lungs. Health care workers should verify that the sample produced is sputum and not saliva. Ideally health care workers should observe patients producing the sputum sample, while keeping sufficient distance when the patient coughs. If all has been done to get the best possible specimen this should be sent to the laboratory and examined. The laboratory should process all sputum samples received and should *not* dispose of any sputum specimen even when they think it is mostly saliva.

Reporting: Sputum smear results are reported by the presence of acid-fast bacilli (AFB) observed[2].

- Positive smear results: A patient with at least one acid fast bacillus (AFB+) in at least one sputum sample is considered a definite case of TB.
- Negative smear results: A patient with two negative sputum-smear results may not have PTB, or the patient may have *smear negative* PTB, or EPTB. Some reasons for the smear negative sputum results in PTB patients include:
  - Early stage of PTB, with no cavities

[2] Acid-fast bacilli. All mycobacteria are acid fast. This means that they do not lose their colour when exposed to acid during the staining process. This makes them stand out in the colour red, against a blue or green background, easy to observe for the microscopist. Because *M.tb* is the most common mycobacterium causing PTB, we assume that all AFB found in the sputum of a TB suspect are *Mycobacteria tuberculosis.*

- Low bacillary load, which may be detected on sputum culture
- Sputum specimen of poor quality (saliva)
- Severely immunocompromised HIV-positive patients
- False negative results

Errors in recording specimens and reporting results, mix-up of specimens at health facility level or in the laboratory, inadequate or poor quality sputum sample (e.g. saliva or specimen stored too long, dried out, overgrown by other bacteria) can lead to false positive or false negative results.

4.3.2.2 Rapid molecular diagnostics

Rapid DST should be requested according to algorithms in ***Error! Not a valid bookmark self-reference.***, *Figure 5* and *Figure 6.*

a) Xpert MTB/RIF

Developed in 2009, the Xpert MTB/RIF is considered an important breakthrough in TB diagnostics. It is the first molecular test that is simple and robust enough to be introduced outside sophisticated laboratory settings. Xpert MTB/RIF detects *M.tb* as well as rifampicin resistance-conferring mutations with a high degree of specificity. The assay provides results directly from sputum in less than two hours.

Specimen collection for the Xpert MTB/Rif test is the same as for smear and culture examination. However, only one sputum sample is required for the selected categories of patients.

Registration of TB cases diagnosed using Xpert MTB/RIF: In addition to registration by smear results (smear-positive and smear-negative), TB cases for whom an Xpert MTB/RIF is performed should have this result recorded as well. Patients in whom the Xpert MTB/RIF detects *M.tb* with no rifampicin resistance should be registered as *Xpert MTB/RIF positive without rifampicin resistance* TB cases. All TB cases with an Xpert MTB/RIF result showing *M.tb* resistant to rifampicin should be registered as *Xpert MTB/RIF positive with rifampicin resistance*. If *M.tb* is not detected, the result should be recorded as *Xpert MTB/RIF negative*. If isoniazid resistance is confirmed by conventional or molecular techniques, the case should be registered as MDR-TB.

b) Line-probe assay (LPA)

LPAs detect resistance by detection resistance-conferring mutations in the DNA of the mycobacteria. They perform well when used directly on smear-positive sputum specimens (with sensitivity for rifampicin resistance exceeding 97% and specificity exceeding 99%), thus they are of value in rapid screening of patients suspected of MDR-TB. LPAs are however as complex to perform as conventional culture and DST methods and require skilled and well-trained laboratory personnel, as well as adequate laboratory space and design to reduce the risk of false-positive results.

Processing of smear-positive specimens for direct testing should be performed in a BSL-2 laboratory, whereas performing LPAs on positive cultures requires a BSL-3 laboratory, including a class I or class II microbiological safety cabinet. Laboratory technicians require training in either BSL-2 or BSL-3 safety precautions and in how to perform the LPA

LPA is indicated only in selected cases according to *Figure 5* and *Figure 6.*

4.3.2.3 Chest X-ray examination

Chest radiography is *not* a substitute for bacteriological examination. Under normal circumstances, diagnostic chest X-ray examination for TB should only be considered after two sputum smear examinations are found negative. Chest radiography does not add value in making a diagnosis of PTB when sputum examination is already positive. Routine chest X-ray examination in TB suspects is therefore not indicated.

Chest radiography in combination with other clinical evidence is supportive for making a diagnosis of TB but one must be aware that many conditions can show TB-like changes on X-ray pictures. HIV positive patients who have TB may have normal chest radiographs, thus a normal chest radiograph cannot reliably exclude TB in these patients.

Chest radiography for TB suspects and patients should only be performed under the following conditions:

- a patient with at least two negative sputum-smears who does not improve on broad-spectrum antibiotics
- the condition of the patient does not allow waiting for smear examination results (sputum smear examination must still be performed in these patients regardless of the X-ray examination results)
- breathless patients, irrespective of sputum-smear results (possible pneumothorax, pleural effusion, atelectasis) to facilitate emergency intervention
- a patient with frequent or severe haemoptysis in order to exclude malignancy or bronchiectasis
- a patient with a history of working in mines (silicosis) or other occupational exposure to pulmonary irritants (poultry or ostrich farms, textile factory)
- a patient in whom any other pathology is suspected (e.g. CCF, Kaposi sarcoma).
- as indicated in the management of patients with drug-resistant tuberculosis (DR-TB).

Box 5: Importance of chest x-ray examination

Chest radiography only provides *supportive* evidence in the diagnosis of TB

An abnormal chest radiograph is *not firm proof* of presence or absence of TB disease, particularly in a patient who has had PTB before

The abnormalities on chest radiographs may be caused by many other diseases and/or manifestations of a previous episode of TB

4.3.2.4 Diagnostic mycobacterial culture and drug susceptibility testing (C/DST)

Culture is a more sensitive diagnostic test than direct microscopy. Only 500 bacilli /ml are needed to get a positive growth. Indications for diagnostic mycobacterial culture are according to the algorithms in ***Error! Not a valid bookmark self-reference.***, *Figure 5* and *Figure 6.* In addition, culture should also be performed on:

- Gastric aspirate specimens in paediatric TB suspects who cannot produce sputum (DST is only necessary if there are risk factors for DR-TB *(*see *Table 3*).
- Any specimens other than sputum, from a patient with suspected EPTB (such as aspirates and biopsies). DST should only be performed if there are risk factors for DR-TB *(*see *Table 3*).

Indications for conventional TB culture and drug susceptibility testing (C/DST) include

- All specimens showing resistance to R and/or H on rapid testing.
- Where rapid molecular DST is indicated, but cannot performed.

Table 3: Risk factors for drug-resistant TB (DR-TB)

RISK FACTORS FOR DR-TB	COMMENTS
Failed initial treatment (*new patient regimen*) in a new TB patient	These patients should be investigated for DR-TB before switching to retreatment regimen with FLDs, if appropriate.
Failed retreatment with FLDs, i.e. patients who remain smear positive after a full course of supervised *retreatment regimen* with FLDs	These patients have perhaps the highest MDR-TB rates of any group, often exceeding 80%.
Exposure to a known DR-TB case	Most studies have shown close contacts of MDR-TB patients to have very high rates of MDR-TB.
Failure of anti-TB treatment in the private sector (or unclear treatment history)	A detailed history of medicines used is essential. If both isoniazid and rifampicin were used, the chances of MDR-TB may be high. Sometimes second-line anti-TB medicines may have been used, and this is important information for designing the 2nd line treatment regimen.
Patients who remain sputum smear positive in the 3rd month while on TB treatment with either the *new patient regimen* or *retreatment regimen* with FLDs	This group of patients is at risk for DR-TB, but rates can vary considerably.
Relapse and return after default following a course of TB treatment	Certain histories in these patients may additionally point to possible DR-TB; for example, erratic medicine use, early relapses or previous use of second line medicines.
Exposure in institutions that have a high DR-TB prevalence (including health-care workers)	Patients who frequently stay in crowded settings, prisoners and health-care workers in clinics, laboratories and hospitals can have high rates of DR-TB.

Figure 4: Diagnostic flow-chart for pulmonary TB at primary care level (nurse)

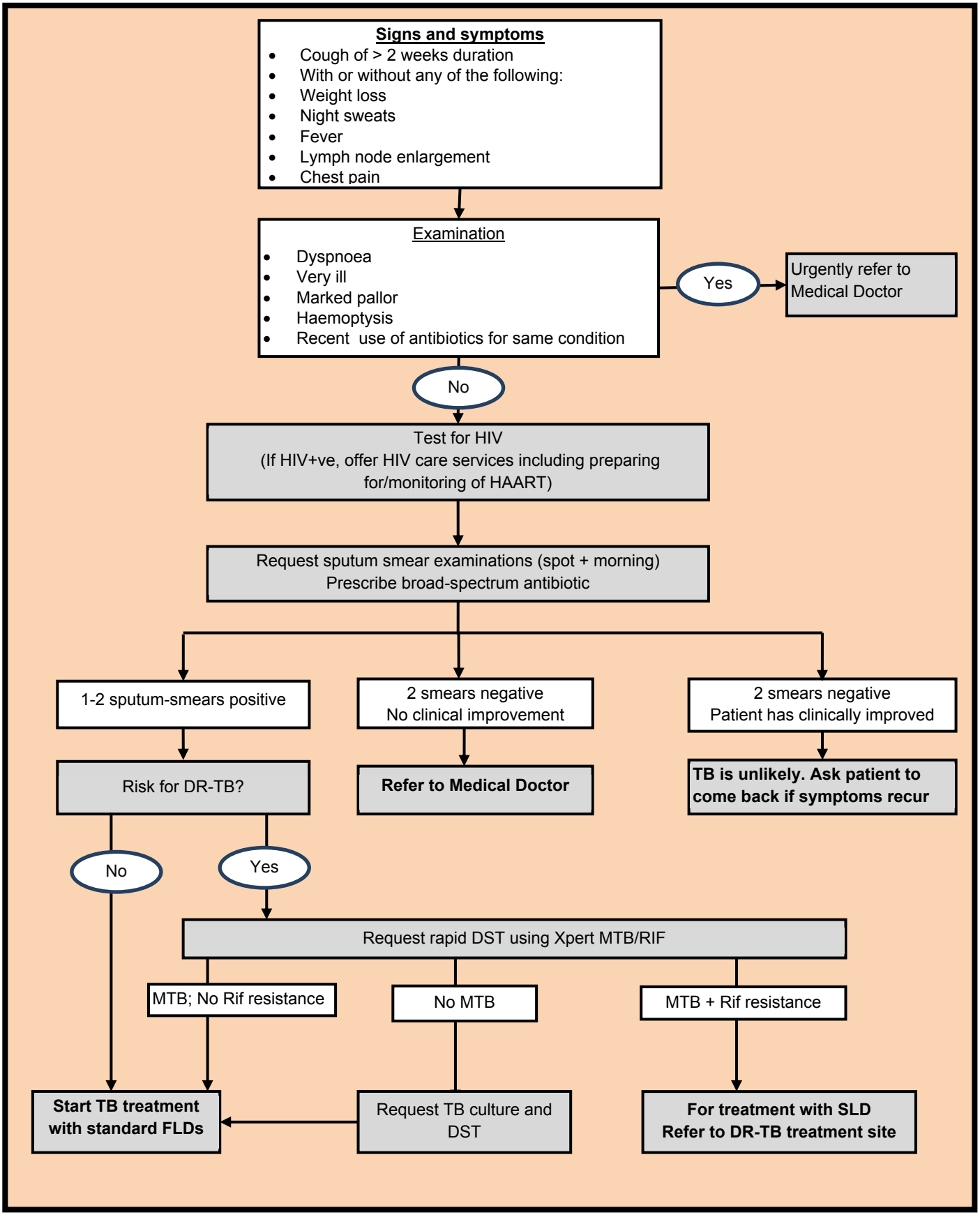


Figure 5: Diagnostic flow chart for pulmonary TB at referral level (medical doctor): patient not very ill

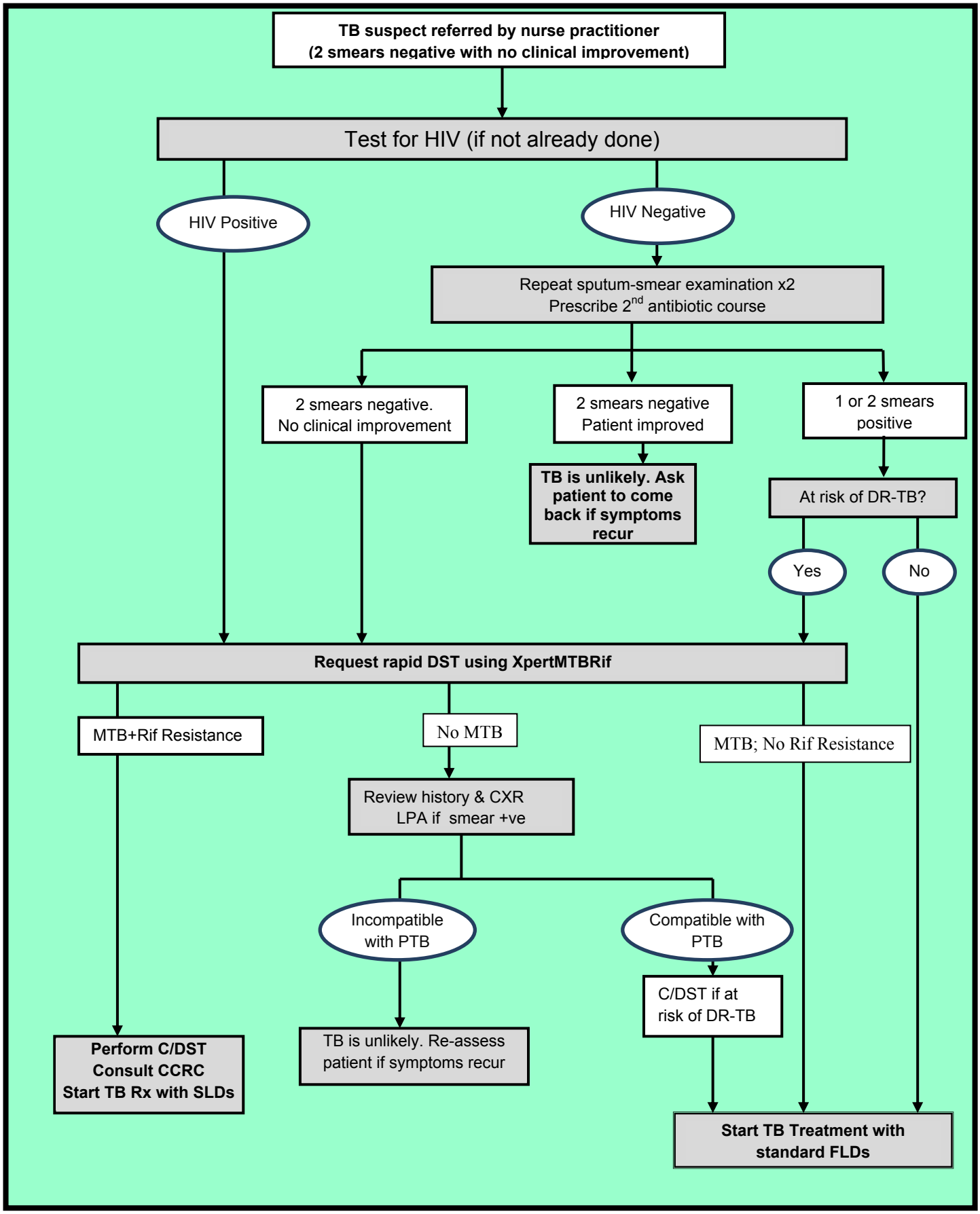
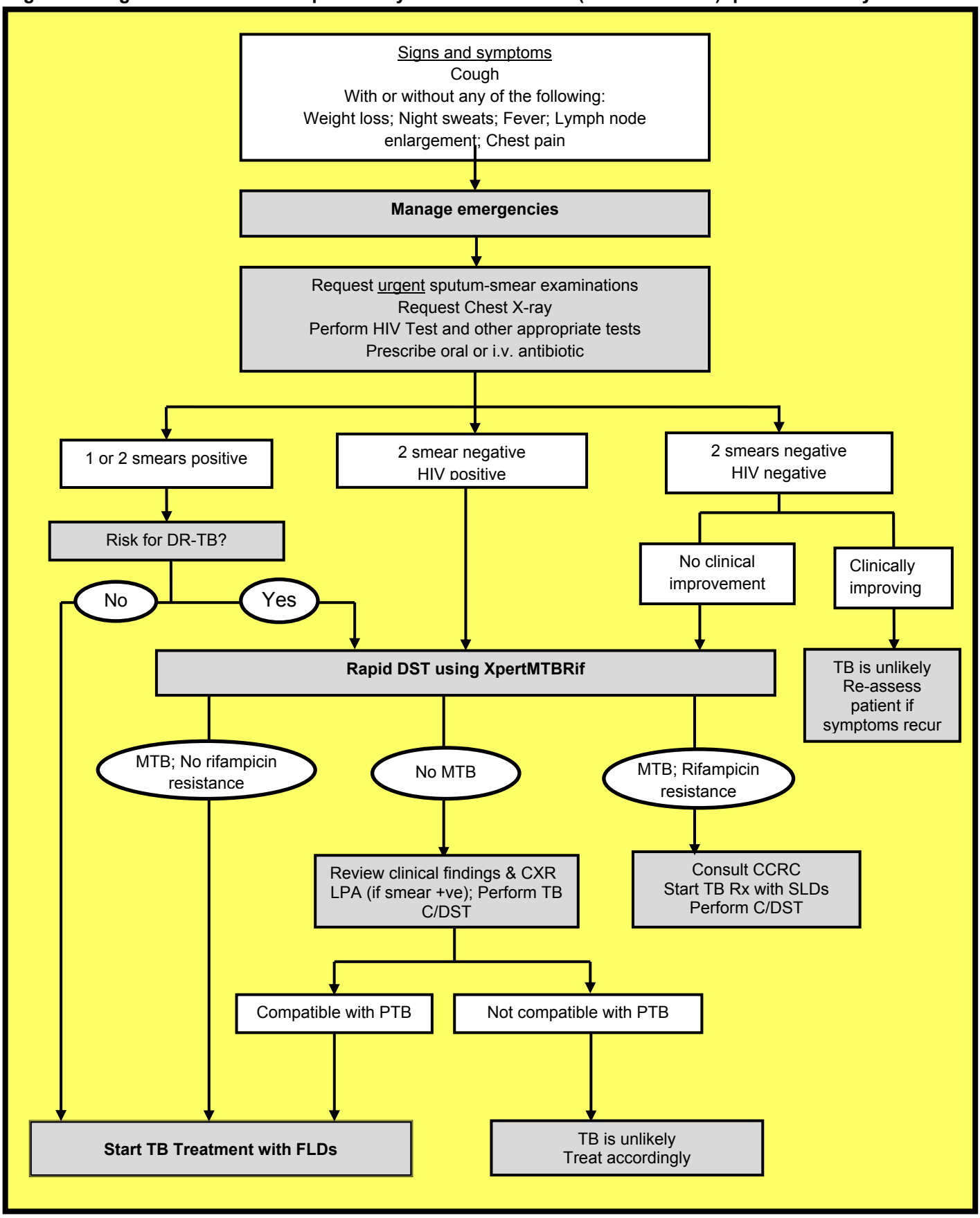


Figure 6: Diagnostic flow chart for pulmonary TB at referral level (medical doctor): patient severely ill



4.4 TB diagnosis in the context of HIV/AIDS

Information on the HIV status including CD4 count is important to make a more accurate and faster diagnosis of TB. Other benefits are that the patient would benefit from ART, cotrimoxazole preventive therapy (CPT), and general care and support for HIV related conditions.

4.4.1 'Diagnostic' HIV testing

The cornerstone for the diagnosis of TB in the adult remains sputum-smear microscopy. The approach to diagnosis is the same in all patients, but more complicated in a patient who is severely immunocompromised. It is thus advisable to perform an HIV test as part of the diagnostic work-up of the patient. This approach to HIV testing is called "diagnostic" HIV testing. Pre- and post-test counselling must be provided for the patient or his family (if the patient is very ill).

4.4.2 Presentation of TB in PLHIV

TB is common in PLHIV, but the diagnosis can be challenging. The HIV-infected TB patient whose immune system is relatively intact may present in the same manner as TB in the HIV-negative patient, with typical symptoms such as cavitary or upper lobe pulmonary disease, positive sputum smear microscopy, etc. However, the HIV-infected TB patient with advanced immunodeficiency is more likely to present with sputum-smear negative pulmonary disease and disseminated TB (blood borne, extra-pulmonary), making a firm diagnosis (with positive sputum smear or culture) more difficult.

Table 4: Features of TB disease in PLHIV

FEATURES OF TB	EARLY HIV INFECTION	LATE HIV INFECTION
PTB	Often resembles post primary (adult) PTB	Often resembles primary (childhood) PTB
Sputum smear results	Often positive	Often negative
Chest X-ray examination	Cavities and/or upper lobe infiltration	Infiltrates with no cavities May affect any part of the lung Pleural or pericardial effusion with or without mediastinal glands
Tuberculin test	Often positive	Often negative
TB lymphadenitis	Less common	More common
Miliary TB	Less common	More Common
TB meningitis	Less common	More common

4.4.3 Chest radiography in HIV Positive Patients

The radiographic appearance of TB in HIV positive patients is related to the degree of immunocompetence. During the early stages of HIV disease, the chest radiographs are more likely to show typical upper lobe cavitations. The appearance becomes increasingly more atypical with advancing immune suppression. In most HIV-infected patients with pulmonary disease, non-specific infiltrates are present, which may or may not be TB.

4.4.4 Mycobacteria other-than *M.tb* (MOTT)

Cases of MOTT have been reported in Namibia, though the prevalence is not known. As in other parts of the world where MOTT have been reported, it is associated with the increasing HIV epidemics. Typical anti-TB medicines are sometimes not effective in treating MOTT. The treatment of MOTT requires broad-spectrum antibiotics depending on the type of mycobacterium identified. On identifying MOTT,

the laboratory should routinely specify those of clinical importance (Mycobacterium Avium Complex (MAC), Mycobacterium kansasii, etc).

4.5 Sputum-smear negative PTB

Sputum-smear negative PTB is a diagnosis that should only be made after smear microscopy report shows that two initial smears are negative. Diagnosis of new sputum-smear negative PTB is then made after carefully eliminating other pulmonary diseases that may present in the same way. This is even more important in patients who are HIV positive as they often suffer from other infections at the same time, which may mimic TB.

4.5.1 Criteria for the diagnosis of sputum-smear negative PTB

Diagnosis of *smear-negative PTB* can be made if a patient has symptoms suggestive of PTB and fulfils the following conditions:

A. Have sputum samples that are smear-negative but culture-positive for *M.tb*, or

B. Have at least two sputum specimens at the start of treatment that are negative for AFB and the clinician has decided to treat with a full course of anti-TB therapy.

The above criteria should apply to most cases. However, in practice it may be difficult to adhere to these principles. If a patient is critically ill, as often occurs in patients with HIV who are severely immunocompromised, the clinician may have to make a presumptive diagnosis of PTB and start TB therapy while waiting for the repeat sputum examinations or culture results. An example is when a patient is very weak, dyspnoeic and unable to produce sputum. In such cases, the clinicians are advised to treat empirically in order to save the patient's life.

Please note that a trial of broad-spectrum antibiotics is no longer recommended to be used as a diagnostic aid for smear-negative PTB in persons living with HIV.

4.5.2 Differential diagnosis of sputum-smear negative PTB

In any patient with negative sputum smear examinations (or cultures) the diagnosis can only be made by a clinician after careful consideration of other diseases. Often in smear negative PTB, the diagnosis is missed in life but made only at autopsy. *Table 5* lists the most common diseases that should be considered and excluded before a diagnosis of smear-negative PTB is made.

Table 5: Diseases that can present like sputum-smear negative PTB

DISEASE	DESCRIPTION
Pneumonia	• Rapid onset of symptoms. Chest X-ray examination shows localised opacity without cavitations as seen in PTB, especially so if they are in the upper part of the lung. A raised white blood cell count is in favour of bacterial pneumonia. A rapid fall of temperature after a course of antibiotics makes the diagnosis likely to be pneumonia. • Pneumonia is common in the immunocompromised patient. The common causative organism in adults is *Streptococcus pneumonia* which responds well to penicillin/ ampicillin or co-trimoxazole. • Pneumonia due to *Pneumocystis jirovecii* (PCP) (previously called *Pneumocystis carinii*) is a common complication of advanced HIV infection. Patients present with dry cough and severe dyspnoea, whereas PTB disease generally presents with a productive cough. Chest radiograph features are often normal or show a bilateral diffuse interstitial shadowing. Definitive diagnosis of PCP depends on finding the microscopic cysts in the sputum. The condition progresses rapidly and can be fatal. It

	is best to start treatment with high dose cotrimoxazole. PCP can be prevented with cotrimoxazole preventive therapy (CPT).
Pulmonary Kaposi Sarcoma	• Occurring almost exclusively in immunocompromised patients, chest X-ray examination shows nodular or diffuse infiltrates that might be confused with TB. Kaposi sarcoma presents with purple nodules or patches on the skin and mucous membranes. ART is the most effective treatment.
Lung cancer	• The tumour may sometimes break down into a cavity which can be seen on the chest radiograph. An infection beyond a bronchus blocked by a tumour may cause a lung abscess with a cavity. If the sputum is negative diagnosis is often made on bronchoscopy. A solid rounded tumour may be difficult to distinguish radiologically from a rounded tuberculous lesion. A patient with lung cancer is almost always a smoker. Palpate for an enlarged lymph node behind the inner end of the clavicle, a common place for a secondary tumour.
Lung abscess	• Presents with a lot of purulent foul smelling sputum. The patient usually has a high fever and is very ill. If the purulent sputum is repeatedly negative for TB, a lung abscess is more likely. The white blood cell count is usually high.
Bronchiectasis	• Also presents with copious purulent sputum. Bronchiectasis often develops over a long time due to recurrent bronchitis and other chest infections, including previous PTB. Persistent moist, coarse 'crackles' may be repeatedly heard over the same area of the lung.
Asthma	• Wheeze is not common in TB but it may occur occasionally due to: a) Enlarged lymph nodes, which may obstruct a bronchus or even the trachea b) Tuberculous bronchitis. Either of these may cause a localised wheeze. Remember patients with severe asthma may be on long-term corticosteroid medicines (e.g. prednisolone) which may weaken the patient's defences against TB. They can then develop TB as well as asthma. Asthmatic patients who are on treatment and who develop a cough, fever or lose weight should have their sputum examined for TB.

4.5.3 Management of patients with two negative sputum smears.

Where applicable, clinicians can prescribe appropriate broad spectrum antibiotics (e.g. amoxicillin) to a patient with two negative sputum smears who are ambulatory. The patient should be advised to report immediately if the condition deteriorates. The patient should return for re-assessment after one week. If the patient doesn't have any complaints, s/he will be advised to go home and report again if the same signs and symptoms recur. If sputum-smears are positive on re-assessment, then the diagnosis of PTB is made. If, however, both smears are negative, and the patient's condition has not improved or has worsened, the patient should have a chest X-ray. When the X-ray image and the general signs and symptoms are compatible with TB and other lung diseases are excluded, a diagnosis of sputum-smear negative PTB is made.

4.5.4 Management of the severely ill TB suspect

All TB suspects who are severely ill should be admitted in hospital. The clinician should start intra-venous antibiotic treatment with suitable antibiotics. Meanwhile efforts must be made to obtain sputum for a smear examination, if not yet done. Label the specimen as '**urgent'** and request the laboratory to process and provide the report on ***the same day***.

When sputum smears are negative, and the patient improves on the prescribed antibiotics, it may be assumed that the patient has a lung infection not caused by *M.tb*. When the smears are negative and the patient does not improve on antibiotic treatment, a chest X-ray may be useful to provide supportive

evidence for PTB. The clinician should take into consideration the HIV status of the patient. If the patient is HIV positive and severely immunosuppressed (CD4 count less than 200/µl), PTB is likely. The clinician may make the diagnosis of smear negative PTB and initiate TB treatment. If the sputum smear is positive, the diagnosis of smear positive PTB is made.

4.5.5 "Trial" therapy for TB

There is no role for trial therapy in the management of TB. A proper diagnosis must be made before starting treatment.

4.5.6 Bronchoscopy

This is a useful method to make a diagnosis of PTB or other diseases. Direct observation of the interior of the lung with the bronchoscope can show typical Kaposi sarcoma, bronchogenic carcinoma and TB lesions. Biopsies taken on bronchoscopy can help to differentiate between TB and other diseases. This method is done under local anaesthesia and is reported to be 92% effective in obtaining positive bacteriology in patients with PTB, if combined with bronchio-alveolar lavage. Bronchoscopy is not a routine TB diagnostic tool in Namibia but is very important investigation at the referral hospitals in the hands of experienced physicians.

4.5.7 Tuberculin skin test

The tuberculin skin test (TST) is only helpful in diagnosing *TB infection* in a person who is immunocompetent, and has very limited value in the clinical diagnosis of TB disease since a positive or negative result does not prove or disprove that a person has TB disease. The TST test is mostly recommended for determining TB infection in an otherwise healthy person, mostly a child who has been recently exposed to a patient with TB disease.

The Mantoux test is the TST used Namibia; *Box 6* summarises how it is performed and interpreted.

Box 6: How to perform and interpret the Mantoux test

The Mantoux test is applied as follows: Using a short fine needle and special syringe calibrated for contents of 0.1ml portions, 0.1ml is drawn from a vial with Purified Protein Derivate (PPD) and - after proper disinfection of the skin - injected intradermally on the inner side of the lower left arm, at the junction of the upper and middle third. After 48-72 hours the skin is examined for induration at the injection site. The diameter of the induration is measured at its largest diameter. The outer edge of the induration is best determined using a ballpoint. Draw the ballpoint inwards towards the induration; where it meets resistance draw a short line oblique to the radial line; do the same on the opposite side; measure the distance between the two oblique lines in millimeters; this is the exact distance of induration.

Mantoux test results and interpretation

	Negative	Positive
HIV-	0-9mm induration	10mm or more
HIV+	0-4mm induration	5mm or more

A positive test is proof of infection with *M.tb.* It is never proof of active TB. Only positive bacteriology is firm proof of TB. A positive tuberculin test result can support a diagnosis of TB in the presence of other clinical evidence of TB.

A false positive result is rare in the tuberculin skin test once there is agreement on the criterion for a positive result. Infection with Mycobacteria Other Than Tuberculosis (MOTT) can also cause an induration, but usually not as strong as an infection by *M.tb.* It is for that reason that the criterion for a

tuberculin test being positive is the size of the induration.

Boosting phenomenon

The boosting phenomenon may occur when two successive tuberculin tests are applied within months to a person who has had BCG long before or who has had a latent TB infection in the past. With the first tuberculin test being negative, the second test may be positive, which may be erroneously interpreted as a recent tuberculin test conversion, or recent *M.tb* infection. This is erroneous because the second increased induration is only the result of a boosting of pre-existing cellular immunity caused by the first of the two tuberculin injections. Physicians who use the tuberculin test for monitoring recent infection in health care settings should be particularly aware of this phenomenon. In persons with a negative result, it may be useful to repeat a second tuberculin test after 2-4 weeks to ensure that there has not been a previous infection (or a BCG vaccination in the past).

A negative test result indicates – but is not firm proof - that the person is not infected by mycobacteria. There are many reasons why the result might be false negative. These include:

- Incorrect test application (subcutaneous injection instead of intradermal); inactive tuberculin,;
- The patient is severely immune suppressed. This happens in patients with advanced AIDS (and low CD4 counts); very cachectic patients; severely malnourished children.

Effects of previous BCG vaccination

BCG vaccination is given to all newborns in Namibia. The tuberculin test will become mildly positive after BCG vaccination. *M.tb* infection will create a much stronger reaction than BCG. Similarly, environmental mycobacteria are very common in Namibia and also create a positive tuberculin test result. Usually the induration is well below 10mm. That is the reason for deciding on 10mm or more as the cut-off point for infection by *M.tb.*

4.6 Diagnosis of extra-pulmonary tuberculosis

Extra-pulmonary tuberculosis (EPTB) is much less common than PTB, except in patients with advanced HIV infection where it may be more frequent. It may have many different manifestations depending on the organ that is affected. The initial infection would probably be in the lungs; TB bacilli may then spread via the blood stream and the lymph nodes to various parts of the body. Sometimes TB bacilli directly enter organs other than through the lungs.

4.6.1 Medical history

The same general signs and symptoms as for PTB will occur in EPTB, such as tiredness, loss of appetite, weight loss, and night sweats. Presence or absence of these signs and symptoms should always be elicited from the patient. Specific complaints such as pain and swelling are caused by the inflammation of the affected organ. Many patients with EPTB may also have concomitant PTB, because the lungs are the most common port of entry of the TB infection. Patients should therefore be questioned about signs and symptoms of PTB and have sputum examination performed.

4.6.2 Investigations

4.6.2.1 Fine- or wide needle aspiration in lymph node TB

Needle aspiration is mostly used in diagnosing lymph node TB. A needle is inserted into the centre of the swollen lymph node, and material is aspirated into the needle. All specimens should be sent for smear microscopy, mycobacterial culture as well as cytology or histology. However, if casseous material is seen, the patient should be commenced on anti-TB treatment while awaiting the laboratory results.

Figure 7: Diagnostic flow-chart for lymph node enlargement

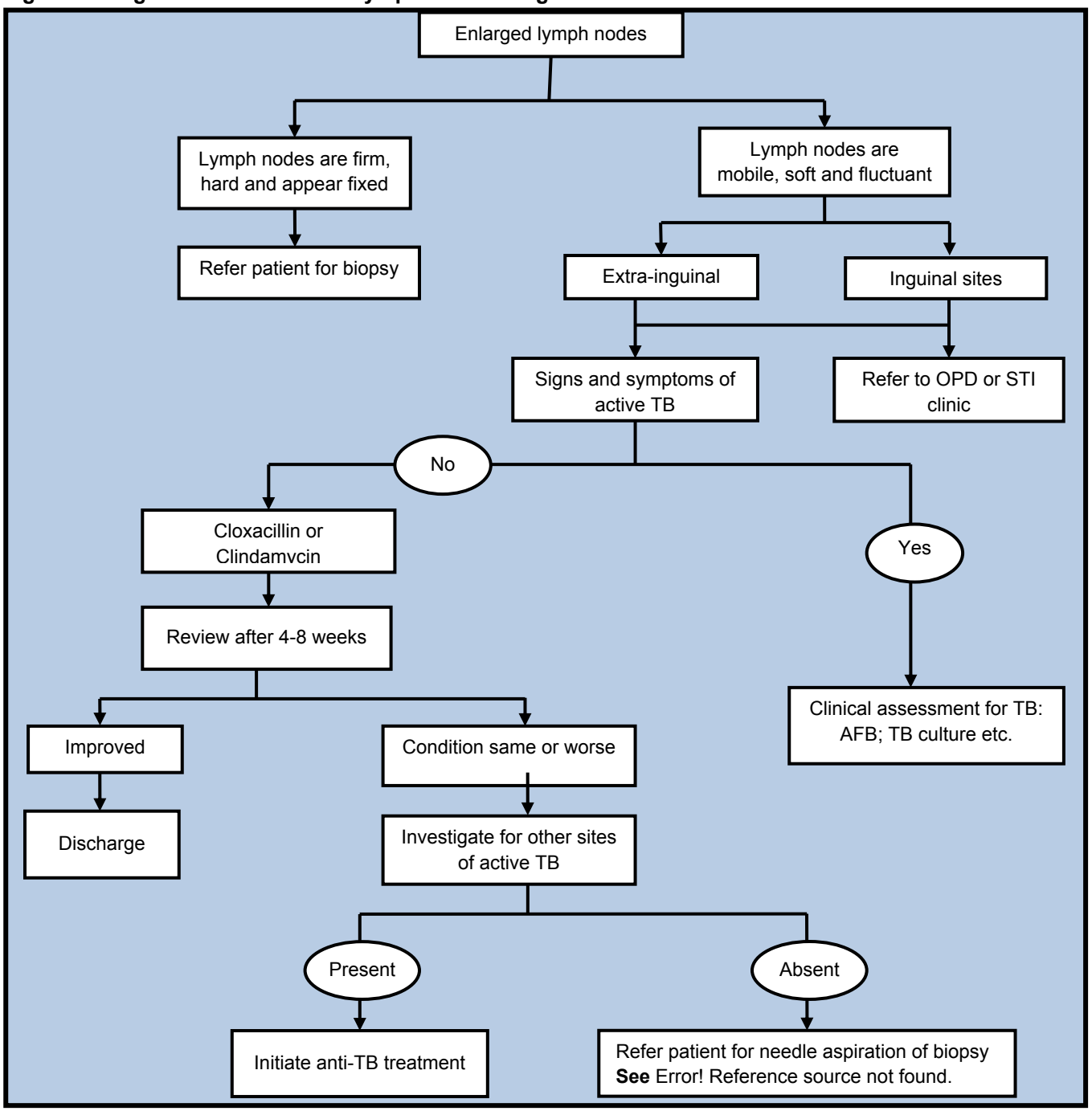
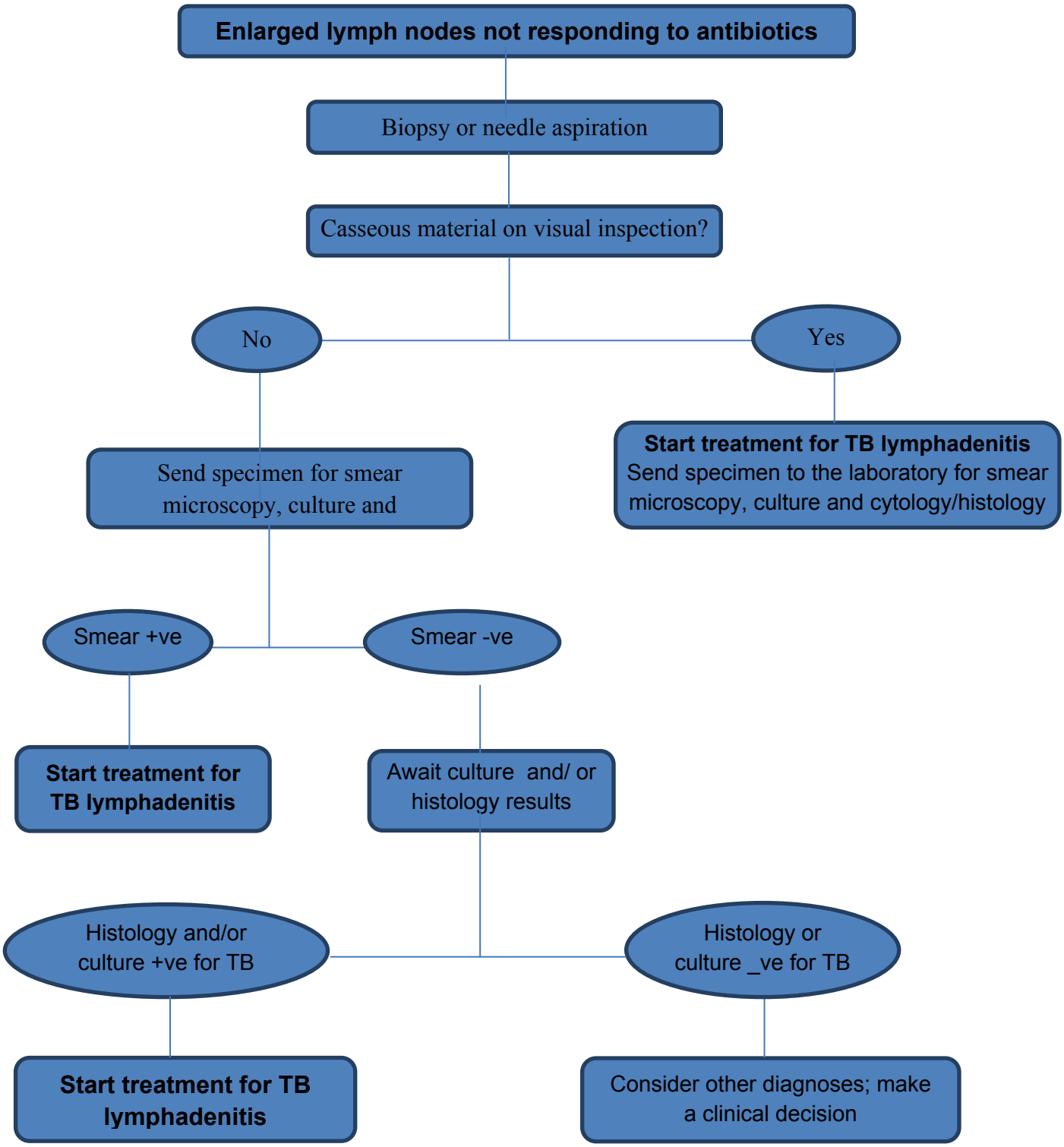


Figure 8: Diagnostic flow-chart for TB lymphadenitis with needle aspiration or biopsy



4.6.2.2 Biopsy

A biopsy from the affected organ can be obtained during a surgical procedure on patients undergoing investigation or excision of a diseased organ. The final diagnosis should be made on histology.

4.6.2.3 Pleural and peritoneal fluid

Between 97 and 99% of all pleural effusions in areas where HIV prevalence is high are caused by TB. In TB pleurisy, an exudate accumulates in the pleural cavity. Simple aspiration of pleural fluid is enough to exclude causes other than TB. The aspirate forms a web when left standing and shows a high protein content on analysis. The gram stain is negative. Examination yields smear-positive results in less than 10% of cases. Ascites due to TB in the peritoneum also presents as an exudate.

4.6.2.4 Cerebro-spinal fluid (CSF)

A lumbar puncture should be performed when TB meningitis is suspected in a patient. The CSF obtained should be submitted for microscopy (including India ink and gram staining), bacterial culture, biochemistry and staining for AFB. If the gram stain and testing for Cryptococcus are negative, TB meningitis should be considered, even when smear is negative for AFBs.

4.6.2.5 Urine

When TB of the renal and urinary system is suspected, mycobacterial **culture** examination of three morning urine specimens can confirm the diagnosis.

4.6.2.6 Genital fluids

When genital TB is suspected, menstrual fluid or material obtained from dilatation and curettage should be examined for AFB and mycobacterial culture should be performed. Smear examination for AFBs as well as mycobacterial culture should be performed on ascitic fluid obtained at laparotomy in patients with suspected adnexal TB

4.6.3 Differential diagnosis of extra-pulmonary tuberculosis

The following table summarises the different clinical features and differential diagnoses for the many different manifestations of EPTB. The most common EPTB manifestations after lymphadenitis are: pleurisy, peritonitis (or other forms of gastrointestinal TB), meningitis, spondylo-discitis (spinal TB), arthritis, uro-genital TB, and pericarditis.

Table 6: Clinical features and differential diagnoses for extra-pulmonary tuberculosis

Type of EPTB	Clinical Features	Diagnosis	Differential Diagnosis
Lymph-adenopathy	• General features of TB disease usually mild • Mildly tender • Common in cervical nodes • Matted together • Often causes chronic fistulas	• Needle aspiration • Lymph node biopsy (caseation-cheesy material seen on visual inspection)	• Persistent Generalised Lymphadenopathy (PGL) in HIV+ patient • Carcinoma, • Sarcoidosis, • Pyogenic abscess
Miliary TB	• Very sick patient • Fever • Weight loss • Hepato-splenomegaly • Tubercles in the choroid of the eye	• Chest X-ray examination: diffuse, uniformly distributed small miliary shadows • Pancytopenia, • Bacilli in CSF • Biopsy of bone marrow or liver shows TB granulations	• AIDS (if active TB can be excluded) • Septicaemia • Disseminated carcinoma
Pleural effusion	• Chest pain • Breathlessness • Mediastinal shift on X-ray • Decreased breath sounds • Stony dullness on percussion of chest	• Chest X-ray examination: unilateral uniform white opacity often with concave upper border • Aspiration of straw coloured fluid • Pleural biopsy (not routinely done except for suspected malignancy) • Pleural fluid chemistry for protein and LDH	• Malignancy • Post pneumonia effusion • Pulmonary embolism
TB pericarditis (mostly presenting as pericardial effusion)	• Cardiovascular features • Pericardial friction rub	• Chest X-ray examination: a large globular heart • ECG (ST and T wave changes) • Cardiac sonar (echocardiography)	• Cardiomyopathy • Any cause of heart failure
Abdominal TB (peritoneum or intestines)	• Ascites • Weight loss • Abdominal mass • Intestinal obstruction	• Chest X-ray examination (to exclude PTB) • Abdominal tap (ascitic fluid chemistry) • Abdominal ultrasound • Peritoneal biopsy • Abdominal X-ray examination (including barium studies in suspected malignancy) • Cytology/Histology	• Malignancy • Liver disease
TB meningitis	• Irritability/confusion • Fever • Weight loss • Headache • Decreasing consciousness • Fits • Neck stiffness	• CSF (microscopic and chemical examination)	• Viral or bacterial meningitis • Cryptococcal meningitis
TB spine	• Back pain • Psoas abscess • Spinal cord compression with paresis or paralysis	• X-ray examination of spine • MRI • Tissue biopsy	• Secondary malignancy
TB bone	• Chronic osteomyelitis • Fistula	• X-ray examination • Biopsy • Culture	• Malignancy • Other bacterial infection
Hepatic TB	• Hepatomegaly	• Ultrasound scan • Liver biopsy	• Hepatoma • Amoebic abscess • Hepatitis of any cause

Renal TB	• Frequency • Dysuria • Haematuria • Loin pain • Oedema	• Sterile pyuria • 3 early morning urine specimens for mycobacterial culture • IV pyelogram	• Bilharzia • Carcinoma • Nephritis
Adrenal glands	• Hypo-adrenalism (Hypotension, raised urea, low serum sodium) • Usually combined with miliary TB • Common in HIV infected patients • High mortality	• Ultrasound scan • X-ray examination (shows calcifications)	• Malignancy
Female genital TB	• Infertility • Pelvic infection • Ectopic pregnancy	• Pelvic examination • X-ray examination of genital tract • Biopsy, urine for mycobacterial culture	• Sexually transmitted diseases (STD) Malignancy
Male genital tract	• Pain and swelling of epididymis	• Tissue biopsy • X-ray kidney • Urine for mycobacterial culture	• STD • Malignancy
Upper respiratory tract TB	• Hoarseness • Pain in ear • Pain on swallowing	• Laryngoscopy • Oesophagoscopy • ENT referral	• Carcinoma of vocal cords • Carcinoma of oesophagus

TB meningitis carries a high mortality and is particularly frequent in small children. The diagnosis is sometimes difficult to differentiate from other diseases. *Table 7* lists the diagnostic approach to the diagnosis of TB meningitis.

Table 7: Differential diagnosis of TB meningitis

Disease	CSF White cells	Protein	Glucose	Microscopy
TB meningitis	Elevated (L>PMN; PMN raised initially)	Increased > 1g/dl	Decreased or markedly decreased	AFB rare, not to be relied on
Cryptococcus meningitis	Elevated L>PMN	Increased	Normal or slightly decreased	Positive India ink staining or cryptococcal antigen test
Partially treated bacterial meningitis	Elevated both PMN and L	Increased	Decreased	Bacteria on Gram stain (rarely)
Viral meningitis	Elevated L>PMN	Increased but less than < 1g/dl	Normal (low in mumps or H. Simplex)	No organisms identified
Secondary syphilis	Elevated L>PMN	Increased	Normal	Dark background microscopy needed to identify AFB
Rare diseases in Namibia				
Late stage Trypanosomiasis *(Travel history to Central or West Africa)*	Elevated (L>PMN)	Increased	Decreased	Motile trypanosomes
Tumour (carcinoma/lymphoma)	Elevated (L>PMN)	Increased	Decreased	Cytology shows malignant cells
Leptospirosis	Elevated (L>PMN)	Increased	Decreased	Cytology shows spirochetes
Amoebic meningitis	Elevated (L>PMN)	Increased	Decreased	Amoebae

4.7 Haematological and biochemistry examinations in TB patients

Laboratory examinations should only be done when their result will influence the management of the patient. *Table 8* provides information on what is (or is not) useful to examine routinely in a patient newly diagnosed with TB. Some tests are desirable if they can be done at start of treatment while others are indicated when a patient develops complications. Repeat laboratory examinations (beyond sputum smears) are only indicated when a patient develops complications. The large majority of TB patients tolerate the first-line TB medicines very well; e.g. routine liver function tests in a patient doing well on treatment are not indicated.

Table 8: Other laboratory examinations

Examination	Indication	Remarks
Erythrocyte Sedimentation Rate (ESR)	• None	• ESR will be elevated in any serious disease or infection (high sensitivity) • ESR is too unspecific to disprove TB disease when it is normal (low specificity)
Haemoglobin (Hb)	• Not routinely indicated • Indicated in a clinically anaemic patient	• Can serve as a baseline for treatment of anaemia
Liver Function Tests (LFT)	• Not routinely indicated • Indicated when patient has jaundice, is seriously nauseated or vomiting, or when patient has a history of liver disease	• Can serve as a baseline in case of abnormalities and previous liver disease history • Elevation of liver enzymes up to 3x normal value when on TB medication is acceptable and may not warrant interruption of TB treatment
Urine	• Not routinely indicated • Indicated when the patient has signs and symptoms of higher or lower urinary tract infection (due to TB or other causes) or diabetes	• Urine culture is useful when TB of the urinary tract is suspected
Adenosine Deaminase (ADA)[3]	• TB pleural effusion, **only** if there is any doubt about the diagnosis	• The levels of adenosine deaminase (ADA), an enzyme found in most cells, are increased in TB pleural effusions

Box 7: Summary of criterion for diagnosis of TB disease in an adult

The following criteria apply before a diagnosis of TB disease is made in a patient with signs and symptoms compatible with TB disease:

- Presence of at least one positive sputum smear
- Presence of one positive culture for *M.tb*
- Positive histology
- Clinical picture and consistent fluid chemistry (pleural fluid etc.)
- Negative sputum-smears with no improvement on treatment with broad-spectrum antibiotics and a TB compatible chest radiograp

[3] Several reports have suggested that an elevated pleural fluid ADA level predicts tuberculous pleurisy with a sensitivity of 90 to 100% and a specificity of 89 to 100%. Specificity is increased when the lymphocyte/neutrophil ratio in the pleural fluid (of > 0.75) is considered together with an ADA concentration of > 50 U/L

5 MANAGEMENT OF TUBERCULOSIS

5.1 Introduction

Anti-TB chemotherapy is the most important intervention for the control of TB in any population. Chemotherapy kills *Mycobacteria tuberculosis* bacilli from an infectious patient thus stopping transmission in the community. Most patients with smear positive TB become non-infectious within five days of commencing effective treatment.

Evidence from good TB programmes shows that high treatment success rates (85-95%) can be achieved when:

- TB treatment is provided at the patient's convenience, for instance close to the patient's home, at his/her workplace or at the nearest health facility
- the patient is well informed about the treatment
- the patient is supported by relatives, community workers and health staff to complete the treatment as prescribed
- health care workers at all levels fully adhere to the technical treatment guidelines of the national TB programme.

5.2 Patient categories and definitions

For rational and effective management of patients with TB it is very important that every patient is categorised correctly, before chemotherapy is started. Uniform criteria to define a TB case are needed for:

- proper patient registration and case notification
- selecting appropriate standard treatment regimens
- standardising the process of data collection for TB control
- evaluating the proportion of cases according to site, bacteriology and treatment history
- cohort analysis of treatment outcomes
- accurate monitoring of trends and evaluation of the effectiveness of TB programmes within and across districts, countries and global regions.

Cases of TB are classified according to:

- the level of certainty
- anatomical site of disease
- bacteriological results (including drug resistance)
- history of previous treatment;
- HIV status.

5.2.1 Case definitions by level of certainty

The TB case definitions below are based on the level of certainty of the diagnosis and on whether or not laboratory confirmation is available.

a) **Tuberculosis suspect**: Any person who presents with symptoms or signs suggestive of TB. The most common symptom of pulmonary TB is a productive cough for two weeks or more, which may

be accompanied by other respiratory symptoms (shortness of breath, chest pains, haemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).

b) **Case of tuberculosis**: A definite case of TB (defined below) or one in which a health care worker (clinician or other medical practitioner) has diagnosed TB and has decided to treat with a full course of TB treatment.

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

c) **Definite case of tuberculosis:** A patient with *M.tb* complex identified from a clinical specimen, either by culture or by a newer method such as rapid molecular tests; a pulmonary case with one or more initial sputum smear examinations positive for acid-fast bacilli (AFB) is also considered to be a "definite" case.

5.2.2 Case definitions by anatomical site of TB disease

In general, recommended treatment regimens are similar, irrespective of site. Defining the site is important for recording and reporting purposes and to identify the more infectious patients – those with pulmonary involvement, who will be further subdivided by smear status (see section below).

Pulmonary tuberculosis (PTB) refers to a case of TB (defined above) involving the lung parenchyma. Miliary TB is classified as pulmonary TB because there are lesions in the lungs. Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lung parenchyma, constitutes a case of *extra*pulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of *pulmonary* TB.

Extrapulmonary tuberculosis (EPTB) refers to a case of TB (defined above) involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. Diagnosis should be based on at least one specimen with confirmed *M.tb* or histological or strong clinical evidence consistent with active EPTB, followed by a decision by a clinician to treat with a full course of anti-TB chemotherapy. The case definition of an EPTB case with several sites affected depends on the site representing the most severe form of disease. Unless a case of EPTB is confirmed by culture as caused by *M.tb*, it cannot meet the "definite case" definition.

5.2.3 Case definition by bacteriological results

Bacteriology refers to the smear status of pulmonary cases and the identification of *M.tb* for any case by culture or newer methods.

Smear positive pulmonary TB refers to a case where one or more sputum smear specimens at the start of treatment are positive for AFB.

Smear-negative PTB cases are patients with clinical features of PTB and either:

A. Have sputum that is smear-negative but culture-positive for M.tb, or

B. Have at least two sputum specimens at the start of treatment that are negative for AFB and the clinician decides to treat with a full course of anti-TB therapy.

Pulmonary TB smears not done, refers to cases where sputum has not been investigated for TB. Efforts to collect sputum should be made on every TB suspect above the age of 5 years *including those with*

EPTB. Cases without smear results should be the exception rather than the rule and should be recorded as "smears not done" in the TB register.

5.2.4 Case definition by history of previous treatment:

At the time of registration, each patient meeting the case definition is also classified according to whether or not they have previously received TB treatment, as well as the outcome of this previous treatment. It is important to identify previously treated patients because they are at increased risk of anti-TB drug resistance, including MDR-TB. At the start of therapy, specimens should be obtained for DST from all previously treated patients.

New TB patients are patients who have never had treatment for TB, or have taken anti-TB medicines for less than one month. New patients may have positive or negative bacteriology and may have disease at any anatomical site.

Previously treated patients are patients who have received at least one month of anti-TB medicines in the past. They may have positive or negative bacteriology and may have disease at any anatomical site. They are further classified by the outcome of their most recent course of treatment as shown in *Table 9*.

Table 9: Registration group by most recent outcome

REGISTRATION GROUP (ANY SITE OF DISEASE)		BACTERIOLOGY	OUTCOME OF MOST RECENT TREATMENT
New		Positive/negative	N/A
Previously treated	*Relapse*	Positive	Cured
			Treatment completed
	Treatment after failure	Positive	Failed treatment
	Treatment after default	Positive	Defaulted
Transfer in (A patient who has been transferred from another reporting unit/TB register to continue treatment)		Positive/negative	Still on treatment
Other		Positive/negative	All cases who do not fit the above definitions, such as patients • for whom it is not known whether they have been previously treated • who were previously treated but with unknown outcome of that previous treatment • who have returned to treatment with smear negative PTB or bacteriologically negative EPTB

Patients who are sputum-smear positive at the end of (or returning from) a second or subsequent course of treatment are no longer defined as "chronic". Instead, they should be classified by the outcome of their most recent retreatment course: relapsed, defaulted or failed.

5.2.5 Case definition by HIV status

Determining and recording the TB patient's HIV status is critical for treatment decisions as well as for assessing programme performance. The *TB Treatment Card* and *Facility* and *District TB Registers* include information on HIV testing, co-trimoxazole, and ART. Always encourage clients to get tested for HIV and update the *TB Treatment Card* and TB registers when this has been done.

Table 10: Summary of registration categories

Classification	Definition
New	A patient who has never been treated before for TB, or who has taken TB treatment only for less than one month. They may be PTB (smear positive or negative) or EPTB
Previously treated	A patient who has previously received at least four weeks of TB treatment, regardless of the previous outcome. They may be PTB (smear positive or negative) or EPTB; This group includes *relapses*, *treatment after failure*, and *treatment after default*
Pulmonary TB	A patient who has TB affecting the lung parenchyma. This includes disseminated or miliary TB and those with concurrent pulmonary and *extra*-pulmonary involvement
Extra-pulmonary TB	A patient with TB disease involving sites other than the lung parenchyma, without lung involvement
Relapse	A patient who presents with bacteriologically (smear or culture) positive TB after previous treatment with a successful outcome (cured or completed treatment)
Treatment after *failure*	A patient who presents for treatment after treatment failure (smear or culture positive)
Treatment after *default*	A smear positive patient who is started on treatment after previous treatment was interrupted for at least 2 consecutive months (default)
Transfer in	A patient who has been transferred from another recording and reporting unit or TB register to continue treatment. They can be PTB (smear negative or positive) or EPTB

5.3 Treatment of tuberculosis

The MoHSS commits to ensuring that all anti-TB medicines are quality-assured, and management of anti-TB medicines is incorporated into the management of other essential medicines.

Table 11: First-line anti-TB medicines

Generic name	Abbreviation	Mode of action
Rifampicin	R	Bactericidal
Isoniazid	H	Bactericidal
Pyrazinamide	Z	Bactericidal
Streptomycin	S	Bactericidal
Ethambutol	E	Bacteriostatic

5.3.1 Standard treatment regimens for defined patient groups

Namibia maintains WHO recommended standardised TB treatment regimens. Standardised treatment means that all patients in a defined group receive the same treatment regimen, and has the following advantages over individualised prescriptions of medicines:

- it minimises errors in prescription, and thus reducing the risk of development of drug resistance
- it simplifies estimation of medicine requirements at all levels
- it reduces costs
- it ensures regular medicine supply when patients move from one area to another
- treatment results can be compared.

For assigning standard regimens, patients are grouped by the same patient registration groups used for recording and reporting, which differentiate new patients from those who have had prior treatment. Registration groups for previously treated patients are based on the outcome of their prior treatment course: '*failure*', '*relapse*' and '*default*' and '*other*'. Recommended regimens for different patient registration groups are shown in *Table 12* below.

Previous guidelines referred to 'Category 1', 'Category 2' and second line regimens. This terminology has now been replaced with "**new patient regimen**" (standard regimen for new TB patients), "**retreatment regimen with 1st line medicines**" (standard regimen for previously treated patients) and "**DR-TB treatment regimens**"

Table 12: Recommended regimens for new and previously treated TB patients in Namibia

New patients regimen – 2RHZE/4RHE **Initial phase of 2 months of RHZE daily, followed by continuation phase of 4 months of RHE daily (total 6 months)**	
Patient category	• All NEW patients with any form of TB (*see definitions in Table 10)*
Modifications advised on the treatment regimen	• In TB meningitis add streptomycin for at least 2 months to ensure maximum bactericidal efficacy; total duration of treatment in these cases is 9-12 months • Streptomycin should not be used in pregnancy • In severe forms of EPTB other than meningitis, total treatment duration may be extended to a maximum of 9 months[4]
Laboratory monitoring of treatment & action to be taken	For follow up of all new patients, one sputum-smear examination should be performed: • at 6 weeks of treatment, and • after 5 months of treatment (if smear was positive at the beginning) If follow up **sputum is positive at 6 weeks** or if the patient is not improving clinically, then • the patient needs to be reassessed by the doctor • in patients who are smear positive at 6 weeks, extend the initial phase by 1 month and repeat sputum-smear examination at 10 weeks (2 ½ months) of treatment If still sputum-**smear positive at 3 months** (10 week results) then: • send one sputum sample for rapid DST • review the results of rapid DST • change to continuation phase of treatment if appropriate If sputum-**smear negative at 3 months** (10 weeks results): • change to the continuation phase of treatment If sputum is **smear positive after 5 months** of treatment: • send one sputum for rapid DST +/- follow-up C/DST • register patient as "treatment failure" • establish if this is true medicine failure (i.e. patient was on strict DOT and still failed) in which case inform the CCRC with a view to starting 2nd line treatment • if failure is due to patient not taking medicines, the retreatment regimen with first line medicines can be considered.
Chest X-ray examination	There is no indication for routine X-ray examination for monitoring clinical progress in patients on *first line* anti-TB therapy.

[4] Severe forms of EPTB are: TB meningitis, spinal TB, abdominal TB, bilateral pleural effusion, pericardial effusion, bone and joint TB involving more than one site. EPTB elsewhere, e.g. lymph node TB, is considered non-severe TB.

End of treatment	In initially sputum-smear positive patients, if smears are negative at 2 (or 3 months) and after 5 months, and the patient has taken 6 months of treatment: • discharge patient and record as ***"cured"*** In initially sputum-smear positive patients, unable to produce sputum at the end of treatment and patient has taken 6 months of treatment: • discharge patient and record as ***"treatment completed"*** In initially sputum-smear negative patients (or EPTB), who have completed 6 months of treatment: • discharge patient from TB treatment and record as ***"treatment completed"***

Retreatment regimen with 1st line medicines – 2RHZES/1RHZE/5RHE **Initial phase of 2 months of RHZES daily, followed by 1 month of RHZE daily, followed by continuation phase of 5 months of RHE daily (total 8 months)**	
Patient categories (see definitions)	• Relapse • Treatment after default • Treatment after failure, with susceptibility to R and H • Other
Modifications advised on the regimen	• In TB meningitis duration of treatment is 9-12 months • Streptomycin should ideally not be used in the pregnant patient eligible for the retreatment regimen, but this risk needs to be balanced against the risk of withholding the medicine • In severe forms of EPTB other than meningitis, treatment duration may be extended to a maximum of 9 months
Monitoring of treatment & Actions to be taken	• Before TB treatment is started, collect one additional sputum sample and send it for DST • Perform **one** sputum-smear examination at: ✓ 10 weeks of treatment, ✓ 5 months of treatment, and ✓ 7 months of treatment If **sputum-smear positive at the 3 month visit** (10 week results): • Follow up on, and review baseline DST results (if not already done so). If results show pan-susceptible TB, are indeterminate or are unavailable, then collect sample for a rapid DST (and C/ DST if indicated) • Review the results of rapid DST • Change to continuation phase, if appropriate If **sputum-smear positive at the 6 month visit** (5 month results): • Send sputum for DST* • Register patient as "treatment failure" • Refer to CCRC with a view to starting the standard regimen for DR-TB patients If **sputum-smear positive at the 8 month-visit** (7 month results): • Send sputum for DST* • Register patient as "treatment failure" • Refer to CCRC with a view to starting the standard regimen for DR-TB patients
Chest radiography	There is no indication for routine X-ray examination to monitor clinical progress during anti-TB chemotherapy. Chest radiography is indicated when a patient fails a retreatment regimen.

End of treatment	In the patient who was initially sputum-smear positive, and smears are negative at 5 months and 7 months, and has taken 8 months of treatment: • Discharge patient and record as ***"cured"*** In the patient who was initially sputum-smear positive and is clinically well but is unable to produce sputum at the end of treatment having taken 8 months of treatment: • Discharge patient and record as ***"treatment completed"*** In the patient who was initially sputum-smear negative or who had EPTB, who has completed 8 months of treatment and is clinically well: • Discharge patient from TB treatment and record as ***"treatment completed"***
Important notes	• All patients must have a DST done before starting the retreatment regimen with first-line medicines to exclude DR-TB. A rapid DST is appropriate in those who are sputum-smear positive. • The result of DST should lead to a change of regimen if: the patient has MDR-TB; monoresistance to R; resistance to H and E; or R and E. Consultation with the CCRC is required in all such cases.

*Due to the advent of rapid molecular-based DST; most patients with MDR-TB and PDR-TB will quickly be identified after starting the retreatment regimen with first-line medicines, and will therefore be moved to appropriate second line treatment.

5.3.2 Treatment dosages by weight categories

5.3.2.1 Fixed dose combinations

The WHO continues to recommend the use of fixed-dose combinations (FDCs) as they are thought to prevent acquisition of drug resistance due to inadequate therapy, which may occur with separate ("loose") medicines. With FDCs, patients cannot choose which medicines to ingest. Prescription errors are likely to be less frequent because dosage recommendations are more straightforward, and adjustment of dosage according to patient weight is easier. The number of tablets to ingest is smaller and may thus encourage patient adherence.

5.3.2.2 Single dose formulations

Using FDCs does not obviate the need for separate medicines; reasons to continue having limited supplies of single-dose formulations of anti-TB medicines include the following:

- Some patients might develop serious adverse effects to one medicine in the FDC, which will require the use of single dose formulations in a specific regimen that does not have the offending, e.g. medicine-induced hepatitis;
- Some patients with DR-TB may still benefit from selected first-line anti-TB medicines;
- The recommended dose by weight band may be unsuitable for some patients.

Table 13: Dosages of FDC formulations

ADULTS		
Body weight in kg	**Initial phase 2 months** [RHZE] [R150/H75/Z400/E275] *Number of tablets*[a]	**Continuation phase 4 months** [RHE] [R150/H75/E275] *Number of tablets*[a]
29 and below	Use paediatric FDCs (R60/H30/Z150; R60/H30) with ethambutol or single dose formulations calculated per medicine by body weight	
30-37	2	2
38-54	3	3
55-74	4	4
75 and over	5	5
For FDC doses for children <12 years of age, please refer to Table 26		

Table 14: Dosages of single anti-TB medicines

Generic name	Abbreviation	Adult dosage Daily treatment in mg/kg/body weight (range)	Maximum daily dose (mg)
Rifampicin	R	10 (8-12)	600
Isoniazid	H	5 (4-6)	300
Pyrazinamide	Z	25 (20-30)	-
Streptomycin[a]	S	15 (12-18)	1000
Ethambutol	E	15 (15-20)	-

[a] *Patients aged over 60 years may not be able to tolerate more than 500–750 mg daily, the dose should thus be reduced to 10 mg/kg per day in patients in this age group. Patients weighing less than 50 kg may not tolerate doses above 500–750 mg daily.*

Table 15: Dosages of single formulation anti-TB medicines by formulation

MEDICINE/ FORMULATION	ADULTS	
	Pre-treatment weight Dosage for injection / number of tablets	
	50kg or more	Under 50 kg
Rifampicin 150mg tablet Rifampicin 450mg	4 1 tablet plus 1 tablet of 150mg	3 1
Isoniazid 300mg tablet Isoniazid 100mg tablet	1 -	1 -
Pyrazinamide 500mg tablet	3	2
Ethambutol 400mg tablet	3	2
Streptomycin injection[b]	1g	750mg
	CHILDREN	
	Calculate dosage by kg /body weight pre-treatment Average dose (range)	
Rifampicin 150mg tablet	15 (10-20)	
Isoniazid 100mg tablet	10 (10-15)	
Pyrazinamide 500mg tablet	35 (30-40)	
Ethambutol 100mg tablet	20 (15-25)	
Streptomycin injection[c]	15 (12-18)	

[b] *Streptomycin: see table below for streptomycin dosing by weight band*

Table 16: Daily dose of streptomycin for adults by weight band

Weight (Kg)	< 60 years 15mg/kg	≥ 60 years 10mg/kg
30-37	500mg	330mg
38-54	660mg	500mg
55-74	1.0g	750mg
≥ 75	1.0g	750mg

5.4 Treatment monitoring

Monitoring of treatment is done using:

- Sputum-smear examination in patients who were initially sputum-positive;
- Records on DOT and clinic attendance;
- Improvement of general clinical condition;
- Increase of body-weight.

Sputum-smear follow-up of a patient who is initially smear-negative may be performed at the end of the intensive phase, but it is often not useful at other times unless there are indications that the TB disease is progressing. This can be caused by non-adherence to treatment or possible drug resistance.

5.4.1 The initial (intensive) phase of treatment

The intensive phase of treatment is a critical phase in which four or more medicines ensure that the majority of TB bacilli are killed and resistant bacilli have no chance to survive. After this, we shift to a less intensive phase of treatment - the continuation phase.

Box 8: Directly Observed Treatment 1

It is important that each daily dose during initial phase treatment is provided as DOT

5.4.2 The continuation phase of treatment

During this phase the patient is treated with fewer TB medicines because the population of live TB bacilli is now small, and the likelihood of it containing naturally resistant mutants is very small.

Box 9: Directly Observed Treatment 2

Each daily dose during the continuation phase should be given as DOT as well. This is particularly important in patients on a retreatment regimen with 1st line medicines

5.5 Definitions of treatment outcomes

The table below shows the definition of standardised treatment outcomes.

Table 17: Definitions of treatment outcomes

Outcome	Definition
Cure	A patient whose sputum smear or culture was positive at the beginning of the treatment and who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.
Treatment completed	A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion
Treatment failure	A patient whose sputum smear or culture is positive at 5 months or later during treatment. These should be recorded as '*treatment failure after 5 months*.'
	Also included in this definition are patients found to harbour a DR-TB strain that necessitate changing the patient to a DR-TB regimen at any point during the treatment, whether they are smear negative or positive. Such outcomes should be recorded as '*treatment failure before 5 months*.'
Died	A patient who dies for any reason during the course of treatment.
Defaulted	A patient whose treatment was interrupted for at least 2 consecutive months.
Transfer out	A patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown.
Treatment success	The sum of those cured and completed treatment

5.6 Adjunctive treatment in tuberculosis disease

5.6.1 Pyridoxine (vitamin B6)

Health personnel can prevent some medicine-induced side-effects, such as isoniazid-induced peripheral neuropathy which usually presents as numbness or a tingling or burning sensation of the hands or feet and occurs more commonly in pregnant women and in people with HIV infection, alcohol dependency, malnutrition, diabetes, chronic liver disease or renal failure. All adult patients should therefore receive preventive treatment with pyridoxine 25mg/day along with their anti-TB medicines. Children over 5 years of age should be given 12.5 mg daily as preventive dose. It should be noted that the prophylactic dose for patients receiving 2nd line anti-TB medicines is much higher than that for patients on first line regimens (see *Chapter 7*).

When an adult patient has developed peripheral neuropathy s/he should be treated with 50-75mg (can be increased up to a maximum of 200mg) pyridoxine daily until symptoms have disappeared, after which s/he should continue on 25mg of pyridoxine daily.

5.6.2 Steroids

Steroid treatment should be considered for management of TB patients with the following conditions:

- Severe allergic reactions to medicines;
- Pericardial effusion and peritoneal effusion,;
- Pleural effusion, when the effusion is extensive enough to cause respiratory distress;
- TB of the eye, the larynx, the kidney;
- TB meningitis;
- TB of the adrenal glands ;
- A patient with TB who is critically ill and is likely to die within the next few days.

The treatment is to be given by experienced clinicians in hospital settings only.

Table 18: Dosage of prednisolone

Disease	Dosage (adults)	Dosage (children)
TB meningitis	*45mg b.i.d. for 4 weeks; 15mg b.i.d. for next 2 weeks then decrease gradually over several weeks according to clinical progress	*2-4mg/kg daily (up to a maximum of 60mg per day) The higher dose is for the more severely ill child
TB pericarditis	*45mg b.i.d. for 4 weeks; 15mg b.i.d. for next 4 weeks; then decrease gradually over several weeks according to clinical progress	
TB pleural effusion	*20mg b.i.d. for 2 weeks; then decrease rapidly	
**The dosage of prednisolone has been increased by half for the first 2-4 weeks. This is because rifampicin reduces the levels of prednisolone in the body.*		

5.7 TB in special situations and management of side effects

The treatment of TB during pregnancy and breastfeeding, and in liver disorders and renal failure is discussed below.

5.7.1 Pregnancy and breastfeeding

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. With the exception of streptomycin, the first line anti-TB medicines are safe for use in pregnancy; streptomycin is ototoxic to the foetus and should generally not be used during pregnancy.

A breastfeeding woman who has TB should receive a full course of TB treatment, including pyridoxine supplementation. Timely appropriate chemotherapy is the best way to prevent transmission of tubercle bacilli to the baby. Except in cases of DR-TB, the 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, if it was not given at birth.

5.7.2 Liver disorders

Patients with the following conditions can receive the usual anti-TB regimens provided that there is no clinical evidence of chronic liver disease:

- hepatitis B or C virus infection
- a past history of acute hepatitis
- current excessive alcohol consumption.

However, hepatotoxic reactions to anti-TB medicines 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 performed at the start of treatment, if possible. If the serum alanine aminotransferase (ALT) level is more than three times the upper limit of normal before the initiation of treatment, the regimens below should be considered in consultation with clinical mentors, specialist physicians or the CCRC. The more unstable or severe the liver disease is, the fewer the hepatotoxic medicines that should be used. It should be noted that TB itself may involve the liver and cause abnormal liver function. In some cases of concurrent acute (e.g. viral) hepatitis not related to TB or TB treatment, it may be preferable to defer TB treatment until the acute hepatitis has resolved.

Possible regimens include[5]:

- Two hepatotoxic medicines (rather than the three in the standard regimen):
  - **9RHE**: 9 months of isoniazid and rifampicin, plus ethambutol
  - **2HRSE/6HR**: 2 months of isoniazid, rifampicin, streptomycin and ethambutol, followed by 6 months of isoniazid and rifampicin
  - **9RZE:** 6–9 months of rifampicin, pyrazinamide and ethambutol
- One hepatotoxic medicine: **2HES/10EH:** 2 months of isoniazid, ethambutol and streptomycin, followed by 10 months of isoniazid and ethambutol
- No hepatotoxic medicines: **24SELfx**: 18–24 months of streptomycin, ethambutol and levofloxacin

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

5.7.3 Management of skin reactions

Before attributing skin symptoms or rash to TB medications, it is important to assess if it was present before commencement of anti-TB therapy or if it can be attributed to another cause. If a patient develops itching without a rash; mild erythema or few papules and there is no other obvious cause, the recommended approach is to try symptomatic treatment with antihistamines and skin moisturisers, and continue anti-TB treatment while observing the patient closely. If a moderate skin rash (more extensive symptoms) develops, all anti-TB medicines must be stopped, pending resolution while on adequate hydration and symptomatic treatment (e.g. antihistamine, steroids).

If the rash is severe (including skin desquamation, mucositis, blister/bullae formation, fever) stop **all** medications, including anti-TBs, analgesics and ARVs, and hospitalise the patient urgently while providing intravenous rehydration and steroids. These cases require specialised care.

Once the reaction has resolved, anti-TB medicines are re-introduced one by one, starting with the medicine least likely to be responsible for the reaction (rifampicin or isoniazid) at a small challenge dose, such as 50 mg isoniazid. The dose is gradually increased over 3 days. This procedure is repeated, adding one medicine at a time (see *Figure 9).* A reaction after introducing a particular medicine implicates that medicine as the cause of the reaction. The alternative regimens listed in *Section 5.7.2* above are also applicable when a particular medicine cannot be used because it was implicated as the cause of a cutaneous reaction.

Figure 9: Example of a stepwise re-introduction of TB medications after a skin rash

Medicine	Challenge Doses		
	Day 1	Day 2	Day 3
H	50 mg	150 mg	300 mg
R	75 mg	300 mg	600mg
Z	250 mg	1.0 g	1.5 g
E	100 mg	500 mg	1.2 g
S	125 mg	500 mg	1 g

Adapted from: TB/HIV: A Clinical Manual, 2nd edition. World Health Organisation. 2004.

[5] These regimens are for exceptional situations and should be considered only after wide consultation

5.7.4 Renal failure and severe renal insufficiency

The recommended initial TB treatment regimen for patients with renal failure or severe renal insufficiency is the standard new patient regimen. 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 medicines at the following doses is recommended: pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg).

While receiving isoniazid, patients with severe renal insufficiency or failure should also be given pyridoxine in order to prevent peripheral neuropathy. Streptomycin should be avoided in patients with renal failure because of an increased risk of nephrotoxicity and ototoxicity. If streptomycin must be used, the dosage is 15 mg/kg, two or three times per week, to a maximum of 1 gram per dose, and ideally serum levels of the medicine should be monitored.

5.7.5 Management of medicine-induced hepatitis

Of the first-line anti-TB medicines, isoniazid, pyrazinamide and rifampicin all can cause liver damage (medicine-induced hepatitis). In addition, rifampicin can cause asymptomatic jaundice without evidence of hepatitis. It is important to try to rule out other possible causes before deciding that the hepatitis is induced by the TB regimen.

The management of hepatitis induced by TB treatment depends on:

- whether the patient is in the intensive or continuation phase of TB treatment;
- the severity of the liver disease;
- the severity of the TB; and
- the capacity of the health unit to manage the side-effects of TB treatment.

If it is strongly suspected that the liver disease is caused by the anti-TB medicines, all medicines should be stopped. Most patients will tolerate this interruption and recover appropriately. If the patient is severely ill with TB and it is considered unsafe to stop TB treatment, a non-hepatotoxic regimen consisting of streptomycin, ethambutol and levofloxacin can be started.

If TB treatment has been stopped, it is necessary to wait for liver enzymes to revert to normal and clinical symptoms (nausea, abdominal pain) to resolve before reintroducing the anti-TB medicines. If the signs and symptoms do not resolve and the liver disease is severe, the non-hepatotoxic regimen consisting of streptomycin, ethambutol and levofloxacin should be started (or continued) for a total of 18–24 months.

Once medicine-induced hepatitis has resolved, the medicines are reintroduced one at a time. If symptoms recur or liver function tests become abnormal as the medicines are reintroduced, the last medicine added should be stopped. Since ethambutol and streptomycin are not hepatotoxic, they may be introduced first, followed by rifampicin because it is less likely than isoniazid or pyrazinamide to cause hepatotoxicity, and is the most effective agent. After 3–7 days, isoniazid may be reintroduced. In patients who have experienced jaundice but tolerate the reintroduction of rifampicin and isoniazid, it is advisable to avoid pyrazinamide.

Alternative regimens depend on which medicine is implicated as the cause of the hepatitis. Possible regimens include the following: [6]

- if rifampicin is implicated, a suggested regimen without rifampicin is 2 months of isoniazid, ethambutol and streptomycin followed by 10 months of isoniazid and ethambutol.
- if isoniazid cannot be used, 9 months of rifampicin, pyrazinamide and ethambutol can be considered.
- if pyrazinamide is discontinued before the patient has completed the intensive phase, the total duration of isoniazid and rifampicin therapy may be extended to 9 months.
- if neither isoniazid nor rifampicin can be used, the non-hepatotoxic regimen consisting of streptomycin, ethambutol and levofloxacin should be continued for a total of 18–24 months.

Reintroducing one medicine at a time is the optimal approach, especially if the patient's hepatitis was severe. The Central Medical Stores (CMS) procure limited quantities of single-dose anti-TB medicines for use in such cases.

Table 19: Symptom-based approach to managing side-effects of anti-TB medicines

Side-effects	Medicine(s) probably responsible	Management
Major		***Stop responsible medicine(s) and refer to clinician urgently***
Skin rash with or without itching	Streptomycin, isoniazid, rifampicin, pyrazinamide	Stop anti-TB medicines (depends on severity-see 5.7.3)
Deafness (no wax on otoscopy)	Streptomycin	Stop streptomycin
Dizziness (vertigo and nystagmus)	Streptomycin	Stop streptomycin
Jaundice (other causes excluded), hepatitis	Isoniazid, pyrazinamide, rifampicin	Stop anti-TB medicines
Confusion (suspect medicine-induced acute liver failure if there is jaundice)	Isoniazid, probably most other anti-TB medicines	Stop anti-TB medicines
Visual impairment (other causes excluded)	Ethambutol	Stop ethambutol
Shock, purpura, acute renal failure	Rifampicin	Stop rifampicin
Decreased urine output	Streptomycin	Stop streptomycin
Minor		***Continue anti-TB medicines, check medicine doses***
Anorexia, nausea, abdominal pain	Pyrazinamide, rifampicin, isoniazid	Give medicines 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; non-steroidal anti-inflammatory medicines, or paracetamol
Burning, numbness or tingling sensation in the hands or feet	Isoniazid	Pyridoxine 50–75 mg daily (can be increased to a maximum of 200mg daily)
Drowsiness	Isoniazid	Reassurance. Give medicines before bedtime

[6] These regimens are for exceptional situations and are considered with wide consultation

Side-effects	Medicine(s) probably responsible	Management
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 (can occur inadvertently due to poor adherence)	Change from intermittent to daily rifampicin administration

5.8 Gold standards for managing TB

5.8.1 DO'S

For TB treatment to be effective and result in treatment success, clinicians and nurses should adhere to the following principles:

- Adhere to the NTLP treatment regimens;
- Prescribe the correct dose for the weight band and adjust the dose if weight increases;
- Maintain the prescribed regimen until completion of the full course, unless a patient becomes a failure or develops severe side-effects requiring regimen change;
- Apply Directly Observed Therapy (DOT) for at least:
  - The first two months of treatment in all new patients, and preferably for the full course;
  - The full duration of treatment of patients treated with the re-treatment regimen;
- Ensure that treatment is given for 7 days a week during the entire treatment
- All TB medicines are taken at the same time. If the patient has gastro-intestinal problems all medicines should be taken immediately after a light meal.

5.8.2 DON'TS

- Do not use one anti-TB medicine (monotherapy) in a patient who is sick and thus might have TB disease, especially in HIV positive patients
- Do not add one medicine to a failing regimen as it might lead to drug resistance;
- Do not deviate from the regimens prescribed in these guidelines, unless on the advice of the CCRC, for very specific patients with rare side-effects or resistance patterns.
- Do not give "trial TB treatment";
- Do not use any of the second-line anti-TB medicines, except when patients fit the eligibility criteria (see *Chapter 7*), and in exceptional circumstances for patients with severe adverse reactions to first line anti-TB medicines.

5.9 Patient management and support

5.9.1 A patient centred approach

TB treatment is quite demanding for the patient. The daily intake of medicines for a period of 6 to 8 months is very difficult for most patients. This must be brought to the attention of the patient from the onset of treatment by the clinician or the nurse. It has commonly been observed that without strong ongoing psychological support from nurses, close relatives and the community (employers in particular) many are tempted or will actually stop their TB treatment when they start feeling better. This is

particularly so, when the costs (real financial costs for medicines or transportation, or the cost of spending time visiting a clinic) are higher than the perceived benefits of completing the TB treatment once a patient feels better. It is therefore important to support each TB patient in such a way that it becomes more attractive and easy to complete treatment, rather than stop it. This can only be achieved when we create a patient-centred treatment delivery system, that is well accessible (geographical, cultural and financial), patient-friendly, compassionate, creative and convenient for each patient.

5.9.2 Adherence by health-care workers

It is very important that all anti-TB treatment is prescribed according to the patient categories and regimens prescribed in these guidelines. Doctors and nurses are encouraged to follow the TB management principles stated in these guidelines. Deviation from these guidelines can lead to development of resistance, including resistance to rifampicin and isoniazid (MDR-TB).

5.9.3 Patients' adherence

The default rate among new smear positive cases has been going down from 10% in 2005 to 4% in 2008. This has been a result of DOT implementation throughout the country. The health services and community have the collective responsibility of ensuring that patients started on TB treatment take all their medicines as prescribed.

5.9.4 Tracing of patients interrupting treatment

When a patient does not turn up for his daily DOT appointment or for collection of a weekly or 2-weekly medicine supply, the TB nurse should put the *TB Treatment Card* aside as this patient is a potential defaulter. Efforts to trace the patients should start as soon as possible with assistance of relevant resources. After one week without the patient or his DOT supporter attending the facility, the TB nurse should make an effort to trace the patient or his DOT supporter. After the patient has been traced, the reasons for treatment interruption are established and treatment is continued as before.

A patient is declared a defaulter if treatment has been interrupted for a period of at least 8 consecutive weeks and all efforts to put the patient back on treatment have failed. Efforts to trace the patient should therefore be made before s/he is classified as a defaulter. The expression "defaulter tracing" is therefore incorrect, although it is frequently being used.

5.9.5 Management of patients who interrupt treatment, and those who have defaulted

The management of patients who interrupted treatment is complex and takes into consideration several variables (sputum-smear status, stage of treatment, degree of remission of the disease after the previous treatment, probability of drug susceptibility or resistance) that may be difficult to assess. The actions to be taken under such conditions are described in the following table.

Table 20: Actions after interruption of treatment and after default

<table>
<tr><th colspan="4">Interruption for less than 1 month</th></tr>
<tr><td colspan="4">• Trace the patient
• Establish the cause of interruption and, where possible, solve the problem
• Continue treatment and prolong it to compensate for the doses not taken</td></tr>
<tr><th colspan="4">Interruption for 1 – 2 months</th></tr>
<tr><th colspan="2">Action 1</th><th colspan="2">Action 2</th></tr>
<tr><td rowspan="3">• Trace patient
• Solve the cause of interruption
• Obtain 2 sputum samples for smear microscopy
• Continue treatment while waiting for results</td><td>If smears negative or EPTB</td><td colspan="2">• Continue treatment and prolong it to compensate for missed doses</td></tr>
<tr><td rowspan="2">If one or more smears positive</td><td>Treatment received < 5 months</td><td>• Collect sputum for rapid DST
• Continue treatment and prolong it to compensate for missed doses if susceptible
• Monitor closely</td></tr>
<tr><td>Treatment received ≥ 5 months</td><td>• Manage as a treatment failure
• Collect sputum for rapid DST & review the results
• Consider retreatment regimen if adherence was poor prior to defaulting, and it is presumed to be pan-susceptible TB
• Final treatment regimen may depend on DST results and consultation with CCRC</td></tr>
<tr><th colspan="4">Interruption for 2 months or more (defaulter)</th></tr>
<tr><td rowspan="3">• Obtain 2-3 sputum smears
• Solve the cause of interruption, if possible
• No treatment while waiting for sputum smear results</td><td>Negative smears or EPTB</td><td colspan="2">Clinical decision on individual basis whether to restart or continue treatment , or no further treatment</td></tr>
<tr><td rowspan="2">One or more smears positive</td><td>Was on new patient regimen</td><td>• Collect sputum for rapid DST and review the results
• Start retreatment regimen with FLD if appropriate and if presumed to be susceptible TB</td></tr>
<tr><td>Was on retreatment regimen with FLDs</td><td>• Collect sputum for rapid DST and review the results
• Treatment regimen may depend on DST results and consultations with the CCRC</td></tr>
</table>

5.9.6 Directly Observed Treatment and patient support

DOT during the entire treatment course is the best method to ensure full adherence and treatment success. In a strict definition, DOT is the act of observing a TB patient swallowing his prescribed medicines, while a broad definition of DOT is providing continuous psychological (moral) support to the patient in his endeavour to successfully complete his TB treatment. This requires an empathetic attitude from the DOT supporter, and a genuine commitment to help the patient with his problems. This also requires continuity in the patient-provider relationship, in order to create bonding and mutual respect. During the admission phase the healthcare worker discusses the possible options for DOT with every patient, until a DOT

supporter that best suits the needs of the patient has been identified. The TB patient record card will be kept at the nearest TB clinic, where the patient or his DOT supporter will come to collect TB medicines on a regular basis. The nurse at the TB clinic will provide the DOT supporter with a *Community Based DOT Card (TB 07)*, on which each daily DOT intake is recorded. When a new supply of medicines is collected the nurse will check the DOT card and ensure that medicine intake was daily. When the patient wishes to move to another address or wants to change the DOT supporter, s/he should report this to the TB clinic, which will facilitate the transfer and record this in the *Facility TB register*.

5.10 The organisation of treatment

5.10.1 Hospital admission

While it is not mandatory to admit patients on first line anti-TB treatment, it is often necessary to keep a patient in hospital until the conditions for proper ambulatory DOT have been established. During this admission the patient should undergo a full clinical assessment including HIV testing. They should only be discharged if they are fit enough to continue ambulatory treatment, if they understand all they need to know about their TB treatment and after a DOT supporter has been identified and educated.

During admission the patient should receive the following care:

- Education on TB treatment and importance of testing for HIV;
- HIV testing and counselling;
- Comprehensive clinical care for diseases other than TB, including STIs and HIV;
- Education on co-trimoxazole preventive therapy (CPT) and ART, if HIV positive;
- Education on proper nutrition;
- Education on the need to have a treatment supporter who takes co-responsibility for DOT during the entire TB treatment.
- Anti-TB medicines, which should be given under direct observation. This will serve to prime the patient for ambulatory DOT
- Information on the community-based organisations operating in the patient's locality, as well as the services they provide.

5.10.2 Registration

After TB diagnosis, the patient is immediately registered in the *Facility TB Register*, and anti-TB treatment is started without delay. No TB patient should be treated without being registered.

5.10.3 Information, education and communication on TB and HIV

As soon as possible the patient should receive information and education on TB disease, its treatment and duration, and possibilities of social and nutritional assistance during treatment. It is very important that the patient understands the link between TB and HIV, and the importance to the clinician of knowing the patient's HIV status. It is poor clinical practice and highly stigmatising not to discuss HIV with a TB patient. Each TB patient is worried that s/he has HIV, and knowing the HIV status of each patient is important for good patient management. If the patient is unable to communicate the family should be informed about the need of HIV testing and counselling. If the patient does not want to be tested this decision must be respected, but opportunities should be created to continue offering the patient additional counselling and testing whenever they are ready.

The TB patient with HIV needs extensive education and information, and should fully understand the benefits of additional treatment for HIV. The patient should be told about cotrimoxazole preventive treatment, and when and how best s/he can be started on ART. The importance of disclosing HIV status to relatives and friends who can support him during both TB and HIV treatment should also be discussed.

5.10.4 Nutrition

Good nutrition during TB treatment is important for a good recovery of the patient, even more so when the patient also has HIV. A balanced diet with high protein content is recommended. TB patients with advanced HIV infection need additional support if they have gastro-intestinal problems such as diarrhoea, or candidiasis.

5.10.5 Ambulatory DOT

Once a patient has been started on treatment, s/he can be referred to the health facility nearest their place of residence. This health facility will be responsible for the provision of TB medicines, monitoring the patient's treatment (by sputum-smears), as well as tracing the patient who has missed an appointment. TB clinics should be held on fixed days each week for patients attending at one- or more weekly intervals, and daily for patients coming for health facility DOT. This TB Treatment Centre will again discuss with the patient, how best DOT can be ensured at the patients' convenience. The following options of DOT are discussed with the patient:

5.10.5.1 Health facility-based DOT

DOT is provided at a health facility that is situated conveniently close to the patients' home or on his way to work. The patient takes the medicines every day under observation by the health care worker, except on weekends when the patient will take his/her anti-TB medicines at home.

5.10.5.2 Community-based DOT

Various options for community-based DOT exist, and the patient should be assisted to select the most suitable DOT option. It should be noted however that this option is not fixed, as the patient might need to change from one option to another during TB treatment.

a) Workplace DOT

DOT can be provided by a healthcare worker in the medical services at the work place, or by a lay person in the organisation. If this is a feasible option for the patient, the health facility nurse or field promoter should contact the employer or supervisor and discuss the possibilities of workplace DOT with the relevant person. The workplace DOT supporter should then come to the clinic with the patient where both should receive intensive education and instructions on the TB treatment, and the importance of daily DOT. A *CB-DOT Card* should be opened and given to the workplace DOT supporter. The health facility nurse or TB field promoter should record details of the workplace DOT supporter on the *TB Treatment Card* and in the *Facility TB Register*.

TB medicines are given to the workplace DOT supporter for periods of 1 to 2 weeks in the intensive phase, and periods of 2 to 4 weeks during the continuation phase. When coming to collect more TB medicines, the patient or DOT supporter should bring the CB-DOT card and the blister cell sheets of the previous period. The nurse or TB field promoter should verify that daily DOT is recorded, count any remaining tablets, and copy the doses taken on the *TB Treatment Card* which is kept at the clinic. A new supply of TB medicines is provided, and recorded on both *CB-DOT Card*, and recorded on *TB Treatment Card*.

b) Guardian-based DOT

A guardian is a lay-person the patient selects from his home or his neighbourhood, who is willing to take joint responsibility for the patient's TB treatment. When the patient is a child, the guardian will most likely be one of the parents. The guardian should come to the hospital or the TB treatment centre and receive intensive education and information on TB and its treatment and the importance of DOT until the end of treatment.

The guardian's name and address are recorded on the *TB Treatment Card* and in the *Facility TB Register*. *A CB-DOT card* is opened for the patient, and the guardian is instructed on how to record each daily intake of TB medicines. TB medicines are given to the guardian or patient for periods of 1-2 weeks in the intensive phase, and periods of 2-4 weeks during the continuation phase. When coming to collect more TB medicines, the patient or guardian brings along the *CB-DOT Card* and the blister cell sheets of the previous period. The nurse or TB field promoter should verify that daily DOT is recorded, count any remaining tablets, and copy the doses taken onto the *TB Treatment Card* which is kept at the clinic. If all is well a new supply of anti-TB medicines is provided, and recorded on both *CB-DOT Card* and the *TB Treatment Card*.

c) Community health worker-assisted DOT

A community health worker or home-based care worker, in the neighbourhood of the patient, takes responsibility for daily DOT at the patient's house (or the CHW's house), or at another agreed location during the full treatment period. Name, address and possibly telephone number of the CHW must be known and recorded on the *TB Treatment Card, TB Patient Identity Card and CB-DOT Card*.

5.11 Roles and responsibilities of various care providers in DOT

5.11.1.1 Nurse

The nurse in the TB treatment unit is the cornerstone of a well-functioning TB programme, as s/he is responsible for ensuring that the patient completes treatment successfully. It requires talent, skill, experience and interest to motivate a patient to successful completion of treatment. Managing a TB clinic is not a task any nurse can do well. S/he must be knowledgeable about all aspects of TB and HIV management and must be able to discuss confidently with any patient about issues around TB and HIV. Additionally s/he must be patient, compassionate, empathetic and creative in finding solutions to the patients' individual problems related to the disease or the treatment.

Box 10: Importance of a designated TB nurse

It is important that nurses are carefully selected as "TB nurses", based on the required attitude and personal interest in TB; that they stay on as TB nurses for a prolonged period of time in order to become experienced and competent via in-service training, and should receive on-the-job training from their supervisors.

Box 11: Staff rotation

Frequent and poorly structured rotation of nurses at the TB clinic at short intervals of 3-6 months may cause lack of continuity, incompetence, and many patients to default due to disruption of established rapport.

5.11.1.2 Medical officer

The role of the medical officer is mainly limited to the diagnosis of TB and the management of complications. The large majority of the TB patients do not need to see a doctor again after diagnosis, in

the absence of complications and when completing treatment. Most patients can be managed well by the TB nurses. The following patients should be reviewed by the doctor:

- All retreatment patients at the end of the initial phase. In addition to reviewing the clinical picture and smear results, this review should also include a review of the pre-treatment DST results.
- All patients who are not improving on treatment, including those who are smear-positive on follow-up smear examination.
- Patients for whom the regimen has been modified due to side effects.
- Patients with EPTB. These patients require thorough clinical assessment as part of their monitoring. Often there is need to assess complications of the TB, as in the case of spinal TB, TB meningitis and pericardial TB.

5.11.1.3 Field promoters

Field promoters are lay persons from the community who may be attached to a health facility or to other TB treatment points in the community, who have been trained in TB-DOT and TB case-finding. They provide support to the TB nurses regarding IEC, observation of treatment, recording and tracing of patients who interrupt treatment. They also support community education on both TB and HIV.

5.11.1.4 Home-based care workers

Home-based care workers can play an important role in TB case-finding and TB-DOT, as many PLHIV develop TB disease in the course of their illness. They are well situated in the community to identify TB suspects and refer them for TB examination and in some cases act as DOT supporters for those on treatment for TB.

Table 21: Summary of roles and responsibilities of clinician and nurse in TB care

Role/ responsibility	TB Nurse	Medical officer (doctor)
TB diagnosis	Identify TB suspects Organise sputum-smear examination	Identify TB suspects Diagnose all forms of TB
Initiation of treatment	Classification of patient Registration of the patient Prescription of correct regimen Organisation of DOT	Classification of patient Prescription of correct regimen
Follow-up sputum-smear examination	Sputum collection according to NTLP guidelines	Ensures that follow-up sputum samples are collected in line with NTLP guidelines
Culture/DST examination	Sputum collection for C/DST as requested by the doctors, or as scheduled according to treatment guidelines	Identification of cases requiring C/DST Review of DST results
DOT	Organise most convenient DOT option for the patient, administer Clinic based DOT	Technical backstopping for nurses
Discharge from treatment	Discharges PTB patients who are fit, and having completed treatment	Assesses all other patients due for discharge
Management of minor side-effects	Diagnoses, advises and provides simple remedies described in these Guidelines	Diagnoses, advises and provides simple remedies described in these guidelines
Management of major	Diagnoses and refers to doctor	Diagnosis and management of all

Role/ responsibility	TB Nurse	Medical officer (doctor)
side-effects		patients
Management of patient with treatment failure	Diagnoses and refers to doctor	Diagnosis and management according to guidelines
Management of patient who returns after default	Diagnoses and refers to doctor Manages new treatment plan	Diagnosis and management according to guidelines

6 TUBERCULOSIS IN CHILDREN

6.1 Background

Globally, children less than 15 years old comprise 10-15% of all reported cases of TB. The source of TB infection in a child is usually an adult, generally a family member living in the same household, with sputum-smear positive PTB. TB in children therefore reflects failed TB control in adults.

Young children (<4 years old), and those with risk factors such as malnutrition and HIV infection are at particular risk for primary progressive TB because of their weak immune systems. Children who develop TB usually do so within 2 years of infection, and are less likely to present with reactivation disease.

Management of TB is similar in adults and children. This chapter will primarily focus on the special considerations specific to management of TB in children.

6.2 Prevention

6.2.1 BCG

Bacille Calmette-Guérin (BCG) is a live, attenuated *Mycobacterium bovis* vaccine given by intradermal injection administered soon after birth and which offers some protection to infants and young children against disseminated TB. The protective efficacy of BCG in young HIV-uninfected children against TB meningitis and miliary TB is estimated to be 73% and 77% respectively.

The policy in Namibia is to routinely administer BCG at birth to all infants unless the infant presents with symptomatic HIV infection. This policy takes into consideration that almost all HIV-infected infants are asymptomatic at birth and to not routinely vaccinate all infants at that time would pose significant risk to non-HIV infected infants in a setting of high TB prevalence. An exception to the above is the infant born to a mother with suspected or confirmed TB. BCG should be withheld while screening for and managing active disease or infection in such infants (see *Section 6.6.3*).

6.2.1.1 BCG disease and BCG IRIS

Complications associated with BCG vaccination occur in a 1-2% of children and include injection-site lesions, adenitis and very rarely, disseminated disease. Disseminated disease, a condition associated with very high mortality, is generally estimated to occur in 5 infants per one million vaccinated. Before the HIV era, infants with disseminated BCG disease usually had rare congenital immunodeficiencies. The rate of disseminated disease in HIV-infected infants is much higher.

BCG disease can present any time after the vaccination, and may also occur as part of Immune Reconstitution Inflammatory Syndrome (IRIS), soon after starting antiretroviral treatment. It may be classified as follows:

- *Local* - lesion at site of injection, including abscess or severe ulceration
- *Regional* - involvement of any regional lymph nodes (axillary or supraclavicular) or other regional lesions beyond site of injection. This may include enlargement, suppuration and fistula formation
- *Distant* - confirmed disease at one site other than the regional lymph nodes or local injection site such as pulmonary secretions, CSF, urine, bone and distant skin lesions
- *Disseminated* – disease occurring at two or more sites other than the regional or local site and/or at least one positive bone marrow or blood culture

BCG IRIS can be defined as BCG-associated local, regional, distant or disseminated disease that occurs in HIV-infected children generally within 3-6 months of initiating ART, irrespective of immunological proof of immune reconstitution. The classification, definitions and management of BCG IRIS is the same as for other BCG disease in HIV-infected infants.

All cases of BCG disease conforming to the above definitions should be officially reported as vaccine-related adverse events. Management of BCG disease will vary depending on the affected site and the HIV status of the child, as shown in***Error! Reference source not found.***. If BCG disease is suspected, consult a specialist.

Table 22: Management of BCG disease

Site	HIV-negative	HIV-positive
Local or Regional	Observe. Consider therapeutic aspiration or excision if: • fluctuant node or abscess, • persistent, rapidly enlarging node, • fistula formation, or • presence of large injection site abscess	Consult a specialist (possible medical treatment) Consider therapeutic aspiration if node fluctuant. Follow-up 2-4 weekly. Consider excision biopsy if no improvement. Initiate ART if not yet commenced.
BCG IRIS (Local or Regional) with no suspected dissemination	Not applicable	Observe. Follow-up 2-4 weekly Continue ART Consult a specialist
Distant or Disseminated	Consult a specialist. Treat medically.* Monitor for toxicity.	Consult a specialist. Treat medically.* Initiate ART if not yet commenced, taking into consideration potential medicine interactions. Monitor for toxicity.

*Medical treatment for a minimum of 9 months:

- H 15-20 mg/kg/day
- R 20 mg/kg/day
- E 20-25 mg/kg/day
- Z 20-25 mg/kg/day (for 2 months or less if *M.tb* excluded)
- Levofloxacin 7.5 -10 mg/kg/day

Dual infection with *M. bovis* (from the BCG) and *M.tb* may occur especially in countries with a high TB prevalence such as Namibia. Therefore, although *M. Bovis* is resistant to pyrazinamide, treatment should include pyrazinamide in the first two months because it is often difficult to confirm BCG disease and to rule out infection with *M.tb* or dual infection.

6.2.1.2 BCG vaccination and HIV

HIV-infected infants who are routinely vaccinated with BCG at birth while still asymptomatic, and who later develop AIDS are at increased risk of developing disseminated BCG disease with an all-cause mortality of >75%. The risk is estimated to be 407 to 1300 per 100,000 HIV-infected infants. This represents a major increase in mortality over that in the general population.

For this reason, BCG vaccination would not generally be recommended for *known* HIV-infected infants. However, HIV-exposed infants in Namibia are tested for HIV at 6 weeks of age, long after the routine BCG immunisation is currently given. A strategy to delay routine BCG for HIV-exposed infants with unknown status, the majority of whom will be HIV-negative, until *confirmed* HIV negative, could result in many such infants becoming infected with, and dying from TB. Hence even HIV-exposed newborns in Namibia, a high TB prevalence setting, should be given BCG vaccination unless they already show signs of HIV infection.

6.2.2 TB isoniazid preventive therapy (IPT)

All children <5 years old (whether HIV positive or negative) who have had contact with sputum positive TB patients, including infants born to mothers with infectious TB disease, should have supervised isoniazid preventive therapy once active TB disease has been excluded. Except for perinatal exposure, screening for signs and symptoms of TB is generally thought to be a sufficient screen.

In addition, any HIV-positive child in whom active TB has been excluded and who has never previously had IPT is eligible for TB-IPT, whether there has been known exposure to active TB or not.

Simple screening questions to be asked for children include probing for:

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

If the answer to any of the screening questions is a "Yes", investigations for TB and other diseases is required. This should include a thorough physical examination; chest radiography and possibly a TST along with any other relevant tests (see *Section 6.3*).

All infants born to mothers with TB disease should be investigated thoroughly (see *Section 6.6*) whether or not they have symptoms.

The dosage for TB-IPT is isoniazid 10 mg per kg (range 10-15 mg/kg, maximum 300mg) daily for 6 months. This is an increase from the previously recommended dosage due to studies which have shown that children metabolise isoniazid more quickly than adults. *Table 6-2* is a weight-banded dosage chart that will assist in prescribing of IPT to children.

Table 23: Weight-banded dosage for isoniazid use in children

Weight range (kg)	Number of H100 tablets per dose daily	Dose (mg)
<5	½ tablet	50
5-9.9	1 tablet	100
10-13.9	1 ½ tablets	150
14-19.9	2 tablets	200
20-24.9	2 ½ tablets	250
≥25	3 tablets or one adult tablet	300

Pyridoxine may be given along with isoniazid in HIV-infected children to prevent isoniazid associated neuropathy. A dose of 12.5 mg/day is suggested for children 5-11 years of age, and 25 mg/day for children ≥12 years.

It is important to follow up children started on TB-IPT on a monthly basis. This allows ongoing screening for TB disease as well as promotion of completion of 6 months of the preventive treatment.

6.3 Diagnosis of TB in children

The diagnosis of TB in a sick child relies on a thorough assessment of all the evidence from a careful history, clinical examination including growth assessment and relevant supporting investigations such as CXR examination and TST. Bacteriologic confirmation of infection would be ideal but is often not possible.

Clinicians should exercise a high index of suspicion in a child presenting with suggestive symptoms, especially with HIV-infected children. Nevertheless, clinicians should always consider other diseases to avoid over-diagnosis and unwarranted treatment for TB. As in adults, diagnosis by "trial therapy" is not recommended in children.

Box 12: Key features suggestive of TB in children

The presence of *three or more* of the following strongly suggests a diagnosis of TB:

- Chronic symptoms suggestive of TB
- Physical signs highly suggestive of TB
- Chest X-ray examination findings suggestive of TB
- A positive TST

Close contact with a smear-positive TB case further increases the likelihood of TB

6.3.1 History

A detailed and careful history should be taken, which should include the following.

Contact history:

- Household or other close contact with a person with TB
- Household or other close contact with anyone with a chronic cough
- Household / family member with HIV (such persons would be more likely to have TB than HIV-negative household contacts)

Previous medical history:

- Previous TB treatment and outcome of treatment
- Previous TB-IPT
- Previous HIV test result

Current illness:

- Progressive, unremitting cough that is not improving and has been present for 2 weeks
- Unexplained fever (temperature ≥38°C) for 2 weeks
- Night sweats
- Fatigue
- Weight loss or failure to thrive: stagnation or decrease in growth noted on growth chart

Weight for age -2 to -3 z-score[7] (underweight) or less than -3 z-score (severely underweight)

- Decreased appetite
- Respiratory infection or meningitis not responding to antibiotics
- Febrile illness not responding to anti-malarial medication in a malarious area

6.3.2 Clinical examination

A good clinical examination should look for signs consistent with TB disease, which may include:

Lymphadenopathy

- Large painless, generally soft, lymph nodes with or without fistula formation – particularly cervical

Respiratory signs

- Tachypnea
- Adventitious sounds on auscultation
- Reduced air entry or dullness to percussion in lower lung field(s) (pleural effusion)
- Audible wheeze due to enlarged intra-thoracic lymph nodes

Cardiac signs

- Pericardial friction rub, distant / muffled heart sounds (pericardial effusion)

Abdominal signs

- Distended abdomen with or without ascites

Bones and joints

- Gibbus deformity due to collapsed vertebrae in the spine
- Progressive non-painful swelling or deformity of joints or bone, with or without sinus formation

Central nervous system

- Change in temperament, convulsions, coma - especially if sub-acute, developing over several days (meningitis)

6.3.3 Bacteriological confirmation of tuberculosis

Pulmonary TB is the most common type of TB seen in children, but children rarely have smear positive sputum, making the diagnosis of PTB difficult to confirm. Contributing factors include the inability of small children to produce sputum, the fact that children tend to swallow sputum, and the greater likelihood of having primary TB infection in children. As with adults, diagnosis of EPTB may require tissue sampling for confirmation.

Particular effort should be made to collect specimens for culture and DST before or at the start of treatment for children with previously treated TB or those suspected of exposure to DR-TB.

6.3.3.1 Sputum

a) *Sputum expectoration:* Older children are often able to produce sputum. Spot and early morning specimens should be obtained following the methodology described in *Chapter 4*.

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[7] **z-scores** refer to standard deviations. -2 z-score is -2 standard deviations from the mean. A child whose weight is -2 z-score, is underweight. A child whose weight is -3 z-scores, is severely underweight.

b) *Sputum induction with saline:* Deep coughing can be induced by inhalation of an aerosol of warm, sterile, hypertonic (5%) saline and is a useful procedure for children and adults who cannot cough up sputum. The procedure should be performed by staff who have been trained to do it. It should be carried out in a well-ventilated place and all personnel in the room should wear N95 respirators.

The patient should fast for 3-4 hours prior to the procedure to prevent vomiting and aspiration. In addition, the procedure should *not* be done if the child is bleeding, or has respiratory distress, reduced level of consciousness or a history of significant asthma.

A bronchodilator such as salbutamol should be administered to reduce the risk of wheezing. Nebulised hypertonic saline should then be administered for 15 minutes or until 5ml of solution has been fully administered, whichever comes first. Chest physiotherapy may be necessary to mobilise secretions. Older children may then be able to expectorate and sputum can be collected. For younger children suction of the nasal passages or nasopharyngeal aspiration may be done to collect specimens.

Induced sputum is watery and resembles saliva; therefore specimen bottles should be clearly labelled *'induced sputum'*.

6.3.3.2 Gastric aspiration

Because children with TB may swallow sputum containing *M.tb*, gastric aspiration can be used to confirm the diagnosis in children who are unable to expectorate spontaneously and where induced sputum cannot be obtained. This procedure should only be done if a culture for *M.tb* is to be requested, in addition to the smear since other mycobacteria or contaminants in the stomach may also give a positive smear. The diagnostic yield of a set of 3 gastric aspirates is 25-50%, therefore *a negative gastric aspirate smear or culture does not exclude TB.*

The highest yield of gastric aspirate specimens for TB is in the morning when the child has been fasting for at least 4 hours. The procedure usually requires 2 people.

Box 13: How to perform a gastric aspirate

> Insert the appropriately-sized nasogastric tube, attach a syringe and withdraw 2-5 ml of gastric contents. If no fluid is aspirated, insert 5-10 ml of water or normal saline and attempt to aspirate again. Withdraw at least 5-10 ml of fluid. If this is unsuccessful, attempt a maximum of 3 times. The extracted fluid should be decanted into a specimen container with an equal volume of 8% sodium bicarbonate. This neutralises the stomach acid and therefore prevents destruction of the tubercle bacilli. The specimen should then be forwarded to the laboratory for smear microscopy and mycobacterial culture as mentioned above.

Gastric aspiration should not be done if the child has a low platelet count or another bleeding disorder.

6.3.4 Diagnosis of extrapulmonary TB (EPTB)

Bacteriological confirmation should be sought if possible in cases of suspected EPTB. The approach will vary with the site (see *Table 24)*, and is similar to that used in adults except that children may require sedation or general anaesthesia to obtain some specimens.

Table 24: Diagnostic procedure for suspected EPTB in children

Site	Procedure
Peripheral lymph nodes (especially cervical)	Fine-needle aspiration or biopsy
Miliary TB	Chest radiography
TB meningitis	Lumbar puncture (head CT scan if available)

Pleural effusion	CXR, consider pleural tap
Abdominal TB	Abdominal ultrasound, tap of ascitic fluid
Osteoarticular TB	x-ray examination, joint tap or synovial biopsy
Pericardial effusion	Chest radiography, cardiac ultrasound, consider pericardial tap

6.3.5 Chest radiography (x-ray examination)

Although radiography findings tend to be non-specific in children, they can provide supportive evidence of PTB disease. Abnormalities seen on chest radiographs include:

- Widened mediastinum due to enlarged hilar or mediastinal lymph nodes
- Persistent parenchymal opacification (generally with ipsilateral hilar lymphadenopathy)
- Miliary infiltration in the lungs
- Pleural effusion, especially in older children
- Rarely, cavitation may occur in older children and adolescents

Overlapping chest radiograph findings may be seen in children with other pulmonary conditions. This is especially common in children with HIV (see *Section 6.3.9*).

6.3.6 Tuberculin Skin Test (TST)

The TST has a supportive role in the diagnosis of TB in symptomatic children when used with other diagnostic tests. A positive test result suggests *infection* with *M.tb*, not TB disease. Children should not be commenced on treatment for TB solely on the basis of a positive TST.

The sensitivity of TST is reduced by HIV infection, severe malnutrition and severe TB disease. The positivity of the TST result decreases with increasing immunosuppression.

TST should be regarded as positive in high risk children such as those with HIV infection and severe malnutrition if the diameter of induration is ≥5mm when read between 48-72 hours later. In all other children (including those who have had BCG vaccination) a diameter of ≥10mm indicates a positive test.

6.3.7 HIV test

As in adults, TB is more common in HIV-infected children. The risk for developing TB in HIV-infected children in a TB endemic setting in South Africa was 20 times higher than the risk for HIV-uninfected children. An HIV test should be performed for all children suspected of or diagnosed with TB. This will allow appropriate initiation of treatment for HIV as well as TB, and will improve survival.

All HIV positive children or those HIV-exposed infants with unknown HIV status who have TB should be started on cotrimoxazole prophylaxis. A plan should be made to commence ART for all HIV positive children.

6.3.8 Use of score charts for the diagnosis of TB in children

In the absence of a confirmed diagnosis of TB, a scoring system was often regarded as a useful way to evaluate a child's history, signs and symptoms. Scoring systems are difficult to validate as diagnostic tools due to lack of a reference diagnostic "gold standard" in children. Because of overlapping clinical features of HIV and TB, scoring systems are even less reliable in identifying TB in HIV-positive children

than in HIV-negative children. Scoring systems are therefore not included in these guidelines in favour of a thorough assessment of the history and clinical features and use of sound clinical judgement.

6.3.9 Diagnostic challenges in HIV positive children

HIV makes the diagnosis of TB in children more difficult. Malnutrition is a common presenting feature in children with TB disease and with HIV infection. Children with HIV commonly have acute and chronic respiratory disease caused by pathogens other than *M.tb* but with similar clinical and radiological features. In addition there is often co-infection or other respiratory co-morbidity, thus possibly masking response to therapy. *Box 14* summarises some of the causes of lung disease that can be confused with TB in HIV-infected infants and children.

Box 14: Other causes of lung disease in HIV infected children

Causes of lung disease in HIV-infected infants <1 year of age in general order of frequency:

- Bacterial pneumonia: pneumococcus, staphylococcus, gram negative organisms. TB can present as acute pneumonia in this age group
- PCP: common cause of severe, fatal pneumonia in the 2-6 month age group, therefore all infants with pneumonia should be given high-dose cotrimoxazole in addition to other therapy
- CMV pneumonia: sometimes co-infection with PCP, probably more common than previously recognised as it is difficult to confirm a diagnosis
- Viral pneumonia: (e.g. respiratory syncytial virus) often associated with bacterial co-infection
- Mixed infection: commonly seen with PCP, bacterial and viral pneumonia and TB
- Measles: usually see a typical rash
- LIP: uncommon in infants

Causes of lung disease in HIV-infected children 1-14 years of age in general order of frequency:

- Bacterial pneumonia: pneumococcus, staphylococcus, gram negative organisms – very frequent, often recurrent
- TB
- LIP: especially 2-6 years of age, persistent or recurrent, associated with clubbing and parotid enlargement
- Bronchiectasis: cough with purulent sputum, associated with clubbing, complicates recurrent bacterial pneumonia, lymphocytic interstitial pneumonia or TB
- Viral pneumonia: often associated with bacterial co-infection
- Mixed infection: commonly seen with bacterial and viral pneumonia, LIP and TB
- Measles: usually see a typical rash
- Kaposi Sarcoma: usually see characteristic lesions on skin or on palate
- PCP: rare in this age group
- Other fungal pneumonia: probably rare

PCP = pneumocystis pneumonia; CMV = cytomegalovirus; RSV = respiratory syncytialvirus

6.4 Treatment of TB in children

Many children may be treated as outpatients; however children with severe disease should be hospitalised. Children with any of the following conditions must be admitted to hospital:

a) respiratory distress
b) severe forms of EPTB such as TB meningitis, miliary TB, spinal TB and pericardial TB
c) severe adverse reactions such as hepatotoxicity.

It is also reasonable to admit any child in whom it is not possible to ensure good adherence to treatment due to social or logistical reasons.

As with adults, the choice of TB treatment regimen in a child is determined by whether the child has new TB, previously treated TB, or DR-TB, irrespective of HIV status. TB treatment in children should be given daily (7 days per week) during the intensive and continuation phases of therapy. Response to TB treatment in even young and immunocompromised children is generally good and swift.

6.4.1 Standard first-line treatment regimens

The standard regimens for new patients (*new patient regimen)* and for previously treated patients (*retreatment regimen with FLDs*) is the same for children as for adults. Exceptions to the 6 month regimen for new patients are the treatment of TB meningitis and osteo-articular (bones and joints, including spinal) TB for which duration of treatment is longer. *Table 25* summarises the anti-TB treatment regimens for children. Consultation with the CCRC and other specialists is recommended for complicated cases.

Table 25: Treatment regimens for use in children with TB

Indication for treatment for PTB and EPTB	Regimen
Standard regimen for new patients (*new patient regimen*)	2HRZE / 4HRE
Standard regimen for previously treated patients (*retreatment regimen* with first line medicines)	2HRZES / 1HRZE / 5HRE
TB meningitis and osteo-articular TB	2HRZE / 10HRE

All children receiving first line treatment regimens will have ethambutol as part of their regimen. This change from the previous guideline takes into account the high prevalence of primary isoniazid resistance in Namibia, thus making it unsafe to treat any form of TB disease with less than 4 oral medications during the initial phase. Inclusion of ethambutol in the continuation phase covers the possibility of isoniazid-resistant TB which would otherwise result in inadvertent rifampicin "monotherapy" if ethambutol was not added. Previous concerns about using ethambutol in children were addressed by WHO in a 2006 publication based on evidence from multiple studies which concluded that children of all ages can safely be given ethambutol in daily doses of 20mg/kg/day.

6.4.2 Recommended dosages

Current evidence shows that serum levels for all four oral first line anti-TB medicines are lower in children compared to adults when given at standard doses. For this reason, in 2010 WHO revised daily dosage recommendations for children less than 12 years old as shown in *Table 26*.

Table 26: Recommended dosages of first-line anti-TB medicines for children <12 years old

Medicine	Recommended daily dose	Daily dosage range in mg/kg (maximum)
Isoniazid (H)	10mg/kg	10-15 (300mg)
Rifampicin (R)	15mg/kg	10-20 (600mg)
Pyrazinamide (Z)	35mg/kg	30-40 (2000mg)
Ethambutol (E)	20mg/kg	15-25 (1200mg)
Streptomycin (S)	15mg/kg	12-18 (1000mg)

FDC tablets with the revised proportions of medicine components (in line with the new guidelines) were not available at the time of publication of these guidelines. Therefore in order to achieve the required dosage in children <12 years old, supplemental isoniazid should be added to the available paediatric

FDCs in addition to ethambutol, which is not included in the FDC, as shown in *Table 27* and *Table 28*. Children ≥12 years old should have treatment based on their weight according to the adult dosage table for FDCs.

Table 27: Medicine combination for initial phase of TB treatment for children <12 years old

Body weight (kg)*	Initial phase				
	[RHZ] "Paediatric" (R60/H30/Z150)	***[RHZE] "Adult" (R150/H75/Z400 /E275)***	***Additional H100***	***E100***	***E400***
	Number of tablets / sachets	Number of tablets	Number of tablets	Number of tablets / sachets	Number of tablets
6.5-7.4	1½		½	1½	
7.5-9.9	2		½	1½	
10-12.9	2½		½	2	
13-14.9	3		1	3	
15-19.9	4		1	3	
20-24.9	5		1		1
25-29.9		2	1½		
30-34.9	1	2	1		
35-39.9		3	½		

*for infants <6.5 kg, calculate doses of individual medicines and give separately

Pyridoxine should be given along with isoniazid in HIV-infected children to prevent isoniazid associated neuropathy. A dose of 12.5 mg/day is recommended for children 5 to 11 years of age, and 25 mg/day for children ≥12 years.

Table 28: Medicine combination for continuation phase of TB treatment for children <12 years old

Body weight (kg)*	Continuation phase				
	[RH] "Paediatric" (R60/H30)	***[RHE] "Adult" (R150/H75 /E275)***	***Additional H100***	***E100***	***E400***
	Number of tablets / sachets	Number of tablets	Number of tablets	Number of tablets / sachets	Number of tablets
6.5-7.4	1½		½	1½	
7.5-9.9	2		½	1½	
10-12.9	2½		½	2	
13-14.9	3		1	3	
15-19.9	4		1	3	
20-24.9	5		1		1
25-29.9		2	1½		
30-34.9	1	2	1		
35-39.9		3	½		

**for infants <6.5 kg, calculate doses of individual medicines and give separately*

Streptomycin is used in TB patients who were previously treated with first line anti-TB medicines. It is given in addition to the four oral medicines for the first 2 months of treatment. Streptomycin should be given IM daily from Monday to Friday. *Table 29* gives weight-banded doses for streptomycin.

Table 29: Streptomycin dosages for children

Body weight (kg)	Streptomycin injection 1000 mg vial
≤ 7	100 mg
8-9	125 mg
10-14	175 mg
15-19	250 mg
20-24	300 mg
25-29	400mg

6.4.3 Adjunctive steroid therapy

Corticosteroids are of benefit in cases of TB meningitis, TB pericarditis and complications of airway obstruction caused by TB lymphadenitis. Prednisolone should be given at a dose of 2mg/kg/day for 4 weeks. The dose should then be gradually reduced over 1-2 weeks before stopping. The dosage can be increased to 4mg/kg/day (maximum: 60mg/day) in the case of seriously ill children to account for increased steroid metabolism induced by rifampicin.

6.4.4 Monitoring therapy

It is recommended that all children with TB receive directly observed therapy (DOT) for the complete duration of therapy. Parents and caregivers need to be counselled about the importance of adherence for the full treatment period and the potential adverse effects of the medicines. This counselling should be repeated at each follow-up visit.

Children should be assessed by a health care worker at 2 and 4 weeks after treatment initiation, at the end of the intensive phase, and every month thereafter until treatment is completed. At each visit there should be:

- A symptom assessment including, for example, presence of cough, fever, poor appetite, and fatigue
- A weight measurement
- A directed physical examination depending on symptoms
- An assessment of adherence to treatment
- An inquiry about any adverse events
- Review of any relevant specimen collections done or due
- Assignment of date for next visit

Adherence is assessed by reviewing the treatment card. If medicines have been dispensed to the caregiver (DOT supporter) to take at home, they should be asked to show any remaining tablets that they have, and should demonstrate to the HCW the number of each type of tablet that the child is taking. TB treatment dosages must be adjusted according to increase in weight. The new treatment dosages should be carefully explained and demonstrated to the caregiver.

Bacteriologic response to TB therapy in children should be monitored in the same way as in adults (*Chapter 5*). A follow-up sputum specimen for microscopy should be obtained at 6 weeks and after the 5th month of treatment for any child who was sputum smear positive at diagnosis, unless this would mean an

invasive procedure such as gastric aspiration. Regimen adjustments and the need for specimens for culture and DST should follow the schedule outlined for adults (*Chapter 5*).

Routine follow-up CXR examination is not indicated. Many children have a radiological response which lags behind the clinical response to treatment. CXR examination is only useful if the child is not clinically improving despite good adherence to anti-TB treatment.

If there is poor response to anti-TB therapy (poor or no weight gain, persistent cough, fever or malaise, etc.) the child should be referred to the next level of care for further assessment and management. Collection of specimens for smear microscopy and C/DST is very important in such children as well as actively trying to identify an adult index case, as this will guide future management. These children may have DR-TB, an unusual complication of PTB, other causes of lung disease, or poor adherence to treatment. In HIV-infected children on ART, virological failure could be a cause.

6.4.5 Adverse events

Children generally tolerate anti-TB treatment better than adults, and have fewer adverse reactions. The commonest severe adverse event due to anti-TB therapy in children is hepatotoxicity. For HIV infected children, there is also the risk of IRIS (see below) and overlapping toxicities with ART and CPT. All adverse events should be reported to the TIPC.

6.4.6 IRIS

Anti-TB treatment can be associated with a transient worsening of clinical disease a few days or weeks after starting therapy. The frequency of these reactions is increased in HIV-positive individuals on ART and is called immune reconstitution inflammatory syndrome (IRIS). It usually occurs within 3 months of starting ART. Diagnosis and management of IRIS in children is the same as in adults (see *Chapter 8*).

6.4.7 Treatment outcomes

Outcomes definitions following anti-TB treatment in children are the same as for adults. A child's TB outcome category should be recorded on his/her *TB Treatment Card*. In addition, the diagnostic and outcome categories as well as the date and weight at the start and end of treatment should be recorded in the child's health passport.

6.4.8 DR-TB

Children usually develop TB disease as an immediate consequence of primary infection, and as such they typically have fewer mycobacteria than adults. Therefore, anti-TB drug-resistance developing during treatment is uncommon. Most drug-resistance found in children is a result of primary infection from an index case with a drug-resistant strain. In consultation with CCRC, it may be recommended for a symptomatic child who is a close contact of an known DR-TB case and in whom a mycobacterial culture cannot be done or is negative, to receive treatment according to the resistance pattern of the isolate from the contact.

DR-TB should be managed according to schedules described in *Chapter 7*, in close consultation with CCRC. Despite worries about the limited experience with the use of 2nd line medicines in children, DR-TB is life-threatening and hence no anti-TB medicines are absolutely contraindicated. Children generally tolerate 2nd line anti-TB medicines well.

6.5 Management of TB/HIV co-infection in children

HIV-infected children with PTB and those with EPTB are clinically eligible for CPT and ART irrespective of CD4 count.

6.5.1 Cotrimoxazole preventive therapy (CPT)

All HIV-positive children are eligible for CPT. If a child with TB is newly diagnosed with HIV, it is important that they receive CPT as soon as possible because it improves their overall outcome. The dosage of cotrimoxazole for use in CPT is given in *Table 30* below.

Table 30: Recommended doses of cotrimoxazole for CPT for children

Age	Cotrimoxazole dosage
6 weeks to 5 months	2.5 ml daily*
6 months t0 5 years	5 ml daily*
6 years to 14 years	10 ml* or one 400mg/80mg tablet daily
>14 years	2 x 400mg/80mg tablets daily

*Paediatric cotrimoxazole suspension contains 200mgSMZ/40mgTMP per 5 ml

6.5.2 When to start HAART in HIV/TB co-infected children not already on HAART

There is significant evidence, that mortality from delaying the start of ART in TB co-infected children greatly outweighs any risk from medicine toxicity or IRIS. The *National Guidelines for Antiretroviral Therapy (2010)* recommend that:

- start ART in all HIV-infected individuals with active TB irrespective of CD4 cell count; and
- start TB treatment first, followed by ART as soon as possible within 8 weeks after starting TB treatment

6.5.3 Preferred ART regimens for children with TB/HIV co-infection:

Because of significant interactions between rifampicin and certain antiretrovirals (ARVs) such as protease inhibitors and nevirapine, these ARVs are best avoided in children being treated for TB with rifampicin. *A paediatric HIV specialist should be consulted before final selection of ARVs for any individual child, especially those already on ART.* See the *National Guidelines for Antiretroviral Therapy* for further details.

- 2NRTIs
  - For children with sexual development (Tanner) Stage I-III, the preferred choice is zidovudine (AZT) (or stavudine-d4T- for young children on paediatric ARV FDCs) with lamivudine (3TC)
  - For children with more mature sexual development, Tanner Stage IV or V, the preferred choice is tenofovir (TDF) with 3TC
- Plus NNRTI
  - Efavirenz (EFV) is the only applicable and available NNRTI that can be safely used with rifampicin. Its use is however restricted, to children ≥3 years old *and* weight ≥10 kg

Special considerations:
For children <3 years old or <10kg, for whom EFV may not be given, the following options apply for use during TB treatment:

- Triple NRTIs: abacavir (ABC)/(AZT or d4T)/3TC or
- 2 NRTIs with "superboosted" lopinavir/ritonavir (LPV/RTV) - this requires giving additional ritonavir (RTV) to ritonavir-boosted lopinavir (LPV/r) to achieve an equivalent total dose of LPV and RTV.

If a child is on *first line ART with 2NRTIs and an NNRTI* when diagnosed with TB, change the NNRTI to EFV if ≥3 years old *and* weight ≥10 kg and not already on EFV. If <3 years old *or* weight <10 kg change to one of the options above for that age group.

If a child is on *first line ART with 2NRTIs and LPV/r*, the options include adding additional RTV to the LPV/r ("superboosted" LPV/RTV), changing LPV/r to ABC, or changing LPV/r to EFV.

If a child is on *second line ART with 2-3 NRTIs and an NNRTI* when diagnosed with TB, change the NNRTI to EFV if ≥3 years old *and* weight ≥10 kg and not already on EFV. If the child is <3 years old or <10 kg: consult an HIV specialist. It would not be safe to use a triple NRTI option as or to change to EFV as the child has already failed first line HIV treatment.

If a child is on *second line ART* with 2-3 NRTIs and LPV/r and is diagnosed with TB, add additional RTV to LPV/r to achieve "superboosted" LPV/RTV.

Remember: two weeks after TB treatment with rifampicin is completed, the child should change to the usual first line regimen, or to the regimen he/she was taking before starting TB treatment. This is particularly important if the child has been given a triple NRTI regimen, which is less robust than an NNRTI- or PI-based regimen, or "super-boosted" LPV/RTV since once rifampicin is no longer in the blood stream causing increased metabolism of PIs, the resultant blood level is likely to be toxic.

ARVs and anti-TB medicines have overlapping potential toxicity in children as in adults (refer to the *National Guidelines for Antiretroviral Therapy)*. If a co-infected child is required to be on d4T and isoniazid, look out for peripheral neuropathy and supplement with pyridoxine.

6.6 TB in pregnancy and during the neonatal period

6.6.1 Background

TB accounts for nearly 15% of maternal mortality in southern Africa, and the relative risk of death is 3.2 higher in TB/HIV co-infected compared to HIV-uninfected mothers. With a very high prevalence of TB in Namibia it is inevitable that some pregnant women will present with TB. The risk of developing TB in pregnancy is 10 times higher in HIV-infected women than in HIV-uninfected women. About 2% of HIV-infected pregnant mothers are diagnosed with TB in TB endemic settings. Vertical transmission of TB to the infant in mothers with untreated or partially treated TB is 15-16%. Before the advent of anti-TB treatment, a 10-50% mortality rate in pregnant women with TB was observed.

Infants born to mothers with TB have significantly worse outcomes with more prematurity, intra-uterine growth restriction, low birth weight and perinatal death compared to women without TB. In addition, the perinatal transmission of HIV in mothers with TB/HIV co-infection is more than twice as high as in HIV-

infected mothers without TB. It is therefore essential to carefully look for and diagnose HIV and TB in pregnant women.

6.6.2 Diagnosis and management of TB in the mother

The main risk factor for perinatal mortality due to TB is starting TB treatment late in the mother, after the 1st trimester. However often mothers are diagnosed with TB only after TB is suspected or confirmed in the infant. The clinical presentation of TB in pregnancy is variable and may be challenging. Some symptoms of pregnancy such as fatigue can mask TB symptoms. The commonest form of TB seen in pregnant women is PTB, and the most common form of EPTB is pleural effusion, with, as expected, an increased incidence in HIV-infected mothers compared to HIV-uninfected mothers.

All pregnant women should be screened for TB with the screening questions and utilising a high index of suspicion at each visit. If active TB is excluded, and the woman has HIV, isoniazid preventive therapy should be started.

If a pregnant woman answers "yes" to any of the screening questions, she should be evaluated for TB disease. The diagnostic process should be expedited because the earlier in pregnancy TB is diagnosed and treated, the better the maternal and neonatal outcomes.

If a pregnant woman is diagnosed as having TB, anti-TB treatment should be started immediately with the standard regimen for new patients. Treatment of previously treated pregnant women is complicated because streptomycin should be avoided if possible due to its toxicity in pregnancy. If streptomycin is thought to be beneficial in such cases, the attending clinician should discuss with CCRC to determine the safest and best option.

If the woman is co-infected with HIV, ART should be started as soon as the woman is stable on TB treatment, within 8 weeks.

6.6.3 Congenital and neonatal TB

Mode of transmission

Young infants with TB have either acquired the infection congenitally or soon after birth. Congenital TB refers to in-utero infection through haematogenous spread via the umbilical vein, or at the time of delivery through aspiration or ingestion of infected amniotic fluid or cervico-vaginal secretions. These infants usually present within the first week of life and have a poor prognosis. True congenital TB is rare, but is likely being under-diagnosed. TB in young infants is more commonly a result of post-partum exposure to a close contact with infections TB, usually the mother. This may be referred to as "neonatal TB". TB is not transmitted through breast milk, although a breastfeeding infant is at increased risk of acquisition of TB through respiratory transmission the mother has TB.

Clinically it may be neither possible nor necessary to distinguish between congenital TB and TB acquired after birth since the management is the same. The TB exposed neonate may be asymptomatic or symptomatic.

Diagnosis of neonatal TB

Onset of symptoms of TB is usually a few days to a few weeks post-partum. Symptoms and signs of TB are usually non-specific and include:

- Fever

- Lethargy, poor feeding
- "Neonatal sepsis" (disseminated TB)
- Irritability, seizures (meningitis)
- Prematurity, low birth weight (intrauterine growth restriction)
- Poor weight gain
- Respiratory distress, progressive non-resolving pneumonia
- Hepatosplenomegaly
- Abdominal distension with ascites
- Anaemia, thrombocytopaenia, disseminated intravascular coagulation
- Jaundice
- Ear discharge, skin pustules, paravertebral abscess
- Lymphadenopathy
- Chorioretinitis

The differential diagnosis of congenital TB includes neonatal sepsis and other congenital infections (toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, Epstein-Barr virus, syphilis and HIV). A poor response to antimicrobial therapy should alert the clinician to look for TB.

The most important clue to the diagnosis of TB in the newborn is a maternal history of TB or HIV infection. Critical points in the maternal history include:

- non-resolving pneumonia
- contact with an index case of TB
- recent commencement of anti-TB treatment

Management of neonates exposed to maternal TB

TB-exposed infants may initially appear well. Therefore all newborns that are known to be exposed to mothers with infections TB, or with symptoms consistent with congenital TB should be investigated for TB. The BCG vaccination routinely given to infants at birth should be delayed until possible TB disease or infection has been diagnosed and managed. If the infant is found to be HIV positive, BCG should be withheld completely.

Table 31 outlines the evaluation and management of infants exposed to maternal TB and symptomatic infants with no known TB exposure.

Table 31: Management of infants exposed to maternal TB and symptomatic infants with no known TB exposure

	TB-exposed and asymptomatic	TB-exposed and symptomatic	Symptomatic but no known TB exposure
Evaluation	• Thorough clinical examination • 3x morning nasopharyngeal or gastric aspirates for smear microscopy & mycobacterial culture • Chest radiography	• Thorough clinical examination • 3x morning nasopharyngeal, gastric or tracheal (if intubated) aspirates for smear microscopy & mycobacterial culture • Chest radiography	• Thorough clinical examination • 3x morning nasopharyngeal, gastric or tracheal (if intubated) aspirates for smear microscopy & mycobacterial culture • Chest radiography

	• Mother: endometrial sample for DM & culture if < 72h after delivery • Determine mother's HIV status if not known	• Mother: endometrial sample for smear microscopy & mycobacterial culture if <72h after delivery • DM & culture of ear swab, urine, abscess aspirate, LN biopsy (if lymphadenopathy) • Consider smear microscopy & mycobacterial culture of CSF, liver biopsy, bone marrow aspirate • Determine mother's HIV status if not known	• Mother: endometrial sample smear microscopy & mycobacterial culture if <72h after delivery • Other relevant samples for smear microscopy & mycobacterial culture. • Determine mother's HIV status if not known
Management	• DO NOT give BCG at birth • Give IPT while awaiting results • If HIV-exposed, do HIV test and give CPT at 6 weeks • Start HAART if HIV + • Follow infant regularly to ensure active TB does not develop • Change to standard regimen for TB if infant's or mother's smears/cultures positive • Continue to monitor clinical status • Give BCG 2 weeks after completion of IPT unless infant HIV +	• DO NOT give BCG at birth • Start full TB treatment before all results of tests received if TB likely • If another cause found, give IPT • If HIV-exposed, do HIV test and give CPT at 6 weeks • Start HAART if HIV+ • Monitor for weight gain / improvement in symptoms • Give BCG 2 weeks after completion of TB treatment unless infant HIV +	• DO NOT give BCG until TB ruled out • Treat as indicated • If HIV-exposed, do HIV test and give CPT at 6 weeks • Start HAART if HIV + • Give BCG when decision made *not* to treat or 2 weeks after completion of TB treatment unless infant HIV +

In evaluating the infant it is important to send all specimens for mycobacterial culture as well as smear examination because in the majority of reported cases of confirmed congenital TB disease, the diagnosis was confirmed by culture. The mother's endometrial sample can be obtained through curettage.

Congenital TB infection progresses almost universally and very quickly to TB disease. For this reason full treatment is recommended even if the infant is asymptomatic.

Breast feeding is recommended for infants as it can be critical for child survival. TB is not transmitted through breast milk, and although anti-TB medicines are excreted into breast milk in small amounts, there is no evidence that they can induce drug resistance. The mother should wear a surgical mask when handling and feeding the infant. If the mother is known to have DR-TB, the clinician should consult the CCRC to discuss the management of the infant.

7 DRUG-RESISTANT TUBERCULOSIS

7.1 Overview

Development and spread of DR-TB must be prevented at all costs by implementing an effective DOTS strategy. Patients with DR-TB should be managed in consultation with the Central Clinical Review Council (CCRC), established in early 2009 to review and approve all regimens intended for patients with DR-TB in Namibia. In addition, the CCRC provides advice on other aspects of clinical care for patients with TB. The CCRC comprises of key NTLP and DSP staff, technical advisors, clinicians as well as laboratory staff, who meet regularly to discuss cases forwarded by regional teams.

7.1.1 DR-TB and HIV/AIDS

Evidence from industrialised countries has frequently shown an association between HIV infection and MDR-TB. This is often caused by patients with MDR-TB mixing with HIV infected patients in hospital wards and congregate settings. Good infection control measures in hospitals and other congregate settings are therefore important to protect other patients and health care workers, and especially those who are HIV positive, from nosocomial MDR-TB infection.

7.1.2 Definitions

It is important to use clear and unambiguous definitions for the different forms of TB drug resistance, as this may have implications for patient management as well as surveillance. *Drug resistant tuberculosis* refers to active TB caused by bacilli resistant to one or more anti-TB medicines.

Patterns of resistance

Four different categories of DR-TB can be described:

• **Mono-resistance:** resistance to one anti-TB medicine.

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

• **Multidrug resistance *(MDR)***: resistance to isoniazid and rifampicin with or without resistance to other medicines.

• **Extensively drug-resistance *(XDR)***: resistance to any fluoroquinolone, and at least one of three injectable second-line medicines (capreomycin, kanamycin and amikacin), in addition to MDR.

7.1.3 The mechanisms for the development of DR-TB

M.tb has the ability to undergo spontaneous mutation, resulting in bacilli that are resistant to any of the known anti-TB medicines. The probability of the occurrence of spontaneous mutants resistant to individual anti-TB medicines is as follows:

Isoniazid	:	1 in every 1,000,000 cell divisions
Rifampicin	:	1 in every 1,000,000,000 cell divisions
Streptomycin	:	1 in every 1,000,000 cell divisions
Ethambutol	:	1 in every 100,000 cell divisions
Pyrazinamide	:	1 in every 10,000 cell divisions

Spontaneous development of MDR-TB strains is extremely rare and would occur once in every 10^{15} cell divisions (the product of the two probabilities of isoniazid and rifampicin mutation). The probability of the presence of resistant mutants in a person, therefore largely depends on the number of *M.tb* bacilli in a

person's body. The lower the bacillary load, the lower the probability of harbouring naturally resistant mutants. This explains why in preventive therapy of a person with latent tuberculosis infection treatment with only one anti-TB medicine is effective and does not create drug-resistance. On the other hand a person with TB has many millions of *M.tb* bacilli and monotherapy will almost invariably lead to resistance against this one medicine.

All the *M.tb* bacilli in the body of a TB patient can be killed if a combination of at least 3 to 5 different and effective anti-TB medicines is given in the intensive phase when the bacterial population is still large; and at least 2 or 3 different effective anti-TB medicines are given in the continuation phase.

Development of resistance to anti-TB medicines in the community can be decreased by:

- Prescription of standardised and effective regimens, including for patients with MDR-TB.
- Ensuring uninterrupted supply of medicines
- Ensuring that patients adhere to treatment.

Table 32: Factors that influence the emergence of DR-TB

Factors facilitating the emergence of MDR-TB	Factors that prevent the emergence of MDR-TB
Health care workers prescribe inadequate TB treatment regimen to patient with TB disease • Too low medicine dosage • Inappropriate combination • Too short duration • Monotherapy	• Train health care workers on national TB treatment guidelines, • Supportive supervision to ensure adherence to guidelines
Use of sub-standard anti-TB medicines	Use of quality assured anti-TB medicines
Patient does not take all TB medicines as prescribed • Inadequate intake of prescribed medicines • Inadequate combination of medicines • Duration of treatment too short • Irregular & selective intake of medicines	Use a combination of three measures: • Use of FDC medicines • DOT during TB treatment • Provide good patient support during the entire treatment using a patient-centred approach

7.2 Likelihood of MDR-TB in a TB patient

MDR-TB may rarely occur in a patient who has never been treated for TB before. This can only happen if that person developed MDR-TB after having been infected by an infectious MDR-TB source. It is much more common to have MDR-TB after having been treated for TB before.

Health care workers must, however, be alert that the probability of MDR-TB is much higher in a new patient with TB who was a close contact of a patient with known MDR-TB, or in a patient who relapses or fails after having been treated with a retreatment regimen. In addition, new TB patients with HIV are more likely to deteriorate if they have DR-TB which is not detected and treated early.

Table 33: Probability of MDR-TB in different patient categories

Patient category	Risk
New patient, never treated for TB before	Very low
Patient, who relapses after treatment with a standard regimen for new TB patients	Low-moderate
Patient, previously defaulted from standard regimen for new TB patients	Low
Patient who failed on standard regimen for new TB patients	Moderate-high
Patient, who relapsed after a retreatment regimen with FLDs	Moderate-high
Patient, who previously defaulted from a retreatment regimen with FLDs	Moderate
Patient who failed on a retreatment regimen with FLDs	High

It is clear from *Table 33* that all patients on a retreatment regimen with first line anti-TB medicines should be managed as high risk patients for DR-TB, ensuring that they adhere to and complete their treatment under supervision.

7.3 Use of second-line anti-TB medicines

There are currently several second-line anti-TB medicines available in Namibia. It is important that these medicines are used strictly according to these guidelines to prevent further resistance against these "last resort" second-line medicines. Inappropriate use of these medicines will inevitably lead to the emergence of further resistance and create a growing number of incurable patients, including XDR-TB.

Table 34: Groups of anti-TB medicines available in Namibia

Grouping	*Medicines*
Group 1: First-line oral agents	isoniazid (H); rifampicin (R); ethambutol (E); pyrazinamide (Z)
Group 2: Injectable agents	kanamycin (Km); amikacin (Am); capreomycin (Cm); streptomycin (S) [a]
Group 3: Fluoroquinolones	levofloxacin (Lfx)
Group 4: Oral bacteriostatic second-line agents	ethionamide (Eto); cycloserine (Cs); para-aminosalicylic acid (PAS)
Group 5: Agents with unclear role in DR-TB treatment (not recommended by the WHO for routine use in DR-TB patients)	clofazimine (Cfz); amoxicillin/clavulanate (Amx/Clv); high-dose isoniazid (High-dose H); clarithromycin (Clr)

Box 15: When to use second-line anti-TB medicines

Second-line anti-TB medicines should only be prescribed for patients who meet the eligibility criteria and after consultation with the Central Clinical Review Council (CCRC)

7.4 Eligibility criteria for treatment with second-line anti-TB medicines

The following patient categories are eligible for treatment with second-line anti-TB medicines:

Proven MDR-TB: Resistance to at least isoniazid and rifampicin

Proven poly-drug resistant TB:

- Resistance to isoniazid and ethambutol +/- streptomycin (susceptible to rifampicin)
- Resistance to rifampicin and ethambutol +/- streptomycin (susceptible to isoniazid)

Proven mono-resistance to rifampicin

Other categories of patients eligible for 2nd line medicines

The following are eligible for 2nd line treatment after considering all the circumstances around the patient.

- Relapse, failure or treatment-after-default on second-line treatment
- Infants who are diagnosed with TB and whose mothers have smear positive DR-TB
- Patients who failed the first-line retreatment regimen with positive smear or culture

Table 35: Eligibility for treatment with second-line anti-TB medicines

A. Patients eligible to start on the standard second-line anti-TB regimen after consultation with the CCRC	
Patient characteristics	**Management**
A patient who failed retreatment regimen with first line anti-TB medicines; and has a positive sputum smear or a positive culture of *M.tb.*	• Stop all anti-TB medicines • Collect sputum specimen for rapid DST • Start the patient on the standard second-line anti-TB regimen (after consulting the CCRC). • After DST results become available, the regimen can be adjusted according to drug susceptibility profile
A patient who has a relapse, failure, or who returns after default, after having been treated with second-line TB treatment; and who is sputum-smear or culture positive. *This patient is likely to have additional resistance to second-line anti-TB medicines.* *In case of a relapse s/he might have been re-infected, with a drug susceptible strain*	• Stop all anti-TB medicines • Collect 2 separate sputum specimens for C/DST, with a special request to additionally test for resistance against second-line anti-TB medicines. • Start the patient on a new second-line anti-TB treatment regimen (after consultation with the CCRC). • When DST results are received, the regimen can be adjusted according to drug susceptibility profile, in the event that there is no resistance against second-line anti-TB medicines.
A patient with laboratory DST result showing resistance to at least isoniazid and rifampicin (MDR-TB).	• Stop all anti-TB medicines, if applicable • Start patient on the appropriate 2nd line anti-TB regimen in consultation with the CCRC
A patient with laboratory DST result showing resistance to at least rifampicin or isoniazid with another medicine	• If applicable, stop all anti-TB medicines • Collect sputum samples for C/DST • Start patient on the appropriate regimen in consultation with the CCRC
TB patient who is a close contact of another patient with bacteriologically confirmed MDR-TB and is a small child, or is immunosuppressed	• Collect sputum or gastric aspirate samples for C/DST • Consider empirical treatment with 2nd line anti-TB medicines, in consultation with the CCRC, based on the resistance pattern of the source case.

B. Patients NOT IMMEDIATELY eligible to start standard second-line anti-TB treatment	
Patient characteristics	**Management**
Patient who relapses after retreatment with 1st line anti-TB medicines *Relapses that occur in the first year after previous TB treatment usually reflect poor adherence to treatment in the continuation phase and/or acquired resistance. Relapses occurring later after completion of previous treatment are more likely to be caused by re-infection with a new strain of TB bacilli.*	• Collect a sputum sample for rapid DST and/or conventional C/DST • Start patient on a 1st line retreatment regimen (standard regimen for previously treated patients) • When DST results are received, the regimen can be adjusted according to the drug susceptibility profile or the patient continues retreatment regimen • If culture is negative, consider the likelihood of DR-TB (depending on other risk factors) and make individual decision to continue the retreatment regimen or start the standard second-line regimen after consulting the CCRC.
A patient who "Returns after Default" after having been treated with retreatment regimen with first-line anti-TB medicines and is sputum-smear positive	
Adult TB patient who is a contact of another patient with bacteriological confirmed MDR-TB	

C. Patients who are NOT eligible for treatment with second-line TB medicines	
Patient characteristics	**Management**
Patients who relapse or who return after default, who are sputum-smear negative	See *Chapter 5*
Patients with severe side-effects to one of the first-line anti-TB medicines	• These patients can be effectively managed with a regimen that does not contain the medicine that causes the side-effect, provided the initial phase contains at least 3-4 first-line anti-TB medicines, and the continuation phase has at least 2 medicines. • Consult the CCRC if two or more first-line anti-TB medicines cannot be used.

7.5 Second-line anti-TB treatment regimens

While individualised treatment regimens are the ideal for treating MDR-TB patients, it is sometimes necessary to start on a standard second-line regimen before DST results are available.

Table 36: Standardised regimen for MDR-TB in Namibia

Initial Phase		Continuation Phase	
Medicines	**Minimum duration in months**	**Medicines**	**Minimum duration in months**
Kanamycin Ethionamide Levofloxacin Cycloserine, and Pyrazinamide +/- Ethambutol subject to susceptibility + High dose pyridoxine	Eight months *and* lasting at least four months after culture conversion	Ethionamide Levofloxacin, and Cycloserine +/- Ethambutol + High dose pyridoxine	18 months

NB: Individualised regimens are only to be designed in consultation with the CCRC. Care should be taken to evaluate the medical history for possible resistance which may have developed, but may not be apparent from the laboratory results. As such, treatment for poly-drug resistant TB should never rely solely on DST results.

All doses of second-line anti-TB therapy must be directly observed for the entire duration of therapy.

7.6 Management of patients who return after defaulting from second line anti-TB treatment

All efforts have to be made to prevent patients from defaulting anti-TB treatment through the provision of patient-friendly services and by ensuring family members and treatment supporters are fully involved in the care and support of the patient.

Health care workers should ensure that patients fully understand why their MDR-TB treatment should not be interrupted and the consequences of poor adherence, i.e. poorer prognosis, higher risk of failure, putting family members and contacts at risk, and having to receive more complicated and longer treatments. In particular poorly managed second-line treatment may result in XDR-TB. It is sometimes justifiable **not to treat** habitual interrupters, due to the risk of amplifying resistance and spreading resistant strains.

Table 37: Weight based dosing of 2nd line TB medicines for adults and children

Medication (common presentation)	Doses per day	Total daily dose by weight class				
		Children (mg/kg)	Adults<33kg mg/kg	Adults 33-50 kg	Adults 51-70 kg	Adults >70 kg
Isoniazid	1	(10) 10-15	4-6	200-300mg	300mg	300mg
Rifampicin	1	(15) 10-20	10-20	450-600mg	600mg	600mg
Ethambutol	1	(20) 15-25	25	800-1200mg	1200-1600mg	1600-2000mg
Pyrazinamide	1	(35) 30-40	30-40	1000-1750mg	1750-2000mg	2000-2500mg
Kanamycin	1	(30) 15-30	15-20	500-750 mg	1000 mg	1000 mg
Capreomycin	1	(30) 15-30	15-20	500-750mg	1000 mg	1000 mg
Levofloxacin (250, 500mg)	1	(10) 7.5-10	750 mg	750 mg	750 mg	750-1000 mg
Ethionamide (250mg)	1-2	(20) 15-20	15-20	500 mg	750 mg	750-1000 mg
Cycloserine	1-2	(20) 10-20	15-20	500 mg	750 mg	750-1000 mg

(250mg)[e]						
P-aminosalicylic acid (4g sachets)[a]	2-3	(300) 150-300	150	8g	8g	8-12g
Clofazimine[b]	1	-	3-5	100mg	100mg	200mg
Amoxycillin+clavulanic acid[c] (500/175mg or 875/125mg)	2-3	-	45 (amoxicillin component)	2000mg	2000mg	2000mg
Clarithromycin (500mg)	2	-	15	1000mg	1000mg	1000mg
High dose Isoniazid (different from usual dose)	1	-	16-20	600-900mg	900mg	900mg
Linezolid[d]	1	-	-	600	600	600
Imipenem/cilastatin[d] (iv injection)	4	-	-	2000-4000mg	2000-4000mg	2000-4000mg

[a] *PAS - If Sodium PAS is used, it may require different dosing; check with manufacturer's recommendations.*

[b] *Clofazimine – Some clinicians begin at 300mg daily and reduce to 100mg after 4-6 weeks.*

[c] *Amoxycillin+clavulanic acid – Dosages for DR-TB not well defined.*

[d] *Normal adult dose –not available in Namibia at the time of publication of these guidelines*

[e] *Pyridoxine should always be given at a dose of 50mg for every 250mg of cycloserine used, maximum dose is 200mg*

Table 38: Management of patients returning after defaulting from second-line TB treatment

Patient characteristics	Management
Patient has had 4 weeks or longer of 2nd line TB treatment, and is sputum-smear (DM) positive	• Collect one sputum specimen for C/DST, including DST to 2nd line anti-TB medicines • Give intensive counselling to the patient and his family members / treatment supporters • Discuss the case with the local MDR-TB management team , and determine social eligibility to continue second-line anti-TB treatment • Record previous outcome as 'Defaulted' and • re-register the patient as 'previously treated with 2nd line medicines' • Re-start second line anti-TB treatment in consultation with the CCRC, and adjust regimen as appropriate when DST results become available.
Patient has taken 4 weeks or longer of 2nd line TB treatment, and is sputum-smear (DM) negative	• Collect one sputum specimen for C/DST, to all first-line and second line anti-TB medicines • Continue the previous MDR-TB treatment regimen from where it was interrupted If culture is positive: • Give a final treatment outcome as 'defaulted' from previous regimen • Re-register the patient for the new treatment episode • Re-start second line anti-TB treatment in consultation with the CCRC

	If culture is negative: • Continue previous MDR-TB regimen from where it was interrupted • Delete earlier "default" outcome and update the report • Final treatment outcome will be determined from the current regimen
Patient has taken less than 4 weeks of MDR-TB treatment and is sputum-smear positive on return	Restart the MDR-TB regimen which the patient interrupted
Patient has taken less than 4 weeks of MDR-TB treatment and is sputum-smear negative on return	Restart the MDR-TB regimen which the patient interrupted

7.7 Adjuvant therapy

Vitamin B6 (pyridoxine) should be given to all patients receiving cycloserine to prevent neurological side effects. The standard dose is 50mg of pyridoxine for every 250mg of cycloserine. All patients should also receive multivitamin supplements. If supplements with minerals are given (zinc, iron, calcium, etc.) they should be dosed apart from the fluoroquinolones, as they can interfere with the absorption of these medicines.

Gastric protection with H_2 blockers (e.g. ranitidine 150mg once daily) or proton pump inhibitors (e.g. omeprazole 20mg once daily) is sometimes warranted, particularly in patients receiving ethionamide and PAS.

Corticosteroids can be beneficial in conditions such as severe respiratory insufficiency and central nervous system or pericardial involvement (prednisolone dose: 1 mg/kg and gradually decreasing to 10 mg per week when a long course is indicated). Injectable corticosteroids are often used initially when a more immediate response is needed.

7.8 Recording and reporting

Recording and reporting are essential for monitoring and evaluation at district, regional and national level of the rational use of second-line anti-TB medicines for MDR-TB and other forms of anti-TB drug resistance, as well as the treatment outcomes.

The following are the recording and reporting requirements for DR-TB:

- Each patient with DR-TB must be recorded in the DR-TB register, on a new row, and with a new unique DR-TB registration number. This is primarily the responsibility of the DTLC. The patient's registration information as well as the treatment progress must be recorded on the DR-TB patient treatment card.
- All patients with DR-TB must be notified to the regional TB and leprosy coordinator and subsequently to the NTLP on the monthly notification form.
- In addition, all patients eligible for 2nd line anti-TB treatment must be discussed with the CCRC before starting treatment.
- Interim treatment outcomes are reported for time to sputum/culture conversion, 6 months, 12 months, 18 months, and at end of treatment (final treatment outcome).

- Namibia Institute of Pathology (NIP) will notify the NTLP of all cultures growing *M.tb strains* showing drug-resistance. This will allow NTLP to cross-check the MDR-TB notification system and monitor MDR-TB detection as part of the routine surveillance system;
- Data on DR-TB cases must be aggregated at district and regional levels on a quarterly basis.
- The NTLP will review notifications and treatment results on a quarterly basis;
- The CCRC should be consulted in the case of complications during treatment requiring adjustment of the regimen. All such events should be duly recorded on the DR-TB Patient Booklet (TB 09).

7.8.1 Categories of patients for MDR-TB registration

As the specific characteristics of previous treatment experience are likely to affect outcomes, two classifications according to previous treatment history exist:

Classification according to history of previous anti-TB medicine use,

This is mainly used to assign the appropriate treatment regimen.

- **New**: A patient who has not previously received anti-TB treatment, or has received anti-TB treatment for less than one month. Patients may also be placed in this group if they had sputum collected for DST at the start of the *new patient regimen* and then switched to MDR-TB treatment based on those DST results. The classification will only apply if DST was performed within one month of the start of treatment (even if the DST result is received more than one month after initiating treatment).
- **Previously treated with first-line anti-TB medicines only**: A patient who has been treated for at least for TB with only first-line anti-TB medicines.
- **Previously treated with second-line medicines**: A patient who has been treated for at least one month for TB with one or more second-line anti-TB medicines, with or without first-line medicines.

Classification according to the outcome of their previous treatment (commonly referred to as the patient's "registration group").

The registration groups are the established groups used in the standard recording and reporting system, with additional sub-grouping of patients treated after failure. This grouping allows analysis of the target groups for DST, epidemiological monitoring and projection of future numbers of MDR-TB cases. Again, classification is determine77d by treatment history at the time of collection of the sputum sample that was used to confirm MDR-TB. The groups are as follows:

- **New**: A patient who has not previously received anti-TB treatment, or has received anti-TB treatment for less than one month.
- **Relapse**: A patient whose most recent treatment outcome was "cured" or "treatment completed", and who is subsequently diagnosed with bacteriologically positive TB by sputum smear microscopy or culture.
- **Treatment after default**: A patient who returns to treatment, bacteriologically positive by sputum smear microscopy or culture, following interruption of treatment for two or more consecutive months.
- **Treatment after failure of initial treatment**: A patient who has received initial treatment for TB (new patient regimen) and in whom treatment has failed. Failure is defined as sputum smear positive at five months or later during treatment.

- **Treatment after failure of retreatment**: A patient who has received retreatment for TB and in whom treatment has failed. Failure is defined as sputum smear positive at five months or later during treatment.
- **Transfer-in**: A patient who has transferred in from another register for treatment of DR-TB to continue treatment.
- **Other**: There are several types of patients who may not fit into any of the above categories. Examples may include the following: sputum smear positive patients with unknown previous treatment outcome; sputum smear positive patients who received treatment other than the standard new patient or retreatment regimen (possibly in the private sector); previously treated patients with extrapulmonary or smear-negative TB; patients who have received several unsuccessful treatments, were considered incurable by health staff and who have lived with active TB disease with no or inadequate treatment for a period of time.

Classification according to site

- **Pulmonary:** Refers to TB with signs of lung parenchymal involvement
- **Extrapulmonary:** TB disease at any site other than the lung parenchyma. Please note that where both extrapulmonary and pulmonary involvement occurs, the patient should be classified as having PTB.

Classification according to form of resistance

- Poly-drug resistance
- MDR-TB
- XDR-TB
- Suspected MDR-TB
- Rifampicin monoresistance

Classification according to HIV status

- HIV positive
- HIV negative
- Unknown HIV status

7.8.2 Interim Outcome Definitions for MDR-TB Patients

Close clinical and bacteriological patient monitoring is of paramount importance when managing DR-TB. Sputum for smear and mycobacterial culture should be collected monthly. Due to the lower sensitivity of sputum smear microscopy and its inability to distinguish viable from nonviable organisms, it is preferable to use mycobacterial culture results for clinical decision making.

Smear or Culture conversion: Patients who began second-line therapy with a positive smear or culture will be considered to have converted after having two negative smears or cultures taken at least 30 days apart. In the event that the patient did not have a positive smear or culture at the beginning of treatment, smear or culture conversion is defined as two negative consecutive smears or cultures, taken at least 30 days apart, after initiation of treatment for DR-TB.

Time interval to smear or culture conversion: This refers to the interval between the date of MDR-TB treatment initiation and the date of the first of these two negative consecutive smears or cultures. The time to conversion should be recorded separately for culture and smear conversions.

It should be noted that the *date of sputum specimen collection* should be used, and not the date the result was printed/obtained.

7.8.3 Treatment outcome definitions for patients with DR-TB

The following are the mutually exclusive definitions of the possible outcomes of patients on treatment for MDR-TB. They rely on the use of mycobacterial culture.

- **Cure:** A patient who has completed treatment according to the NTLP guidelines and has at least five consecutive negative cultures from samples collected at least 30 days apart in the final 12 months of treatment. A patient may still be considered cured if only one positive culture containing less than 10 colonies is reported during that time. However, in order to meet the criteria for cure, a positive culture must be followed by a minimum of three consecutive negative cultures, taken at least 30 days apart (in patients with a positive culture late in treatment, treatment may be extended to satisfy the criteria for cure).
- **Treatment Completed:** A DR-TB patient who has completed treatment according to NTLP guidelines but does not meet the definition for cure or failure due to lack of bacteriologic results.
- **Died**: A DR-TB patient who dies for any reason during the course of treatment.
- **Treatment default:** A DR-TB patient whose treatment was interrupted for two or more consecutive months. Patients who are removed from treatment by clinicians due to persistent, short (< 2 months) interruptions should also receive a default outcome.
- **Treatment failure:** A DR-TB patient with more than one positive culture out of the five cultures performed in the last 12 months of treatment. A patient will also be considered a treatment failure if one of the final three cultures taken during treatment is positive, or if s/he is persistently culture-positive and a clinical decision has been made to terminate treatment early. Patients permanently removed from treatment due to medicine intolerance should also receive a treatment failure outcome.
- **Transfer out:** A DR-TB patient who has been transferred to another reporting and recording unit and for whom the treatment outcome is unknown.

7.8.4 Cohort analysis

Because of the long treatment duration the time points used for cohort analysis are different from those for patients on first-line anti-TB regimens. All patients should be analysed in two different cohorts:

- **Treatment cohort** includes only patients who start treatment. It is defined by the date of start of treatment.
- **Diagnostic cohort** includes patients diagnosed with DR-TB (identified in the register by date of diagnosis) during a specific period. These cohorts may include patients who have not been started on treatment.

7.8.5 Time frame of MDR-TB cohort analysis of treatment outcomes

In each quarter, all DR-TB patients are included in the cohort analysis of treatment outcomes based on the date of DR-TB treatment initiation. To account for the long duration of MDR-TB treatment regimens, final cohort analysis should be performed 36 months after last patient enrolment. Interim treatment

outcomes may be assessed at 6, 12, 18 and 24 months to monitor patient progress. Patients still on treatment at the end of a designated cohort treatment period must also be explicitly identified as such; this is a provisional outcome until a final outcome is available.

The performance of the DR-TB management is eventually measured in a cohort analysis using three different registration categories. Some patients may be registered twice during one cohort period (failure or default patients who are re-registered); therefore, the cohort analysis should identify the total number of treatment episodes. Stratifying cohort analyses by category of patient (new, return after default,) will prevent the repeated inclusion of a patient in a single analysis.

7.9 Organisation of DR-TB treatment

7.9.1 Admission in hospital

All patients on treatment for DR-TB should ideally be admitted in hospital during the intensive phase, or at least until smear or culture conversion.

*On admission, or initiation of treatment, the following are minimum requirements***:**

- Clinical assessment, including weight
- Baseline sputum smear microscopy and C/DST
- Blood for Full Blood Count (FBC); Urea, creatinine and electrolytes (U&E); Liver function tests (TFT), Thyroid function tests (TFT), CD4 count and urine for pregnancy test (if applicable)
- HIV counselling and testing, and assessment for ART if HIV positive. (if already on ART, consider a test for the viral load)
- Chest radiography
- Assessment by a social worker
- Audiometry
- Health education and signing of consent form.

7.9.2 Discharging from the hospital

Patients with MDR-TB are normally eligible for discharge after completing the intensive phase, or at least after culture conversion.

Discharge can be done ONLY when adequate arrangements for out-patient DOT have been made.

- If a patient is being discharged to another district, the formal procedure should be to transfer that patient to their nearest hospital before allowing them to go home.
- Discharging DR-TB patients is initiated by the doctor following the guidelines in consultation with the DTLC, the social worker and the DOT providers, preferably at the DR-TB committee meeting. The DTLC coordinates the patient's management thereafter, including
  - Liaising with the social worker to ensure an enabling environment for the patient to continue treatment.
  - Arranging with the TB focal nurse and the DOT field supervisor/promoter at the nearest clinic or DOT point regarding the aftercare of the patient.

- Meeting with the patient's family members to provide continuing health education, and supporting them on the preferred DOT option.
- Where possible, an environmental health inspector should assess the patient's residence and offer advice on environmental controls that can minimise transmission of TB.

- Clear information should be given to the patient on the following:

1. How often the patient collects his/her medicine
2. When and where the next appointment is; at the DOT point, clinic and hospital
3. When the next sputum sample is needed
4. What to do if there is a problem
5. How to transmission at home and in the community

Table 39: Treatment monitoring for DR-TB in intensive phase and the continuation phase

	Intensive Phase	Continuation Phase
ON ADMISSION	• Take a detailed history and conduct a full examination • Measure the weight • Collect sputum samples for baseline sputum smear microscopy and C/DST • Perform HIV counselling and testing • Collect blood for FBC, U&E, LFT, TSH, CD4 count (if HIV+), HIV viral load (if HIV+ and on ART), • Perform chest radiography • Perform a urine pregnancy test (if applicable) • Refer the patient for baseline audiometry • Conduct health education and ensure that the patient signs the treatment consent form in the DR-TB Treatment Booklet. The patient must be given adequate time, to ensure readiness • Conduct a social assessment (by a medical social worker)	
DAILY	• Measure temperature • Watch the patient swallow his/her medication and sign for every dose taken • Observe the clinical condition and possible side effects	• Watch patient swallow medication and sign on *DR-TB treatment card* (if at the health facility) or *community based DOT card* (if in community)
WEEKLY	• Record on the side effect monitoring chart • Review by the doctor (more frequently if necessary)	• Medicines collected from clinic by field promoter or DOT supporter (if applicable)
MONTHLY	• Collect 2 sputum samples for smear microscopy and mycobacterial culture • Collect blood for U&E • For HIV positive patients, check ART and cotrimoxazole prescription • Measure weight • Conduct a social assessment (by social worker)	• Review the patient at clinic/hospital (by a nurse) • Measure the weight • Screen for side effects and fill in side effects monitoring form • Order medicines from the hospital • For HIV positive patients, check ART and cotrimoxazole prescription • Collect sputum for smear microscopy

EVERY 3 MONTHS	• Collect blood for LFT • Refer patient for audiometry	• Sputum for smear microscopy and mycobacterial culture • Blood for LFTs (if still on pyrazinamide) • Patient seen by doctor with results
EVERY 6 MONTHS	• Perform chest radiography	• Perform chest radiography

7.9.3 Out-patient management of DR-TB

Management of out-patients with DR-TB depends on whether the patient is still receiving the injectable medicine or not. For patients still on the intensive phase, monitoring is as outlined in *Table 39*. The patient must take the medicines, including the injectable under daily supervision by a nurse at a clinic or hospital.

During the continuation phase: Daily supervision can be decentralised as follows:

- The TB nurse orders medicines from the hospital/DTLC on a named patient basis once a month.
- The TB focal nurse at the clinic packages a weekly supply of medicines, and the field promoter collects these from the clinic once a week.
- The patient swallows all doses daily at the DOT site; or at another location under observation by the field promoter or trained DOT treatment supporter. The field promoter also observes for any side effects and reminds the patient about his/her clinic visits.
- The patient goes to the clinic once a month to be seen by the TB focal nurse, who will assess the patient for side effects and record on the side effects monitoring chart.
- The TB nurse collects a sputum sample every month (smear microscopy) and two sputum samples (smear microscopy and culture) every three months.
- The patient is reviewed at the hospital by the doctor every 3 months, or more frequently if necessary.
- On completion of treatment, the doctor discusses with the DR-TB committee and the CCRC before discharging.

Box 16: Second-line treatment and DOT

SECOND-LINE TB TREATMENT IS ADMINISTERED AS DOT

7.9.4 The role of chest radiography

Chest X-ray examination should be performed at the beginning of second-line treatment and every six months thereafter as reference points should the patient requires additional interventions such as surgery. Chest radiography is also indicated when there is clinical evidence that the patient may have complications such as pneumothorax, severe pleural effusion or empyema.

7.10 Prevention of nosocomial transmission of DR-TB

The following precautions should be applied to minimise the risk of nosocomial transmission of DR-TB:

- DR-TB patients, when admitted, should be nursed in isolation from non-DR-TB patients and any other patients;

- DR-TB patients should always wear a surgical mask when leaving the isolation area and whenever in contact with visitors or health care workers;
- Health care workers should always wear N95 (FFP2) respirators whenever they are working on the DR-TB ward. It is very important that these respirators are correctly applied for them to be effective;
- The DR-TB treatment facility should ideally be located in a separate building within the hospital compound to avoid DR-TB patients easily mingling with other patients in the hospital;
- Rooms in the DR-TB treatment facility should have wide windows which should be kept open at all times to allow for natural ventilation.
- Visitors to infectious DR-TB patients should not be allowed to enter the patients' rooms unless it is unavoidable. Visitors and patients should meet only in an outdoor open area.

7.11 Close contacts

Close contacts are defined as persons who share the same household with a patient, or worked closely with the patient in the 2 years prior to the establishment of the diagnosis in the index case. A list of close contacts should be made for each patient. These contacts should be examined for active TB and those found to have active TB should be investigated for DR-TB.

HIV negative adults should be managed with first-line anti-TB medicines while awaiting the results, and have the regimen adjusted as soon as DST results become available. Immunosuppressed or paediatric patients should be reviewed in consultation with the CCRC because of the possibility of starting an empirical DR-TB treatment regimen. All close contacts should receive health education on TB, including DR-TB.

If active TB has been excluded, close contacts should be reviewed periodically and advised to return whenever symptoms occur. There is currently no effective chemo-prophylactic therapy with second-line anti-TB medicines.

7.12 Special situations

7.12.1 Children

There is limited reported experience using the second-line anti-TB medicines for extended periods of children. Careful consideration of the risks and benefits of each medicine should be made. Open and comprehensive discussion with the patient and family members is critical from the outset. Given the life-threatening nature of MDR-TB, there are no medicines that are absolutely contraindicated in children. The dosages of the second-line medicines should be adjusted to the weight of the patient. Monitoring monthly weights is therefore especially important in paediatric cases, with adjustment of doses as the child gains weight.

7.12.2 Pregnancy and lactation

The safety and efficacy of DR-TB treatment in pregnant women is not well documented. All female patients of childbearing age should undergo pregnancy test on initial evaluation, and birth control is strongly recommended for all women receiving DR-TB chemotherapy.

Pregnancy is not a contraindication to the treatment of active DR-TB, since active disease poses great risks to the life of the mother and foetus. Pregnant patients should be carefully evaluated, taking into

consideration gestational age and severity of the DR-TB. The risks and benefits of DR-TB treatment should be considered carefully, with the primary goal being smear conversion in order to protect the health of the mother and child, both before and after birth.

The following considerations apply to the management of pregnant patients:

- Since the majority of teratogenic effects occur in the first trimester, therapy may be delayed until the second trimester unless life-threatening symptoms occur.
- Patients in the third trimester have reduced risk of teratogenicity, although aminoglycosides may still damage the foetal ear.
- Capreomycin is the second-line injectable of choice in pregnant women but it should be prescribed in consultation with the CCRC.

Table 40: Safety of anti-TB medicines during pregnancy

Medication	Safety class*	Comments
Ethambutol	B	Experience in pregnant patients suggests it is safe to use
Pyrazinamide	C	Use with caution. Most references suggest it is safe to use
Kanamycin	D	Documented toxicity to developing foetal ear. Risks and benefits must be carefully considered. Avoid use when possible
Levofloxacin	C	Use with caution. No teratogenic effects seen in humans when used for short periods of time (2-4 weeks). Associated with permanent damage to cartilage in weight-bearing joints of immature animals. Experience with long-term use in gravid patients is limited, but given bactericidal activity, benefits may outweigh risks.
Ethionamide	C	Avoid use. Teratogenic effects observed in animal studies; significantly worsens nausea associated with pregnancy
Cycloserine	C	No significant evidence of toxicity in pregnant patients; animal studies have not documented toxicity
Capreomycin	C	Generally avoided in pregnancy due to congenital deafness seen with streptomycin and kanamycin. There are case reports of its safe use in pregnancy
PAS	B	Not adequately studied, but no teratogenicity known.

*Safety classification: A = safety established using human studies; B = presumed safety based on animal studies; C = uncertain safety, no human studies, and animal studies show an adverse effect; D = unsafe, evidence of risk that may be justifiable under certain clinical circumstances.

7.12.3 DR-TB in mothers with young infants

Newborn infants are at high risk of developing DR-TB. If possible mothers with DR-TB should avoid close contact with infants till smear and culture negative. The family should be requested to look after the baby, and safe infant feeding practices instituted.

Effects of DR-TB medications on the nursing infant have not been fully studied. The use of infant formula is a way to avoid any unknown adverse effects due to continued close contact between mother and child. However, the use of infant formula will depend on multiple factors, including the patient's resources, safety of water supply, and bacteriological status of the mother. If the setting is not appropriate for infant formula, then breastfeeding may be considered while attempting to minimise close contact. The second-line anti-TB medicines are not contraindicated in mothers who choose to breastfeed.

7.12.4 Diabetes mellitus

The treatment of MDR-TB in a diabetic patient will result in poorer TB treatment outcome if blood sugar levels are not well controlled. The responsibility often falls on the physician treating the patient for MDR-TB to ensure proper diabetic care. In addition, diabetes may potentiate adverse effects, especially renal dysfunction and peripheral neuropathy. Diabetes mellitus must therefore be managed closely throughout treatment. There must be good communication between the clinician managing treating the diabetes and the one managing the DR-TB.

7.12.5 Renal insufficiency

Renal insufficiency due to longstanding TB disease is not uncommon. Second-line anti-TB medicines that rely on renal clearance for most of their elimination include the aminoglycosides, ethambutol, cycloserine and fluoroquinolones. Metabolites of pyrazinamide are also primarily cleared by the kidneys. Great care should thus be taken in the administration of second-line medicines in patients with renal insufficiency, and the dose and/or the interval between dosing should be adjusted accordingly.

The creatinine clearance (CrCl) is used to determine the required dose adjustment in renal insufficiency, and is estimated thus:

$$\textit{Estimated creatinine clearance} = \frac{\textit{(140 – Age) x (body weight in kg) x } \mathbf{1.23}}{\textit{serum creatinine, µmol/l}}$$

(multiply the result of the above by 0.85 in female patients).

Normal values for CrCl are 97 to 137ml/min in men and 88 to 128ml/min in women.

Table 41: Dose adjustment of anti-TB medicines in renal failure

Medicine	Change in dosage?	Change in frequency?	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving haemodialysis
Isoniazid	No change	No change	300 mg once daily
Rifampicin	No change	No change	600 mg once daily
Pyrazinamide	No change	Yes	25–35 mg/kg per dose 3 times per week (not daily)
Ethambutol	No change	Yes	15–25 mg/kg per dose 3 times per week (not daily)
Levofloxacin	No change	Yes	750–1000 mg per dose 3 times per week (not daily)
Cycloserine	Yes	Yes	250 mg once daily or 500mg 3 times per week
Ethionamide	No change	No change	250–500 mg per dose daily
PAS	No change	No change	4 g/dose, twice daily
Streptomycin	Yes	Yes	12–15 mg/kg per dose 2-3 times per week (not daily)
Capreomycin	Yes	Yes	12–15 mg/kg per dose 2-3 times per week (not daily)
Kanamycin (or Amikacin)	Yes	Yes	12–15 mg/kg per dose 2-3 times per week (not daily)

General recommendations

1. To take advantage of the concentration-dependant bactericidal effect of many anti-TB medicines, standard doses are given unless there is intolerance.

2. The medicines should be given after haemodialysis on the day of haemodialysis (this also allows for the easy administration if DOT is three times per week).
3. Monitoring of serum concentrations should be considered to ensure adequate medicine absorption, without excessive accumulation, and to assist in avoiding toxicity.
4. Data are currently not available for patients receiving peritoneal dialysis. In the interim, begin with doses recommended for patients receiving haemodialysis and verify adequacy of dosing using serum concentration monitoring.
5. The appropriateness of 250 mg daily doses of cycloserine has not been established. There should be careful monitoring for evidence of neurotoxicity (if possible, measure serum concentrations and adjust accordingly).
6. Caution should be used with the injectable agents in patients with renal function impairment because of the increased risk of both ototoxicity and nephrotoxicity.

7.12.6 Psychiatric problems during DR-TB chemotherapy

There is a high baseline incidence of depression and anxiety in patients with DR-TB, often connected to socioeconomic factors related to the disease. Any psychiatric illness identified at the start of or during treatment should be addressed fully. Treatment with psychiatric medications, individual counselling, and/or group therapy may be needed to manage the patient suffering from a psychiatric condition or adverse effects. Group therapy has been very successful in providing a supportive environment for the DR-TB patient and may be helpful for patients with or without psychiatric conditions. It is therefore recommended that all facilities managing DR-TB patients hold regular group sessions where patients share experiences, and discuss challenges related to their treatment, under the guidance of a member of the facility DR-TB management team that they trust, preferably a social worker.

Patients with substance dependence should be offered treatment if possible. Complete abstinence from alcohol, smoking or recreational drugs should be strongly encouraged. However, active alcohol or drug use is not an absolute contraindication to treatment. If treatment is repeatedly interrupted due to the patient's addiction, TB treatment should be suspended until after successful therapy for the addiction. Good DOT gives the patient contact with and support from health care providers that often aids greatly in being successful in reducing substance dependence.

Cycloserine has a higher incidence of adverse effects in both the psychiatric patient and the alcohol or drug dependent patient. However, if cycloserine is required in the regimen, it should be used in these patients and the patients closely observed for adverse effects.

Clinicians treating DR-TB patients should work closely with a social worker and psychiatrist and have a system in place for psychiatric emergencies, including psychosis, suicidal ideation, and any situation that involves the patient posing a danger to himself or to others.

7.12.7 HIV

Routine HIV testing and counselling is strongly recommended for all patients diagnosed with DR-TB. HIV positive patients in general have a higher rate of adverse reactions, both to TB and non-TB medicines. All HIV positive patients with DR-TB should receive ART. None of the second line anti-TB medicine in the standard regimen is contraindicated for use with ARVs; although modifications may be necessary with rifampicin-containing second line regimens, and if levofloxacin is to be given in a patient taking buffered didanosine.

8 TUBERCULOSIS AND HIV

8.1 Background

Many countries in the region, including Namibia, experienced a large increase in TB patients during the 1990s due to the escalating HIV epidemic. This happens through two mechanisms:

- Reactivation of latent TB infection to TB disease, due to HIV-related immunodeficiency. This is the main driving force behind the current TB epidemic.
- Rapid progression from recent TB infection to TB disease. TB infection in PLHIV can rapidly progress to active disease. In the absence of HIV infection, the lifetime risk of developing TB disease is approximately 10%. However, a person with both HIV and TB infection has a 5-10% risk of developing TB disease *annually*. In 2010 the rate of HIV among patients with all forms of TB was 55% in Namibia.

TB is by far the leading cause of death in PLHIV in sub-Saharan Africa. Failure to promptly diagnose and treat TB in PLHIV contributes to premature mortality and TB transmission in the community.

8.2 TB/HIV Collaborative Activities

The goal of collaborative TB/HIV activities is to reduce the burden of TB and HIV in populations affected by both diseases by expanding the scope of TB and HIV control programmes. The objectives underlying this goal are:

- to establish the mechanisms for collaboration between TB and HIV control programmes;
- to reduce the burden of TB in people living with HIV; and
- to reduce the burden of HIV in TB patients.

8.2.1 Establishing the mechanism of collaboration

For TB/HIV collaborative activities to be effective the following steps need to be taken:

8.2.1.1 Set up a coordinating body for TB/HIV activities at all levels:

This means that there should be an enunciated mechanism through which the management of TB/HIV patients is addressed at national, regional, district and facility levels; as well as within the community health services. Regions and districts are therefore particularly recommended to ensure that there is a forum for discussion of TB/HIV issues.

8.2.1.2 Conduct surveillance of HIV prevalence among TB patients:

All TB patients should be offered HIV testing and counselling as early as possible. Patients who initially decline HIV testing should still be offered the chance to be tested at subsequent visits. Data on HIV status of TB patients should be reported on a quarterly basis; aggregation of these data provides very useful information for programme planning and implementation.

8.2.1.3 Joint TB/HIV planning:

Joint planning and coordinated management are particularly important for:

- Joint resource mobilisation, both financial and human, at all levels. .
- Capacity building, including training.
- TB/HIV advocacy, communication and social mobilisation (ACSM).

- Enhancing community involvement in collaborative TB/HIV activities through support groups for PLHIV and community-based organisations. Communities can be mobilised to advocate for resources and help implement collaborative TB/HIV activities.
- Operational research to inform national policy and strategy development, taking account of cultural, geographical and resource diversity.

8.2.1.4 Monitoring and evaluation of collaborative TB/HIV activities

This provides the means to assess quality, effectiveness, coverage and delivery of collaborative TB/HIV activities. Indicators are integrated within the monitoring and evaluation system of NSF for HIV and TBL MTP-II.

8.2.2 Decrease the burden of TB in persons living with HIV

8.2.2.1 Intensified TB case-finding (ICF):

ICF involves screening for symptoms and signs of TB in settings where HIV infected people seek care. All HIV infected persons should be screened for TB at every opportunity. ICF needs to be established in all HIV counselling and testing (HCT) centres, hospitals, prisons and other congregate settings where both TB and HIV are common. Referral mechanisms and communication and education to clients and staff need to be implemented routinely. The following sites should be considered important for intensified TB case-finding:

- HIV care clinics
- medical wards
- HCT centres
- antenatal clinics
- out-patient departments

The following TB screening questions should be asked to all PLHIV visiting any of the above sites:

Box 17: Screening questions for active TB

Yes	Symptoms to ask about	No
	Current cough?	
	Weight loss?	
	Night sweats?	
	Fever?	
	Swellings in the neck, armpits or groin (Lymph node enlargement)?	

Clients who answer "Yes" to any of these questions should be investigated for active TB. If already on TB-IPT, it should be stopped until TB is ruled out.

8.2.2.2 Isoniazid preventive therapy (TB-IPT):

TB-IPT is very effective in preventing TB in individuals who have latent infection with *M.tb*. Persons who qualify for TB-IPT include:

- HIV-positive persons in whom active TB has been excluded
- 0 -5 year old children who are close contacts of patients with infectious TB

- Close contacts of a smear-positive TB patient who have medical conditions that suppress the immune system, such as Hodgkin's disease, leukaemia, or diabetes mellitus, or who have been on immunosuppressive therapy like chronic steroids or cancer chemotherapy.

Individuals with both HIV infection and latent TB infection have a 5-10% *annual* risk of developing active TB, compared to HIV-negative individuals whose *lifetime* risk is only 10%. Six months of daily isoniazid reduces the risk of active TB in HIV-infected patients by at least 60%. The safety of TB-IPT has been well established in pregnancy and in children. Risks of TB-IPT include isoniazid-induced hepatitis, peripheral neuropathy, and inadequate treatment of persons with active TB with the potential development of isoniazid resistance. Following the strict criteria for TB-IPT eligibility, along with proper monitoring and follow-up, will minimise these risks.

To qualify for TB-IPT the HIV-positive individual must:

- Be healthy (TB-IPT should not be given to patients who are unwell, particularly where there is no explanation for the illness)
- Have no symptoms or signs of TB – **current cough, fever, weight loss, night sweats, enlarged lymph nodes**, or fatigue, blood in sputum, chest pain, diarrhoea, shortness of breath and loss of appetite
- Have no history of alcoholism
- Have no history of active liver disease, liver insufficiency, or jaundice
- Have no history of hypersensitivity to isoniazid
- Have no history of exfoliative dermatitis
- Be motivated for TB-IPT after being educated about the benefits, possible side-effects and risks

Precautions:

Persons starting TB-IPT must be warned about possible side-effects.

- INH-induced hepatitis will present with nausea and vomiting accompanied by passing dark urine and/or generalised itching.
- Peripheral neuropathy manifests as burning, numbness or tingling in feet and/or hands.

If any of these symptoms develop, the patient must stop taking INH and report immediately to the nearest health facility for assessment and management. Health-care workers should always check clients for signs and symptoms of hepatitis, neuropathy and skin itching when they come to collect INH.

Dosage:

- Isoniazid 10 mg/kg bodyweight (up to a maximum of 300mg/per day) is given daily for a period of 6 months.
- Pyridoxine 25 mg daily is administered with the INH to decrease the risk of neuropathy. The risk of developing neuropathy increases in patients who are also on D4T.
- Temporary TB-IPT interruption, although not ideal, is acceptable, as long as the patient completes a total of 6 months of treatment within a 9 month period. In non-adherent patients, prophylaxis should be discontinued and no further efforts should be made to restart it.

- Only one 6-month course of TB-IPT is given to an individual patient. Its efficacy lasts for approximately two years, after which PLHIV have the same risk of developing TB disease as before the TB-IPT. Currently, there is no recommendation to repeat TB-IPT after two years.

Recording and reporting: All details of the person receiving TB-IPT must be recorded as required in the IPT register and the TB-IPT identity card or other patient-held record. IPT status should also be recorded in the HIV patient care booklet (if HIV positive).

8.2.2.3 TB infection control in health facilities and other congregate settings

The risk of infection with *M.tb* is increased within health facilities and other congregate settings (e.g. prisons, police and military barracks), where people with TB and HIV frequently congregate. Measures to reduce TB transmission include administrative, environmental and personal protection measures, which are aimed at generally reducing exposure of staff to *M.tb.*

a) Administrative measures should include early recognition, diagnosis and treatment of TB suspects, particularly those with PTB, and separation of PTB suspects from others, until a diagnosis is confirmed or excluded.

b) Environmental protection should include maximising natural ventilation and fully utilising any other additional installations which reduce the concentration of infectious particles in the air.

c) Personal protection should include protection of the HIV-positive persons (and staff) from possible exposure to TB, and offering TB-IPT if eligible.

8.2.3 Decrease the burden of HIV in TB patients

8.2.3.1 Provide HIV testing and counselling:

All TB patients should be offered provider-initiated HIV counselling and testing (PICT) at every opportunity because of the following benefits:

- CPT and ART in HIV-infected patients have been shown to improve morbidity and prolong survival following successful TB treatment, but cannot be provided if the TB patient's HIV status remains unknown;
- Knowing one's HIV status is important for individual behavioural change, preparing for the future, and reducing stigma. This applies to each TB patient as well as the health-care worker providing care.

8.2.3.2 HIV prevention for patients with TB:

Comprehensive HIV prevention messages and tools for reducing risk behaviour should be offered to all TB patients, including referral to PMTCT services and screening for sexually transmitted infections. TB clinics should have IEC material addressing HIV prevention and should also offer condoms.

8.2.3.3 Co-trimoxazole preventive therapy:

Cotrimoxazole preventive therapy (CPT) has been shown to reduce morbidity and mortality in HIV-infected TB patients through the prevention of opportunistic infections such as pneumocystis pneumonia, other pneumonias, diarrhoea, malaria and toxoplasmosis. Cotrimoxazole 960mg daily should be started concurrently with TB treatment in PLHIV. Patients who are allergic to sulphur medicines should take dapsone 100 mg daily instead. It is continued until the CD4 count is above 350 on at least 2 consecutive tests performed at least 6 months apart.

8.2.3.4 Anti-retroviral therapy in patients with TB:

Antiretroviral therapy (ART) improves survival in HIV-positive patients. In addition, ART reduces TB rates by up to 90% at an individual level and by 60% at a population level, as well as reducing TB recurrence rates by 50%. ART should be initiated for *all* PLHIV with active TB regardless of CD4 cell count. TB treatment should be started first, followed by ART as soon as possible and within 8 weeks of starting TB treatment.

What ART regimens to start?

The recommended first-line ART regimens for TB patients are those that contain efavirenz (EFV), since interactions with anti-TB medicines are minimal. Rifampicin, an important component of TB treatment, interacts with many medicines, including many ARVs. Rifampicin decreases blood levels of protease inhibitors by approximately 80%, nevirapine by 30-50%, and efavirenz by 25%. This effect on efavirenz is not clinically significant and efavirenz can be used with rifampicin. At standard doses, efavirenz (EFV) in combination with tenofovir-lamivudine (TDF/3TC) is effective (see *Box 18*).

Because of concerns related to teratogenicity, efavirenz should not be used in women of childbearing potential without adequate contraception, nor should it be used for women who are in the first trimester of pregnancy. Alternatives are also needed for patients who are intolerant to efavirenz or are infected with a strain of HIV that is resistant to NNRTIs.

Box 18: Recommended ART regimens for adults in Namibia (MoHSS, 2010)

- ***Preferred 1st line choice in TB patients*:**
  - **tenofovir (TDF) + lamivudine (3TC) + Efavirenz (EFV)**
  - *Acceptable alternative*: zidovudine (AZT) + lamivudine (3TC) + Efavirenz (EFV)
- ***Efavirenz-free alternatives in TB patients:***
  - TDF + 3TC + LPV/r 400mg/ritonavir 400mg (superboosted)
  - AZT + 3TC + LPV/r 400mg/ritonavir 400mg (superboosted)
  - TDF + 3TC + AZT (*temporary*, until rifampicin is stopped)
- ***1st line HAART choices in patients not on rifampicin*:**
  - *Preferred 1st line:* TDF + 3TC + NVP (use EFV if CD4>350)
  - *Alternative 1st line:* AZT + 3TC + NVP (use EFV if CD4>350)
  - *ARV naïve pregnant women:* TDF + 3TC + NVP (EFV is option if CD4>350 after 1st trimester)
  - *With HBV co-infection:* TDF + 3TC + NVP (EFV if ALT>5times ULN)
- ***2nd line HAART choices (consult an HIV specialist)*:**
  - *Not on rifampicin*: AZT + TDF + 3TC + LPV/r
  - *On rifampicin*: AZT + TDF + 3TC + LPV/r (400mg/400mg)

For patients on rifampicin, alternatives to efavirenz are

1. Triple nucleoside regimens:
   e.g. tenofovir (TDF) + lamivudine (3TC) + zidovudine (AZT)
   These combinations are short term and the patient should be switched to a NNRTI containing regimen two weeks after stopping rifampicin.
2. A lopinavir based regimen super-boosted with ritonavir:
   TDF or AZT+3TC with LPV/r 400mg+ritonavir 400 mg BD (poorly tolerated).

When to start ART?

TB treatment should be commenced first and ART subsequently commenced, as soon as possible and within 8 weeks of starting TB treatment. The rationale for starting ART soon after TB diagnosis is that

case-fatality among TB/HIV patients occurs mainly in the first 2 months of TB treatment. However, early initiation of ART means an increased number of tablets for the patient, which may discourage treatment adherence. There is also increased risk of adverse effects, medicine interactions and IRIS.

Immune Reconstitution Inflammatory Syndrome (IRIS)

The Immune Reconstitution Inflammatory Syndrome (IRIS) is a spectrum of clinical signs and symptoms resulting from the restored ability to mount an inflammatory response associated with immune recovery. It can present with the signs and symptoms of a previously subclinical and unrecognised opportunistic infection, as a paradoxical worsening several weeks into therapy, or as an autoimmune disease such as Grave's disease (hyperthyroidism) in the context of immune recovery on ART.

Mild to moderate IRIS is relatively common in patients with TB started on ART; it has been reported in up to one-third of patients in some studies. However, it is relatively rare in its severe forms. The syndrome can present as fever, enlarging lymph nodes, worsening pulmonary infiltrates, or exacerbation of inflammatory changes at other sites. It generally presents within 3 months of starting ART and is more common when CD4 cell count is low (<50 cells/mm3). Most cases resolve without intervention and ART can be safely continued. In severe cases steroids are beneficial; in very severe cases temporary discontinuation of ART with continuation of TB therapy may be required.

IRIS is a diagnosis of exclusion. Patients with advanced AIDS may show clinical deterioration for a number of other reasons. New opportunistic infections or previously subclinical infections may be unmasked following immune reconstitution and cause clinical worsening. IRIS can also be confused with TB treatment failure. In addition, HIV-positive TB patients may be demonstrating progression of TB disease due to drug-resistance. IRIS is not a reason to switch patients to second-line ART, although the ART regimen may need to be adjusted to ensure compatibility with the TB treatment.

Organisation of combined TB treatment and ART in the co-infected patient

In order to minimise the burden to the patient it is advisable that the patient receives both anti-TB and ARV medicines from one health facility nearest to his home or workplace. ARV medicine collection should therefore be made accessible in health facilities that also offer TB therapy, or vice versa. When DOT is being given outside the health facility, ideally the ARV "treatment supporter" should also be the "DOT supporter", directly observing ingestion of both the ARVs and anti-TB medicines.

9 TUBERCULOSIS INFECTION CONTROL AND PREVENTION

9.1 Introduction

There are three types of prevention relevant to the management of TB:

- Preventing TB infection (primary prevention)
- Preventing TB disease (secondary prevention)
- Preventing TB morbidity and mortality (tertiary prevention)

The DOTS strategy can be considered as a combination of primary and tertiary prevention. By advocating early diagnosis and adequate treatment of infectious TB patients it prevents transmission of TB infection to uninfected persons in the community, and it also prevents TB death and disability in those patients with the disease.

9.2 Preventing TB infection: Tuberculosis infection control (TB-IC)

Administrative, environmental and personal respiratory protection should be implemented according to the *National Tuberculosis Infection Control Guidelines*. All health care facilities should have infection control plans outlining the implementation of TB-IC in the specific facilities:

9.2.1 The TB Infection Control Plan

Every health facility and setting should have a written infection control plan that outlines a protocol for the prompt recognition, separation, investigation and referral of patients with suspected or confirmed TB. Areas which should be prioritised in the health facilities include areas where diagnosed or undiagnosed TB patients are found, such as out-patient screening areas, waiting areas in medical outpatient departments, HIV care clinics, medical wards, TB clinics and TB wards.

The facility TB-IC plan should include the following measures:

- Prompt screening of all patients after arrival at the facility to identify persons with symptoms of TB or those who are being investigated or treated for TB disease (patients with *undiagnosed* sputum-smear positive TB form the highest health risk to patients and staff).
- Instructing the TB suspects and patients on respiratory hygiene/cough etiquette**.** This includes instructing them to cover their nose and mouth when coughing or sneezing, and providing face masks or tissues to assist them in covering their mouths. Face (surgical) masks help prevent the spread of *M.tb* from the patient to others. Paper tissues are less likely to be used effectively but are less costly and less likely to identify people as TB suspects with the attendant risk of stigma. Tissues and face masks should be disposed of in waste receptacles.
- Placing TB suspects and cases in a separate well-ventilated waiting area such as a sheltered open-air space is ideal in warm climates;
- Speeding up management of TB suspects so that they spend as little time as possible in the facility; including rapid diagnostic investigation and ensuring that persons reporting TB treatment are adhering to their treatment;
- Optimising the use of environmental control measures. This includes implementation of the “open window policy” as well as maintenance of ultraviolet germicidal irradiation (UVGI) units and other environmental control measures where these are installed.

- Training and educating all staff on TB and the TB-IC plan (should include special risks for TB for HIV positive health workers and patients, and need for diagnostic investigation for those with signs or symptoms of TB).
- Providing voluntary HIV counselling and testing for staff, with adequate access to confidential HIV care and treatment;
- Providing support for health-care workers found to be HIV-positive and implementing measures to reduce their exposure to TB (particularly MDR- and XDR-TB)
- Monitoring the TB-IC plan's implementation and correcting any inappropriate practices and enforcing adherence to institutional policies.

Table 42 summarises the actions that should be taken with all potential TB patients in health facilities to minimise the risk of transmission of TB within health facilities.

Table 42: Five steps to prevent transmission of TB in health care settings.

STEP	ACTION	DESCRIPTION
1	**Screen**	Early recognition of patients with suspected or confirmed TB disease is the first step in the plan. A staff member should be assigned to screen patients with cough of more than 2 weeks or who are under investigation or on treatment for TB. These patients should be attended to without delay.
2	**Educate**	Persons identified in **1** above should be instructed on cough hygiene. This should include covering their mouth and noses on coughing, sneezing and where possible be provided with face masks or tissues for use in this regard. Patients should be encouraged to do this at all times; not just when in the facility.
3	**Separate**	Promptly separate patients identified in **1** above from other patients. They should wait in a separate, well ventilated waiting area, and instructed in cough hygiene as in **2** above.
4	**Provide HIV care Services**	Symptomatic patients should be triaged to the front of the line while seeking services (e.g. HIV counselling and testing, medication refills etc) for prompt attention and reduce time to expose other persons to *M.tb*.
5	**Investigate for TB**	TB diagnostic investigations should be done promptly

9.2.2 Other areas to be addressed by the TB IC Plan

Outpatient management

One of the most effective means of reducing the risk of nosocomial transmission is to avoid hospitalisation where possible and manage ambulatory TB patients on an outpatient basis. This strategy works best where there are strong community-based DOT services.

If patients are hospitalised, frequent evaluation should be carried out for possible discharge with continuation of therapy as out-patients. Outpatient treatment should **not** be provided in the same rooms where TB suspects are evaluated. Treatment schedules should be convenient to the patient to avoid defaulting. Outpatient treatment should strictly be DOT and provided by an individual who is available and acceptable to the patient.

Infection control committees should ensure that patients who are discharged for ambulatory treatment are well informed about TB-IC measures while at home. This is particularly important for patients with DR-

TB who may continue to be infectious for prolonged periods of time. It should always be remembered that some patients on first line TB treatment might be harbouring undiagnosed DR-TB, therefore it is still important to emphasise infection control practices to all TB patients on treatment.

There is no danger in sharing food and eating utensils with a TB patient on TB treatment, if the patient observes cough etiquette and basic household hygiene. It is the inhalation of *M.tb* bacilli, not the physical contact with the patient or the sharing the same food or food utensils that causes TB infection.

Inpatient Management

Ideally all infectious TB patients should be isolated from non-TB patients as well as from other TB patients. Where this is not possible, separation should be practised till the patients are non-infectious.

Always attempt to:

- Limit the number of areas in the facility where exposure to potentially infectious TB patients may occur;
- Establish separate wards, areas, or rooms for confirmed infectious TB patients. These wards should be located away from other wards with non-TB patients (especially paediatric wards, medical wards with immune-compromised patients) preferably in separate buildings;
- Where only a single ward is available, separate the area within the ward and keep TB patients in a well-ventilated area. The direction of the airflow in such settings should always be away from patients without TB;
- Introduce and enforce that infectious TB patients are limited/restricted in their movements within the hospital, or otherwise wear a face mask when this cannot be avoided;
- Patients with suspected or confirmed DR-TB should be strictly isolated from patients without DR-TB. This is important because DR-TB patients may be able to transmit their infection to other TB patients.

Drug-resistant TB patients

Patients with DR-TB require specialised management at a referral centre for relatively longer periods. These patients are infectious for a long period with resultant increased risk for nosocomial transmission. They should be placed in a separate area or building in a facility, preferably in ventilated individual patient rooms where the possibility of contact with other patients without TB, or with presumed drug susceptible TB is not possible. Where this is not possible, and a large number of patients are suspected or have confirmed DR-TB cases, then a separate ward or a section of the existing ward should be designated for these patients.

9.3 Personal protective interventions

Personal protective interventions aim to prevent the inhalation of infectious respiratory aerosols. They should be used together with administrative and environmental controls in situations where there is an increased risk of pathogen transmission. Personal protective interventions include use of personal respirators. Respirators are the last line of defence for HCWs against nosocomial *M.tb* infection and should be closely fitted to the face to prevent leakage around the edges. If the respirator is not fitted correctly, infectious droplet nuclei can easily enter a person's airways, potentially resulting in infection. N95 respirators are recommended for use by HCWs. They are disposable but can be re-used repeatedly for several weeks up to a month if they are properly taken care of.

Without appropriate administrative and environmental controls, respirators will **not** adequately protect the HCW from infection. However, respirators may serve as a valuable complement to administrative and environmental infection control measures. Each facility should identify their high risk areas where respirators should be used and include this in the TB-IC plan.

The main factors responsible for the deterioration of respirators are humidity, dirt, and crushing. They should be stored in a clean dry location. One method is to fold a light towel around the respirator (being careful not to crush it). Plastic bags should never be used since they retain humidity.

A respirator fit testing programme should be incorporated into the infection control plan of each health facility. Fit testing should be conducted prior to the use of a respirator and annually thereafter.

9.4 Other methods of preventing TB disease

9.4.1 BCG vaccination

BCG (Bacille Calmette-Guerin) vaccination provides good protection in children against severe forms of TB (miliary TB and TB meningitis), reducing the associated mortality and morbidity. BCG vaccination is therefore part of the Namibian EPI package and is recommended for all newborn babies irrespective of the HIV status of the mother; except in newborns whose mothers have sputum-smear positive TB. In the event that a child is seen at a much older age – not having had a BCG vaccination, a tuberculin skin test may be performed first to see whether the child has already been infected. With a positive tuberculin test there is no need for BCG vaccination; if tuberculin test is negative BCG can be given.

9.4.2 TB-IPT in preventing TB disease

TB-IPT is very effective in preventing TB disease in persons who have been infected with TB bacilli (also called secondary chemoprophylaxis) (see *Chapter 8*).

9.5 Contact examination and management

9.5.1 Household contacts

Household contacts of an infectious TB patient are particularly at risk of becoming infected and developing TB disease. Over 50% of cases of TB disease in young children, who are the main victims of household transmission, develop TB within 5 years of infection. Routine examination of household contacts can be useful and result in:

- Identifying persons who have undiagnosed active TB
- Identifying persons who are likely to have TB infection but without active disease, who can benefit from TB-IPT.

9.5.2 Management of household contacts of TB patients

In all patients with TB

- The TB patient should be informed about the potential risks of disease in their contacts, in particular children under 5 years of age and any person who is known to be HIV positive.
- The health-care worker should interview the patient with infectious TB and note down the details of contacts on the back of the *TB Patient Treatment Card*, and fill in *TB Contact Investigation Slips (TB 12)* for each contact. The name of the contact should be clear on these cards.

- The TB patient should deliver the TB contact cards to the respective household contacts, explaining the purpose and the benefit of the card and advising all contacts to report to the TB clinic indicated on the card.
- The health-care worker or field promoter should additionally visit the households to ensure that all contacts are traced and screened for possible TB, and then treated appropriately.
- Household contacts reporting to a TB clinic are recorded on the *TB Treatment Card* of the patient (if attending at the same clinic); checked for signs and symptoms of active TB, and checked for eligibility of IPT;
- Contacts eligible for IPT are educated, recorded and started on IPT.
- Patients with signs and symptoms of TB are examined and investigated for TB.
- If the patient is supported by a community-based DOT supporter, the supporter should also be asked to provide TB-IPT to eligible household contacts as DOT

9.5.3 Heath care workers

Staff working in health care institutions and congregate settings with high TB prevalence are at risk of infection with TB. This includes nurses, doctors, porters, cleaners, caterers as well as volunteers and counsellors. Staff with HIV are at a particularly high risk of rapid progression to TB disease if they become infected or re-infected due to exposure to *M.tb* in the facility.

Health facility staff therefore should be included in training programmes on TB-IC, including regular refresher trainings. The TB-IC measures recommended in these guidelines should reduce time persons with undiagnosed TB spend in the health-care settings and should improve ventilation and thus dilution of *M.tb* bacilli in the environment. Staff at risk should be encouraged to know their HIV status, and those known to be HIV-positive should be offered TB-IPT and must be assigned to areas with lower risk for occupational exposure to TB.

Members of staff who develop any symptom of TB should be fully investigated for TB. The facility TB-IC plan should nominate designated staff who will initiate the TB investigations, while maintaining confidentiality of the affected workers.

10 ADVOCACY, COMMUNICATION AND SOCIAL MOBILISATION (ACSM)

10.1 What is ACSM?

ACSM stands for advocacy, communication and social mobilisation.

Advocacy: Advocacy seeks to ensure that national and local governments remain strongly committed to implementing TB control policies. Advocacy often focuses on influencing policy-makers, funders and international decision-making bodies through a variety of channels. The different types of advocacy are:

- *Policy advocacy*: informs senior politicians and administrators how an issue will affect the country, and outlines actions to take to improve laws and policies
- *Programme advocacy*: targets opinion leaders at the community level on the need for local action
- *Media advocacy*: validates the relevance of a subject, puts issues on the public agenda, and encourages the media to cover TB-related topics regularly and in a responsible manner so as to raise awareness of possible solutions and problems.

Communication: Behaviour-change communication (BCC) aims to change knowledge, attitudes and practices among various groups of people. It frequently informs the public on the different health services and the latest medical interventions available. Effective BCC and messages need to convey more than just the medical facts as, on their own, these facts do not necessarily motivate people to visit a TB clinic or complete their treatment. The messages should explore the reasons why people do or do not take action on the information they receive, and then focus on changing the actual behaviour by addressing the identified causes.

BCC creates an environment through which affected communities can discuss, debate, organise and communicate their own perspectives on TB. It aims to change behaviour – such as persuading people with symptoms to seek treatment – and to foster social change, supporting processes in the community or elsewhere to spark debate that may shift social mores and/or eliminate barriers to behavioural change.

Always remember the golden rule whenever you communicate: **RUTH (R**espect, **U**nderstanding, **T**rust and **H**onesty)

Social mobilisation: Social mobilisation brings together community members and other stakeholders to strengthen community participation for sustainability and self-reliance. Social mobilisation generates dialogue, negotiation and consensus among a range of players that includes decision-makers, the media, NGOs, opinion leaders, policy-makers, the private sector, professional associations, TB-patient networks and religious groups. At the heart of social mobilisation is the need to involve people who are either living with active TB or have suffered from it at some time in the past. Empowering TB patients and the affected community helps to achieve timely diagnosis and treatment completion, especially among families of TB patients

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

10.2 TB control challenges that can be addressed through ACSM

TB control presents many challenges, such as:

- Delayed detection and treatment
- Lack of access to TB treatment
- Difficulty in completing treatment
- Lack of knowledge and information about TB that can lead to stigma, discrimination and delayed diagnosis and/or treatment
- Stigma and discrimination that can prevent people from seeking care and diagnosis;
- Misunderstandings and myths surrounding TB, including the belief that it is "untreatable"
- Weak political support for TB programmes
- Insufficient funding for TB programmes.

Despite increased attention and funding in recent years, these challenges have been difficult to overcome. ACSM strategies however contribute to addressing many of them successfully. *ACSM is therefore a very important component of TB control programme.*

A multipronged approach should be implemented to disseminate information through IEC materials and simultaneously through community-based activities to involve and sensitise communities and facilities providing diagnostic and treatment services for TB.

The key messages are:

1. TB is curable even in HIV-infected people,
2. TB treatment is free, and
3. TB patients should complete their treatment course.

These activities implemented in a planned and systematic manner will enable communities to become TB literate. TB literate communities will generate demand for DOT and access health facilities for treatment when TB symptoms arise. The communities will know the 'do's and 'don'ts' on preventive aspect of TB and thereby will be free of TB related stigmas. Ongoing regular and systematic sensitisation of communities will lead to social mobilisation and will result in health seeking behaviour. It will also help with treatment adherence and result in reduction adverse treatment outcomes. Advocacy on TB control issues will increase the priority given to the TB programme. It will assist in resource mobilisation and will ensure high level support.

Monitoring of ACSM activities is essential. Therefore regular documentation is necessary. Monitoring and evaluation of ACSM activities should be part of routine planning activities and regular supportive supervisory visits. It should appear on the work plans of districts and regions and should have a budget. Feedback from the field visits is critical for modification and improvement in activities.

10.3 Documenting ACSM activities

ACSM activities are not 'one-time'; they must be ongoing. Need based action plans on ACSM activities should to be in place so that the activities can be systematically monitored. Activities must generate demand for DOT and increased programme priority at all levels. The following are the reasons for documenting ACSM activities:

- To help programme managers to monitor ACSM activities, both in number and quality
- To assist the system in evaluation of ACSM activities and assess the impact on programme indicators like case detection rates, treatment success rates and default rates.
- To assist programme managers in assessment of action plans and re-planning of activities and improve wherever necessary
- To make ACSM activities an integral part of the programme, therefore it should be highlighted in the annual work plans at all levels.

ACSM reporting should be included in the routine quarterly TB reports based on the *ACSM Documentation Form (TB 20)*.

10.4 Patient education

10.4.1 General patient education

Good patient education is the cornerstone for achieving high treatment success rate by preventing patients from treatment interruption and default. Since patients have different cultural and educational backgrounds, patient education can only be effective if each patient is approached as an individual, each with his own specific problems and background. This requires specific skills and the right attitude from the educator, and most importantly, sufficient time.

For anti-TB chemotherapy to be successfully completed, each patient must fully understand what it entails: different medicines, duration, possible side-effects, importance of completing the treatment and taking every medicine as prescribed, and the possibility of HIV co-infection and treatment. The educator must verify that the patient has fully understood the message by asking the patient and the DOT supporter to explain the information in his/their own words. Many different people can and should provide TB education: nurse, TB field promoter, HIV/AIDS counsellor, and doctors, peer educators, DTLC, DOT supporter etc. Care must be taken that their messages are consistent and mutually re-enforcing.

The following approach is considered desirable to achieve full understanding by the patient and his/her DOT supporter:

- When possible a period of hospital admission for intensive high quality patient education and organisation of ambulatory DOT.
- The DTLC in collaboration with the TB field promoter has the overall responsibility of ensuring that each TB patient is properly informed and fully understands the implications of TB disease and treatment.
- It is advisable that the DTLC and the HIV counsellor jointly plan and implement education to each individual patient and his/her treatment supporter.
- To maximise effectiveness of patient education and information the following educational materials should be available and provided to each patient and DOT supporter: patient information leaflet in all major languages, DOT supporter leaflet.
- The TB patient card includes a patient education checklist to guide the TB educator(s) and ensure that all important aspects of information are covered and understood by the patient.

- Other educational materials can support the process of patient education, such as flip charts and videos.
- The involvement of TB field promoters in patient education is highly recommended, particularly if they are former TB patients who have successfully completed their treatment.

Box 19: Patient education

It is much more cost-effective to invest time in patient education and support than in tracing of patients who interrupt their treatment.

10.4.2 Principles of patient education

Every educator should bear in mind that the diagnosis of TB is often perceived as a shock by the patient. The first IEC session might therefore focus on acceptance of the diagnosis;

- Assume that each patient with TB will be worried about having HIV, and that not addressing represents a missed opportunity for HIV prevention and patient management.
- Education is a dialogue, not a lecture.
- Involve patient companions (family, relatives and friends) in the education sessions.
- Always encourage the patient and his/her companions or treatment supporter to ask questions.
- The educator should try to put himself in the position of the patient
- Allow sufficient time for each session
- Use several approaches repeating the same messages: group discussion, individual dialogue, leaflets, flip-charts etc.
- Provide the patient and his companions with information leaflets in the language they can read and understand
- Verify that the patient has understood the message(s) by asking him/her to repeat the message(s) in his/her own words
- Try to avoid providing too much information at the same time.

10.4.3 What each patient and his/her DOT supporter needs to know

During initial (admission) phase:

- TB is curable, if treatment is taken as prescribed.
- TB treatment is available free of charge at any government or mission health facility.
- TB is an infectious disease that is transmitted from one person to another by coughing, and appropriate cough hygiene reduces transmission.
- The patient may already have infected other people who may also develop TB. The patient should therefore encourage other people with whom s/he is in close contact to have themselves checked for TB disease when they are ill or display symptoms.
- It is important to identify a DOT supporter and determine where and when medication will be administered.
- All close contacts under 5 years of age are likely to have been infected and can benefit from TB-IPT.
- Explain the duration of initial and continuation phases of TB treatment.

- Explain which pills s/he will take during the full treatment course; show and explain number, colour and frequency.
- Once treatment with these medicines has begun, symptoms of TB disease will disappear quickly; but the medicines still need to be continued daily until the end of the prescribed treatment period.
- Failure to adhere to this treatment may cause TB disease to start again, with great risks for the health of the patient, because the second time around the treatment is likely not to work as well.
- Because of the risk of transmitting TB to the community, it is the patient's responsibility to complete the TB treatment the first time. Interrupting treatment puts the community at risk.
- Sputum-smear examinations are required at certain intervals to monitor the progress towards cure. Explain to the patient when the examinations are required.
- TB and HIV are different diseases, but HIV is common in TB patients.
- TB can be cured, even when you have HIV.
- It is important for the nurse or doctor and the patient to know the patient's HIV status so that the patient can have access to better treatment, including ART.

Additional information for returning treatment interrupters:

- Adjustments need to be made to the treatment provided;
- Repeated treatment interruption will not be tolerated, and may eventually result in a decision by the health authorities to enforce hospitalisation for the full duration of treatment.

Examples of verification questions to be asked from each patient:

- "What is the disease you have?"
- "How is this disease spread?"
- "What can you do to avoid infecting others?"
- "How will you be treated?"
- "Can TB be cured?"
- "What medicines will you take and for how long?"
- "Are TB and HIV/AIDS the same? Explain"
- "Why is it important to know your HIV status when you have TB?"
- "How can you benefit from knowing your HIV status?"
- "Why is it important to have a DOT supporter?"
- "What are common side-effects and what can you do about them?"
- "Which are serious side-effects that must make you come to the hospital immediately?"

During treatment:

- Re-emphasise the need for follow-up visits and investigations
- Patient should inform the staff at the clinic when s/he intends to travel. An adequate supply of medicines can then be given to cater for the period of travelling
- Patient should inform the staff at the clinic when s/he intends to move to another area. The clinic staff will then write the transfer letter and give advice as to where treatment can be continued.

At the end of treatment:

- TB may occur again, especially if one is HIV positive;
- The patient should report immediately to the TB clinic, when s/he notices similar symptoms, to be examined for recurrence of the disease.

10.5 Community education

It is important for all sectors of the community to understand TB prevention, disease and management. Important partners in community education on TB are: community leaders, schools, all organisations working on HIV, businesses and private health sector; and specific sectors with a very high TB burden (prisons, police holding cells, hostels for migrant workers, army barracks).

10.5.1 Messages to stress during community education

- Namibia has one of the worst TB epidemics in the world.
- TB is caused by bacilli that are passed on from one person to another, and is not caused by witchcraft, dust or inheritance.
- Everybody who has a cough for two weeks or more, or has coughed up blood should go to a clinic or hospital to have his/her sputum examined for TB.
- TB treatment is free of charge in government and mission health facilities.
- TB can be cured completely if you come early when you are ill and take the treatment to the end.
- TB patients who are not on treatment are spreading TB disease within their families and communities.
- TB patients on treatment are not infectious and do not need to be isolated or shunned; but rather need support and encouragement to complete their treatment.
- There is no danger in being close to a TB patient who is on TB treatment: touching, sleeping, or sharing food or eating utensils is safe.
- TB and HIV are different diseases, but HIV is common in TB patients.
- TB can be cured, even when a person has HIV.
- All TB patients should have an HIV test, so that those who are HIV positive can also be treated for HIV.

10.5.2 What communities can do to prevent TB?

- Identify friends and colleagues with chronic cough, weight loss, and prolonged fever and advise them to be tested for TB and HIV.
- Advise people to hold their elbow before their mouth when they cough (cough hygiene).
- Ventilate and clean houses, barracks and prison cells on a daily basis.
- Build houses that have wide windows for ventilation and sunlight.
- Avoid overcrowding in prisons, barracks and private homes, if possible.

10.5.3 What leadership can do in the fight against TB?

- Stress the importance of fighting this curable but widespread disease, TB.

- Allocate sufficient human and financial resources to fight TB.
- Mention the need to fight TB in public addresses.
- Stress that TB and HIV often go together - but not always - , and that every HIV infected patient should be regularly screened for TB, while every TB patient should be tested for HIV in order to access life-saving HIV care if HIV positive
- Be sincerely committed to fighting poverty and HIV, as both are fuelling the TB epidemic.

11 MONITORING AND EVALUATION

11.1 Introduction

Establishment of a reliable recording and reporting system is an essential part of the DOTS strategy. Analysis of reports and indicators taken from the routinely collected data helps in assessment of progress and performance of different aspects of the programme. These guidelines are accompanied by revised recording and reporting forms as well as new forms to enable the collection of data on interventions for TB control. In addition to submitting data to national level, each health facility, district and region should fully utilise the data they collect in order to improve general TB control activities in their catchment area. Easy generation of reports through the use of electronic TB registers will facilitate this.

11.2 Records (TB01-TB14)

The recording and reporting forms (TB01-TB20) are annexed to these guidelines.

TB 01: Sputum Examination Register

This register should be kept in each health facility and in the TB clinic. When a TB suspect has been identified the date his sputum specimens were received and sent to the laboratory should be written in the register. Laboratory results will be copied in the sputum examination register, and the time elapsed between sending and receiving the results (turn-around-time, TAT) recorded. The TAT should ideally not exceed 48 hours. When the patient is sputum-smear positive TB treatment should be started without delay and the date recorded. The patient can be traced to his home address if the sputum is positive and s/he has not returned to collect the result.

TB 02: Drug Susceptibility Testing (DST) Register

The DTLC should keep this register as a record of all patients who have DST requested. Its purpose is to ensure that all patients at risk for DR-TB have a DST requested and are adequately followed up. Whenever a DST is requested for the first time in a patient or in a contact of a DR-TB patient, a number is allocated and their name is entered. It will also apply to patients who have had a DST before, but in whom a change in drug susceptibility patterns is suspected. Results should be actively followed up and entered (within a week for rapid DST, and within 2 months for conventional culture and DST).

TB 03*:* TB Patient Treatment Card

This card contains information about the patient's details (name, age, sex, address, and contact details), the patient's diagnostic classifications, results of initial and follow-up sputum-smear examinations, treatment regimen, medicine doses, initial and follow-up body weight, HIV status, and medicine collection data.

This card is issued after a patient is diagnosed with TB and treatment is started. The card must be completed in full in order for it to be useful both for the patient and for gathering accurate information for programme analysis. The TB Patient Treatment Card should be kept at the health facility at which the patient receives his/her anti-TB medicines. The card should not be transferred with the patient in the event that a patient relocates. A new card will be issued at the referral TB treatment site when the patient reports and hands in his/her referral form.

TB 04*:* TB Patient Identity Card

The TB Patient Identity Card contains an extract of the information of the TB Patient Treatment Card. This card is provided to the patient at the start of TB treatment. Daily DOT must be recorded on this card

in the intensive phase of the treatment. Unlike the TB Patient Treatment Card the patient must keep it with his/her health passport. It serves as a special passport to any health facility in the country and the patient can access treatment upon presentation of the card.

The TB nurse should advise the patient to keep the card safely even after completing treatment as it is a reference document for TB for the rest of his/her life. When the patient falls ill, the card must be presented to the doctor or nurse along with the health passport.

TB 05: Facility Tuberculosis Treatment Register

This register is maintained in health facilities attending to TB patients. It facilitates easy and quick recording and monitoring of regular attendance of patients during treatment.

TB 06: The District Tuberculosis Register

The TB register is the cornerstone of the NTLP monitoring and evaluation system. It records essential information for notification and treatment outcomes by district. The register must always be kept up-to-date with data on sputum-smear examinations and treatment outcomes. The DTLC should update the District TB register with new information from the Facility TB Treatment Register during each clinic supervision visit. The information in the District TB Register should be entered in the District Electronic TB Register (ETR.net). This is an electronic copy of the TB register.

At every opportunity the ETR.net should be updated and regular reports generated from it for local use. During the review meetings, the paper-based registers and the ETR.net will be compared.

TB 07: Community-based DOT Card

This form should be used by DOT supporter for each patient who is on ambulatory treatment. It should be kept by the DOT supporter, who records on it each day DOT is administered to the patient. The nurse in the health facility from where TB medications are collected will indicate the period for which medicines were issued on the form. The form has enough space to record the patient's ambulatory DOT for second-line TB medicines for up to 18 months.

TB 08: Tuberculosis Patient Transfer Form

The TB *Patient Transfer Form* should be completed in triplicate and the original given to the patient who wishes to move to another district for continuation of his/her TB treatment. The second copy should be sent to the receiving district PMO, for the attention of the DTLC, while the third copy remains in the booklet. The DTLC at the receiving district will record the patient in the *District TB Register* as a "Transfer In" patient and will open a new *TB Treatment Card*, recording all the information on the *TB Patient Transfer Form.* The patient can continue his treatment as required and his treatment outcome is captured in the *District TB Register*.

The outcome of treatment is recorded on the bottom section of the *TB Patient Transfer Form*, and the slip should be sent back to the transferring district. The true treatment outcome can now be captured in the treatment outcome analysis of the transferring district where the patient was first registered, and then the notation "transfer-out" is deleted and replaced by the true treatment outcome reported by the district where the patient was transferred to.

NB: The treatment outcome of transfer out should be temporary and should approach zero in the annual cohort analysis.

TB 09: DR-TB Patient Booklet

This booklet is used for patients managed with second-line anti-TB medicines at DR-TB treatment centres. It is given a different colour, blue, to make it readily distinguishable from the treatment cards for patients on first-line anti-TB medicines. The *DR-TB Patient Booklet* includes additional sections for recording DOT during continuation phase and monitoring of adverse effects of second-line medicines. The booklet should always be kept at the health facility where the patient receives TB treatment. On discharge from the DR-TB treatment centre, a duplicate of the booklet should be made for the district where the patient will continue treatment, and sent to the PMO, attention DTLC, by registered mail. A *TB Patient Transfer Form* will accompany the patient

TB 10: Drug-resistant Tuberculosis (DR-TB) Register

The DR-TB register is the cornerstone of programmatic management of DR-TB (PMDT). It records essential information for notification and treatment outcomes by district. The register must always be kept up-to-date with data on sputum smear and culture examinations and treatment outcome. The DTLC will keep one DR-TB register per district. The following categories of patients will be recorded in the DR-TB register regardless of whether they are on treatment or not: confirmed MDR-TB, Poly-drug resistant TB, rifampicin monoresistance and XDR-TB,. In addition, patients who are started on empirical second line treatment should be recorded as suspected cases of MDR-TB.

TB 11: Drug-Resistant Tuberculosis Patient Transfer/Referral Form

This form should be completed for all patients on treatment for DR-TB being transferred from one district to another. The reason for the transfer must be documented and communicated with the patient and patient's relatives to solicit their support.

The form has two tear-off feedback forms, one to acknowledge receipt of the patient and the other to inform the referring facility of the final outcome. The MoHSS medical referral form or cover letter signed by doctor in charge of treating the patient should also be completed and attached to the DR-TB Patient Transfer/Referral form.

TB 12: Tuberculosis Contact Investigation Slip

All smear-positive patients should have their contacts identified and a Contact Investigation Slip should be completed for each contact. The details of the outcome of the contact tracing should be recorded on the tear-off slip.

TB 13: Client Isoniazid Preventive Therapy Card

This card is for persons who receive isoniazid preventive therapy (IPT). It contains an IPT number, personal patient information, start and end dates of IPT, and dates of 4-weekly medicine collections. These clients should not be registered in the *District or Facility TB Register*; they must instead be registered in the *IPT Register*.

TB 14: Isoniazid Preventive Therapy (IPT) Register

All clients receiving IPT should be recorded in the *Health Facility TB-IPT Register* for purposes of monitoring of client adherence and IPT outcomes. Patients entered in this register include contacts who are less than 5 years old, and those with other immunosuppressed contacts. A similar register should be kept in the HIV clinic.

11.2. Reports (TB15-TB20)

TB 15: District Quarterly Tuberculosis and Leprosy Report

Divided into:

- **Tuberculosis and leprosy case-finding:** This report is generated from individual patient notification data recorded in the *District TB Register* and the Leprosy Register[8]. The district data are again aggregated to regional and national level. The report is of critical importance to monitor the trend of TB notifications and may give an indication of the trends in TB incidence as well as the diagnostic performance at all levels. The DTLC is responsible for the timely and complete submission of correct reports to the District PMO and the RTLC, within 15 days after the end of the quarter as indicated in *Table 43*. A similar report should be produced for each health facility in order to monitor the distribution of TB patients.
- **District Quarterly Report on Treatment Outcomes:** This report is generated from individual patient data recorded in the *District TB Register*. The district data are again aggregated to regional and national level. This report is of critical importance to monitor the performance of various levels in treatment outcomes. A similar report should be produced for each health facility in order to monitor the performance of TB management per health facility. The DTLC is responsible for the timely and complete submission of correct reports to the District PMO and the RTLC, and these reports should reach national level within 15 days after the end of the quarter.

  To avoid double registration, patients who were "Transferred-in" are not included in treatment outcome analysis in the quarterly treatment outcome analysis of the receiving district. The treatment outcome should instead be included in the report of the transferring district. The final outcome analysis and reporting for the national level should not have the column on transfer out as at this stage all transferred patients should have an outcome. Otherwise patients from this category may be recorded as defaulters if they do not fit into any of the categories of dead, failed treatment, treatment completed, or cured.

TB 16: TB/HIV Quarterly Report Form

This form is similar to the District TB and Leprosy Quarterly reform, but it specifically focussing on reporting TB patients who are known to be HIV infected.

TB 17: The DR-TB Quarterly Reporting Form

This report aims to aggregate data on DR-TB per district by cases notified in that reporting quarter, classified as MDR-TB, XDR-TB, poly-drug resistant TB, or have no DST results. In addition, this report also shows the gross and net burden of DR-TB cases in the district each quarter, the HIV status, and the interim outcome analysis. The reporting periods are the same as for the district quarterly report discussed above (*Table 43*).

TB 18: Quarterly Outcome Report for Isoniazid Preventive Therapy (IPT)

This report should be compiled quarterly and summarises the outcome of contacts and other at-risk individuals commenced on IPT during the same quarter of the previous year. Outcomes for under-five contacts of smear-positive cases and those for adults commenced on IPT due to immunosuppressive conditions should be reporter separately.

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[8] Not included in these guidelines

TB 19: District Quarterly Report on Community-based Tuberculosis Care (CBTBC)

This form summarises the implementation of community-TB care activities and should be completed by the DTLCs with input from the organisations providing CBTBC services in the district.

TB 20: Namibia ACSM Documentation Format

This form should be part of quarterly reporting and includes information on all ACSM activities implemented in the district during the quarter under review.

11.3. TB review meetings

Review meetings are important meetings during which TB programme officers at all levels review their data and find solutions to challenges hampering TB control efforts in their locality. Continuity of these meetings is important for improving data quality and utilisation at local level.

Review meetings will be conducted as follows:

1. **Regional quarterly review meetings:** At these meetings, all districts in a particular region will come together and review their TB and leprosy data. This forum is used for data cleaning as well as to produce the district and regional quarterly TB reports. Additionally this is also used for capacity building on TB and leprosy data management. It is expected that regions will start including these meetings in their annual budget requests.
2. **Zonal review meetings:** At these meetings, a number of regions (two to four) will come together and review their TB and leprosy data. This forum focuses more on data analysis and programme performance and should be used to build capacity on data utilisation for decision making.
3. **National review meetings:** These should be held annually and will aid the national level in monitoring trend and putting measures in place to improve or change strategies as necessary. The national meeting seeks to leverage regional expertise and inter-programme collaboration.

Table 43: Reporting dates and periods for case-finding and treatment outcome

Reporting deadline	Reports to be submitted
15th of January	TB Case-finding Report, previous Quarter 4 of previous year (1 October – 31 December) Treatment Outcome Report Quarter 1 previous year (1 October – 31 December)
15th of April	TB Case-finding report Quarter 1, same year (1 January – 31 March) Treatment Outcome Report Quarter 2 of previous year (1 January – 31 March)
15th of July	TB Case-finding report Quarter 2, same year (1 April – 30 June) Treatment Outcome Report Quarter 3 previous year (1 April – 30 June)
15th of October	TB Case-finding report Quarter 3, same year (1 July – 30 September) Treatment Outcome Report Quarter 4 previous year (1 July – 30 September)

11.4. Supervision

11.4.1. Introduction

Supportive supervision is an essential activity, which all NTLP staff must do on a regular basis. The objectives of supportive supervision can be summarised as follows:

- To check if clinic and staff performance is satisfactory, relative to NTLP technical guidelines and outcome indicators;

- To check for gaps in understanding and performance weaknesses that can be remedied through on-the-job training or in-service training;
- To identify contextual factors that inhibit or enhance proper implementation of NTLP technical policies;
- To motivate and support health staff to perform well.

11.4.2. Competence and motivation

A person's performance in a job is determined by several factors, of which competence and motivation are the most important. Continuous monitoring of the competence and motivation of health staff is therefore part of the supervisor's task. The profile of competence of staff working in TB control is:

Attitude

- An interest in TB as a major public health problem affecting people's prospects to an improved life;
- Empathic character; a person interested in the fate of individual patients s/he is managing;
- Results oriented; achieving good patient adherence to treatment and high treatment success rate.

Knowledge

- NTLP guidelines
- TB epidemiology and TB control.

Skills

- Communication and coordination
- Clinical practice
- Organisation
- Supervision
- Training
- Recording and reporting.

11.4.3. Important aspects of supervision

For supervision to be effective the following principles should be adhered to:

- The attitude of the supervisor is supportive, not necessarily policing all the time;
- Supervision is done regularly, preferably following a pre-arranged schedule;
- Supervision is done is a structured manner, with the aid of a structured checklist or questionnaire;
- Feedback is given on-the-spot, verbally as well as in writing;
- Supervision reports are copied to relevant people in the administrative hierarchy
- Future supervision should take recommendations from previous supervisions into consideration.

11.5. Frequency of supervision by different levels

11.5.1. District TB and Leprosy Coordinators (DTLC)

The DCC should provide reliable transport for the planned visits by the DTLC. The DTLC should supervise all health facilities monthly in the rural areas and weekly in urban areas. The visit should take place on a scheduled clinic day. Health staff should be observed as the clinic is being conducted. The

DTLC should not conduct the clinic, but should provide guidance, advice and training to the dedicated TB clinic nurse. Praise should be given where performance is good, constructive criticism and on-the-job training if the performance is below standard.

For successful performance of the programme, the TB treatment centre should open on time and be staffed with competent nurses. Only then can health staff credibly demand that patients stick to their appointments. The DTLC should use a checklist for each visit to a health unit, and verify each time that previous recommendations were implemented. S/he should make a clinic visit schedule for the entire year for all clinic visits and indicate on it when the visit is planned. This schedule should be distributed to all heads of health units, as well as the RTLC and the DCC.

11.5.2. Regional TB and Leprosy Coordinator (RTLC)

Regional management should provide reliable transport for the planned visits by the CHPA or SHPA who has the responsibility for TB and leprosy (thus called Regional TB and Leprosy Coordinator). The DTLC's work should be regularly supervised by the RTLC through field visits and during quarterly regional DTLC meetings. The RTLC should observe the DTLC during his/her work. The competence checklist can also be used as a checklist for the DTLC's performance. The RTLC should give the DTLC feedback on the assessment of his/her performance. It is good practice for the RTLC to make a report of the supervision visit and send copies to the DTLC, DCC, CMO and national level.

11.5.3. National level

National level should be provided with reliable transport for scheduled supervision visits to regions, and each region should be visited at least once a year. The staff should also use a standardised approach to supervision using a checklist, and should give feedback to the RTLC on his/her performance. A written report of the supervision visit should be sent within 2 weeks to the RTLC and Regional Director.

11.6. Information sharing

RTLCs and DTLCs should write a brief annual report that will be distributed to their superiors and lower levels in the NTLP. This report should describe the performance of the programme in the region according to work plan; indicate the epidemiological trends for TB and include an annual plan for improvement of the national, regional and district performance. The national level should compile an annual report and publish it by end of second quarter of each year.

12. MANAGEMENT OF ANTI-TB MEDICINES

12.2. Introduction

Management of medicines is an essential part of any health care system, but even more critical to the success of a TB programme. This is because TB is a difficult disease to cure, requiring multi-drug regimens for long treatment periods. Ensuring an effective medicine supply and management system is one of the sub-components of the Stop TB strategy. Non-availability to a patient of any of the anti-TB medicines at any time is a serious weakness in a TB programme and can contribute to the emergence of TB drug resistance. Moreover, it undermines the credibility of the TB programme in the eyes of the patient and the community, and is a serious challenge for committed TB programme coordinators and health care workers looking after TB patients.

Each health-care worker in charge of medicines supply in a health facility should be familiar with the *Managing Pharmaceutical Stores Manual* as well as the *Pharmaceutical Standard Operating Procedures*. This manual and the SOP comprehensively cover all aspects of stock control and storage for pharmaceutical items; this chapter only highlights some of the most critical aspects as they relate to the management of anti-TB medicines.

The DTLC in collaboration with the pharmacist /pharmacist assistant should take responsibility for the provision of an uninterrupted anti-TB medicine supply.

12.3. Stock control

A stock control system serves two main purposes. It is effectively implemented if:

- it ensures that the correct items are available in the right amounts, at the time when they are needed;
- it improves accountability.

The advantages of a properly functioning stock control system to the patient, the health-care worker, the district hospital, and medical stores include:

- improved efficiency in the use of financial resources
- prevention of under-stocking and stock-outs
- prevention of overstocking and wastage
- prevention of shortages in case of delays in delivery
- continued service provision even when there are staff changes
- prompt identification of security problems

The most important tool for effective stock control is the proper maintenance of up-to-date stock cards. A proper stock control system which is documented by the effective use of stock cards deals with the three main steps in the medicine distribution and supply cycle:

Step 1: Ordering medicines and related supplies

Step 2: Receiving medicines and related supplies

Step 3: Issuing medicines and related supplies (including removal of excess or expired/damaged items from stock)

12.3.1. Ordering of medicines and related supplies

New supplies of medicines need to be ordered at regular intervals. Whether this is every six weeks or once per month depends on how the system is set up in each particular district. If **too much** of an item is ordered then medicines which might be needed urgently elsewhere will pile up on shelves and eventually expire. If **too little** is ordered then patients will suffer because they will not receive the necessary medication. This can have disastrous consequences for the TB patients, e.g. treatment failure, development of MDR-TB and loss of credibility of the health facility and NTLP.

12.3.2. Guiding principles for the ordering of supplies

Anticipate changes in demand

The quantity of anti-TB medicines required by a health facility is directly related to the number of TB patients registered at the facility. Therefore any increase or decrease in number of TB patients registered will necessitate an increase or decrease in future orders for anti-TB medicines.

- Do not order items simply because they are printed in the order book! Only order the anti-TB medicines that are currently used at your health facility. If there are no TB patients receiving treatment, then it is only necessary to keep a small amount of TB medication for emergencies (e.g. if a TB patient is a visitor to the area and needs his/her medication refilled). If the facility is very near its supply source, then it may not be necessary to stock any anti-TB medicines at all.
- Do not forget that if paediatric TB patients are receiving treatment or prophylaxis at your health facility, it may be necessary to order TB medicines of different formulations (e.g. syrups).
- Know when the order is to be placed and then make sure that the order book is completed and submitted in good time.
- Remember that all items are **ordered in units.** Never record an order as: number of capsules! So if 100 rifampicin capsules are needed fill in "1" in the order column (= 1 unit = 1 container x 100 rifampicin capsules). The unit sizes are pre-printed in the order book.

Be systematic

To ensure that appropriate quantities are ordered it is easiest to systematically follow the steps described below:

Step 1: Perform a physical stock count. This should be done for every item that is normally stocked, not only items that are known to be needed.

Step 2: Decide whether or not to order a particular item. Check whether the physical stock is equal to or less than the **minimum** stock indicated on the stock card. If it is, order enough units to make up the **maximum** stock. If the physical stock is greater than the **minimum** stock, do not order the item!

Step 3: Complete your order book. Fill in the appropriate amount for the items you want to order.

Reorder quantity = Maximum Stock Level – Stock On Hand

Stock management definitions

Order interval is the time between two orders. If orders are placed once a month, then the order interval is one month.

Minimum stock (reorder level) is the stock which represents the average consumption of a particular item during a period that is twice the order interval. If three units of isoniazid tablets are used per order interval, then the minimum stock level is 3 x 2 = 6 units. If the stock level equals or falls below the minimum stock level, the item should be reordered. Each item in a store has its own minimum stock which should be indicated on the stock card.

Maximum stock defines the maximum number of units of a particular item there should be in stock –do not stock more than this. The number must be written on the stock card and *should equal the average consumption of that item in a time covering four times the order interval.* This means that if the average consumption is three units of isoniazid tablets per order interval, then the maximum stock for isoniazid is 3 x 4 = 12 units. In this example, you should not store more than 12 units of isoniazid at a time.

Minimum and maximum stock levels can both change over time according to changes in consumption. For anti-TB medicines, these levels will change as the number of TB patients change. The initial calculations should be done by the person in charge of the store *together with* the DTLC, regional pharmacist or pharmacist's assistant. When these numbers are used for ordering the first time, they should be recalculated at the latest after two months. After this, the minimum and maximum stock levels should be recalculated every three or four months.

12.3.3. Receiving medicines and related supplies

When receiving supplies from the district hospital or the medical stores the following must be carefully checked;

- Are the number of boxes received the same as indicated on the delivery note?
- Are all the boxes sealed and intact?
- Check if the items received tally with those recorded on the 'goods received note', i.e. have **the right items** in **the right unit size** and in **the right quantity** been supplied?
- Do the medicines have satisfactory expiry dates (at least four times the order interval from the date of receipt)?
- Are all containers intact (nothing damaged or tampered with?)

If there are any problems with the quantity, type, expiry date or condition of any items received then contact the supplying facility immediately by telephone to report the problem. In addition make a written statement detailing the problems found, keep one copy for your reference and send one copy to the supplying facility.

Box 20: Maintenance of stocks

Do not forget to update the stock cards after new goods have been received and with each issue of the medicine.

12.3.4. Issuing medicines and related supplies

Each time supplies are issued it should be **recorded in the stock card**. Issuing of supplies includes the following:

- Removing stock from the store to the dispensing and/or treatment rooms (remember to issue stock showing the earliest expiry dates first; FEFO rule, see *Section 12.3*)

- Issuing stock to the outreach team
- Removing stock from the store for pre-packing
- Sending stock which is not needed (excess stock) back to the district hospital/medical store
- Removing expired medicines from the shelf and sending them to the district hospital
- Removing broken containers from the shelf

12.4. How to avoid wastage due to expired stock

Following the basic rules mentioned above will help to avoid wastage of medicines due to expiry.

FEFO rule: This refers to First Expiry First Out (FEFO). When new supplies are received, put them at the back of the shelf and always issue stock at the front first. However, if the expiry date of the new stock is earlier than that of the existing (old) stock, put the new stock in front so that it is used up first. This will prevent expiry of medicines.

Box 21: FEFO rule

Always follow the FEFO Rule (First Expiry – First Out):
Always issue that stock which will expire first

In addition the following should also be routinely done:

Clearly mark containers of medicines with short expiry date (less than 12 months) – this will help bring these items to your attention when you are placing an order and dispensing medicines.

Return excess stock to the supplying facility (hospital/medical stores) as soon as you are aware of it. Once you realise that you are unable to use all of an item before its expiry date, or that you have more than the calculated stock of an item, then return it to your supplying facility (district hospital or medical stores) with documentation to show from whom it is being returned.

12.5. Monitoring stocks of anti-TB medicines

In order to manage stock levels of anti-TB medicines in districts, the DTLCs together with the pharmacists/ pharmacist's assistants should produce monthly anti-TB FDC and DR-TB medicine stock reports, from all health facilities treating TB patients. This information will then be forwarded by the pharmacist to the Regional Pharmacist who should discuss any problems with the RTLC and take appropriate action where needed, as well as forwarding the information to the NTLP.

These data are needed in order know the stock situation of these critical medicines in the country. This will help to monitor the stock levels countrywide and identify problems in stock control of these vital medicines.

12.6. TB medicines stock control at Central Medical Stores

The NTLP should collaborate closely with the Division: Pharmaceutical Services by providing accurate data regarding predicted numbers of patients requiring anti-TB medication as well as specifications of all anti-TB medicines. This is important so that the Central Medical Stores (CMS) can enter into contracts for the correct quantities and types of each of the anti-TB medicines. Accurate information of number of TB patients will also assist CMS to maintain suitable stock levels of all anti-TB medicines, thus avoiding stock-outs.

12.7. Roles of different players in the management of anti-TB medicines

12.7.1. Role of Division: Pharmaceutical Services

- Ensuring availability of all anti-TB medicines at all times by strengthening medicine supply management through improved procurement, storage and distribution at all levels of health care
- Providing safe, efficacious, high quality and cost effective anti-TB medicines
- Strengthening the quality assurance system to ensure that safe and high quality medicines are supplied
- Promoting rational use of anti-TB medicines by prescribers, dispensers and clients.
- Improving human resource capacity for management of all medicines including anti-TB medicines

12.7.2. Role of the DTLC in the management of anti-TB medicines

- Diagnosing, registering and notifying all forms of TB.
- Consulting the CCRC when needed in conjunction with the doctor in charge.
- Ensuring all prescriptions conform to national guidelines and are reflected in the registers and the TB treatment cards.
- Ordering anti-TB medicines from the pharmacy every 1-3 months
- Supervising packaging of medicines for peripheral clinics and DOT points, and provision of DOT.
- Ensuring continuous supply of medicines and proper storage, as well as reporting on usage of medicines.
- Informing the pharmaceutical staff of new cases and their regimens promptly so that the pharmacy can organise the medicine for the newly registered cases.

12.7.3. Role of the pharmacist / pharmacist's assistant in the management of anti-TB medicines

- Addressing pharmaceutical issues as a member of the local TB committee
- Supplying medicines to the TB clinic or TB ward as requested.
- Assisting the DTLC in forecasting needs.
- Ordering medicines from the relevant distribution channels
- Preventing stock-outs.

12.7.4. Role of the TB focal nurse in the management of anti-TB medicines

- Supervising DOT
- Orders supplies from the TB clinic or pharmacy
- Making weekly (or daily) packages to hand to treatment supporters or field promoters
- Directly ensuring that treatment supporters or field promoters provide DOT as requires

12.7.5. Role of treatment supporters or field promoters in the management of anti-TB medicines

- Collecting weekly supplies from the clinic/TB nurse
- Ensuring that medicines get to the patients on time
- Observing patients swallowing their prescribed medicines

- Reporting any problems to the DTLC/ TB nurse.

Table 44: List of anti-TB medicines available in Namibia

Medicine	Formulation
[RHZE] adult	Fixed-dosage combination tablet: [R150mg; H75mg; Z400mg; E275mg]
[RH] adult	Fixed-dosage combination tablet: [R150mg; H75mg]
[RHE] adult	Fixed-dosage combination tablet: [R150mg; H75mg; E275mg]
[RHZ] child	Fixed-dosage combination sachets: [R60mg; H30mg; Z150mg]
[RH] child	Fixed-dosage combination sachets: [R60mg; H30mg]
Streptomycin	Powder for injection; 1g vial
Ethambutol	400mg/100mg tablet
Isoniazid	100mg tablet
Isoniazid	300mg tablet
Rifampicin	450, 150mg capsule/tablet
Pyrazinamide	500mg tablet
Ethionamide	250mg tablet
Levofloxacin	250mg tablet
Cycloserine	250mg tablet
Kanamycin	1 g powder for injection
Capreomycin	1 g powder for injection
PAS	4 g sachet
Clofazimine	100mg capsule
Amoxycillin+clavulinic acid	875/125mg tablet
Carithromycin	500mg tablet

13. MYCOBACTERIA OTHER THAN TUBERCULOSIS (MOTT)

Mycobacteria other than TB (MOTT), also termed as non-tuberculous mycobacteria (NTM), are environmental organisms capable of causing chronic disease in humans. MOTT can be very difficult to diagnose, and often require prolonged courses of therapy.

13.1. Epidemiology

MOTT diseases are seen worldwide. However, surveillance data are limited and MOTT infections are non-communicable and therefore not reportable. There are more than 120 identified mycobacteria species known to cause disease in humans. By far, *M. avium* complex (MAC) and *M. kansasii* are the most common MOTT species causing disease in humans. MAC refers to two mycobacterial species, *M. avium* and *M. intracellulare*. These species constitute nearly half of all mycobacterial infections. Although considered a similar pathogen, *M. avium* is common in disseminated disease, whereas *M. intracellulare* is more common in respiratory infections. The remaining cases of MOTT involve numerous other mycobacterial species, most commonly *M. kansasii, M. gordonae*, *M. chelonae, M. fortuitum,* and *M. abscessus*. MOTT is commonly isolated in both natural and indoor water sources, which are the primary reservoir for most human infections. Multiple species, particularly *M. kansasii*, *M. xenopi,* and *M. simiae* are commonly recovered from most municipal water sources. As such, not all MOTT isolates represent true infections.

Box 22: Significance of isolating MOTT in a specimen

MOTT isolates may represent :

- **Contamination,**
- **Colonisation, or**
- **True infection**

13.2. MOTT diseases in humans

Pulmonary manifestations account for 94% of cases of MOTT, but infections involving the skin, bones, and lymph nodes do occur. Disseminated disease may occur and, without treatment, is frequently fatal.

Chronic pulmonary disease is the most common clinical manifestation of MOTT. The majority of cases are caused by MAC, followed by *M. kansasii.* The risk for infection increases in immunosuppressed patients or those with structural lung disease, particularly chronic obstructive pulmonary disease (COPD) and bronchiectasis. Parenchymal scarring and fibrosis from prior TB infection also increase risk of MOTT. This often poses a challenge to health care workers as reactivation of TB should be considered in cases of suspected MOTT infections.

MOTT lung disease is almost always associated with symptoms such as chronic or recurring cough, sputum production, and dyspnoea. Constitutional symptoms such as fever, fatigue, malaise, night sweats, and weight loss may occur. Haemoptysis, although uncommon, can occur. Clinically, MOTT may be similar to active pulmonary TB, especially with infections caused by *M. kansasii*.

13.2.1. Pulmonary MOTT

There are two main pulmonary manifestations of MOTT: cavitary/fibronodular) disease and nodular bronchiectatic lung disease, each with a unique epidemiology and clinical course.

Cavitary/fibronodular disease is the traditionally recognised presentation of MOTT lung disease. In developed countries there is a strong male predominance, and typically patients are in their late 40s and 50s. Cigarette smoking, COPD, and alcoholism are common. Apical fibrocavitary changes are typical. Cough, haemoptysis, and constitutional symptoms are common, and this disease is radiographically and clinically indistinguishable from pulmonary TB. In addition, acid-fast bacillus smears may be strongly positive, adding further confusion. Untreated cases are often rapidly progressive and can result in extensive lung cavitation and fibrosis, leading to respiratory failure.

Nodular bronchiectatic disease typically occurs in older women (80%) without a previous history of lung disease. Smoking and alcoholism are not common associations. Patients often share a common body morphological type: thin body habitus, pectus excavatum, kyphoscoliosis, joint hypermobility, and mitral valve prolapse. This clinical pattern has been commonly labelled the "*Lady Windermere syndrome*." X-ray images typically reveal peripheral small nodular tree-in-bud densities in a bronchovascular distribution. Focal cylindrical bronchiectasis predominates, and the right middle lobe and lingual are most often involved. This anatomic distribution likely results from impaired mucociliary clearance as a result of thoracic anatomic abnormalities (pectus excavatum and kyphoscoliosis). This form of lung disease is typically milder and more indolent and progresses slowly over years. However, disease progression is common and significant disability or even death may occur.

Hypersensitivity-like pneumonitis: MOTT can rarely present as a hypersensitivity-like pulmonary syndrome, commonly known as 'hot tub lung'. This is likely to be a manifestation of both parenchymal inflammation and active infection. Mycobacteria are resistant to disinfectants and growth is enhanced by hot, humid environments, especially standing water sources such as hot tubs or other undrained indoor sources. Clinical disease is often subacute and is predominated by cough, dyspnoea, and fever. Nodular inflammation of the lungs is common and may progress to hypoxemic respiratory failure. Similar to other forms of hypersensitivity pneumonitis, patients are typically younger and non-smokers. Results of x-ray imaging are always abnormal and commonly reveal diffuse nodular infiltrates and ground glass opacities. These are typically distributed in a centrilobular or bronchiocentric pattern, differentiating it from other hypersensitivity pneumonitis or sarcoidosis. Histopathologic examination is that of non-necrotising granulomas and organising pneumonia. The disorder is diagnosed by the isolation of MOTT with compatible clinical, radiographic, and pathologic findings.

Corticosteroid therapy may facilitate recovery and improve gas exchange. Antimycobacterial therapy may also hasten recovery and prevent the uncommon development of chronic disease. The prognosis is good and a prompt resolution of symptoms is expected following treatment.

13.2.2. Disseminated MOTT Infection

Disseminated MOTT is a life-threatening illness that occurs almost exclusively in patients with advanced AIDS. It is rarely encountered in other forms of immunosuppression, but it has been reported following renal or cardiac transplantation, chronic corticosteroid use, and leukaemia. The majority of infections are caused by *M. avium* and *M. kansasii*. Prior to effective antiretroviral therapy, nearly 40% of patients with CD4 counts less than 10 developed disseminated MOTT within 1 year. The risk for disseminated MOTT infection increases with progressively lower CD4 counts. It typically occurs with CD4 counts below 25 but those with counts less than 50 are at risk.

Clinical findings include anaemia, fever, night sweats, weight loss, and hepato-splenomegally. In patients initiating antiretroviral therapy, disseminated MOTT may occur as part of an immune reconstitution inflammatory syndrome (IRIS). This MOTT-associated paradoxical reaction produces an intense local inflammatory reaction to indolent MOTT infections in individuals taking ART for HIV infection. It is manifested by painful suppurative lymphadenopathy, pulmonary infiltrates, and skin abscesses.

Successful treatment requires treatment of both HIV and MOTT infections. Macrolides are the cornerstone of therapy for disseminated MOTT. Although they are highly effective, resistance and treatment failure occurs in 50% of those receiving macrolides alone. Monotherapy is therefore contraindicated in disseminated MOTT infections, and regimens should include ethambutol and rifampicin.

13.2.3. Mycobacterial lymphadenitis

Lymphadenitis is an uncommonly recognised manifestation of mycobacterial infection. In the absence of HIV infection, MOTT lymphadenitis rarely occurs in adults and is primarily a disease of children. In fact, cervical adenitis may be the most common form of MOTT disease in children. The vast majority (80%) of culture-proven disease is caused by MAC, with the remaining cases caused by *M. scrofulaceum, M. malmoense,* and *M. haemophilum*.

Clinical manifestations of MOTT lymphadenitis are frequently insidious in onset and are rarely associated with systemic symptoms. Nontender, unilateral (95%) adenopathy is the most common finding and typically involves the submandibular, submaxillary, cervical, or preauricular lymph nodes. Although it is uncommon, affected nodes may rapidly enlarge, rupture, and form draining sinus tracts.

MOTT lymphadenitis is diagnosed by isolating the causative organism from lymph node cultures. In suspected cases, excision biopsy is preferred as fine-needle aspiration or incision and drainage of the involved nodes may result in fistulae formation with chronic drainage. It is important to exclude *M.tb* as the cause of the lymphadenitis, especially in adults where greater than 90% of culture proven mycobacterial lymphadenitis is caused by *M.tb.*

The treatment of MOTT lymphadenitis is complete surgical excision of the involved lymph nodes. Surgical resection is associated with a 95% success rate. In the absence of other sites of infection, medical therapy is rarely needed.

13.3. Diagnosis of MOTT Disease

13.3.1. Clinical features

The diagnosis of MOTT must be based on a high level of clinical suspicion that is compatible with symptoms and features found on x-ray images. Typical symptoms of pulmonary MOTT include chronic or recurring cough, sputum production, and dyspnoea. Constitutional symptoms such as fever, fatigue, malaise, night sweats, and weight loss may occur. In particular features of *M. Kansasii* are similar to pulmonary TB.

Disseminated MOTT presents with anaemia, fever, night sweats, weight loss, and hepato-splenomegaly occurring in severely immunosuppressed individuals.

A presumptive diagnosis based solely on clinical and x-ray findings, especially in normal, immunocompetent hosts, may not be correct.

13.3.2. Radiology

Fibronodular/cavitatory disease is not distinguishable from pulmonary TB on chest x-ray images. Nodular bronchiectasis presents with nodular tree-in-bud features in addition to bronchiectasis. In addition, pulmonary MOTT tends to occur in patients with pre-existing structural lung damage.

13.3.3. Sputum microscopy and culture for MOTT

Sputum microscopy is positive for acid-fast bacilli. Isolation of MOTT in culture is essential for the diagnosis of MOTT lung disease. In cases of pulmonary disease (the most common site of infection), bronchial cultures should be obtained. Patients should have at least 3 sputum specimens collected on separate days, and MOTT should be confirmed by positive results in at least 2 of these 3 specimens. Bronchoscopic washing may be a useful diagnostic tool if available.

In the right clinical setting, a single positive culture from bronchoscopy washing or lavage may be considered diagnostic. Specimens obtained from biopsy (transbronchial lung biopsy, surgical lung biopsy, or excisional biopsy from infected tissue) are also diagnostic if they produce isolation of MOTT or show granulomatous inflammation on histopathologic examination. In the right clinical setting with highly suspicious clinical and radiological findings, tests in which cultures are negative should be repeated as isolation of MOTT is often difficult.

A single positive culture may be indeterminate to provide a reliable diagnosis of MOTT. Contamination is common, especially with sputum samples. Even rinsing of the mouth with tap water can cause false positive results. Likewise, cleaning the bronchoscope or culture plates with tap water can also result in contamination and false-positive results.

Therefore, a reliable diagnosis must be based on both a highly suspicious clinical picture and confident microbiologic studies. Without this, all positive cultures should be highly scrutinised, especially with less common species or in species known to be common contaminants (*M. gordonae, M. mucogenicum, M. terrae, M. kansasii, and M. abscessus).*

Runyon's classification

When solid culture medium is used, it is often possible to distinguish between the various types of clinically significant MOTT based on growth patterns as follows:

- ⇨ Isolates of MOTT which form colonies on subculture in 7 days or fewer, are referred to as 'rapidly growing mycobacteria,' (*M. abscessus*)
- ⇨ Isolates of MOTT that require more than 7 days to form mature colonies on subculture are termed 'slowly growing mycobacteria' (e.g. *M. kansasii & M. avium* complex)
- ⇨ Isolates of MOTT that change colour when exposed to light are called "photochromogens" (*M. Kansasii)*
- ⇨ Isolates of MOTT that do not change colour when exposed to light are called "non-photochromogens" (*M. avium* complex)

13.3.4. Differential diagnosis

The presentation of MOTT may be similar to that of active TB. Both can produce cavitary pulmonary infiltrates, extra-pulmonary disease, granuloma formation, haemoptysis, and constitutional symptoms. Therefore, TB must be excluded in all cases of suspected MOTT, especially with acid-fast bacillus smear positivity. In fact, TB is both much more common and is a higher public health threat than MOTT. Other

pulmonary granulomatous diseases such as sarcoidosis and fungal infection can resemble MOTT and should be included in the differential diagnosis.

13.4. Treatment of MOTT disease

13.4.1. Treatment regimens

The treatment of MOTT disease is seldom straightforward. Prolonged durations of therapy are frequently needed and eradication is unlikely. Often patients describe the treatment as being worse than the disease, as some patients will not have progressive disease. The decision to treat must be balanced between the risk of disease progression and unnecessary exposure to the cost and toxicity of medications; in other words, not all patients with MOTT disease need treatment. Clinicians must make careful considerations about whether or not to treat their patients.

Cure of MOTT infection may not necessarily be the goal of therapy in all patients. For some, palliation of symptoms or minimisation of disease progression may be a reasonable objective. For all patients who begin treatment, a reasonable goal may be symptomatic, radiographic, and microbiologic improvement.

Nodular bronchiectatic MOTT

- Clarithromycin 1000 mg daily (or 500 mg twice a day) or azithromycin 250 mg daily,
- Rifampicin 10 mg/kg/day (maximum 600 mg/day) or rifabutin 150 to 300 mg
- Ethambutol 15 mg/kg/day

Cavitary/fibronodular disease or severe symptomatic MOTT

- Clarithromycin 1000 mg daily (or 500 mg twice a day) or azithromycin 250 mg daily,
- Rifampicin 10 mg/kg/day (maximum 600 mg/day) rifabutin 150 to 300 mg
- Ethambutol 15 mg/kg/day
- Amikacin or streptomycin for 2 to 3 months should be considered in severe cases.

Confirmed MOTT by species

In addition to the above regimens depending on clinic-radiological presentations, some modifications may be necessary firm identification of the species is available.

- In *M. kansasii* infections, isoniazid should be added as *M. kansasii* is often susceptible.
- In *M. abscessus* (rapidly growing) infections, cefoxitin should be added to the treatment.

13.4.2. Treatment success

This is defined by resolution (or control) of symptoms and conversion of sputum cultures. Sputum cultures should be obtained monthly during therapy to help assess treatment response and guide the duration of therapy. Clinical improvements within 4 to 6 months of beginning therapy and negative sputum cultures typically occur within 6 to 12 on adequate therapy.

Treatment should be continued **for up to 12 months of documented negative sputum cultures.** Therefore, the typical duration of treatment is 18 to 24 months, but it can be longer for some.

13.4.3. Treatment failure

This is common and is considered if there is no clinical improvement after 6 months or no negative sputum culture after 12 months of appropriate therapy. Treatment failure may be related to treatment

noncompliance or intolerance, anatomic defects (cavitation or bronchiectasis), or drug resistance (especially to macrolides).

Relapses and re-infections are also common and may not be related to drug susceptibility.

Macrolide resistance occurs and typically results from macrolide monotherapy or the concomitant use of quinolones. Regimens that do not include ethambutol are also associated with the development of drug resistance.

Surgical resection has been shown to improve outcomes in some patients with MOTT infection and should be considered as an adjuvant or alternative to medical therapy.

12. APPENDICES

Appendix 1: Responsibilities, functions and tasks of the various levels of the NTLP

1. National level

Overall responsibility

Planning, resource mobilisation, supervision, monitoring and evaluation of TB and leprosy control at all levels.

Functions and tasks

- Advising the Director for the Directorate of Special Programmes in the MoHSS on all matters concerning TB and leprosy control.
- Advising regional management committees on all matters pertaining to TB and leprosy control.
- Formulation of national strategic plans for TB and leprosy control.
- Publication of an annual report on TB and leprosy, focussing on annual and long-term NTLP targets.
- Technical supervision of TB and leprosy staff at regional level through the surveillance system, bi-annual and quarterly meetings, and frequent supervisory visits.
- Monitoring adherence by clinicians in hospitals and clinics to NTLP technical guidelines regarding diagnosis and treatment.
- Supporting the Pharmaceutical Services Division in monitoring the procurement and rational distribution of anti-TB and anti-leprosy medicine supplies in all health facilities.
- Participating in training of all staff on TB and leprosy control at all levels of the health system
- Maintaining active contact, coordination and cooperation with other partners and departments within the ministry, as well as institutions or sectors relevant to the control of TB and leprosy outside the MoHSS.
- Initiating and coordinating operational research on TB and leprosy.
- Advising and assisting NIP on all aspects related to the functioning of a well-accessible quality assured laboratory network for sputum-smear examination, culture and DST.
- Planning, coordination and implementation of an advocacy, communication and social mobilisation campaign on TB and leprosy, in collaboration with relevant stakeholders.
- Developing and disseminating effective patient education materials on TB and leprosy.
- Participating in resource mobilisation initiatives and preparing an annual budget for national level activities.

2. Regional level

Overall responsibility

Planning, implementation and monitoring and evaluation of TB and leprosy control in the region. The C/SHPA responsible for TB and leprosy control is functionally the Regional TB and Leprosy Coordinator (RTLC).

Functions and tasks

- Advising the District Management Teams on all aspects of TB and leprosy control.
- Advising the DTLCs and the District Management Teams on the implementation of the strategic plan on TB and leprosy.
- Conducting regular (at least quarterly) supportive supervisory visits to districts and DTLCs.
- Collecting, analysing and forwarding data aggregated by the DTLCs to national level on a quarterly basis, within 15 days after the end of the quarter.
- Organising quarterly DTLC meetings for performance monitoring and continuing education on TB and leprosy control.
- Organising and participating in training of staff on TB and leprosy.
- Developing a budgeted annual work plan based on the national strategic plan.
- Monitoring the rational distribution of anti-TB and anti-leprosy medicines in each district.
- Initiating and coordinating the implementation of operational research on TB and leprosy in the region.
- Initiating and coordinating advocacy, communication and social mobilisation activities within the region.

3. District level

Overall responsibility

Planning, implementation, and monitoring and evaluation of TB and leprosy control in the district. The nurse responsible for TB and leprosy control in the district is functionally referred to as the District TB and Leprosy Coordinator (DTLC).

Functions and tasks

- Advising the District Management Team on all matters of TB and leprosy control.

- Advising general health staff involved in TB and leprosy care in peripheral health units on all aspects of TB and leprosy management and control in line with NTLP technical guidelines and strategic plan.
- Monitoring the implementation and performance of TB treatment clinics and community-based TB care providers through monthly visits to each unit.
- Formulation of budgeted annual work plans.
- Monitoring the rational distribution of anti-TB and anti-leprosy medicines in all treatment clinics.
- Timely collecting, aggregating, analysing and forwarding of TB and leprosy data from each clinic, to the RTLC on a quarterly basis. Organising and participating in training for staff relevant for NLTP activities as to address identified needs.
- Initiating and coordinating health education activities to the community, through agricultural shows, public meetings, visit to schools.

4. Health facility

For the day-to-day execution of TB and leprosy control activities in health units at least one member of staff per health unit (preferably 2) should be properly trained and have proven competence in TB and leprosy patient management.

Professional education and rank should not be major selection criteria for becoming a dedicated TB nurse. Instead, interest, attitude, motivation and communication skills are important attributes. **Frequent rotation of nurses in TB clinics must be avoided as this disrupts continuity of care, resulting in poor case management and record keeping, as well as poor treatment outcomes.**

Overall responsibility

The main responsibility of the health facility is implementation of diagnosis and treatment of TB, maintaining up-to-date records, as well as coordination and supervision of community-based TB care providers in line with NTLP technical guidelines.

Functions and tasks

- Diagnosis of TB and leprosy according to the NTLP guidelines.
- Maintaining all records for TB and leprosy suspects and patients, as well as results of contact tracing.
- Giving patient education ensuring that each patient understands all aspects of treatment
- Giving health education to the public on the signs and symptoms of TB and leprosy.
- Providing directly-observed therapy for TB patients attending for DOT at the clinic
- Issuing 2- or 4-weekly supplies of anti-TB medicines to DOT-providers (anti-TB medicines and IPT), and ensuring that the patients are receiving their treatment under supervision.
- Maintaining adequate stocks of anti-TB medicines at all times
- Recording patient attendance and medicine collection in the appropriate NTLP forms.
- Identifying patients who need urgent referral according to the NTLP guidelines.
- Tracing patients who interrupt treatment in close collaboration with CBTBC providers.
- Training and supervising CBTBC providers in the catchment area of the clinic.

5. Community Health Workers (CHWs)

This applies to all supportive staff providing education and support for TB suspects and patients (includes TB field promoters, lifestyle ambassadors, home-based care providers, and other community-based health service providers). All CHWs need to be knowledgeable on TB signs and symptoms and assist in TB control through identification and referral of patients with signs and symptoms of TB, education on TB disease of the community and screening contacts of TB patients. CHWs can play an important role as DOT providers.

Appendix 2: Health facility supervision checklist

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

HEALTH FACILITY SUPERVISION CHECKLIST

District	TB clinic
Name supervisor	Designation
Current date	Date last visit

A. NAMES OF PERSONS MET AND THEIR DESIGNATION

B. CLINIC QUALIFICATIONS			
Is (are) there dedicated TB nurse(s)?	Number:	Yes	No
If so what is/ are their name(s):			
For how long have they been doing TB work? (indicate number of months/years)			
When did s/he/'they receive their last TB case management training?			
Is there a focal doctor for DR-TB and is h/she specifically trained in the management of DR-TB in Namibia		Yes	No
Is there a focal nurse for DR-TB and is h/she specifically trained in the management of DR-TB in Namibia		Yes	No
When did s/he receive their trainings?			
Does your facility/district have a DR-TB committee?			

C. BURDEN OF TUBERCULOSIS (compare with electronic register)	
# TB patients on initial phase	
# TB patients on continuation phase	
# No of DR –TB	
# No of XDR	
# of TB patients known their HIV status	
# of TB patients tested HIV positive	
Do you have a TB Infection Control focal person?	
Total	

D. DISTRIBUTION OF TB-DOT		
# and % of patients on Health Facility-DOT (HF-DOT)		%
# and % of patients on Community-Based-DOT (CB-DOT)		%
# and % of patients on workplace (DOT)		%
# of TB Field promoters in Health Facility/clinics # CB-DOT providers in the community		
Names of organisations involved in TB Care and CB-DOT:		

E. TREATMENT OUTCOMES (new sputum smear patients in last 2 quarters)															
Last 2 Q's	Registered	Cured		TC		Died		Failed		Def		Transfer		Evaluated	
		#	**%**	**#**	**%**	**#**	**%**	**#**	**%**	**#**	**%**	**#**	**%**	**#**	**%**
Q															
Q															

F. PATIENT EDUCATION AND COMMUNICATION		
Does the clinic have sufficient supply of IEC materials on TB	Yes	No
On a sample of patients, is their knowledge of TB satisfactory?	Yes	No

G. RECORD KEEPING (take a sample of five TB Treatment Cards) (tick correct answer)			
TB Treatment Card	Good	Fair	Poor
Treatment cards are kept orderly and confidentially			
Treatment cards kept up-to-date			
Dosages are correct for patient weight			
Each patients receives the correct regimen			
Sputum-smears examined as required (pre-treatment /follow-up)			
Is body weight taken as required?			

DST is recorded in each patient on Cat II or MDR-TB regimen			

TB Registers (compare paper with electronic register)	Yes	No
Are all registers available: Facility/district/MDR	Yes	No
TB register up-to-date with TB Treatment Cards	Yes	No
All patients on TB-treatment are registered	Yes	No
TB patients are recorded in the correct categories	Yes	No
All patients (>10 years of age) with PTB have sputum-smear examinations done	Yes	No
Each patient has information on type of DOT (HF-DOT/CB-DOT)	Yes	No
HIV status is recorded for each patient (+/-/?)	Yes	No
Electronic TB register		
Is the data up to date and in accordance with the M&E tools	Yes	No
Are the data clerk and DTLC trained in ETR	Yes	No

H. SUPPLIES			
Anti-TB medicines	Good	Fair	Poor
Stock cards for each specific medicine present			
Each stock card is up-to-date			
Each medicine within range of minimum/maximum stock level			
Each medicines within validity period			
FEFO principle adhered to			
TB COMBI			
Do you have an ongoing TB COMBI project ? If yes, how is the progress?			
How many TB L/A are trained			
Are TB IEC material available in the local languages			
TB Laboratory Investigations			
Turn-around time DM – clinic			
Turn-around time Culture and DST			
Stock level for sputum containers			

I. LABORATORY			
Turn-Around Time of sputum specimens with 48 hours (tick)	80-100%	60-80%	< 60%
# of TB suspects examined in past quarter			
# and % of suspects examined, who are sputum-positive		#	%
# of suspects examined, who are sputum negative		#	%

# and # of suspects who are sputum negative, and have 2 sputum examination results (target >90%)		#	%
# of times External Quality Control done in past year			
Last EQC results (tick)	Good	Fair	Poor
SS examination slides kept for EQC (tick)	Good	Fair	Poor

PROGRESS SINCE PREVIOUS VISIT:

MAIN CURRENT PROBLEMS:

ON-THEJOB-TRAINING/TRAINING NEED:

RECOMMENDATIONS (EXPAND WITH ADDITIONAL SHEET WHEN NECESSARY):

SIGNATURE AND DATE (SUPERVISOR & SUPERVISEE):

Appendix 3: Standard Operating Procedures for Quarterly TB and TB/HIV Review Meetings

Introduction

These SOPs should be used alongside the *National Guidelines for the Management of Tuberculosis,* and definitions of terms as described in the national guidelines will be used.

In order to ensure sustainability, regions are expected to increasingly budget for these meetings as donor funding is expected to gradually decline.

Objectives of the review meetings:

- To strengthen peer review of data collected and analysed by individual districts
- To compile TB, TB/HIV, DR-TB and leprosy notification data for the previous quarter
- To compile treatment outcome data for the previous year
- To harmonize district data and share information on transferred patients among districts
- To harmonize paper-based and ETR.net data
- To present and discuss planned and unplanned activities focusing on TB, TB/HIV and leprosy performed the previous quarter
- To share challenges and solutions to challenges faced in previous quarter
- To share the latest information on TB, TB/HIV and leprosy control

Procedure

Every quarter, each region conducts a 3-day review of their TB data at a venue to be decided by the regional team. At these meetings each district will be represented by the DTLCs, PHC supervisor, facility TB nurses (from the major health facilities), environmental health officer, TB medical officer, and a representative of the community TB care providers and a data clerk if present. The region will be represented by the CHPA/ SHPA or another designated individual.

After these meetings, 5-day zonal meetings will be conducted which will bring together at least two regions, again to share their data and assist each other in cleaning and interpreting the data.

Format of Review Meetings

Presentations from districts on

- TB notification data for quarter
- TB/HIV data (all forms, HIV positive, on CTX, on ART)
- Quarterly DR-TB notification data
- Quarterly leprosy notification data
- Treatment outcome analysis for patients registered during the same quarter of the previous year
- Overview of leprosy in the districts
- Achievements and challenges on planned activities
- Suggestions to overcome challenges

Analysis of district data in groups

- Districts re-analyse their data using district registers
- Transferred-out patients within the region are sought and their outcomes recorded
- Data are finalized for each district

Format of presenting data (2-3 Slides)

- District/Regional population
- Total number of TB cases reported (new and re-treatment)
- New patients: PTB positive/ PTB negative/PTB sputum not done and EPTB
- Retreatment cases of PTB positive (relapses, return after default/failures)
- DR-TB cases (cases notified this quarter and cumulative total notified cases by district)
- *(all above data can be broken down by age and sex, can use graphs/charts/figures)*

Format: Outcome analysis data (2-3 slides)

- For all new smear positive PTB cases for the last quarter
- For all relapses for last quarter
- For smear negative PTB cases, PTB smears-not-done, EPTB (additional)

What to bring to quarterly review meetings: The following documents are critical and should be brought:

- District TB, DR-TB and leprosy registers
- Patient treatment cards
- Current draft quarterly reports (TB and DR TB)
- Previous quarterly reports (TB and DR TB)
- DR TB line-list
- A completed ACSM documentation format for the quarter
- An up to date ETR.net dataset
- Data on:
  - Number of health care workers diagnosed and started on TB treatment
  - Number of health care workers trained on any aspect of TB control in the quarter
  - Status of implementation of TB-IC by district

Implementation of planned activities

- Present what was planned and what was done
- Why some planned activities were not carried out?
- What were the successes and what were failures, and why?
- What are the plans for PMDT at regional and district levels?
- The cost of each activity and source of funding should be reported.

Responsibility

- The DTLCs should ensure that district data are cleaned and corrected before the end of the zonal review meetings
- The DTLCs should ensure that data are collected from different sources
- Funding proposals should be submitted to the national office by the hosting region three weeks in advance
- C/SHPAs from all 13 regions should ensure that these SOPs are adhered to and that the conduct of quarterly review meetings shows consistency
- Verified and signed copies of quarterly reports should be submitted to national level at most within 72 hours of concluding a zonal review meeting
- The C/SHPA and the DTLCs should make copies of the submitted quarterly reports available to the Chief Medical Officers at Regional level and the Principal Medical Officers at district level respectively (within one week of concluding a zonal review meeting).
- The region responsible for hosting the zonal meetings should ensure that review meeting reports are submitted to the Chief Medical Officer at the end of each zonal review meeting (maximum, one week post review meeting)

Appendix 4: Sample Infection Control Plan for Preventing Transmission of Tuberculosis

Name of facility: _____District:_____

Infection Control Committee	Name of representative
Infection Control Committee Chair	
Infection Control Lead Person (ICP)	
Infection Control Committee Members • *Nursing Services* • *Radiology* • *Laboratory* • *DTLC* • *ARV Clinic Represenative* • *Other departments/units*	

The committee meets on the _____ of each month and updates on TB Infection Control are a standing agenda item.

BACKGROUND STATEMENT:
_____hospital/clinic is a health facility that serves patient in _____District, of _____ Region. _____ Region has a TB incidence of ____:100 000 compared to national incidence of ____:100 000. We provide the following services: _____, _____, _____, and _____. In the year _____ the facility had _____ TB patients. Of these, _____ were smear-positive, _____ were smear-negative, and _____ were extra-pulmonary. Of these were _____ retreatment cases, _____ were found to have MDR-TB and _____ had XDR-TB. From all the TB patients, _____ had a known HIV status and _____ tested HIV positive. Of these _____ are on ARV treatment. TB diagnostic services available on site are _____ and _____.

PURPOSE:
The infection control plan outlines strategies to identifying, separating, appropriate treatment and other measures to reduce the risk for TB transmission to patients and health care workers.

AUTHORITY STATEMENT:
The designated Infection Control Lead Person shall have the authority to assess, implement and ensure compliance with this plan for all clinical sites. The signatures of both the Health Facility Manager and Infection Control Committee Chair on the last page of this document give authority and responsibility to the designated ICP.

RESPONSIBILITY:
The facility Infection Control committee has the authority to adapt the plan as needed to maintain the safety and health of patients and staff members.
The Infection Control Person, with the support of the facility administration and Infection Control Committee ensures that the facility consistently follows the practices as outlined below:

Managerial Controls

The Infection Control Lead person will:
1. Monitor implementation of infection control practices on a daily basis.
2. Conduct TB IC training sessions for all staff.
3. Ensure that the written Infection Control (IC) plan will be available to all staff and more often if deemed necessary and display the plan in clinical areas.
4. Provide information and IEC materials on TBIC for all patients and visitors.
5. Perform a TB IC Risk Assessment and Analysis with a performance improvement plan at least annually.

Administrative Controls
In order to reduce the risk of TB transmission for both employees and patients the following TBIC practices will be implemented at our facility. Person(s) responsible for the activities are;

Activity	*Name of person responsible*
Ask all clients for cough upon entering the facility	
Educate all patients and clients on cough etiquette and hygiene	

Provide tissues or face masks to all coughing patients and clients	
Clients who cough will be asked to dispose of tissues or mask using bins provided.	
Clients who cough will be directed to a special waiting area or fast tracked and will be seen first	
Explain the queuing system all clients and patients	
The professional nurse (or nurse staffing the service) will periodically scan the queue for coughing clients.	
TB suspects will promptly be investigated for active TB disease	
Processing of sputums will be expedited to the lab. There will be a tracking mechanism to monitor-turn-aruond time of lab results and regular meetings with lab staff.	
Display posters and provide IEC material on TB IC to all patients and clients	

Environmental Controls

Certain environmental controls have been identified to decrease the risk of TB transmission in the facility.

Activity	*Name of person responsible*
Direction of air flow in each consultation room will be established and marked with a sign.	
HCW should sit with the clean air moving from behind them towards the client.	
Windows or doors will be opened to ensure maximum air flow.	
Signage will be placed to remind HCWs to keep windows and door open	
Fans will be located in appropriate areas (consultation rooms and/or waiting areas) and be operational	
Regular cleaning and maintenance will be performed on all environmental controls and records kept	

Personal Protective Equipment (PPE)

Personal Protective equipment when used in tandem with other IC strategies can also reduce the risk of TB transmission to staff and other within the facility.

Activity	**Name of person responsible**
Fit testing will be done to all health care workers wearing a N95 respirators	
N95 respirators will be available in consultation rooms for HCWs.	
N95 respirators will be used by all HCW working in high risk areas or attending to DR-TB patients	
Offer confidential HIV counselling and testing to HCWs	
Offer ART and IPT prophylaxis to all eligible HCWs	
HIV infected staff will be reassigned if they request	

Signature and date **Health Facility Manager**	**Signature and date** **Infection Control Committee Chairperson**

Appendix 5: Side-effects of anti-tuberculosis medicines

Although most TB patients complete their treatment without any significant medicine side-effects, all patients must be monitored during treatment. Severe adverse medicine reactions are more common in HIV-positive TB patients. Health staff should educate patients on how to recognise symptoms of common side effects and report if they develop such symptoms, and by asking about symptoms when patients report for medicine collections. Significant side effects should be reported to the TIPC (see *Appendix 6*).

Second-line anti-TB medicines are more toxic and less efficacious than the first-line medicines. All physicians should be aware of the main side-effects of these medicines before prescribing to a patient. When serious side-effects arise, clinicians must report to the TIPC.

Decisions to modify second-line anti-TB treatment regimens must be made in consultation with the CCRC.

Isoniazid *(H or INH)*

Contraindications

Known cutaneous or hepatic hypersensitivity reaction.

Active hepatic disease.

Precautions

Monitoring of hepatic transaminases in patients with pre-existing chronic liver disease.

All patients should receive pyridoxine for prevention of peripheral neuropathy.

Medicine interactions

Consider reducing the dosage of carbamezipine and phenytoin in the treatment of patients with epilepsy.

Concomitant aluminium hydroxide decreases the absorption of INH.

Pregnancy

INH is safe in pregnancy.

Minor adverse effects

Mild itching: generally responds well to anti-histamines. In HIV-positive patients, however it can develop quickly into a serious cutaneous reaction.

Some increase in serum levels of hepatic transaminases at the onset of treatment usually resolves spontaneously during treatment, and without clinical significance.

Major side-effects

Cutaneous hypersensitivity reactions during the first weeks of treatment.

Peripheral neuropathy (tingling and numbness of the hands and feet): This is the main adverse effect of INH, common in malnourished patients and with high doses. Peripheral neuropathy is treated with pyridoxine 100mg daily until symptoms disappear, then continue with 25mg daily to prevent recurrence.

Hepatitis is rare. When it occurs stop INH immediately.

Less common are: optic neuritis, toxic psychosis, generalised convulsions, developing during the later stages of treatment in susceptible individuals.

Rifampicin (R or Rif)

Contraindications

Known hypersensitivity to rifampicin

Hepatic dysfunction

Precautions

Women using oral contraceptives are advised to use an oral contraceptive with a higher dose of estrogen (50µg) or a non-hormonal barrier method.

Serious immunological reactions resulting in renal impairment, haemodialysis or thrombocytopenia may occur in patients who resume taking rifampicin after a prolonged interruption of treatment. In this rare situation, it should be immediately withdrawn.

Monitor liver function in the very elderly, in patients who have hepatic disease, and in those with alcohol dependence.

Warn patients that rifampicin can cause reddish coloration of urine, tears, saliva, and sputum (contact lenses can be irreversibly stained).

Vitamin K should be administered at birth, to the newborn of a mother treated with rifampicin to prevent the occurrence of postnatal haemorrhage.

Medicine interactions

Rifampicin induces hepatic enzyme function which may breakdown other medicines more rapidly than normal, and may increase dosage requirements of all medicines metabolised in the liver: e.g. corticosteroids, oral contraceptives, oral hypoglycemic agents, oral anticoagulants, phenytoin, cimetidine, cyclosporine and digitalis glycosides.

Rifampicin decreases the serum levels of antiretroviral medicines of the NNRTI and PI groups.

Biliary excretion of radiocontrast media and sulfobromophthalein sodium may be reduced and microbiological assays for folic acid and vitamin B12 disturbed.

Pregnancy

Rifampicin is safe in pregnancy.
Minor adverse effects
Generally well tolerated by most patients, in recommended dosages.
Reddish coloration of tears, saliva, sputum, urine.
Moderate rises in bilirubin and serum transaminases are common at the onset of treatment, but are usually transient and without clinical significance.
Gastro-intestinal intolerance (nausea, vomiting) are quite common. Advise the patient to take the medicines at bedtime or after a meal.
Major side-effects
Influenza-like syndrome, fever, malaise, bone pains and thrombocytopenia may occur after prolonged interruption of rifampicin treatment (see above).
Exfoliative dermatitis (Stevens-Johnson syndrome) is more common in HIV+ persons. Stop rifampicin immediately and select alternative treatment.
Medicine induced hepatitis. Rifampicin must be stopped immediately and an alternative medicine should replace rifampicin.

Pyrazinamide (Z or PZA)
Contraindications
Known hypersensitivity to pyrazinamide.
Severe hepatic dysfunction.
Precautions
Patients with diabetes should be monitored carefully since blood glucose levels may become labile.
May cause or exacerbate gout.
Pregnancy
Pyrazinamide is safe in pregnancy.
Minor adverse effects
Generally well tolerated by most patients, in recommended dosages
Gastrointestinal intolerance (nausea, vomiting) is quite common. Advise the patient to take the medicines at bedtime or after a meal.
Some patients complain of light flushing of the skin
Moderate rises in bilirubin and serum transaminases are common at the onset of treatment, but are usually transient and without clinical significance.
Asymptomatic hyperuricaemia may occur.
Pain in joints (mostly shoulders and knees) may occur and responds generally well to treatment with analgesics, especially aspirin.
Major side-effects
Gout develops occasionally. This requires treatment with allopurinol.

Ethambutol (Abbr. E or ETH)
Contraindications
Known hypersensitivity to ethambutol
Pre-existing optic neuritis from any cause
Creatinine clearance of less than 50ml/minute
Precautions
Patients should be advised to discontinue treatment immediately and to report to a clinician if their sight or perception of colour deteriorates.
If possible, renal function should be assessed before treatment.
Respect maximum dose for adult and children of 15mg/kg BW in daily treatment.
Pregnancy
Ethambutol is safe in pregnancy and should be used as first choice medicine for TB treatment.
Children
Ethambutol is safe in treatment of children provided maximum daily dose of 25mg/kg is not exceeded.
Minor adverse effects
Early and mild changes in visual acuity and colour vision may occur and are reversible if ethambutol is stopped immediately.
Signs of peripheral neuropathy occasionally develop in the hands and feet. Treat with pyridoxine 100-200mg daily until symptoms disappear, then continue with 25mg daily.
Major side-effects
Blindness may develop if ethambutol treatment is not stopped immediately when mild and early changes in visual acuity and colour vision occur.

Streptomycin (S or SM)
Contraindications

Known hypersensitivity to streptomycin
Auditory nerve impairment
Myasthenia gravis
Precautions
Streptomycin in the treatment of children is only used when absolutely necessary, because of painful injections and irreversible damage to 8th nerve, and the fact that small children do not report loss of hearing.
The elderly and people with renal impairment are at risk of dose-related toxic effects.
Persons with renal impairment can be treated with streptomycin at reduced doses when renal function and plasma levels can be monitored (should not exceed 4µg/ml)
Pregnancy
Streptomycin should not be used in pregnancy. It crosses the placenta and can cause auditory nerve impairment and nephrotoxicity in the foetus.
Medicine interactions
Other ototoxic or nephrotoxic medicines should not be administered to patients receiving streptomycin, including: other aminoglycosides, amphotericin B, cephalosporins, etacrynic acid, cyclosporine, cisplatin, furosemide, and vancomycin.
Streptomycin may potentiate the effect of neuromuscular blocking agents administered during anaesthesia.
Minor adverse effects
Injections are painful and may cause sterile abscesses.
Dosage of streptomycin should be reduced by 25% when vertigo, tinnitus, headache and vomiting occur.
Major side-effects
Hypersensitivity reactions are common and can be severe. Stop streptomycin and do not re-introduce it..
The main adverse effect of streptomycin is ototoxicity (damage to the 8th cranial nerve. The damage to the vestibular apparatus is shown by giddiness or vertigo accompanied by vomiting. Streptomycin is less toxic than other aminoglycosides. Dosage must be reduced by half immediately if renal output falls, if albuminuria occurs or if tubular casts are detected in the urine. Haemolytic anaemia, aplastic anaemia, agranulocystosis, thrombocytopaenia and lupoid reactions are rare major side-effects.

Kanamycin
Adverse reactions
Ototoxicity: Deafness, dizziness.
Reversible nephrotoxicity.
Precautions
Reduce dose if renal function is impaired.
Contraindications
Pregnancy (only as last resort).

Ethionamide
Adverse reactions
Gastro-intestinal: Epigastric discomfort, nausea, metallic taste, belching with rotten eggs smell, vomiting, salivation.
Mental disturbance: Psychotic reaction, hallucinations, depression.
Hypoglycaemia, take extra care if patient is diabetic.
Hepatitis frequent (in 10% of patients) but rarely serious.
Gynaecomastia, menstrual disturbance, impotence, and acne.
Headache
Peripheral neuropathy.
Close monitoring
In patients with diabetes, liver disease, alcoholism, or mental instability.
Contraindication
Pregnancy (teratogenic).

Levofloxacin
Adverse effects
Gastro-intestinal: anorexia, nausea, vomiting.
Nervous system: Dizziness, headache, mood changes, and sometimes convulsions.
Contraindications
Pregnancy (benefit is higher than risk in DR-TB).
Growing children (benefit is higher than risk in DR-TB).
Medicine interaction
With antacids, iron, zinc, sucralfate. When needed, these medicines must be taken at least 3-4 hours before or after a dose of levofloxacin.

Cycloserine
Adverse effects
Nervous system: dizziness, slurred speech, convulsions, headache, tremor, insomnia, confusion, depression, altered behaviour, suicide tendencies.
Rare reactions:
Hepatitis
Generalised hypersensitivity reaction
Closely monitor
Central nervous system reactions
Give pyridoxine medication for prevention of CNS reactions, at 50mg for every 250mg of cycloserine
Check and report undue depression or personality change.
Renal failure: Cautious use in patients with renal failure.
Avoid
In patients with history of epilepsy, mental illness, or alcoholism.

Para-amino Salicylate (PAS)
Adverse effects
Gastrointestinal disturbance: nausea, vomiting, bad taste, pain, gastritis, bloating, constipation, diarrhoea
Rare reactions:
Hepatitis
Hypothyroidism (increased incidence with concomitant ethionamide use).
Closely monitor
Liver function.
Thyroid function (in cases of hypothyroidism, administer thyroid replacement therapy).
Renal failure: Cautious use in patients with renal failure.
Avoid
In pregnancy (relative contraindication).

Appendix 6: Safety Yellow Form for reporting ADRs and medicine use/product problems

Republic of Namibia
Ministry of Health and Social Services

For reporting ADRs and medicine use /product problems

A. Patient Information

TIPC

Patient identifier(initials/code)		*Sex*	*M_____F_____*
Age at the time of event		*Weight in kgs*	

B. Adverse Event/Product problem/Error (*tick where appropriate)*

1. Event/Reaction		**2.Type of Event/Reaction**	
Event/Reaction to ARV/TB/ACT/New medicines/Product		*Adverse Event*	
Serious events with other medicines/Products		*Product problem (e.g. defects/malfunctions)*	
		Product use error (e.g. medication error)	

3. Outcomes attributed to adverse event (tick where appropriate)			
Death (Date:_____/_____/_____)		*Disability or Permanent damage*	
Life-threatening		*Congenital anomaly/ Birth defect*	
Hospitalisation/prolonged hospital stay		*Other serious (important medical events)*	
Required intervention to prevent permanent impairment/damage e.g. use of devices		***4. Date of the Event***	
		5. Date of this report	

6. Describe the Event, Product problem or Product use error and Actions taken

7. Relevant tests/Laboratory investigations done (include dates)

8. Other relevant history, including pre-existing medical conditions (allergies, pregnancy, smoking, alcohol use, liver, kidney problems, race etc)

C. Suspect Product (obtain as much information as possible from product label/packaging)

Name		*Dose/amount*	
Strength		*Frequency*	
Manufacturer		*Route*	
Date of use (From/to or best estimate of duration):			
Event stopped after stopping use? (Yes/No)		*Event stopped after dose was reduced?(Yes/No)*	
Event reappeared after reintroduction (Yes/No)			
Lot number		*Expiry date*	

D. Other products taken by the patient within the last 3 months prior to the reaction

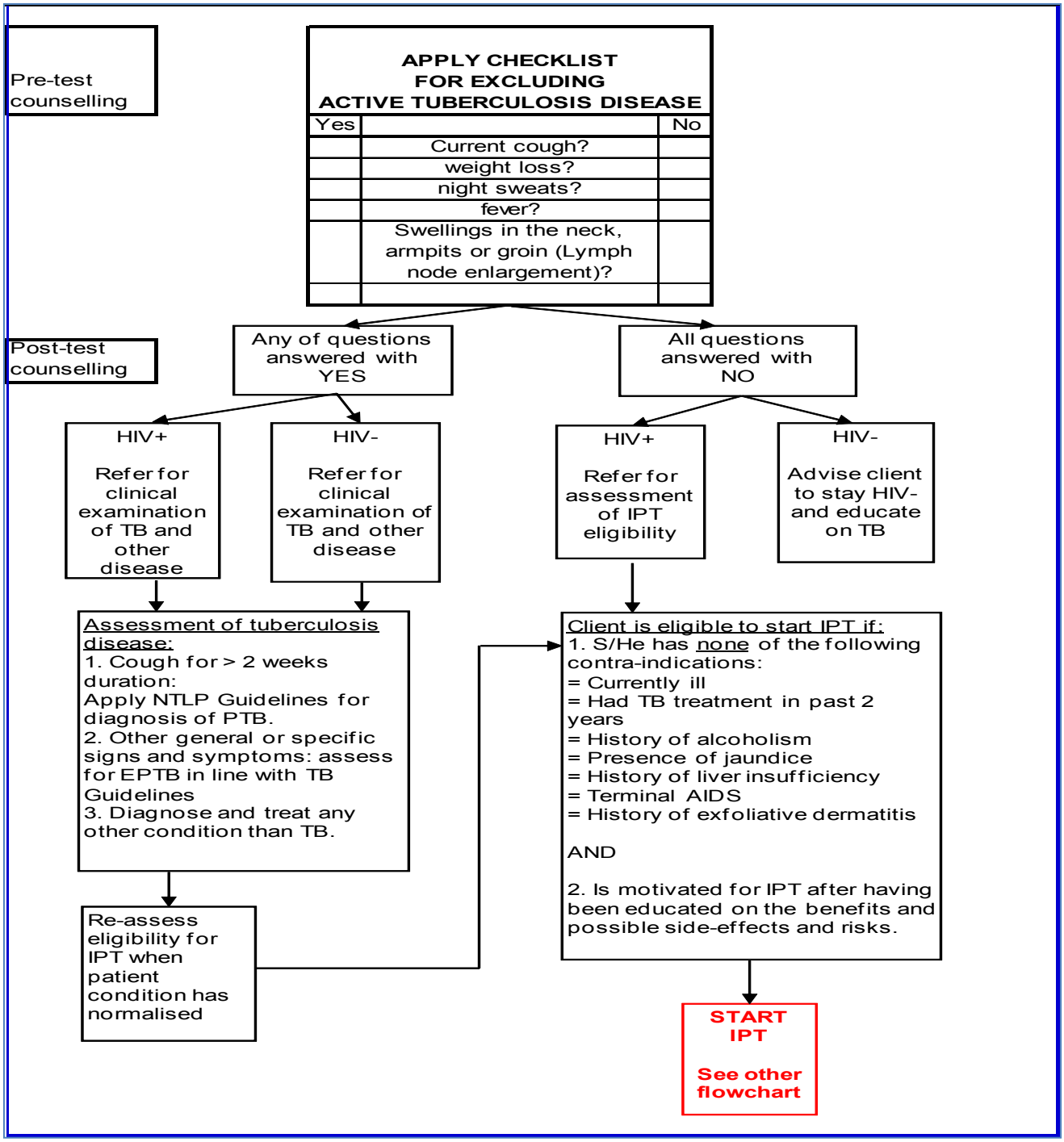
Product name 1		*Product name 3*	
Dosage and dates		*Dosage and dates*	
Product name 2		*Product name 4*	
Dosage and dates		*Dosage and dates*	

E. Information about the reporter

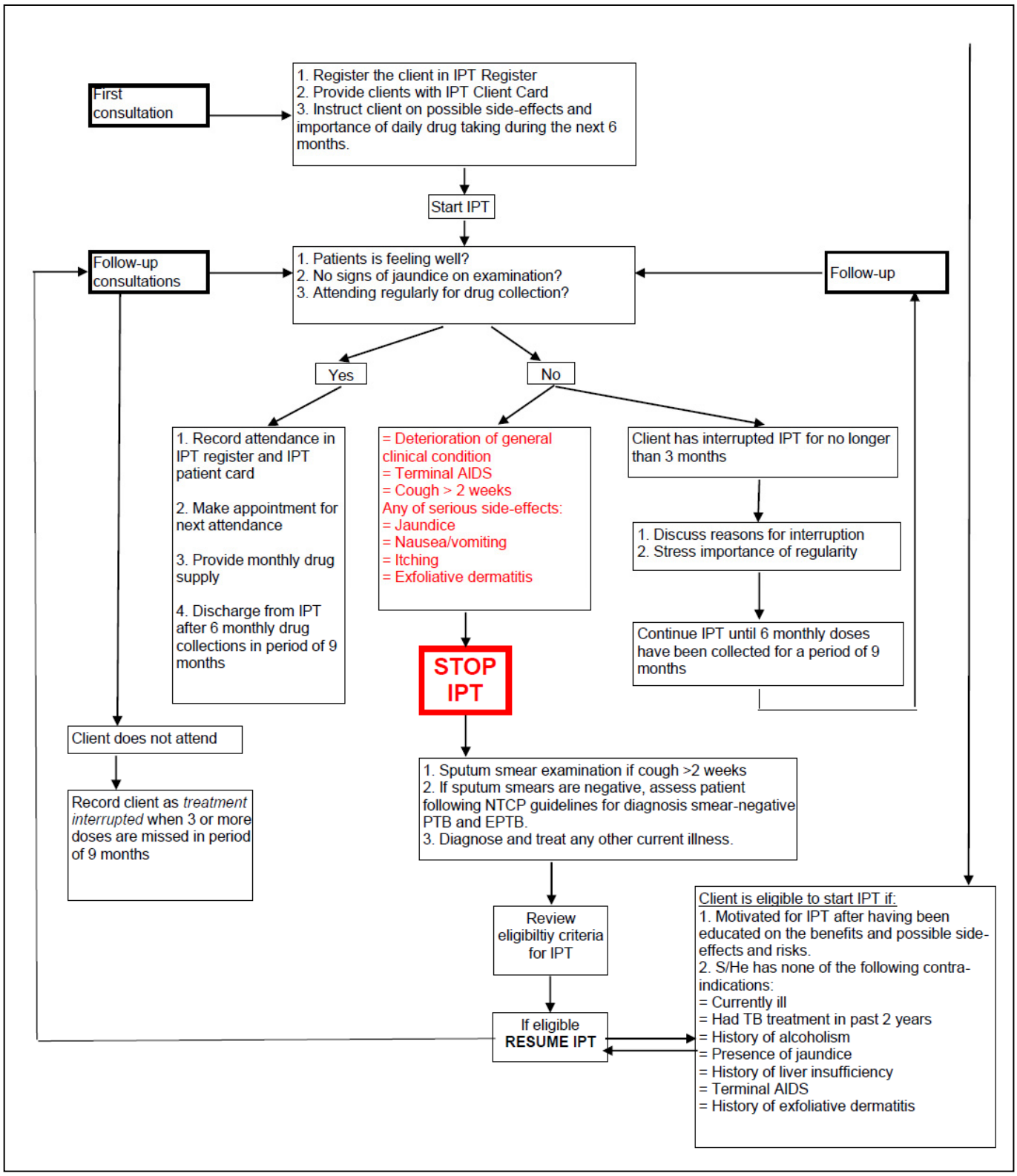
Names		*Profession*	
Telephone		*Fax*	
Region		Email	
Health Facility			

Send/ Fax the completed form to the Therapeutics Information and Pharmacovigilance Centre: Room 21, Basement Area, Windhoek Central Hospital; Tel: 061 203 2312; Fax: 061 226 631

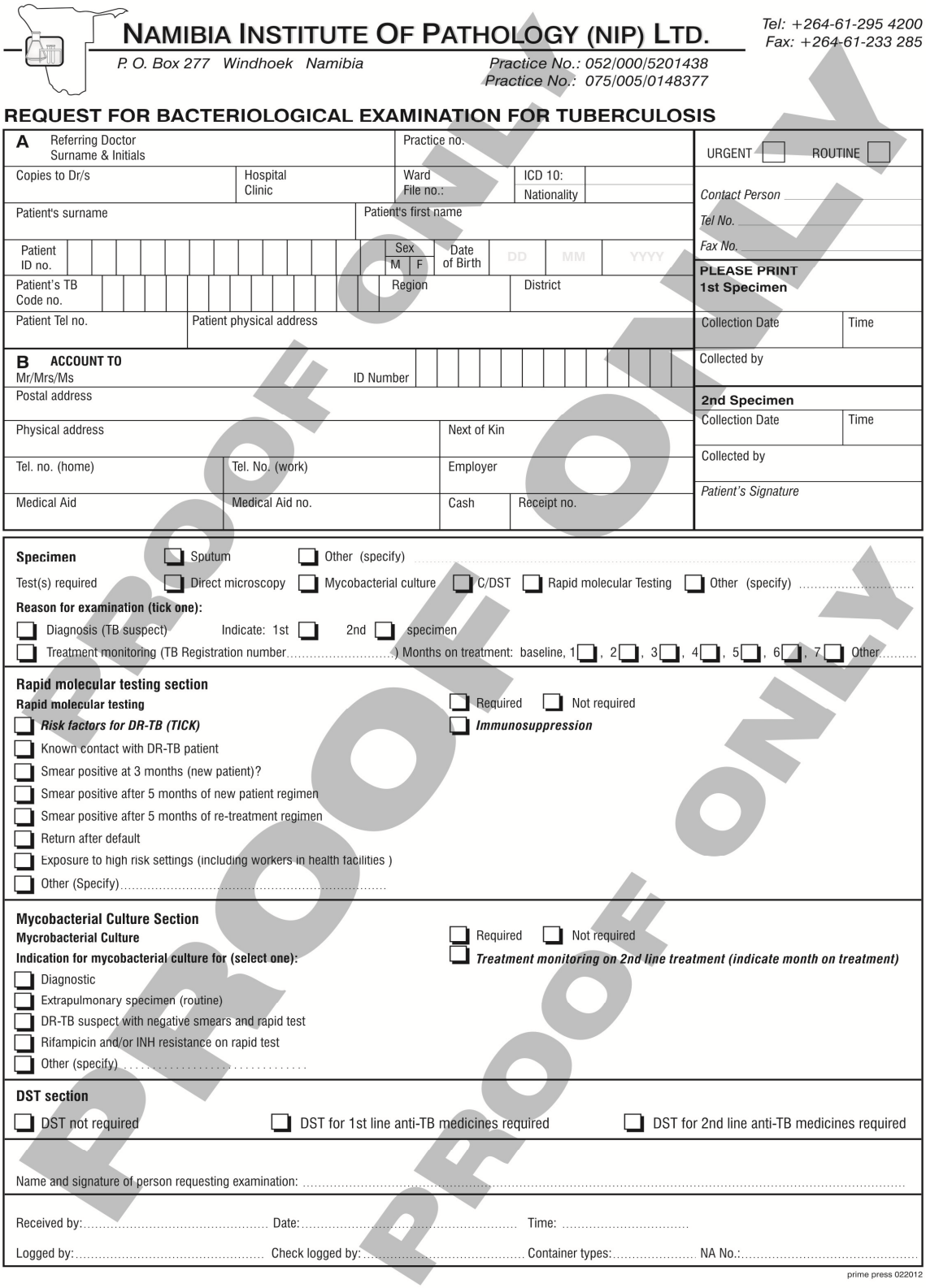
Appendix 7: Tuberculosis screening algorithm in HIV testing and care settings



Appendix 8: Algorithm for the commencement and follow-up of clients on isoniazid preventive therapy



Appendix 9: Laboratory request form for tuberculosis investigations



NAMIBIA INSTITUTE OF PATHOLOGY (NIP) LTD.

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Practice No.: 052/000/5201438
Practice No.: 075/005/0148377

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REQUEST FOR BACTERIOLOGICAL EXAMINATION FOR TUBERCULOSIS

A Referring Doctor Surname & Initials | Practice no. | URGENT ☐ ROUTINE ☐

Copies to Dr/s | Hospital Clinic | Ward File no.: | ICD 10: | Nationality | *Contact Person* | *Tel No.* | *Fax No.*

Patient's surname | Patient's first name

Patient ID no. | Sex M F | Date of Birth DD MM YYYY | **PLEASE PRINT**

Patient's TB Code no. | Region | District | **1st Specimen**

Patient Tel no. | Patient physical address | Collection Date | Time

B **ACCOUNT TO** Mr/Mrs/Ms | ID Number | Collected by

Postal address | **2nd Specimen**

Physical address | Next of Kin | Collection Date | Time

Tel. no. (home) | Tel. No. (work) | Employer | Collected by

Medical Aid | Medical Aid no. | Cash | Receipt no. | *Patient's Signature*

Specimen ☐ Sputum ☐ Other (specify) .....

Test(s) required ☐ Direct microscopy ☐ Mycobacterial culture ☐ C/DST ☐ Rapid molecular Testing ☐ Other (specify) .....

Reason for examination (tick one):

☐ Diagnosis (TB suspect) Indicate: 1st ☐ 2nd ☐ specimen

☐ Treatment monitoring (TB Registration number .....) Months on treatment: baseline, 1☐, 2☐, 3☐, 4☐, 5☐, 6☐, 7☐ Other .....

Rapid molecular testing section

Rapid molecular testing ☐ Required ☐ Not required

☐ ***Risk factors for DR-TB (TICK)*** ☐ ***Immunosuppression***

☐ Known contact with DR-TB patient

☐ Smear positive at 3 months (new patient)?

☐ Smear positive after 5 months of new patient regimen

☐ Smear positive after 5 months of re-treatment regimen

☐ Return after default

☐ Exposure to high risk settings (including workers in health facilities)

☐ Other (Specify) .....

Mycobacterial Culture Section

Mycobacterial Culture ☐ Required ☐ Not required

Indication for mycobacterial culture for (select one): ☐ ***Treatment monitoring on 2nd line treatment (indicate month on treatment)***

☐ Diagnostic

☐ Extrapulmonary specimen (routine)

☐ DR-TB suspect with negative smears and rapid test

☐ Rifampicin and/or INH resistance on rapid test

☐ Other (specify) .....

DST section

☐ DST not required ☐ DST for 1st line anti-TB medicines required ☐ DST for 2nd line anti-TB medicines required

Name and signature of person requesting examination: .....

Received by: ..... Date: ..... Time: .....

Logged by: ..... Check logged by: ..... Container types: ..... NA No.: .....

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Appendix 10: Central Clinical Review Council Consultation Sheet

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

A) History and Clinical Examination

Site/Hospital	
Doctor and Contact Details	
District TB Coordinator and Contact Details	
Patient Name, Age and Sex	
Diagnosis	
Problem(s)	
HIV Status, Latest Cd4 & ART Regimen	
Medical History	
TB History (Date/Year, Initial Rx / Retreatment, Duration & Outcomes, Include any Side Effects)	1. 2. 3. 4.
TB History (2nd Line) (Actual Medicines, Duration Dates if Possible, Include any Side Effects)	
Examination Findings & Chest X-ray	
Current Sputum (Date Taken, DM, Culture, DST)	
Other Investigations Done	
Current Treatment (TB & Other –Include Side Effects)	
Proposed Treatment (By District/Regional Team)	
Social Considerations (Problems and how they are Being Addressed) Assessed by Social Worker (Y/N).....	Dot (Y/N)..... Name of Provider/Organisation.....

B) Sputum Examination Chart

Date Taken	Dm-Insert Worst: *Neg/+/++/+++* (and date received)	Culture *Mtb/Mott/ Neg6wk/Neg2wk*	Resistant: *H/R/S/E Km/Ofx/Eto*	Susceptible *H/R/S/E Km/Ofx/Eto*

H=Isoniazid, R=Rifampicin, S=Streptomycin, E=Ethambutol, Km=Kanamycin, Ofx=Ofloxacin, Eto=Ethionamide

Close Contacts with Known or Suspected DR-TB Case? Yes / No

Name of Contact	Resistance Pattern

Additional Comments/Information (continue on additional sheet if necessary)

.....

……

Person Reporting: .....

Fax Number: :..... Date.....

Appendix 11: List of key indicators for the NTLP

Strategic Result 1: High Quality DOTS and leprosy services expanded and enhanced	
Indicator	**Description**
Proportion of the NTLP budget that is funded	Available funding per year as a proportion of the funding required to fully implement activities according to the costing of TBL MTP-II
Number of district hospitals providing on-site smear microscopy	Number of district hospitals who are able to routinely offer smear microscopy at the hospital without having to refer specimens to another facility.
Proportion of TB patients with documented contact tracing	Number of TB patients with documented contact tracing/ total number of TB patients.
Turn-around time for smear-microscopy results	Time (days) between specimen collection and receipt of results at the health facility.
Treatment success rate (new smear positives)	New smear positive TB cases that successfully complete their treatment/ all new smear positive TB cases registered during a specified time period.
Treatment success rate (re-treatment cases)	Retreatment cases that successfully completed treatment/ among all retreatment cases registered during the specified period
Proportion of TB patients with documented access to DOT during TB treatment	Number of patients with documented DOT/ total number of TB patients.
Proportion of district hospitals reporting stock-outs of first line anti-TB medicines	Number of districts reporting stock outs of longer than two weeks during each calendar year/Total number of districts.
Number of active leprosy case finding assessments done	Comprehensive assessments which include contact tracing and patient retrieval.
Proportion of leprosy patients being treated with the recommended MDT treatment	Number of patients being treated with MDT/total number of leprosy patients reported during that period.
Proportion of districts submitting TB and leprosy quarterly reports in a timely manner	Number of district TB reports submitted within 16 days after the end of a quarter/ total number of district reports submitted.
Strategic Result 2: Increased access to high quality TB/HIV treatment and care interventions	
Proportion of scheduled TB/HIV working group meetings held	Percentage of all scheduled meetings held during each reporting period (quarterly, half yearly and annually)
Proportion of registered TB patients with an HIV result	Number of TB patients with a known HIV result/ total number of TB patients
Proportion of registered HIV positive TB patients on CPT	Number of registered HIV positive TB patients who have taken at least one dose of CPT/ total number of HIV positive TB patients
Proportion of registered HIV positive TB patients who are on ART at the end of treatment	Number of registered HIV positive TB patients on ART at the end of TB treatment/ total number of HIV positive TB patients
Proportion of leprosy patients with a known HIV status	Number of leprosy patients with a known HIV status/ total number of leprosy patients

Strategic Result 3: Programmatic management of drug-resistant TB improved and scaled up	
Proportion of retreatment cases screened for TB drug resistance	Number of retreatment patients with a DST result/ total number of retreatment patients
Proportion of laboratory confirmed MDR-TB patients started on appropriate therapy	Number of MDR-TB patients commenced on treatment /total number of MDR-TB patients diagnosed in the laboratory
Proportion of DR-TB patients receiving social support	Percentage of DR- TB patients, registered over a given time period, who receive social support
Proportion of district hospitals with comprehensive TB-IC measures in place	Number of district hospitals with comprehensive TB-IC measures in place/ total number of district hospitals assessed
Strategic Result 4: General health systems strengthened and effectively supporting TB and leprosy services	
Number of doctors and pharmacists trained in TB and leprosy per year	Number of doctors and pharmacists who will have attended at least one training workshop on TB and leprosy during the year under review
Proportion of districts with district TB and leprosy coordinators who have been in the position for at least 1 year	Number of districts with DTLC's who have been in their positions for at least one year/ total number of districts
Number of nurses and pharmacist assistants trained on TB and leprosy per year	Number of nurses and pharmacist assistants who attended at least one training workshop on TB and leprosy during the year under review
Strategic Result 5: Partnerships for TB control and leprosy eradication strengthened	
Number of TB and leprosy National Steering Committee meetings held	Number of TB and leprosy NSC meetings held during the year under review
Proportion of private health care providers trained on NTLP guidelines	Number of private practitioners trained on NTLP guidelines in the past 3 years/ total number of registered private practitioners
Strategic Result 6: Communities and people with TB and leprosy empowered	
Number of KAP studies conducted during TBL MTP –II	Number of KAP studies conducted during the implementation of MTP II

Tuberculosis recording and reporting tools[9]

[9] *The sample recording and reporting tools are included here for reference only; the actual tools may be formatted differently.*

TB 01: Sputum Examination Register

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Date sputum sent to lab	Name of patient	Sex M/F	Age	Full address of patient (1)	Results of sputum examination and date results received		Average TAT (In days) (2)	Remarks (indicate who suggested the test) 1=Self 2=provider initiated	Comment (3)
					1	2			
1									
2									
3									
4									
5									
6									
7									
8									

(1) Write a complete address that can help you to trace the patient when sputum results are positive.
(2) TAT: Turn-around-time; write the number of days elapsed between the date specimens were sent and date results were received.
(3) Date patient referred for further examination or TB registration number.

TB 02: Drug Susceptibility Testing Register

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

DR-TB Suspect No.	Date	Names & Surname in full	M/F	Age	Address(Physical where possible)	Telephone (Patient & Next of kin)	*HIV result	Risk (Why suspect)**	Date Sample taken for DST	Results of direct microscopy	
										1	2

Key

***HIV result**
1=positive
2=negative
3=unknown

****Risk**
2=Retreatment failure
3=Rx failure in private sector
4=DR-TB contact
5= Relapse/retreatment
6=Default/interrupted Rx

Sputum Microscopy Results
Neg
Scanty
+
++
+++

7=Smear+ at 2-3mo of TB treatment
8=Unclear history of TB treatment
9=Other (specify)

Drug Susceptibility Register…(cont)

	Results of rapid DST (R=resistant S=ssusceptible)		**Results of culture** (MTB Neg2w Neg6w MOTT Other)		**Result of full Drug Susceptibility Testing (DST)** R=resistant, S= susceptible, C=contaminated							**Date of outcome/ clinical decision**	**Outcome/ clinical decision (No TB/ Susceptible TB/ DR-TB/ Died/other) If active TB, insert TB registration number**
	R	**H**	**1**	**2**	**R**	**H**	**E**	**S**	**Km**	**Ofx**	**Eto**		

TB 03: Tuberculosis Treatment Card

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Patient name					Registration number
Address					Tel number:
Age	Sex	M	F	Occupation	
Health facility					Health facility code:
Name CB organisation		Name CB-DOT provider			DOT Code:

CB-DOT code: close relative (1); Guardian-relative, neighbour (2) Workplace (3); Health facility (4); Community Health Worker (5); Other

Diagnostic Classification(*)			
Pulmonary Smear +		New	
Pulmonary Smear -		**Previously treated**	
Pulmonary no smear		Relapse	
		Treatment after Failure	
Xpert MTB/RIF Pos without Rif resistance		Treatment after Default	
Xpert MTB/RIF Pos with Rif resistance		Transfer In	
Xpert MTB/RIF negative			
		Other (Smear –ve or EPTB retreatment's, unknown previous history)	
EPTB: (specify)			

Diagnostic evaluation and monitoring of progress				
	Sputum smears		Body weight	
Timing	Date/result	Date/result	Date	Weight (kg)
Pre-Rx				
2 months				
5-6 months				
7-8 months				
Other:				
Other:				

HIV status and Anti-Retroviral Treatment			
HIV Test result	Pos	Neg	Not done
HAART regimen:		Date started:	
On CPT?: Y / N		Date started:	

Results of Culture and Drug Susceptibility Testing (Indicate **R** for RESISTANT and **S** for SENSITIVE to the listed medicines)					
Indication**	Date and result	H	R	E	S

ANTI-TUBERCULOSIS THERAPY AND OTHER MEDICINES			
Date treatment started		Date treatment ended	
Treatment in New pts (New pt regimen) 2RHZE/4RHE		Treatment in previously treated pts (retreatment) SRHZE/1RHZE/5RHE	

Medicines - Dosage													
	Adult [RHZE] - FDC		R 150mg		H 300 mg		E 400mg		S inj. mg		Co-Trimoxazole. 480mg		
	Child [RHZ] - FDC		Z 400mg		H 100mg		E 100mg		Pyridoxine 25mg		……		

INITIAL PHASE OF ANTI-TUBERCULOSIS CHEMOTHERAPY

Month/ day	*Sign with initials for date of DOT or date medicines are collected. Draw a horizontal line for dates that TB medicines are taken as DOT or SAT at home*																												
	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

* For correct classification follow definitions in the TB guidelines. **Some patients will require rapid DST. (All SS+ve, HIV +ve and all retreatment's)

List of close contacts and action taken (*inner left side*)

Name	Contact traced (Y/N)	Active TB (Yes/No)	Name	Contact traced (Y/N)	Active TB (Yes/No)

Clinical notes

Patient education verification (*inner right side*)
Tick in the columns whether the patient has a good understanding of the questions asked and what it means to him/her.

	At beginning of Intensive phase		**At end of Intensive phase**		**Other time Date:**	
What is the disease you have?	Poor	Good	Poor	Good	Poor	Good
How is this disease spread?						
What can you do to avoid infecting others?						
How will you be treated?						
Can TB be cured?						
What medicines will you take and for how long?						
Why is it important that you never forget to take all your medicines each day?						
Are TB and HIV/AIDS the same? Explain						
Why is it important to know your HIV status when you have TB?						
How can you benefit from knowing your HIV status?						
Why is it important to have a DOT supporter?						
What are common side-effects and what can you do about them?						
Which are serious side-effects that must make you come to the hospital immediately?						
What are “close contacts”?						
Why is it important to inform your close contacts that you have TB disease, and to use the TB contact Card?						
Can you get TB disease again?						
What should you do when you get the same disease symptoms after you have been cured?						
What should you do when you meet somebody who has been coughing for more than 3 weeks?						

CONTINUATION PHASE (*backside*)

Standard regimen for new patients (New patient regimen)	

Standard regimen for previously treated patients (Re-treatment regimen)	

MEDICINES AND DOSAGE					
ADULT FDC-[RHE]-		H 300mg		Pyridoxine 25mg	
CHILD FDC-[RH]		H 100mg		Cotrimoxazole 480mg	
R 450mg		E 400mg			
R 150mg		E 100mg			

CONTINUATION PHASE OF TUBERCULOSIS CHEMOTHERAPY

Month/ day	*Sign with initials for date of DOT or date medicines are collected. Draw a horizontal line for dates that TB medicines are taken as DOT or SAT at home*																														
	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

TREATMENT OUTCOME AND DATE						
Cured	Treatment completed	***Failure before 5/12 of treatment	Failure after 5/12 of treatment	Died	Defaulted	Transfer Out

****These are patients who are registered as failure on the basis of the DST result showing DR-TB or any other patients who are changed to a second line regimen before completing 5 months of treatment with first line regimen.*

Remarks:

Sputum smear examinations (months from starting treatment)

0	2	3	5	7

Remarks

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TB 04: TB Patient Identity Card

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Registration No.				
Name:				
Sex: AGE (years):				
Address:				
Health Facility:----------District:				
DOT provider's name:				
Contacts	Number traced		Number with active TB	
PTB	Smear +		EPTB	Other
	Smear -			

Regimen:	Date Started	Date Ended
New patients: 2RHZE/4RHE		
Retreatment: 2RHZES/1RHZE/5RHE		
Drug-resistant TB		

Treatment Outcome:

INTENSIVE PHASE
(Only mark date when daily medicines were taken)

TB 04: TB Patient Identity Card ….(Cont)

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	32	33	34	35
36	37	38	39	40	41	42
43	44	45	46	47	48	49
50	51	52	53	54	55	56
Extended initial phase:						
57	58	59	60	61	62	63
64	65	66	67	68	69	70
71	72	73	74	75	76	77
78	79	80	81	82	83	84

MEDICINES AND DOSAGES

Pre-Treatment Bodyweight	kg

Adult FDC [RHZE]		R 150/450mg	
Adult FDC [RHE]		H 100/300mg	
Adult FDC [RH]		Z 400mg	
Child FDC [RHZ]		E 400/200mg	
Pyridoxine 25mg		Streptomycin injection	
Co-trimoxazole 480mg		Cycloserine 250mg	
Ethionamide 250 mg		Levofloxacin250mg	
PAS 4g sachets			

CONTINUATION PHASE

Four-weekly medicine collections
(write date when medicines were collected)

1	2	3
4	5	6

TB 05: Facility Tuberculosis Treatment Register

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Year----------

Date of Reg.	Reg. Number	Name (in full)	Sex M/F	Age	Address (in full)	Name of health facility where patient receives treatment	Date treatment started/ Regimen	P/ EP	Category of patient			
									New	Previously treated R/D/F	TI	O

N - New patient **R** – Relapse patient; sputum-smear positive, **F** = Treatment after Failure; **D** = Treatment –after-default, **TI** – Transfer In; patient referred from other treatment clinic; **O** – Other: please specify (includes smear negative or EPTB retreatment cases, unknown previous history).

TB 05: Facility Tuberculosis Treatment Register…. (Cont)

Sputum examinations (months)									Write date and month medicines were collected at 4 weekly period												HIV status	ART	CPT	CB-DOT option	No. of contacts traced	No. of contacts with TB	Date and outcome of Treatment
Initial			2 months		5 months		7 months		1	2	3	4	5	6	7	8	9	10	11	12							
Sm	C	Xpert	Sm	C	Sm	C	Sm	C																			

Xpert – (+) if M.tb is detected on Xpert MTB/RIF ; (-) if M.tb is not detected on Xpert MTB/RIF, or (ND) if Xpert MTB/RIF test is not performed. Cured – sputum-smear negative **TC** – Treatment completed (no smear) **Died** – patient died from any cause **Failure** – Sputum positive at 5 or 7 months, or changed to second line therapy before 5 months **Defaulter** – Interrupted treatment for 2 months **Transfer Out** – Patient moved to another clinic, no outcome known **HIV** – Code 1 = pos; 2 = neg; 3 = unknown **CPT**- insert date of commencement, **ART**-insert date of commencement
Indicate **CB-DOT** code: (1) Guardian (relative, neighbour); (2) Workplace; (3) Health facility; (4) Community Health Worker; (9) Other

TB 06: District Tuberculosis Register

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

YEAR:_____

Date of Reg.	Reg. Number	Name (in full)	Sex M/F	Age	Address (in full)	Name of health facility where patient receives treatment (including private facilities)	Date treatment started/ Regimen	P/ EP	Category of patient			
									New	Previously treated R/D/F	TI	O

N - New patient **R** – Relapse patient; sputum-smear positive, **F** = Treatment after Failure; **D** = Treatment after default, **TI** – Transfer In; patient referred from other treatment clinic
O – Other: please specify, this includes smear negative or EPTB retreatment cases, unknown previous history.

TB 06: District Tuberculosis Register …. (Cont)

Results: Sputum examinations												Date and Treatment Outcomes							HIV status	ART	CPT	DOT options	No. of contacts traced	No. of contacts with TB	Remarks
Initial			2-3 months			5 months			7 months			Cured	Treatment complete	Died	Failure		Default	Transfer Out							
1 Sm	2 Sm	Culture (C)	1	2	C	1	2	C	1	2	C				Before 5/12	After 5/12									

Cured – sputum-smear negative **TC** – Treatment completed (no smear) **Died** – patient died from any cause **Failure** – Sputum positive at 5 or 7 months **Defaulter** – Interrupted treatment for 2 months
Transferred – Patient moved to another clinic, no outcome known **HIV** – Code 1 = pos; 2 = neg; 3 = unknown **CPT**- insert date of commencement, **ART**-insert date of commencement

Indicate **CB-DOT** code: (1) Guardian (relative, neighbour); (2) Workplace; (3) Health facility; (4) Community Health Worker; (9) Other

TB 07: Community-Based DOT Card

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Patient Registration number:	Name and address of DOT provider: Phone number(s): Name of field promoter:……..……....
Name of patient:	
ome address:	Tel number:
Work address:	Tel number:
Name of Health Facility:	Name of health worker (TB nurse):

Date treatment started:		Date treatment ended:	

REGIMEN (TICK)

2HRZE/4HRE		2HRZE/4HRE (children)		2SHRZE/HRZE/5HRE	
Drug-resistant TB (write regimen abbreviation):					

MEDICINES TO BE TAKEN DURING TB TREATMENT		
Type of medicine	Initial Phase (No .of tablets)	Continuation Phase (No .of tablets)
[HRZE] –FDC-adult		
[HRE] – FDC - adult		
[HRZ] – FDC - child		
[HR] – FDC - child		
Other:		
Other:		
Other:		
Other:		
Other:		
Other:		
Other:		
Other:		
Cotrimoxazole 480mg		
Antiretroviral Therapy		

HEALTH WORKER –MEDICINE ISSUE PERIODS

Signature	From	To	**Signature**	From	To

INITIAL PHASE – INDICATE DATE FOR DAILY DOT*

MONTH/Yr	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
	*						

*Insert date & initials

Remarks:

CONTINUATION PHASE*

MONTH/YR	Mon	Tues	Wed	Thurs	Fri	Sat	Sun

TB 07: Community-Based DOT Card…… (Cont)

List of close contacts and action taken (inner left side)

Name	Contact traced (Y/N)	Active TB (Y/N)	Name	Contact traced (Y/N)	Active TB (Y/N)

TB 08: Tuberculosis Patient Transfer Form

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Name of Transferring Health Facility: _____District:_____

Tel / Fax No:_____

Name of Receiving Health Facility:_____District:_____

Tel / Fax No:_____

Name of patient:_____ Registration No: _____

Age:_____ Sex:_____(_F/M_)

Diagnostic category (tick one): New/previously treated (Treatment after failure/default/relapse)/other/ TI

Date treatment started:_____ Expected completion date:_____

Regimen:	Initial phase (Tick)	Relevant F/U smear dates and results	Continuation phase (Tick)	Relevant F/U smear dates and results
New patient: 2RHZE/4RHE				
Retreatment: 2RHZES/1RHZE/5RHE				

MEDICINES AND NUMBER OF TABLETS

Anti-TB Medicines	No. of tablets	Anti-TB Medicines	No. of tablets
4-FDC [RHZE] Adult		Streptomycin injection (dose)	
3-FDC[RHE] Adult		Other:	
2-FDC [RH] Adult		Other:	
3-FDC [RHZ] Child		Other:	
2-FDC [RH] Child		Other:	
Pyridoxine 25mg/100mg		Other:	
Co-trimoxazole 480mg		Other:	
HAART		Other:	

Health Worker Name/Title:_____

Signature:_____ Date Transferred:_____

NOTE: PLEASE CUT-OFF HERE AND SEND SLIP BACK TO TRANSFERRING HEALTH FACILITY AFTER YOU HAVE RECORDED PATIENT'S TREATMENT OUTCOME

Tel/Fax No: _____

Patient Name:_____ Reg. No. at Receiving Health Facility:_____

Your patient was received here on (date):_____ Treatment outcome (date + result): _____

Health Workers Name / Title: _____ Signature: _____

TB 09: Drug-resistant Tuberculosis Patient Booklet

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

(Front Side)

DR-TB Treatment Unit:	**Registration number:**	**Date of registration:**		
Patient name:		**Age:**	M	F
Address:		**Telephone number:**		
Employment/profession	**Mother tongue:**			

Previous TB treatment history:	Number of previous treatments with first-line TB medicines (≥ 4 weeks):	
	Number of previous treatments with second-line TB medicines (≥ 4 weeks):	

Total period anti-TB medicines were taken before (month/years)			**Diagnostic category (tick)**			
Rifampicin (R)			New patient, never treated for TB, or treated for less than 4 weeks			
Isoniazid (H)						
Pyrazinamide (Z)			Previously treated with first-line medicines more than 4 weeks			
Ethambutol (E)						
Streptomycin (S)			Previously treated with second-line medicines more than 4 weeks			
Amikacin/Kanamycin						
Ciprofloxacin (Cfx)			**HIV test result** (tick)	Positive	Negative	Not done
Levofloxacin (Lfx)						
Ethionamide (Et)			If positive, on ART?	Yes	No	
Cycloserine (Cs)			Date ART started D/M/Y			
PAS						

Pulmonary TB		**Extra-Pulmonary TB**				**Body weight** (kgs)

Initial sputum-smear results (date, lab. Number) (neg, positive and grading, not done)	1	2	3
Initial culture results (date, lab number) Negative/positive *M.TB*/contaminated/not done/pending	1	2	
Initial drug susceptibility test: (Date collected, laboratory number, date result) (Res, Sens, not done, pending)	1	2	

List of contacts and actions taken

Name	**Contact traced (Y/N)**	**Active TB (Yes/No)**	**Name**	**Contact traced (Y/N)**	**Active TB (Yes/No)**

Medical History:
(Adverse reactions and allergies to non-TB medications; last menstrual period; method of contraception; pregnancy history)

Other complicating conditions:
(Diabetes, renal insufficiency, hepatitis, drug or alcohol abuse, psychiatric disorders, depression etc.)

Other medicines that the patient is currently taking:

Physical examination:
(General physical condition, blood pressure, length, BMI, full physical examination, urine analysis, liver /kidney function)

Initial screening:

Date:		Potassium:	
Haemoglobin:		Urea:	
Platelets :		ALT:	
White cell count:		Total bilirubin:	
CD4 count:		Blood glucose:	
Viral load:		Pregnancy test:	

X-ray findings:

Summary of Assessment by Social Worker

CONSENT TO TREATMENT FOR DRUG-RESISTANT TUBERCULOSIS

I, _____, ID No_____, hereby consent to being admitted, investigated and treated for drug-resistant tuberculosis. I have been informed that I have drug-resistant TB, which as I have clearly understood, can spread to others and requires close monitoring to determine if the treatment that I am put on is working.

I have been told that **I will receive daily injections for more than 8 months** and that the treatment may continue for up to two years or more. The actual duration of injections and my hospital stay will depend on when laboratory test results confirm that I am no longer able to spread TB to others.

I have been properly counselled that I may suffer side effects from this treatment, such as hearing loss and stomach upset. However, I have chosen to continue this treatment on my own free will because there are no other alternative medicines for my disease.

I will be admitted in hospital to prevent spreading tuberculosis to others and to make sure that I take the medicines every day under direct observation by a health-care worker. I may be transferred from one hospital to another which is better suited to manage my condition, as decided by the medical team. I fully consent to being discharged only after the medical team has confirmed and is satisfied that I am no longer able to spread TB to others.

To prevent the spread of TB to others I may be told to cover my mouth and nose with a surgical/hospital mask and I hereby undertake to do so immediately upon being requested to do so. I will not intentionally or negligently endanger the life of members of my family or public who do not have TB by violating any of the advice given to me to protect others during my treatment and will take all reasonable steps to avoid such an endangerment.

During the course of my admission, I will not leave the hospital without the written and signed approval of the nurse in charge of the ward. I understand the gravity and seriousness of having TB and I have chosen to stay in hospital out of my own free will in order to receive treatment; therefore I shall abide by all of the terms and conditions set out in this consent form and generally by the rules and regulations of the hospital as outlined to me by the hospital authorities.

I further understand that, should I attempt to leave the hospital without consent during my treatment, physical force might be needed in order to restrain me from doing so, and that such restraint may be necessary in order to ensure my treatment period is completed and I agree to such.

I understand that to protect the effectiveness of the medicine the medical team will stop my medicine if:

- I interrupt the treatment myself, or
- there is evidence that the medicine will not work, or
- I suffer serious side effects, or
- I breach the conditions of treatment.

Furthermore, the hospital management reserves the right to ask me to leave the hospital if I disrupt smooth delivery of service at the hospital.

I have read the aforementioned and understand such and sign out of my own free will and without duress.

SIGNED…….DATE…….

WITNESS 1 (HCW)…….. WITNESS 2 (relative/guardian)……

TREATMENT

Date treatment started	Date:		Date:	
	Initial phase	**Dose/day**	**Continuation phase**	**Dose/day**
Standard second-line	Kanamycin		Levofloxacin	
	Levofloxacin		Ethionamide	
	Ethionamide		Cycloserine	
	Cycloserine		Pyrazinamide	
	Pyrazinamide		Ethambutol	
	Ethambutol			
Individualised regimen (based on DST result)	Capreomycin		Capreomycin	
	PAS		PAS	
	Rifampicin		Rifampicin	
	Isoniazid		Isoniazid	
	Streptomycin		Streptomycin	
	Clofazimine		Clofazimine	
	Amox/Clav		Amox/Clav	
	Clarithromycin		Clarithromycin	
	Thiacetazone		Thiacetazone	
Additional treatment	Cotrimoxazole		Cotrimoxazole	
	Pyridoxine		Pyridoxine	
Anti-Retroviral Treatment				
Other medicines				

MONITORING (Treatment duration in months)	**Sputum-smear**			**Culture (worst result)**	**DST (See Guidelines)**	**Body weight Kg**
	1	2	3			
Pre-treatment						
2						
3						
4						
5						
6						
9						
12						
15						
18						
21						
24						

INITIAL PHASE OF TUBERCULOSIS CHEMOTHERAPY																															
Month/	*Sign with initials for date of DOT.*																														
Day	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

CONTINUATION PHASE OF TUBERCULOSIS CHEMOTHERAPY																															
Month/ Day	*Sign with initials for date of DOT or date medicines are collected. Draw a horizontal line for dates that TB medicines are taken as SAT at home*																														
	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

SIDE-EFFECT MONITORING

INTENSIVE PHASE

Adverse effect (indicate grading*)	Week																								Management	Outcome
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24		
Abdominal pain																										
Constipation																										
Decreased hearing																										
Depression																										
Diarrhea																										
Dizziness																										
Fatigue																										
Fever																										
Headache																										
Joint pain																										
Nausea																										
Psychosis																										
Rash																										
Skin discolouration																										
Tinnitus																										
Tremors																										
Vision changes																										
Vomiting																										
Other (list)																										

* Grading: 1 = mild; requiring no intervention 2 = moderate; requiring palliative intervention 3 = severe; requiring change in treatment

SIDE EFFECT MONITORING

Continuation phase

Adverse effect (indicate grading*)	Month **																				Management	Outcome
Abdominal pain																						
Constipation																						
Decreased hearing																						
Depression																						
Diarrhea																						
Dizziness																						
Fatigue																						
Fever																						
Headache																						
Joint pain																						
Nausea																						
Psychosis																						
Rash																						
Skin discolouration																						
Tinnitus																						
Tremors																						
Vision changes																						
Vomiting																						
Other (list)																						

* Grading: 1 = mild; requiring no intervention 2 = moderate; requiring palliative intervention 3 = severe; requiring change in treatment

** Indicate in the first row the month of treatment that continuation phase started

TB 10: Drug-resistant Tuberculosis Register

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Date of Reg. d/m/y	**Unique district DR-TB Register Number**	**Surname & Names in full**	**Sex** M/F	Age	**Address** (Physical where possible)	**Site** of Disease (P/EP)	**Category***	**Classification****	**Date Sample taken for DST**	**Result Of Drug Susceptibility Testing(DST)** (Enter the DST that resulted in the patient being registered as a DR-TB patient. If the DST is pending, it should be filled in when the results are known) R=resistant, S= susceptible, C=contaminated									**DOT options**
										R	H	E	S	Km	Ofx	Eto	other	other	

*** Category**
1. New
2. Previously Rx 1st line
3. Previously Rx 2nd line

****Classification**
1. New
2. Relapse
3. After default
4. After failure of initial treatment
5. After failure of re-treatment
6. Transfer in (from another drug-resistant treatment site)
7. Other

TB 09: Drug-resistant Tuberculosis Register ….. (Cont)

Reasons for Reg.	Date treatment started (d/m/y)	DR-TB Treatment Regimen	**Smear(S) and Culture(c) results during treatment** (insert worst result for that month)																									
			Start of Treatment Month 0		Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 9		Month 12		Month 15		Month 18		Month 21		Month 24	
			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
			d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y	
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Reasons for registration
MDR= confirmed MDR-TB
XDR= confirmed XDR-TB
PDR= confirmed polydrug resistant TB
Rif mono= Rifampicin monoresistant TB
Suspected = Commenced 2nd line Rx with no DST result

Medicine abbreviations

First-line medicines
H= Isoniazid
R= Rifampicin
E=Ethambutol
Z=Pyrazinamide
S=Streptomycin

Second-line medicines
Km= Amikacin
Eto = Ethionamide
Lfx = Levofloxacin
Cs = Cycloserine
PAS = Para-amino salicylate
Cm = Capreomycin
Cfz = Clofazimine
Amx+clv = Amoxycillin with clavulanate
Clr = Clarithromycin
Lzd = Linezolid

TB 09: Drug-Resistant Tuberculosis Patient Booklet ….. (Cont)

Outcome Cured Completed treatment Failed Died Defaulted Transferred Out	**No. of contacts traced**	**No. of contacts with TB**	**TB/HIV information**					**Comments**
			HIV Testing			ART Y/N Start date	CPT Y/N Start date	
Date of treatment outcome			Testing done (Y/N/U)	Date of Test	Result			
/ /								
/ /								
/ /								
/ /								
/ /								
/ /								
/ /								
/ /								
/ /								
/ /								

Notation method for recording smears (for non-centrifuged specimens)

No. AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation method for recording cultures

(if solid culture media is used)

No growth reported	0
Fewer than 10 colonies	Report number of colonies
10-100 colonies	+
More than 100 colonies	++
Innumerable or confluent growth	+++

TB 11: Drug-Resistant Tuberculosis Patient Transfer/Referral Form

Health Facility referred/transferred from: _____ District: _____

Tel: _____ Fax :_____

Health Facility referred/transferred to: _____ District: _____

Tel: _____ Fax :_____

Name of Patient:_____
New address: ……
Tel……
Next of kin name & tel……

DR-TB Registration No: _____ Inpatient / Outpatient (circle)

Age: _____ Sex:_____ Weight: _____kg

Diagnostic category (tick) : MDR ☐ Poly-resistant ☐ XDR ☐ Suspected MDR/ Other ☐

REASON FOR TRANSFER/REFERRAL: ……

DRUG SUSCEPTIBILITY TESTING (DST) RESULTS (Insert R-resistant or S-sensitive)

	DATE (collected)	**H**	**R**	**E**	**S**	**Km**	**Ofx**	**Eto**	**Other(specify)**
Initial	/ /								
Most Recent	/ /								

Date treatment started: _____/_____/_____

Expected completion date: _____/_____/_____

REGIMENS AND REGIMEN CHANGES (tick)

DATE Started/ Altered		**H**	**R**	**Z**	**E**	**Km**	**Lfx**	**Eto**	**Cs**	**PAS**					
/ /															
/ /															
/ /															
/ /															
/ /															
CURRENT REGIMEN															

COMMENT ON ADHERENCE (circle): Good / Poor / Needs supervision **WAS ON DOT** (Y/N) ☐

SPUTUM RESULTS (insert worst**)**

Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**22**	**24**	**Other Latest**
Date																							
DM																							
Culture																							

Next sputum collection due on _____/_____/_____

TB Treatment supplied for _____days. Last dose to be taken on_____/_____/_____

Other treatment (Y/N): HAART ☐ CTX ☐ Pyridoxine ☐
OTHER (SPECIFY) _____

Health Worker Name/Title: _____/_____

Signature: …… Date transferred/referred: ……/……/……

PLEASE CUT-OFF HERE AND SEND SLIP BACK TO TRANSFERRING HEALTH FACILITY AFTER YOU HAVE RECORDED PATIENT'S TREATMENT OUTCOME

PATIENT FINAL TREATMENT OUTCOME UPDATE SLIP

Name of Receiving Health Facility/District: _____

Tel: _____ Fax: _____

Patient Name: _____
Reg. Number: _____

TO _____(Name of referring/transferring facility)

Your patient was received here on (date):_____/_____/_____

TREATMENT OUTCOME: _____ __Date _____/_____/_____

Comments:……
……

Health Workers Name / Title: _____/_____ _____

Signature: ……. Date :…….

……
PLEASE CUT-OFF HERE AND SEND SLIP BACK TO TRANSFERRING HEALTH FACILITY AS SOON AS YOU RECEIVE THE PATIENT.

DR-TB PATIENT DESTINATION UPDATE SLIP

Name of Receiving Health Facility/District: _____

Tel: _____ Fax _____

Patient Name: _____
Reg. Number: _____

TO _____(Name of transferring HCW)

AT_____(Name of transferring facility)

Your patient was received here on (date):_____/_____/_____

Comments:……
……

Health Workers Name / Title: _____ /_____

Signature: ……. Date: …….

TB 12: Tuberculosis Contact Investigation Slip

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

TB CONTACT SLIP

Index Patient Registration No:	
Date:	Health facility:
Name of Health Worker:	

Dear Sir/Madam,
This is to inform you that a close relative, friend, or colleague of yours was recently diagnosed with tuberculosis (TB) disease.

1. Because of the nature of TB disease, it is possible that you might have been infected with TB germs. If you are infected, you may experience the following problems now or some time later:
   - Cough
   - Weight loss
   - Night sweats
   - Fever
   - Swellings in the neck, armpits or groin (Lymph node enlargement)

   If you have any of the above symptoms now, we strongly advise you to visit any health facility and present this slip for medical attention.

2. If there is any close contact living with HIV and children under the age of five years, they should also visit their nearest health facility for assessment and provision of TB preventive medicine if they do not have signs and symptoms of TB.

3. If you are not ill now, you may still become ill with TB after some months or years. To stop this from happening, please visit your nearest health facility for:
   - More information and advice on how to protect yourself from TB
   - Examination by a health care worker
   - Provision of TB treatment or preventive medicine if required
   - HIV counselling and testing
   - Specific treatment in case you are HIV positive

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

TB CONTACT TEAR-OFF SLIP

Index Patient Registration No:	
Name of contact being assessed:	
Address: Telephone number:	
Date:	Health facility:
Name of Health Worker:	

Yes	Symptoms to ask about	No
	Cough for two weeks or more?	
	Weight loss?	
	Night sweats?	
	Fever?	
	Swellings in the neck, armpits or groin (Lymph node enlargement)?	
	Under the age of 5 years?	
	HIV positive?	
	Other Immunosuppressive conditions (Diabetes/cancer/on corticosteroids)?	

If yes to any of the above; visit to nearest health facility for further assessment.

TB 13: Client Isoniazid Preventive Therapy (IPT) Card

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Client IPT Card

Patient Registration No:				
Name of health facility:				
District:				
DOT Provider name (if any):				
Patient Name:				
Age:		Sex:	M	F
Address:				
Reason for IPT (circle the most appropriate one)				
HIV+	TB Contact < 5 years old	Other Immunosuppressive conditions (Diabetes/cancer/on corticosteroids, other)		
Date prophylaxis started:		Date prophylaxis ended:		
Outcome of prophylaxis outcome:				

MEDICINES AND DOSAGES

Bodyweight at start of treatment (kgs):	

Medicine	**# of tablets**
Isoniazid 100mg	
Isoniazid 300mg	

Four-weekly medicine collections

(Record date when medicines were collected)

1	2	3
4	5	6
7	8	9

TB 14: Isoniazid Preventive Therapy (IPT) Register

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Date of Reg.	Reg. number	Name (in full)	M/F	Age	Address (in full)	Name health facility	Category of IPT client (HIV+/ <5//Other)	Date / number of monthly doses collected									Date and outcome of IPT					Remarks
								1	2	3	4	5	6	7	8	9	Completed	Died	Stopped (due to side-effects)	Defaulted	Transferred out	

OUTCOME OF IPT: **Completed:** Collected 6 monthly doses in period of 9 months; **Died:** Died from any disease; **Stopped:** IPT was stopped for medical reasons; **Defaulted:** Collected less than 6 monthly doses within 9 months; **Transfer out:** Was transferred to another clinic, no information on outcome.

TB 15: Tuberculosis and Leprosy Quarterly Report Form

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

District:	**Cases registered in (Quarter), Year**
Region:	Tick or circle on the quarter below
Name of DTLC:	1st Quarter (1 January- 31st March)
	2nd Quarter (1 April-30 June)
Signature: _____ **Date:**	3rd Quarter (1 July -30 September)
	4th Quarter (1 October- 31 December

PART A: QUARTERLY REPORT ON NEW AND RETREATMENT TB CASES, CONTACT TRACING AND HEALTH WORKERS TRAINED

Smear-positive PTB								Smear Negative PTB		Smears-not-done Adults		Smears-not-done <15 Years		Extra Pulmonary TB		TOTALS			Others	
New Cases		Retreatment																		
		Relapses		T. A.D		TAF														
M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	TOTAL	M	F

	M	F
Number of health workers trained in TB		
Number of health workers diagnosed with TB		
Number of contacts traced		
Number of contacts diagnosed with TB		

Age-Sex distribution of new smear-positive TB cases

AGE GROUP IN YEARS																TOTALS		
0-5		6-14		15-24		25-34		35-44		45-54		55-64		65 +				
M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	TOTAL

PART B: HIV TESTING AND LEPROSY

	M	F	New Leprosy cases recorded on register	
TB cases with known HIV status			Pauci-Bacillary	
TB cases who are HIV positive			Multi- Bacillary	

PART C: TREATMENT RESULTS FOR TB CASES FOR SAME QUARTER LAST YEAR

	Cured (smear-negative)	Treatment completed	Died	Failure (smear-positive)	Defaulted	Transferred-out	Total number evaluated
Smear-positive							
Smear-negative							
Extra-pulmonary							
Retreatment							
Smears-not-done ≥ 15 years							
Smears-not-done < 15 years							
Others							

TB 16: TB/HIV Quarterly Report Form

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

District:
Region:
DTLC Name:

Signature: _____ Date:

Cases registered in (quarter), Year:
1st Quarter: 01 January – 31 March
2nd Quarter: 1 April – 30 June
3rd Quarter: 1 July – 30 September
4th Quarter: 1 October – 31 December

PART A: QUARTERLY REPORT ON NEW AND RETREATMENT TB CASES

Smear-positive PTB								Smear Negative PTB		Smears-not-done Adults		Smears-not-done <15 Years		Extra Pulmonary TB		TOTALS			Others	
New Cases		Retreatment																		
		Relapses		T. A.D		TAF														
M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	TOTAL	M	F

Age and sex distribution of smear positive new cases

Age group in years																TOTALS		
0-5		6-14		15-24		25-34		35-44		45-54		55-64		65 +				
M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Total

PART B:

TB HIV COLLABORATIVE ACTIVITIES	M	F
Number of TB/HIV patients on co-trimoxazole prophylaxis		
Number of TB/HIV patients started on or continued on ART		

PART C: TREATMENT RESULTS FOR TB/HIV CASES FOR SAME QUARTER LAST YEAR:

	Cured (smear-negative)	Treatment completed	Died	Failure (smear-positive)	Defaulted	Transferred-out	Total number evaluated
Smear-positive							
Smear-negative							
Extra-pulmonary							
Retreatment							
Smears-not-done ≥ 15 years							
Smears-not-done < 15 years							
Others							

TB 17: DR-TB Quarterly Reporting Form

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

District:	**Cases registered in (Quarter), Year**
Region:	Tick or circle on the quarter below
Name of DTLC:	1st Quarter (1 January- 31st March)
	2nd Quarter (1 April-30 June)
Signature:	3rd Quarter (1 July -30 September)
Date:	4th Quarter (1 October- 31 December

PART A: Quarterly report on DR-TB

Cases registered in this* reporting quarter									
	MDR-TB		XDR-TB		PDR-TB		Suspected MDR-TB/ other		**Totals**
	M	F	M	F	M	F	M	F	
New									
Previously treated with 1st line medicines									
Previously treated with 2nd line medicines									
TOTAL									
Reported by laboratory									

PART B: 6-month interim assessment for patients reported in the ___quarter of 20____(year)

	Cured	Treatment completed	Culture-positive on Rx	Culture-negative on Rx	Died	Failed	Defaulted/ Absconded/ Treatment stopped	Transferred-Out	Total number evaluated
MDR-TB									
XDR-TB									
PDR-TB									
Suspected MDR-TB/Other									
TOTAL									

PART C: Quarterly DR-TB/HIV Report

	DR-TB patients with known HIV status	HIV-positive DR-TB patients	HIV-positive DR-TB patients on ART	HIV-positive DR-TB patients on CPT
Number				

PART D: DISTRIBUTION OF DR-TB CASES THIS REPORTING QUARTER

	MDR-TB	XDR-TB	PDR-TB	Other/ Suspected MDR-TB	TOTALS
Totals registered in this reporting quarter *[from Part A: add M+F]* (A)					
Carried over from last Quarter (B=H at previous quarter)					
Transfer-in this Quarter (C)					
Died during this Quarter (D)					
Transfer out in this Quarter E)					
Discharged from Rx this Quarter. (F) *[Cured + completed]*					
Defaulted & Rx stopped this Quarter. (G)					
Total on Rx at end of Quarter (H=A+B+C-D-E-F-G)					

PART E: TRAINING

Number of Health workers (specify) trained in DR-TB in the Quarter	
Cumulative number of health workers trained in DR-TB in the district	

COMMENTS *(Must include update on suspected MDR-TB cases reported in previous quarter)*

.....

.....

.....

INTERIM AND FINAL OUTCOMES AFTER 12, 18 & 24 MONTHS

PART F: 12-month interim assessment for patients reported in the __quarter of 20__ *(year)*

	(1) Cured	(2) Treatment completed	(3) Culture-positive on Rx	(4) Culture-negative on Rx	(5) Died	(6) Failed	(7) Defaulted/ Absconded/ Treatment stopped	(8) Transferred-out	(sum of 1-8) Total number evaluated
MDR-TB									
XDR-TB									
PDR-TB									
Suspected MDR-TB/Other									
TOTAL									

PART G: 18-month interim assessment for patients reported in the _quarter of 20__ *(year)*

	(1) Cured	(2) Treatment completed	(3) Culture Positive on Rx	(4) Culture Negative on Rx	(5) Died	(6) Failed	(7) Defaulted/ Absconded/ Treatment stopped	(8) Transferred-out	(sum of 1-8) Total number evaluated
MDR-TB									
XDR-TB									
PDR-TB									
Suspected MDR-TB/Other									
TOTAL									

PART H: 24-month outcome assessment for patients reported in the ___quarter of 20___*(year)*

	(1) Cured	(2) Treatment completed	(3) Culture Positive on Rx	(4) Culture Negative on Rx	(5) Died	(6) Failed	(7) Defaulted/ Absconded/ Treatment stopped	(8) Transferred-out	(sum of 1-8) Total number evaluated
MDR-TB									
XDR-TB									
PDR-TB									
Suspected MDR-TB/Other									
TOTAL									

TB 18: Quarterly Outcome Report for Isoniazid Preventive Therapy (IPT)

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Date of Report:		Period/Quarter Reporting On:
Health Facility Name:	Health Facility Number:	District:
Name of DTLC:		Signature:

OUTCOME ANALYSIS

Category	**Completed**		**Died**		**Stopped**		**Defaulted**		**Transfer out**		**Total**	
	No	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
< 5 years contacts												100
Other contacts												100
Total												**100**

Total Number of Clients Registered for IPT in the Reporting Period:	
Total Number Evaluated for IPT in Reporting Period:	
Percentage Evaluated	**%**

TB 19: District Quarterly Report on Community-based Tuberculosis Care (CBTBC)

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

Reporting quarter (tick): □1 Jan – 31 Mar □1 Apr – 30 Jun □1 Jul – 30 Sep □1 Oct – 31 Dec YEAR: 20____

District…….. Name of DTLC…….
Name of Reporting Organization(s):……..... ……
Source(s) of Funding:…….
Name of person submitting report:…… … Date: ……..
Contact details:……..

PROGRAMME ACTIVITIES AND OUTPUTS	Number/%	
1. Number of defaulter/ interrupters		
2. Number of defaulter/ interrupters traced who were put back on treatment		
3. Number of close contacts symptom-screened for TB		
4. Number of TB suspects (close contacts) referred to health facilities for TB examinations		
5. Number/% of TB patients with a known HIV status		
6. Number of TB patients provided with food supplements		
7. Number of patients/former TB patients trained in life-skills activities		
8. Number of TB awareness health educations sessions events conducted		
Activities 09-16 should be disaggregated by gender	Male	Female
9. Number of field promoters in district at end of reporting period		
10. Number of field promoters trained during the reporting period		
11. Number of new TB patients registered during period under review		
12. Total number of TB patients on treatment at the end quarter		
13. Number of DR-TB patients on treatment in the community during period under review		
14. Number of new community members trained as to observe treatment		
15. Number of community members reached through health educations sessions (schools, churches, community etc.)		
16. Number of IEC materials distributed (specify……)		
17. *		
18. *		
19. *		
20. *		
21. *		

**Add any additional indicators that are not included here (eg Global Fund specific indicators).*

Challenges:

Planned activities for next quarter:

Comments/ Additional information:

TB 20: Namibia ACSM Documentation Format

Republic of Namibia
Ministry of Health and Social Services
National Tuberculosis and Leprosy Programme

District Name: Quarter Number: Year:

	Report on community based activity					**Report on I.E.C materials developed & disseminated**			**Report on advocacy activities**					**Report on World TB Day**	
S.N	Activity	Number of activities planned	Number 0f activities conducted in the quarter	Expected output achieved (Yes/No)	Output of the activity	Materials developed (D) / Reproduced (R) / Stock (S)	Dissemination of materials (Yes/No)	Visibility (Places where visible)	Activity	Number of activities planned	Number of activities conducted in the quarter	Expected output achieved (Yes/No)	Output of the activity	Activity	Output

Statement of expenditure:

Activity	Budget	Expenditure
Community based activity		
IEC materials		
Advocacy activities		
World TB day activities		
Total		

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