Ministry of Health & Family Welfare
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World Health Organization
India

TRAINING MODULES (1-4)

FOR PROGRAMME MANAGERS & MEDICAL OFFICERS

National TB Elimination Programme
Central TB Division
Ministry of Health & Family Welfare,
Government of India, New Delhi

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Abbreviations

aDSM	Active Drug Safety Monitoring and Management
ACH	Air Change per Hour
ADR	Adverse Drug Reaction
AE	Adverse Event
AFB	Acid Fast Bacilli
AIC	Airborne Infection Control
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine Aminotransferase
Am	Amikacin
AMC	Adr Monitoring Center
Amx/Clv	Amoxicillin/clavulanate
ART	Anti-retroviral Therapy
ARV	Anti-retroviral
AST	Aspartate Aminotransferase
ATS	American Thoracic Society
Bdq	Bedaquiline
BPL	Below Poverty Line
BTS	British Thoracic Society
CAP	Conditional Access Programme
CBNAAT	Cartridge Based Nucleic Acid Amplification Test
Cfz	Clofazimine
Clr	Clarithromycin
Cm	Capreomycin
CMO	Chief Medical Officer
CP	Continuation Phase
CPT	Co-trimoxazole Preventive Therapy
Cs	Cycloserine
CTD	Central Tb Division
CUP	Compassionate Use Programme

C-DAC	Centre For Development of Advanced Computing
C-DST	Culture and Drug Susceptibility Test
CL-HIV	Children Living With HIV
DAIDS	Division of Aids
DBT	Direct Beneficiary Transfer
DCGI	Drugs Controller General of India
DDG	Deputy Director General
DDS	District Drug Store
DDR TBC	District Dr Tb Centre
DG	Director General
DGHS	Directorate General of Health Services
Dlm	Delamanid
DMC	Designated Microscopy Centre
DOT	Directly Observed Treatment
DOTS	Core Approach Underpinning the Stop TB Strategy for TB Control
DRT	Drug Resistance Testing
DR TB	Drug-resistant Tuberculosis
DR TBC	Drug-resistant Tuberculosis Centre
DSMC	Drug Safety Monitoring Committee
DST	Drug Susceptibility Testing
DTO	District TB Officer
DVDMS	Drug Vaccine Distribution Management System
E	Ethambutol
ECG	Electrocardiogram
ECHO	Extension of Community Health Care Outcomes
EP-TB	Extra-pulmonary Tuberculosis
EQA	External Quality Assurance
Eto	Ethionamide
EU	European Union
FDA	Food and Drug Administration
FEFO	First Expiry First Out

FL LPA	First Line-line Probe Assay
FQ	Fluoroquinolone
GLC	Green Light Committee
GFATM	Global Fund for Aids, Tuberculosis & Malaria
Gfx	Gatifloxacin
GMSD	General Medical Stores Depot
GoI	Government of India
H	Isoniazid
Hh	High Dose Isoniazid
HRCT	High Resolution Ct Scan
ICH	International Conference on Harmonization
ICT	Information Communication Technology
ICMR	Indian Council for Medical Research
IP	Intensive Phase
Ipm	Imipenem
IPAQT	Initiative For Promoting Affordable & Quality TB Test
IQC	Internal Quality Control
IRL	Intermediate Reference Laboratory
ISO	International Standard Organization
Km	Kanamycin
LC	Liquid Culture
LFT	Liver Function Test
Lfx	Levofloxacin
L J	Lowenstein Jensen
LPA	Line Probe Assay
LT	Laboratory Technician
LTFU	Lost To Follow Up
Lzd	Linezolid
MAC	Mycobacterium Avium Complex
MDR TB	Multi-drug Resistant TB
Mfx	Moxifloxacin

Mfxh	High Dose Moxifloxacin
MGIT	Mycobacteria Growth Indicator Tube
MIC	Minimum Inhibitory Concentration
MIS	Management Information System
MO	Medical Officer
MoHFW	Ministry of Health and Family Welfare
MO-DMC	Medical officer-designated Microscopy Centre
MO-PHI	Medical officer- Peripheral Health Institute
MO-TC	Medical officer TB Control
MOTT	Mycobacterium other Than Tubercle Bacilli
MoU	Memorandum of Understanding
Mpm	Meropenem
MR	Mono Resistance
MSS	Monthly Stock Statement
NAAT	Nucleic Acid Amplification Test
NABL	National Accreditation Board for Laboratories
NTEP	National TB Elimination Programme
NDRS	National Drug Resistance Survey
NDR TBC	Nodal Dr TB Centre
NGO	Non-government Organization
NGS	Next-generation Sequencing
NHPS	National Health Protection Scheme
NHM	National Health Mission
NIRT	National Institute for Research in Tuberculosis
NITRD	National Institute For Tuberculosis and Respiratory Diseases
NRL	National Reference Laboratory
NSP	National Strategic Plan
NTI	National TB Institute
NTM	Non-tuberculous Mycobacterium
Ofx	Ofloxacin
OPD	Out Patient Department

PAS	P-aminosalicylic Acid
Pdx	Pyridoxine
PDR	Poly Drug Resistance
PHI	Peripheral Health Institute
PK/PD	Pharmacokinetic/pharmacodynamics
PL-HIV	People Living with HIV
PMDT	Programmatic Management of Drug-resistant Tuberculosis
PP	Private Provider
PQC	Product Quality Compliance
PSM	Procurement and Supply Management
PT	Previously Treated
PTE	Pre-treatment Evaluation
Pto	Protionamide
PvPI	Pharmaco-vigilance Programme of India
QA	Quality Assurance
QSE	Quality System Elements
R	Rifampicin
RNTCP	Revised National Tuberculosis Control Programme
RR TB	Rifampicin Resistant Tuberculosis
R&R	Recording & Reporting
RT-MERM	Real Time Medication Event Reminder Monitor Device
S	Streptomycin
SA	Statistical Assistant
SAE	Serious Adverse Event
SCM	Supply Chain Management
SDG	Sustainable Development Goals
SDS	State Drug Store
SLD	Second Line Anti-TB Drugs
SLDST	Second Line Drug Susceptibility Testing
SLI	Second Line Injectable
SL-LPA	Second Line-line Probe Assay

SME	Supervision, Monitoring & Evaluation
SoP	Standard Operating Procedures
SPC	Specimen Processing Control
STLS	Senior TB Laboratory Supervisor
STO	State TB Officer
STR	Standardized Treatment Regimen
STS	Senior Treatment Supervisor
TALFU	Treatment After Lost To Follow Up
TAT	Turn-around Time
TB	Tuberculosis
TBHV	Tb Health Visitor
Thz	Thioacetazone
ToR	Terms Of Reference
Trd	Terizidone
TU	TB Unit
UDST	Universal Drug Susceptibility Testing
ULN	Upper Limit of Normal
UPT	Urine Pregnancy Test
USAID	United States Agency For International Development
USFDA	United States Food & Drug Administration
WCO India	World Health Organization Country Office for India
WHO	World Health Organization
XDR TB	Extensively-drug Resistant TB
Z	Pyrazinamide

MODULE 1

OVERVIEW OF TB CONTROL IN INDIA

Learning Objectives

In this module we will learn about:

- Pathogenesis of Tuberculosis (TB)
- Burden of TB and its impact (Extent of TB problem in the National and Global context
- Evolution of the National Tuberculosis Control Programme
- Sustainable Development Goals
- End TB strategy
- National Strategic Plan (2017-25)
- Health System structure & functions for delivery of TB care
    - Delivery of TB care in public and private sectors
    - Patient Centric Model of Care

Introduction

The National Tuberculosis Control Programme (NTP) of India was initiated in 1962. A comprehensive review of the NTP in 1992 found that the NTP had not achieved its aims or targets. Based on the recommendations of the 1992 review, the Revised National Tuberculosis Control Programme (RNTCP), incorporating the components of the internationally recommended Directly Observed Treatment Short-course (DOTS) strategy for the control of TB, was developed. RNTCP has now been implemented in the country for more than two decades, and has been expanded geographically to achieve nation-wide coverage in March 2006. The spread of human immuno-deficiency virus (HIV) during the last two decades, emergence of various forms of drug resistant TB and unorganised and unregulated vast private sector pose additional challenges in effective TB control.

Over a period of time, there are several landmark achievements including policy and system preparedness for Universal access to TB care including mandatory notification of TB cases, development of Standard for TB Care in India, Comprehensive Real time TB Information Management System – NIKSHAY, use of rapid molecular diagnostics, successful innovations in Private Sector engagement for TB care- Universal Access To TB Care (UATBC). A considerable progress in addressing Drug Resistant TB with focus on Drug Susceptibility Testing (DST) guided treatment including introduction of newer drugs (like bedaquiline, delamanid), TB and co-morbidities, paediatric TB, nutritional support through Nikshay Poshan Yojana by DBT, active case finding, intensified case finding and urban TB control models has also been made and a major progress has been achieved in advocacy and communication areas.

The programme gives priority in detecting and treating Microbiologically confirmed PTB, thereby aiming to cut the chain of transmission of infection. However, it needs to be remembered that under NTEP all types of TB cases are diagnosed and treated.

Pathogenesis of TB

Source of infection and exposure

Tuberculosis (TB) is an airborne infectious disease caused predominantly by Mycobacterium tuberculosis species of pathogenic bacteria, first discovered in 1882 by Robert Koch. TB is caused by one of several mycobacterial species that belong to the Mycobacterium tuberculosis complex.

Mycobacterium tuberculosis is a fairly large, non-motile & rod-shaped bacterium that are 2-4 micrometer in length and 0.2-0.5 in width. It is an obligate aerobe, so in the classic case of tuberculosis, MTB complexes are always found in the well-aerated upper lobes of the lungs. The bacterium is a facultative intracellular parasite, usually of macrophages, and has a slow generation time, 15-20 hours, a physiological characteristic that may contribute to its virulence.

M. tuberculosis has a waxy coating on its cell surface primarily due to the presence of mycolic acid. This coating makes the cells impervious to Gram staining. Hence, Acid-fast stains such as Ziehl-Neelsen or fluorescent stains such as Auramine O are used to identify M. tuberculosis with a microscope.

Patients suffering from Microbiologically confirmed pulmonary TB (PTB) constitutes the most important source of infection. The infection occurs most commonly through droplet nuclei generated by coughing, sneezing etc., inhaled via the respiratory route. The chances of getting infected depend upon the duration, the frequency of exposure, load and virulence of TB bacilli and the immune status of an individual.

Primary Infection

Entry and establishment of bacilli in human body constitutes infection. It usually takes 6-8 weeks for the establishment and manifestation of infection. Infection is indicated by detection of release of interferon gamma by a positive reaction to a tuberculin skin test (Mantoux test) or Direct IGRA. Primary infection is an infection occurring for the first time in susceptible individuals who are exposed to tubercle bacilli. Droplet nuclei that are inhaled into the lungs, are so small (< 5μm) that they evade the muco-ciliary defences of the bronchi and lodge in the terminal bronchiole or alveoli of the lungs. Subsequently, the bacilli multiply and invade the hilar lymph nodes through the lymphatics. The subpleural lung lesion, lymphangitis and hilar adenopathy together constitute a “primary complex”. In most cases, the host’s immune defences overcome the primary infection, which generally passes unnoticed.

Secondary bacillary multiplication that occurs at the regional lymph nodes causes bacillaemia resulting in the implantation of seedlings of bacilli in different parts of the body, such as the apical & sub-apical areas of the lungs, the meninges & cerebral cortex, intervertebral discs, renal parenchyma and the epiphysial ends of long bones. In such environments, the bacilli continue to multiply as these environments favour their continued growth and multiplication. In a few cases, the infection may develop into progressive primary forms of TB disease such as meningitis and miliary TB. However, in majority of the cases, the multiplication of the bacilli is contained by the host defence mechanism.

Post-primary TB

Post-primary TB disease occurs after a latent period of many months or even years after the primary infection. Disease may occur either due to endogenous reactivation of dormant tubercle bacilli acquired from a primary infection or by exogenous re-infection. Post-primary TB disease usually affects the lungs, but can involve any part of the body except nails and hair.

Risk of infection

A smear positive pulmonary TB case in the general population may infect 10-15 other persons in a year and remain infectious for 2 to 3 years if left untreated.

Risk of developing disease

Tuberculosis is most commonly transmitted by inhalation of infected droplet nuclei which are discharged in the air when a patient with untreated TB coughs or sneezes. TB disease usually affects the lungs, but can involve any part of the body. Pulmonary TB which affects lungs is an infectious form of disease. Extra-pulmonary TB can affect the lymph nodes, pleura, bones and joints, the Genito-urinary tract, the nervous system (meningitis, tuberculoma), abdominal TB (intestines, mesentery, solid organs), skin, etc. All those who get infected do not necessarily develop TB disease. The life time risk of breaking down to disease among those infected with TB is 10–15%, which gets increased to 10% per year amongst those co-infected with HIV. Other determinants such as diabetes mellitus, smoking tobacco products, alcohol abuse and malnutrition also increase the risk of progression from infection to TB disease.

Magnitude of TB

India accounts for more than one fourth of the global TB burden i.e. 27 Lakh out of 1 crore new cases annually. In India, more than 40% of population is infected (prevalence of infection) with Mycobacterium tuberculosis. The table below shows the estimated figures for TB burden globally and for India provided by WHO for the year 2018.

Estimates of TB Burden (2018)	Global (Million)	India	% of Global
Incidence TB cases	10	2.69 Million	27%
Mortality of TB	1.2	440,000	31%
Incidence HIV TB	0.86	92,000	9%
Mortality of HIV-TB	0.25	9,700	4%
MDR-TB	0.5	130,000	24%
Children with TB	1.12	342,000	31%

Annual Risk of Tuberculosis Infection (ARTI)

It is defined as the proportion of individuals getting infected or re-infected with Mycobacterium tuberculosis over a period of one year. This depends upon the burden of infectious cases in the community, the duration and frequency of exposure to the source of infection (smear positive PTB cases), nutritional status, co-morbidities etc. The ARTI in effect reflects the overall infectious pool in the community. Currently, ARTI is not being used under the programme.

HIV co-infection among TB patients

As per the recently released, India HIV Estimates 2017 report, National adult (15–49 years) HIV prevalence in India is estimated at 0.22% (0.16% – 0.30%) in 2017 translating into 21.4 lakhs people living with HIV/AIDS.

In India it is estimated that 92,000 TB patients are living with HIV infection in 2018, which accounts to approximately 9% of the Global burden. Based on available country data, it is estimated that 3% of incident TB patients in India were HIV positive in 2017.

Tuberculosis is the most common opportunistic infection amongst HIV-infected individuals. It is a major cause of mortality among patients with HIV and poses a risk throughout the course of HIV disease, even after successful initiation of antiretroviral therapy (ART). In India 55-60% of AIDS cases reported had TB at any time in their life time, and TB is one of the leading causes of death in 'People living with HIV/AIDS' (PLHIV).

Impact of HIV on TB

The primary impact of HIV on TB is that the risk of developing TB becomes higher in patients with HIV. An HIV-infected person newly infected with TB has a 16-27 times higher chances of developing the disease than among patients infected with TB only. Amongst TB infected PLHIV, 3–10% of persons develop TB per year. Furthermore, HIV-infected TB patients suffer much higher mortality than HIV negative TB patients. Even if TB is successfully treated, recurrence of TB and long-term post-TB mortality among PLHIV is extremely high.

Impact of TB on HIV

In a TB patient infected with HIV, inflammatory response to TB bacilli increases HIV replication. As a result of the increase in number of viruses in the body, there is rapid progression of HIV infection. The viral load can increase by 6-7 folds. As a result, there is a rapid decline in CD4 count and patient starts developing symptoms of various opportunistic infections. Thus, the health of the patient who has dual infection deteriorates much more rapidly than with a single infection. Amongst the AIDS cases, TB is the most common opportunistic infection. The mortality due to TB in AIDS cases is also high.

Paediatric TB

Children in the first five years of their life are likely to suffer from serious and fatal forms of TB, more so, if not vaccinated with BCG. Globally, it is estimated that about 10 lakh children become ill with TB every year, 52% under 5 years of age and 2,33,000 deaths occur annually due to TB among children. It is estimated that 67 million children are infected with TB and therefore at risk of developing disease in the future. Moreover, 25,000 children develop multi-drug resistant TB every year globally. Estimated 2.2 lakh children are affected with TB in India each year. Reliable data on the incidence and prevalence of the disease is not available due to the difficulties in diagnosis of pediatric TB under field conditions.

Drug-resistant tuberculosis (DR-TB)

Drug resistant TB is defined as TB disease where the bacilli is resistance to one or more anti TB drugs. Inadequate or poorly administered treatment regimen (mono-therapy, irregular consumption, frequent interruptions or trial therapy) in taking treatment for TB is the most common cause of acquiring drug resistance.

Multi Drug Resistance (MDR-TB) is defined as tuberculosis disease where the bacilli are resistant at-least to isoniazid (H) and rifampicin (R), with or without resistance to other first line drugs.

As per the recently concluded drug resistance survey data in India, MDR-TB amongst new cases are estimated at 2.84% and amongst re-treatment cases at 11.6%. Extensively Drug Resistant TB (XDR–TB) is a subset of MDR-TB where the bacilli, in addition to being resistant to R and H, are also resistant to fluoroquinolones and any one of the second-line injectable drugs (namely Kanamycin, Capreomycin or Amikacin).

Findings of National Drug Resistance Survey (NDRS) India - 2014-16

DST Pattern	NEW TB case	Previously TB cases	ALL TB cases
Total DST results available	3065	1893	4958
Susceptible to all drugs	2374(77.46 %) (75.93 – 78.92 %)	1196(63.18 %) (60.96 – 65.36 %)	3570(72.01 %) (70.73 -73.25 %)
Any drugresistance	691(22.54 %) (21.10 - 24.1 %)	697(36.82 %) (34.64 – 39.04 %)	1388(28.00 %) (26.77 – 29.29 %)
MDR	87(2.84%) (2.28 – 3.50 %)	220(11.62 %) (10.21 – 13.15 %)	307(6.19%) (5.54 – 6.90 %)

- Any drug resistance among new patients is 22.54%, among previously treated (PT) patients is 36.82% and among all patients 28.02%;
- Any H resistance (16% in all with 11.6% in new and 25.09% in previously treated patients) being the driver for R resistance;
- Almost all RR-TB patients are resistant to H with/without other first or second-line drugs;
- MDR-TB is 6.19% in all patients (2.84% among new and 11.6% among previously treated patients);
- Among MDR-TB patients, additional resistance to other first-line drugs is high at 74.3%. The drug specific resistance in combination with MDR-TB includes:
  - any Streptomycin resistance – 70% in new and 59.09% in PT;
  - any E resistance - 45.98% in new and 46.36% in PT; and
  - any Z resistance – 31.03% in new and 20.45% in PT.
- State level and cluster-wise variations clearly indicate that although the national DR TB situation is well within the range of previous state level surveys, there exist focal epidemics of DR TB in some states.
- Programmatically, MDR-TB (at-least to H & R), Rifampicin resistance (RR-TB) and XDR-TB (at least H, R, second-line injectable [SLI] and fluoroquinolones [FQ]) received priority. As facilities for detecting other varieties of resistance became increasingly available, making available regimens for their treatment also became a programmatic priority.

While prevention of development of drug resistance is of paramount importance for ending TB, early detection and immediate initiation of appropriate regimen and completion of treatment are keys to interrupt on-going transmission, to prevent death and reduce chances of sequelae post-treatment. The programme has so far been able to successfully treat 46% of the cohorts of patients initiated on treatment 30-33 months ago. However, treatment outcomes vary from state-to-state. While few states were able to achieve more than 70% treatment success rate among the diagnosed MDR/RR-TB patients, others could achieve less than 40%, suggesting the variability of the health system to deliver treatment, care and cure. Main reasons attributed for the attrition were death and lost to follow-up (LTFU) during treatment. In India, the great concern is the potential threat of drug resistant TB (DR-TB) with the existing unregulated availability and injudicious use of first and second-line anti-TB drugs in the country.

Socio-economic impact of TB

The estimated loss in economic well-being from TB in India amounted to US$ 23.7 billion in 2006. Mortality accounts for the majority of this burden reflecting the greater number of life-years lost due to premature deaths. The economic burden of TB has fallen by US$ 2.0 billion, or 7.8%, in absolute terms since 1990. On a per capita basis, the economic burden of TB has fallen by 31.1% from US$ 29.9 in 1990 to US$ 20.6 in 2006.

Most of the improvement since the mid-1990s has come through reduced mortality, due to the implementation of RNTCP. Morbidity has also recorded a large improvement reflecting the decrease in prevalence. However, TB remains a significant cause of loss of health, life and economic well-being of India's population.

TB primarily affects people in their productive age group; with important socio-economic consequences for the household. Almost 70% of TB patients are aged between 15 and 54 years. The disease is more common amongst the poorest and the marginalized sections of the community. Whilst two-thirds of cases are male, TB takes a disproportionately larger toll among young females, with more than 50% of cases occurring amongst females less than 34 years of age. In addition, there is a devastating social cost with an estimate of more than 300,000 children forced to leave school because their parents have TB, and more than 100,000 women with TB rejected by their families. Previous studies suggest that on an average, 3-4 months of work-time is lost as a result of TB, resulting in an average potential loss of 20-30% of the annual household income. This leads to increased debt burden, particularly for the poor and marginalized sections (tribal, migrant and urban slums) of the population.

Evolution of Revised National Tuberculosis Control Programme

The National TB Institute (NTI), Bengaluru, was established in 1959 to devise strategies for TB control in India. A scientifically logical and economically feasible national tuberculosis control programme was formulated during 1959 to 1962 at NTI, Bengaluru. The National Tuberculosis Control Programme of India was initiated in 1962 and was originally designed for domiciliary treatment using self-administered standard drug regimens.

The NTP had created an extensive infrastructure for TB control with a network of more than 446 district TB centres, 330 TB clinics and more than 47,600 TB beds. The NTP had also raised the awareness of TB and TB treatment facilities and had succeeded in placing more than 1.3 million patients on treatment annually. Despite the NTP being in existence since 1962, no appreciable change in epidemiological situation of TB in the country had been observed. The HIV-AIDS epidemic and the spread of drug resistant TB were threatening to further worsen the situation.

In view of this, in 1992, GOI, with WHO and SIDA (Swedish International Development Cooperation Agency) reviewed the TB situation and the performance of the NTP. The observations revealed that the NTP, though technically sound, suffered from managerial weakness, inadequate funding, an over reliance on X-ray for diagnosis had frequent interrupted supplies of drugs, and low rates of treatment completion. The Government decided to give a new thrust to TB control activities by revitalising the NTP, with assistance from International agencies.

In 1993, The Revised National TB Control Programme was piloted in a population of 24 Lakh in five states (Delhi, Gujarat, Maharashtra, West Bengal and Kerala). This was later expanded to cover 13 million people by 1995 and 2 crores by 1996.

In 1997, the RNTCP was launched as a national programme with a plan to scale up in a phased manner. The RNTCP thus formulated, adopted the internationally recommend Directly Observed Treatment Short-course (DOTS) strategy as the most systematic and cost-effective approach to revitalise the TB control programme in India.

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Directly Observed Treatment Short course (DOTS) strategy

DOTS is a systematic strategy to control TB disease. This has the following 5 components:

- Political and administrative commitment
- Good quality diagnosis, primarily by sputum smear microscopy and other microbiological tools
- Uninterrupted supply of quality drugs
- Directly observed treatment (DOT)
- Systematic monitoring and accountability

Political and administrative commitment: The government's commitment is measured in terms of continued financial assistance, human resources and administrative support. This priority must be reflected at the National, State, District and local levels.

Quality assured diagnosis through sputum microscopy and other microbiological tools: Under RNTCP, sputum microscopy and other microbiological tools are the tools for detection of infectious TB cases, facilitating categorization of treatment and an objective method for monitoring the response to treatment. Quality assured laboratories are established for this purpose.

Uninterrupted supply of quality drugs: The policy of procurement and distribution of drugs ensures sufficient quality assured anti-TB drugs available at all levels. The unique feature of RNTCP is the use of strips of fixed dose combination of anti TB drugs, as per weight bands, for the entire course of treatment.

Directly observed treatment (DOT): DOT is one of the key elements of the DOTS strategy. In DOT, an observer (health worker or trained community volunteer, or trained family member for selected patients) watches and supports the patient intaking their drugs. Direct observation ensures treatment adherence with the right drugs, in right doses for the right duration.

Systematic monitoring and accountability: A standardized recording and reporting structure which allows for rigorous monitoring and evaluation of the outcome of every patient diagnosed put under treatment is essential. In RNTCP, the key indicators like TB Notification rate and treatment success rates are monitored regularly at every level of the health system. The uniqueness of the programme is that it shifts the responsibility and accountability of cure from the patient to the health system.

Previously the objectives of the RNTCP were to achieve at least 85 percent cure rate among the new smear positive cases initiated on treatment, and thereafter a case detection rate of at least 70 percent of such cases. The RNTCP was built on the infrastructure and systems built through NTP. Major additions to the RNTCP, over and above the structures established under the NTP was the establishment of a sub-district supervisory unit, known as TB unit, with dedicated RNTCP supervisors (STS, STLS) posted, and decentralization of both diagnostic and treatment services, with treatment given under the support of DOT providers. The entire country was covered by March 2006. The programme has made rapid strides ever since its implementation and consistently been achieving global benchmarks of case detection and treatment success rates since 2007.

The widespread implementation of the DOTS strategy has proved to be an effective tool in controlling TB on a mass scale and practised in over 200 countries. The prime task for the next decade was to achieve the Millennium Development Goals (MDGS) and related STOP TB Partnership targets for TB control. The target under MDG for tuberculosis is to halt and begin reversal of incidence of tuberculosis, malaria and other major diseases by 2015.The indicators were to reduce the prevalence and death rates by 50% between 1990 and 2015.

Meeting these targets required a coherent control strategy. The WHO released STOP TB Strategy in 2006 with six principal components to realize the global TB related MDGs by 2015.These were pursuing high quality DOTS expansion and enhancements; Addressing TB, HIV, MDR-TB and other challenges; Contributing to health system strengthening; Engaging all care providers; Empowering patients and communities; and Enabling promoting research.

India adopted the components of STOP TB strategy and strived to achieve targets under it. National AIDS Control Programme (NACP) and RNTCP have developed "National framework of joint TB/HIV collaborative activities" in 2007 which were revised in February 2008 to redefine the scope of TB/HIV collaborative activities being implemented in the country. Programmatic management of drug resistant (DR)TB services began in 2007 and national coverage has been achieved in March 2013. Scope of engagement of all care providers was expanded with revisions in schemes for involvement of private providers and NGOs in 2008 and Global Fund supported engagement of professional associations like Indian Medical Association (IMA) and Catholic Bishop Conference of India (CBCI). Task force mechanisms were established to engage medical colleges to support patient care, training and research.

Emboldened by its achievements, the programme in 12th five-year plan (2012-17) had articulated National Strategic Plan with a vision of TB free India. The goal of the NSP is to achieve universal access to quality TB diagnosis and treatment for all TB patients in the community.

The objectives of the National Strategic Plan are

1. To achieve 90% notification rate for all cases
2. To achieve 90% success rate for all new and 85% for retreatment cases
3. To significantly improve the successful outcomes of treatment of DR -TB cases

4. To achieve decreased morbidity and mortality of HIV associated TB
5. To improve outcomes of TB care in the private sector

To achieve these objectives, RNTCP further strengthened and improved through quality of basic DOTS services aligning sub-district level management unit with health system under National Health Mission (NHM), deploying improved rapid diagnostic tools in the field level, increasing efforts to engage all health care providers, strengthening urban TB control, expanding diagnosis and treatment of DR-TB, improving communication, outreach and social mobilization and promoting research for development and implementation of improved tools and strategies.

A Government order issued by GOI on 7th May 2012 mandates all healthcare providers to notify every TB case diagnosed and/or treated, to local authorities.

To support TB notification and strengthen TB surveillance in general, a case base web-based TB notification system-NIKSHAY was established to provide platform for notification from both public and private sector, decrease lead time of data transmission and increase use of information for programme management for betterment of care of delivery of services at local level. Amendment in this Government order was made on 21st July 2015 for including public health action. Ministry of Health and Family Welfare further notified this in the Gazette of India on 19th March 2018.

Ministry of Health and Family Welfare has notified in the Gazette of India, for prohibiting the import of sero-diagnostic kits for TB and the manufacture, sale, distribution and use of such kits for TB on 7th June 2012.

RNTCP, World Health Organization and other stakeholders jointly prepared standards for TB care in India (STCI) in 2014, which lays down uniform standards for TB care.

National TB Elimination Programme (NTEP)

Government of India has committed to end TB by 2025, five years ahead of the global target under Sustainable Development Goals. The Ministry of Health & Family Welfare is implementing the National Strategic Plan (NSP) for Tuberculosis Elimination (2017-2025) with commensurate resources to rapidly decline TB incidence and mortality in India. The NSP aims to seek the attention of all stakeholders to the most important interventions or activities that will bring about significant changes in the incidence, prevalence and mortality of TB. Key activities include active TB case finding, use of newer and shorter regimen, private sector engagement, financial/nutritional support to TB patients; IT enabled surveillance, preventive and awareness measures. In view of End TB targets, the programme has been renamed from 'Revised National Tuberculosis Control Program (RNTCP) to 'National Tuberculosis Elimination Program (NTEP)

Standards for TB Care in India

The vision of NTEP is that the people suffering from TB receive the highest standards of care and support from all healthcare providers of their choice. It spelt out in the National Strategic Plan (2012-17) to extend the umbrella of quality TB care and control to include those provide by private sector.

The private sector holds a factual predominance of health care service delivery in India. There is very little information about TB patients from the private sector available to the programme and little is known about their quality of treatment, including treatment outcomes. The need for quality and standards for TB care is made particularly acute where a large unorganized private sector accounts for almost half of the TB care delivered in India.

Thus, it was felt essential to develop and disseminate the standards for TB care that is particularly relevant in India context, acceptable to the medical fraternity in both the public and private sector in India. Also, the availability of new diagnostic tools and strategies for early TB diagnosis, emerging evidences on existing regimens and newer regimens and the need for better patient support strategies including addressing social inclusiveness necessitated the development of Standards for TB care in India.

The standards in STCI differ from existing guidelines in that the standards present what should be done whereas guidelines describe how the action is to be accomplished. These standards represent the first what is expected from the Indian healthcare system. It is expected that the standards laid down in STCI are clear and will be accessible to all providers as an easy reference.

Twenty-six standards developed after a National Workshop with support from various public health administrators, programme managers, representative from various professional association (IMA, API, College of Physicians Association of India, IAP, FOGCI, etc) academicians and specialists from public and private sectors (pulmonologists, physicians, surgeons, paediatricians, gynaecologists, orthopaedic surgeons, microbiologists, public health specialists etc.) donors, technical and implementation partners and pharmaceutical companies and pharmacists. There are six standards for diagnosis (standard 1 to 6), five for treatment (standard 7 to 11), nine for public health (standard 12 to 20) and six for social inclusion (standard 21 to 26).

END TB STRATEGY- A holistic approach to end TB

Ending the TB epidemic is a SDG target that requires implementing a mix of biomedical, public health and socioeconomic interventions along with research and innovation.

The End TB Strategy encompasses a package of interventions that can be fully adapted at country level. It has ten components organized under three pillars and four underlying principles.

Implementing the pillars and components of the End TB Strategy while adhering to its underlying principles requires intensified action from and beyond the ministries of health, in close collaboration with all stakeholders including other ministries, communities, civil society and the private sector.

END TB STRATEGY

VISION	A WORLD FREE OF TB Zero deaths, disease and suffering due to TB			
GOAL	END THE GLOBAL TB EPIDEMIC			
INDICATORS	Milestones		Targets	
	2020	2025	SDG 2030	End TB 2035
Reduction innumber of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20%	50%	80%	90%
TB-affected family facing catastrophic costs due to TB(%)	0	0	0	0

PRINCIPLES

A. Government stewardship and accountability, with monitoring and evaluation
B. Strong coalition with civil society organizations and communities
C. Protection and promotion of human rights, ethics and equity
D. Adaptation of strategy and targets at country level, with global collaboration

PILLARS AND COMPONENTS

Integrated, patient-centred care and prevention

A. Early diagnosis of tuberculosis including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
B. Treatment of all people with tuberculosis including drug-resistant tuberculosis, and patient support
C. Collaborative tuberculosis/HIV activities, and management of co-morbidities
D. Preventive treatment of persons at high risk, and vaccination against tuberculosis

Bold policies and supportive systems

A. Political commitment with adequate resources for tuberculosis care and prevention
B. Engagement of communities, civil society organizations, and public and private care providers
C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
D. Social protection, poverty alleviation and actions on other determinants of tuberculosis

Intensified research and innovation

A. Discovery, development and rapid uptake of new tools, interventions and strategies
B. Research to optimize implementation and impact, and promote innovations

THE SUSTAINABLE DEVELOPMENT GOAL

The Sustainable Development Goals (SDGs), are a universal call to action to end poverty, protect the planet and ensure that all people enjoy peace and prosperity. The consolidated goal for health is SDG 3, 2015 which is defined as "Ensure healthy lives and promote well-being for all at all ages". Thirteen targets have been set for this goal, and one of these targets is 'End TB strategy'.

- **Target 3.3, explicitly mentions TB**
  "By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases". Ending epidemics is also now a prominent element of global health strategies developed by WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS) for the post- 2015 era, including the End TB Strategy.

National Strategic Plan 2017-25

The National Strategic Plan (NSP) sets out the strategic direction and key initiatives that the Ministry of Health and Family Welfare will undertake from 2017 to 2025 for working towards achieving the goals of eliminating TB by 2025. We have seen excellent commitment and the progress achieved through the previous NSP period (2012-17), yet much more is required to be done to accelerate the march towards a TB free India.

India's achievements in TB control over the past decade are remarkable. More than 90 million people have been tested, more than 19 million TB patients detected and treated, and millions of lives saved by the RNTCP's efforts.. The country achieved complete geographic coverage for management of drug resistant TB and more than 100,000 MDR TB cases were diagnosed and treated.

In the NSP 2017-2025 we are moving towards rapidly ending the epidemic of TB in India. This necessitates a paradigm shift in approach and strategy. This NSP addresses requirements for achieving the SDG and End TB targets for India and is driven by the 'DETECT-TREAT-PREVENT-BUILD' approach. The focus is on early diagnosis of all the TB patients, prompt treatment with the right drugs and regimens along with suitable patient support systems including financial and nutritional support. This is supplemented by prevention strategies including active case finding, contact tracing and LTBI management in high risk population, and airborne infection control. There is an urgent need for management and financial system upgradation for the TB control programme at all the levels and these issues have been addressed in the said NSP.

This NSP is a framework to provide guidance for the activities of stakeholders including the National and State Governments, Development Partners, Civil Society Organizations, International Agencies, Research Institutions, Private Sector, and many others whose work is relevant to TB elimination in India. The NSP 2017-2025 is a three-year costed plan and an eight-year strategy document. It provides goals and strategies for the country's response to the disease during the period 2017-2025 and aims to direct the attention of all stakeholders to the most important interventions or activities that the programme believes will bring about significant changes in the incidence, prevalence and mortality of TB. These strategies and interventions are in addition to the processes and activities already ongoing in the country.

Vision, Goals and Targets of NSP

The NSP proposes bold strategies with commensurate resources to rapidly decline TB incidence and mortality in India by 2025, five years ahead of the global End TB targets and Sustainable Development Goals to attain the vision of a TB-free India.

VISION: TB-Free India with zero deaths, disease and poverty due to TB

GOAL: To achieve a rapid decline in burden of TB, morbidity and mortality while working towards elimination of TB in India by 2025.

Results Framework (impact and outcome indicators and targets)

IMPACT INDICATORS	Baseline	Target		
	2015	2020	2023	2025
To reduce estimated TB Incidence rate (per 100,000 population)	217 (112-355)	142 (76-255)	77 (49-185)	44 (36-158)
To reduce estimated TB prevalence (per100,000 population)	320 (280-380)	170 (159-217)	90 (81-125)	65 (56-93)
To reduce estimated mortality due to TB (per 100,000 population)	32 (29-35)	15 (13-16)	6 (5-7)	3 (3-4)
To ensure no family should suffer catastrophic cost due to TB	35%	0%	0%	0%
OUTCOME INDICATORS				
Total TB patient notification (in millions)	1.74	3.6	2.7	2
Total patient private providers notification (in millions)	0.19	2	1.5	1.2
MDR/RR TB patients notified	28,096	92,000	69,000	55,000
Proportion of notified TB patients offered DST	25%	80%	98%	100%
Proportion of notified patients initiated on treatment	90%	95%	95%	95%
Treatment success rate among notified DSTB	75%	90%	92%	92%
Treatment success rate among notified DRTB	46%	65%	73%	75%
Proportion of identified targeted key affected population undergoing active case finding	0%	100%	100%	100%
Proportion of notified TB patients receiving financial support through Direct Benefit Transfers (DBT)	0%	80%	90%	90%
Proportion of identified/eligible individuals for preventive therapy / LTBIs - initiated on treatment	10%	60%	90%	95%

Health System structure & functions for delivery of TB care

For a patient centred delivery of TB care, a systematic approach is required involving both public and private sectors.

Delivery of TB care in the public sector

The organisation at the national level consists of the Union Ministry of Health and Family welfare (MoHFW). In each State, the organisation is under the State Department of Health and Family Welfare that is headed by a State Minister and with a Secretariat under the charge of the Secretary/ Commissioner (Health and Family Welfare).

a) **In 2005, National Rural Health Mission (NRHM)** was launched to provide accessible, affordable, accountable, effective and reliable primary health care facilities, to the rural population, especially vulnerable groups. In addition, the National Urban Health Mission (NUHM) was also launched to further strengthen urban health structure and both NUHM and NRHM have been clubbed together under National Health Mission (NHM) from 2013. The vision of NHM is "Attainment of Universal Access to Equitable, Affordable and Quality health care services, accountable and responsive to people's needs, with effective inter-sectoral convergent action to address the wider social determinants of health".

b) **NHM** further aims to provide support to the existing national programmes of health and family welfare including RCH-II, malaria, blindness control, iodine deficiency, filariasis, kala- azar, tuberculosis, and leprosy and for integrated disease surveillance

c) **NTEP** is one of the components under the National Health Mission which is a flagship scheme under Govt. of India. The MoHFW follows equity-based approach to allocate funds under programme to various States. The overall allocation is made on the basis of population of the states, disease burden and socio-economic status. The financial management procedures for RNTCP are well established and administered by the Finance Cell of the Central Tuberculosis Division (CTD). These procedures are documented in manuals and guidelines available on the program's website (www.tbcindia.gov.in).

   i. **Institutional arrangements:** Overall responsibility for financial management of the program is with the, Ministry of Health & Family Welfare (DGHS) a part of the National Health Mission of the MoHFW. At state level these are through state TB cell and at district level through district TB cell.

   ii. **Budget and release of funds:** Program expenditures are budgeted in the Demand for Grants of the MoHFW under the Disease flexi-pool funding arrangement under two separate budget lines for Externally Aided Component (EAC) and General Component (GC).

   iii. **Funds flow:** Funds flow for the program will remain within the existing financial management systems of MoHFW, which operates through the centralized Pay and Accounts Office. Funds are being released to state in 2-3 instalments. All the states are required to submit the annual audit report to CTD by 30th September.

NTEP Organogram

NTEP structure comprises of five levels: National, State, district, sub-district and peripheral health institution level.

National Level

Central TB Division (CTD) manages the National TB Control Programme for the entire country at the central level under AS&DG (RNTCP & NACO) through a National Programme manager, Deputy Director General TB (DDG TB). The financial and administrative control of the programme is managed by the Joint Secretary from the administrative arm of the MoHFW.

The CTD is supported by a National TB Institute (NTI) Bengaluru, six National Reference Laboratories (NRL) including NTI, National Institute for Research in Tuberculosis (NIRT), Chennai, National Institute of Tuberculosis and Respiratory Diseases (NITRD), Delhi, National Japanese Leprosy Mission for Asia (JALMA) Institute for Leprosy and other mycobacterial diseases, Agra, Regional Medical Research Centre, Bhubaneshwar and -Bhopal Memorial Hospital & Research Centre – (BMHRC) , Bhopal. The CTD is also supported by National Task Force for collaboration of Medical Colleges activities in country through ZTF/STF.

Various committees of experts to guide the programme at different levels on technical & policy matters are there supporting Central TB Division.

State Level

The States have total ownership and accountability for the TB control in their state. State Health Society or its equivalent under National Health Mission of the state manages the TB Control Programme. A full-time State Tuberculosis Officer (STO), trained at national level and based at the State TB Cell (STC), is responsible for planning, training, supervising and monitoring the programme in all the districts of their respective states. STO is administratively accountable to the State Government, technically follows the instructions of the CTD, and coordinates with CTD and the districts and is assisted by other technical & secretarial staff.

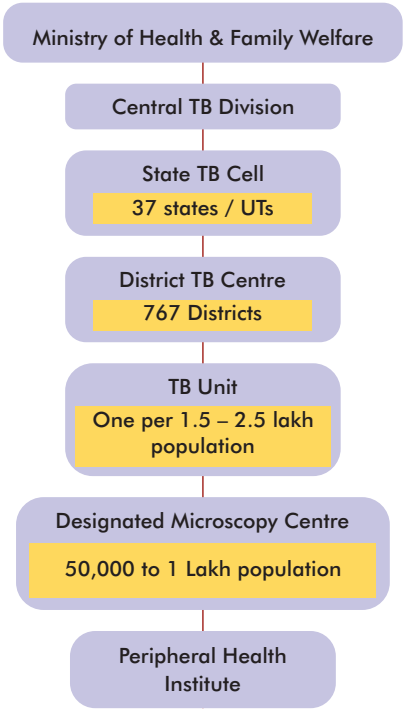
State TB cell is being supported by State TB Training and Demonstration Centre (STDC) in many states through its three units – a training unit, Supervision and monitoring unit and an Intermediate Reference Laboratory (IRL) supporting an effective Quality Assurance system of the Sputum smear microscopy network and laboratory services for PMDT (molecular DR testing and C&DST) in the State. Operational Research is also a component of STDC.

Each state also has one fully operational State Drug Store (SDS) for each 5 crore of population. It is responsible for effective management of medicines and other logistics and ensuring uninterrupted supply of good quality 1st & 2nd line anti-TB medicines for adults and paediatric population.

Organization structure

Supporting Facilities

- National Institutes (3)
- National Reference Laboratories (6)
- Intermediate Reference Laboratories **(29)**
- State TB Training and Demonstration Centre (26)
- Culture and DST Laboratories (42)
- Nodal DR-TB Centre (154)
- CBNAAT Laboratories (1180)



District Level

The key level for the management of primary health care services is the district. The Chief District Health Officer (CDHO) / Chief District Medical Officer (CDMO) / Civil Surgeon or an equivalent functionary in the district is responsible for all medical and public health activities including control of TB. The District Tuberculosis Centre (DTC) is the nodal point for TB control activities in the district. A full-time District Tuberculosis Officer (DTO), trained at national level & based at the DTC, is responsible for planning, training, supervising and monitoring the programme in the district. DTO is assisted by other technical & secretarial staff. The primary role of the DTC is a managerial one.

Sub-District Level (Tuberculosis Unit Level)

Integrating the TB control programme with the health system increases effectiveness and efficiency of TB care and control. India's TB control programme has been mainstreamed efficiently with National Health Mission (NHM).

A major organizational change in NTEP is the creation of a sub-district level (Tuberculosis Unit - TU). The TU is the nodal point for TB control activities in the sub-district. TUs are based mainly in NHM health blocks with the overall aim to align with NHM Block Programme Management Unit (BPMU) for optimum resource utilization and appropriate monitoring. In urban areas the TUs have been created based on a population of 1 per 2,00,000 (range 1.5 – 2.5 lakh) for rural and urban population and 1 per 1,00,000 (0.75 – 1.25 lakh) population in hilly/tribal/difficult areas. The Tuberculosis unit (TU) consists of a designated Medical Officer-Tuberculosis Control (MO-TC), as well as one full-time supervisory staff - Senior Treatment Supervisor (STS). However, One Senior TB Laboratory Supervisor (STLS) will continue to be in 5 lakh population (one per 2.5 lakh population for tribal/hilly/difficult areas). There is a provision of additional STS if more than 300 TB cases are registered in public sector annually in a TU; additional STS if more than 50 private

health establishments are registered in NIKSHAY in a TU and more than 200 TB patients are notified from these private health establishments annually in a TU.

The Block Medical Officer also functions as a Medical Officer TB Control (MO-TC). For the urban TB Units, a medical officer from the health facility where TU is located should be designated, in coordination with CM&HO/DHO to function as a MO-TC. All MO-TCs should be trained in NTEP at a state level institution. MO-TC has the overall responsibility of management of TB Control Programme at the TU and is expected to undertake supervisory visits for seven days in a month. The team of STS and STLS are under the administrative supervision of the MO-TC and the DTO. The TU will have one Microscopy Centre for every 100,000 population (50,000 in tribal, desert, remote and hilly regions) referred to as the Designated Microscopy Centre (DMC However, for complete geographic coverage National programme envisages to expand sputum smear microscopy services at PHC level.). Microscopy Centres may also be established beyond population norms in Medical Colleges, Corporate hospitals, ESIC, Railways, NGOs, private hospitals, etc.

Peripheral Health Institutions (PHIs)

For the purpose of NTEP, a PHI is a health facility which is manned by at least a medical officer. At this level, there are dispensaries, PHCs, CHCs, referral hospitals, major hospitals, specialty clinics or hospitals (including other health facilities), TB hospitals, ART Centres and Medical colleges within the respective district. All health facilities in the private and NGO sectors participating in NTEP are also considered as PHIs by the programme. Some of these PHIs also function as DMCs. Peripheral health institutions undertake tuberculosis case-finding and treatment activities as a part of the general health services. In situations where more than one MO is posted in any of the peripheral health centres, one of them may be identified and entrusted with the responsibilities of the NTEP. There is 1 TB Health Visitor (TBHV) per one lakh urban population to support the urban TB control activities.

TB Laboratory Services

The services of the laboratory are utilized for diagnosing TB & DR-TB cases and for monitoring of treatment of these patients. The Laboratory network under NTEP is a 3-tier system for provision of diagnostic services and maintaining its quality.

A. **The peripheral laboratories** are situated in the public sector like the dispensaries, PHCs, CHCs, referral hospitals, major hospitals, specialty clinics / other sector hospitals / TB hospitals / Medical colleges and in the private/NGO sectors. For establishment of microscopy centre in a lab, it must have adequate physical infrastructure, Binocular microscope and a trained LT. These laboratories are covered under quality assurance mechanisms

I. Some of the labs not having facility for sputum microscopy, function as a sputum collection centres, and such facilities are also established in areas such as the tribal, hilly, desert and difficult to reach areas of the country for improving the access to diagnostic services.

ii. In addition, large hospitals and medical colleges have facilities of digital X-Ray, rapid molecular test (Cartridge based nucleic acid amplification test -CBNAAT & Line Probe Assay - LPA), Fine Needle Aspiration Cytology (FNAC), histopathology, and culture & DST for diagnostic services of TB.

B. **At the state level** a nodal laboratory is designated as Intermediate reference laboratory (IRL) which is usually situated in the State TB Training and Demonstration Centre (STDC) /

medical college/ public health laboratory. The main functions of IRLs are monitoring of laboratory services across the state and maintenance of its quality through external quality assurance. There are 27 IRLs with facilities for culture & DST using Phenotypic (Solid – LJ & Liquid Culture – MGIT) and Genotypic technology (LPA & CBNAAT).

CBNAAT sites

In addition to the culture DST laboratories, CBNAAT centres are also established to diagnose Rifampicin resistance among all TB patients (Universal DST). Usually these are established in DTCs, TB units and Medical Colleges. The country is in the process of expanding CBNAAT site network. They also serve to diagnose TB among presumptive TB cases from key population.

DRTB Centres

DRTB Centres are specialised centres for clinical management of drug resistant TB. At state/regional/division level, there are Nodal DRTB Centres (NDRTBC), to manage seriously ill DRTB cases, DRTB with extensive resistance and DRTB cases to be treated with regimes containing new drugs (Bedaquiline and Delamanid).

At the district level, there are district DRTB Centres (DDRTBC), to manage DRTB cases with MDRTB, and H mono/poly resistance. These centres will function under the guidance of NDRTBCs.

C. **At the central level** there are six designated National Reference Laboratories (NRLs) namely National Tuberculosis Institute, Bengaluru, National Institute for Research in Tuberculosis (NIRT), Chennai, National Institute of Tuberculosis and Respiratory Diseases (NITRD), Delhi, National JALMA Institute, Agra, Regional Medical Research Centre, Bhubaneshwar and Bhopal Memorial Hospital & Research Centre (BMHRC), Bhopal. NIRT Chennai is also a Supra National Reference Lab (SNRL) for World Health Organization (WHO) for the South East Asia Region. NTI is a WHO Collaborating Centre for Training, while NITRD is WHO centre of excellence in TB laboratory services. The NRLs are mainly responsible for External Quality Assurance of Lab network, drug resistance surveillance, training and research.

Delivery of TB care services in the private sector

The private sector referred to in this section is everything outside the ambit of the government run public health initiatives. The private sector in India varies widely in its size, nature of service delivery and the socio-economic groups served. It consists of a wide range of providers from individual medical practitioners of many different systems of medicine, including allopathic as well as Indian Systems of Medicine and Homeopathy, paramedics and even traditional healers who possess no formal training, private hospitals and nursing homes, NGO run hospitals, and corporate sector health care institutions.

The private sector holds a factual predominance of health care service delivery in India. As per National Sample Survey Organization report of 71st round of survey, more than 70% of patients seek care in private clinics or hospitals. Delays in diagnosis, over-diagnosis of TB due to an over-dependence on X-rays, the use of multiple non-standard regimens for inappropriate durations, the lack of a mechanism to ensure the full course of treatment and to record treatment outcomes are some issues of concern in the private sector. Similar problems in varying degrees are encountered in other health sectors as well.

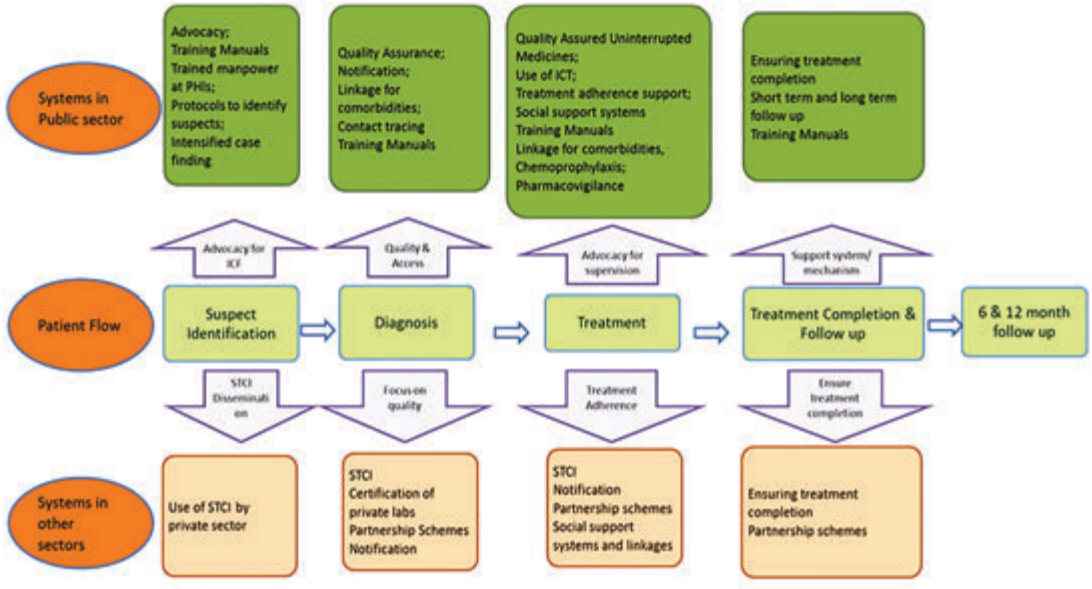
The strategic vision of NTEP is to lay down guidelines and norms for TB care in country. The underlying principle is for NTEP to extend public services to privately-managed patients.

Standards for TB care in India, mandatory TB notification, NIKSHAY, ban on Serodiagnostics and amendments in H1 schedule etc, are among the tools to improve TB care services in private sector. Regulatory tools, however, are limited, and partnership is preferred. Programme staff should understand that NTEP needs private providers more than private providers need the NTEP to achieve TB elimination by providing a patient centric care.

Other approaches include an expanded acceptance by NTEP of internationally approved diagnostic and treatment protocols, reliance on market forces rather than normative exhortation, increased use of accreditation and contracting. Further outreach to private laboratories, increased control of TB drugs, and innovative use of information and communication technologies for TB notification and treatment adherence monitoring. It is important to recognize that partnerships come in a wide variety of shapes and sizes, and operate at all levels, from local to global.

Model of care envisioned for delivery of services in continuum of care of TB patients from being a presumptive TB to the diagnosis, treatment and final treatment outcome in public and private sector is depicted below. It also shows what systems are in place for ensuring the various aspects of patient care in the public sector in the upper half and the other sectors in the lower half. All these systems ensure quality of services being provided to the patients irrespective of the place where the patient seeks care.

Model of Care



Work exercises

Q1. District X has a population of 20 Lakh, with 5 lakhs population residing in hilly tribal areas.

Q2. What is the number of TUs and DMCs that the district is expected to have in place?

Q3. What are the key pillars of END TB Strategy?

Q4. Discuss the organogram of NTEP

MODULE 2

DIAGNOSIS OF TB AND QUALITY ASSURANCE

Learning Objectives

In this chapter the participants will learn about the following:

Section A: Overview of Diagnostics

a. Symptoms of tuberculosis
b. Presumptive TB Patient
c. Screening for TB symptoms
d. Active Case finding from key population
e. Process of Diagnosis
f. Collection of Biological specimens
    I. Tasks to be performed before, during & after collection of sputum
    ii. Use of appropriate form
g. Transportation of Biological specimen
    I. For smear microscopy from collection centres
    ii. For Culture and DST from DMC/DTC/ CBNAAT sites
h. Diagnostic Tools
I. Sputum smear examination (ZN/ FM staining procedure) Rapid Molecular techniques: NAAT (CBNAAT)/ TruNAAT), LPA
    j. Universal Drug Susceptibility Testing
k. Documentation related to diagnostic services
    I. Referral slip
    ii. NTEP Request form for examination of biological specimen for TB
    iii. TB Laboratory register
    iv. TB Notification register
    v. NTEP Laboratory register for culture, CBNAAT and drug susceptibility testing

Section B: External Quality Assurance of Diagnostic services

Introduction

Pulmonary tuberculosis, microbiologically confirmed by Sputum Smear Microscopy, WHO endorsed rapid molecular tests (WRD) or culture, is the most common and infectious form of tuberculosis and forms the major source of infection in the community. Every sputum smear positive patient has the potential to spread infection to 10 – 15 persons annually, if untreated. From the public health point of view, it is of utmost importance to detect and treat all forms of TB as early as possible, to cut the chain of transmission of disease in the community.

Diagnostic services for all forms of tuberculosis such as Extra-Pulmonary tuberculosis, Paediatric TB, HIV-TB and Drug Resistant TB are available under programme.

Sputum Smear microscopy is the primary tool which is reliable, inexpensive, easily accessible and rapid method of diagnosing PTB, where in the bacilli are demonstrated in the sputum specimen of a patient suffering from PTB. Chest X-ray is both a screening and a supportive tool for the diagnosis of smear negative PTB. Solid (LJ) and Liquid Culture (MGIT) methodologies and molecular based diagnostic technologies including Nucleic Acid Amplification Test (CBNAAT/ Truenat), Line Probe Assay etc., are available under the programme.

Definitions:

Presumptive Pulmonary TB refers to a person with any of the symptoms and signs suggestive of TB, including: cough for 2 weeks or more, fever for 2 weeks or more, significant weight loss, haemoptysis, any abnormality in chest radiograph.

Note: *In addition, contacts of microbiologically-confirmed TB Patients, PLHIV, diabetics, malnourished, cancer patients, patients on immune-suppressants or steroid should be regularly screened for sign and symptoms of TB*

The following are also to be investigated as presumptive PTB

a. Contacts of Microbiologically confirmed TB patients having cough of any duration
b. Presumptive /confirmed extra-pulmonary TB having cough of any duration
c. HIV positive patient having cough of any duration

Presumptive Extra Pulmonary TB refers to the presence of organ-specific symptoms and signs like swelling of lymph node, pain and swelling in joints, neck stiffness, disorientation, etc., and/or constitutional symptoms like significant weight loss, persistent fever for 2 weeks or more, night sweats.

Presumptive Paediatric TB refers to children with persistent fever and/ or cough for 2 weeks or more, loss of weight*/ no weight gain and/ or history of contact with infectious TB cases**.

- History of unexplained weight loss or no weight gain in past 3 months; loss of weight is defined as loss of more than 5% body weight as compared to highest weight recorded in last 3 months.

** *In a symptomatic child, contact with a person with any form of active TB within last 2 years may be significant*

Presumptive DR TB refers to the patient who is eligible for Rifampicin resistant screening at the time of diagnosis or/and during the course of treatment for DS TB or H mono/poly. This includes following patients:

- All Notified TB patients (Public and private) - Follow-up positive on microscopy including treatment failures on standard first line treatment and all oral H mono/poly regimen; - Any clinical non-responder including paediatric (if specimen available)

To diagnose TB, appropriate diagnostic test may be used

Importance of properly identifying Presumptive TB cases

Identification of Presumptive TB patient

Most patients with TB attend health facilities for seeking relief of symptoms. It is important to suspect tuberculosis among these chests symptomatic and subject them for sputum examination. These TB patients if not diagnosed will continue to spread the infection. If left untreated it is likely that more than half of them die by three years. Hence, every case of presumptive pulmonary TB should be referred for sputum examination and presumptive EPTB cases for appropriate investigations on time.

NTEP referral slip (Annexure-1)

The referral slips are used by peripheral health workers like ASHA, AWW, Link Workers etc. to refer patients to health facilities for examination or specimen collection. This referral slip has contact details and symptoms of presumptive TB case. At the referred health facilities, Request form for examination of biological specimen for TB is filled up by Medical Officer.

Passive Case Finding: When the Patient Voluntarily reports symptoms to the Medical Officer.

Intensified Case Findings: When the Medical Officer searches for TB symptoms among the individual seeking care in the health facility e.g., ART Centre, Diabetic Clinics, NCD Clinics.

Active Case Finding: When the Community health workers seeks for TB symptoms among the vulnerable key population. The Programme encourages Active Case finding as an intervention for Ending TB

All health workers and community volunteers should be encouraged to identify and refer presumptive TB patients to DMCs for early diagnosis and treatment to prevent further spread of the infection

Screening of vulnerable population

Vulnerable population is a group of people in whom the prevalence or incidence of TB is significantly higher than in the general population. The recommended vulnerable groups to be considered for intensified case finding may be classified as follows:

<table>
<tr><th>Clinical</th><th>Social</th><th>Geographical</th></tr>
<tr><td>Clients attending HIV Care Settings</td><td>Prisoners</td><td>Urban Slums</td></tr>
<tr><td>Substance abuse including smokers</td><td>Occupations with risk of developing TB (mines, coal industry, sand blasting industries, weaving & glass industries, stone crushers, cotton mill workers, tea garden workers, rice mill workers etc.,)</td><td>Hard to reach areas</td></tr>
<tr><td>Co-morbidities like Diabetes Mellitus, Malignancies, patients on dialysis and on long term immunosuppressant therapy</td><td rowspan="6">People in Congregate settings – e.g., night shelters, De-addiction centres, Old age homes</td><td rowspan="6">Indigenous and tribal populations</td></tr>
<tr><td>Health Care Workers</td></tr>
<tr><td>Household & Workplace Contacts</td></tr>
<tr><td>Patients with Past History of TB</td></tr>
<tr><td>Malnourished</td></tr>
<tr><td>Antenatal mothers attending antenatal clinics/MCH clinics</td></tr>
</table>

Adopting a well thought ACSM strategy and integrating it with the planning process for ICF will result in a multiplier effect in case finding efforts.

Utilizing Mobile Medical Units for screening presumptive TB patients in identified and hard to reach areas, using Information & Communication Technology (ICT) tools to enhance case finding are some examples of innovation in ICF which can be adopted.

Screening of Presumptive Pulmonary TB patients:

Patients attending health institutions - government/private need to be systematically screened for cough of two weeks or more. Persons with cough for more than 2 weeks, with or without other symptoms suggestive of TB, should be promptly identified as presumptive pulmonary TB patients. They are to be referred to designated microscopy centre (DMC) for sputum examination using the Request form for examination of biological specimen. Patients belonging to the key population EPTB, HIV and Paediatrics (after X-ray screening in case of children) can be directly referred for CBNAAT.

In a peripheral health institution (PHI), it is expected that at least 2-3% of new adult out patients are chest symptomatic (Presumptive PTB Cases). However, this will vary widely in different settings e.g., chest clinics, Medical Colleges and TB hospitals. A good number of TB patients may be left undetected, if a health facility is identifying and subjecting less than 2 - 3% of new adult outpatient for sputum examination. Further, it is expected that on an average 5-15% of the chest symptomatic subjected for sputum examination are found to be sputum smear positive following standard operating procedures of smear microscopy. This percentage varies depending on the clinical/epidemiological settings.

The number of Presumptive TB patients examined can be expressed as numbers / lakh population. There should be an increasing trend year on year commensurate with more efforts required to detect additional patients.

Sustained efforts have to be taken to examine as many Presumptive TB patients as possible to maximize case detection under the program.

Referral for sputum examination

Specimen from Presumptive Pulmonary TB patients are subjected to sputum smear microscopy at Designated Microscopy Centres (DMC). Presumptive PTB patients attending peripheral health institutions other than DMC are either referred to nearest DMC for sputum examination or their sputum specimens are collected and transported to the DMC as per guidelines. For diagnosis, two sputum specimen have to be examined by Microscopy.

To provide better access for diagnosis of TB all peripheral health institutions including the PHC wherever, laboratory technicians and Binocular microscope are available can be upgraded to designated microscopy centre, irrespective of the population norms or OPD attendance. In addition, DMCs can be established in other public sector undertakings, (e.g., ESI, Railways) private hospitals and NGO health facilities. All DMCs should comply with the Quality Assurance mechanisms as per the External Quality Assurance (EQA) Guidelines.

Tools for diagnosis Pulmonary TB in adults

Anatomical Site of TB	Type of TB	Type of TB	Geographical
Pulmonary / Extra-Pulmonary	Drug Sensitive TB	1. Sputum smear microscopy (Zeihl-Neelson Staining /Fluorescence staining) 2. Solid and liquid culture	NAAT
	Drug Resistant TB	1. Liquid culture & DST 2. Solid culture & DST	1. NAAT 2. LPA

- Sputum smear microscopy
- Nucleic Acid Amplification Test (NAAT)
- Sputum culture and DST for diagnosis of Drug Resistant TB
- Line Probe Assay for diagnosis of MDR/XDR TB

Supportive tools for the clinical diagnosis of TB

- Chest X-ray and other radiological tests
- Tuberculin Skin Test (TST), Interferon Gamma Release Assay (IGRA) and other blood tests, Histopathology and other tissue-based tests.

Diagnostic Tools

Tools for microbiological confirmation of TB

Under the programme acceptable methods for microbiological diagnosis of TB are:

A. Sputum Smear Microscopy (for AFB):

- Zeihl-Neelsen Staining
- Fluorescence staining

B. Culture:

- Solid (Lowenstein Jensen) media
- Automated Liquid culture systems e.g. BACTEC MGIT 960, BacT Alert or Versatrek etc.

C. Drug Sensitivity Testing:

- Modified Proportionate Sensitivity Testing (PST) for MGIT 960 system
- Economic variant of Proportion sensitivity testing (1%) using LJ medium

D. Rapid molecular diagnostic tests:

- Line Probe Assay (LPA) for MTB complex and detection of RIF & INH resistance (FL LPA) and FQ and SLI resistance (SL LPA)
- Nucleic Acid Amplification Test (NAAT) (CBNAAT/Truenat)

Smear microscopy being the most commonly used method for microbiological diagnosis of TB for the last several decades, has had enormous value in TB diagnosis but with limited sensitivity, more so in children and PLHIV. Under the programme, two methods of microscopy are currently being used- ZN stain-based microscopy using conventional microscope and Light Emitting

Diode based Fluorescent Microscopy (LED FM).

Culture though highly sensitive and specific method for TB diagnosis, requires 2-8 weeks to yield results and hence does not help in early diagnosis. However, culture will be used for follow up of patients on drug resistant TB treatment to detect early recurrence. In addition, it is also used for long term follow up for DS TB patients as per programme guidelines, to ensure relapse free cure.

Liquid culture system– Mycobacteria Growth Indicator Tube system (MGIT-B is an automated culture system that detects the growth of mycobacteria. The culture results are usually available up to 42 days. DST results are available 14-26 days after the cultures turn positive.

Molecular Assays– Polymerase Chain Reaction (PCR) based technologies using various modifications are used for detecting the presence of putative resistance genes (rpoB for rifampicin, katG and inhA for Isoniazid etc.,).

The most widely evaluated and used assays are Line Probe Assays (LPA) which are based on in-situ hybridization on nitrocellulose strips of specific genetic targets for resistance genes. These are now available for RIF and INH resistance (MDR-TB) and also for XDR-TB (gyrA and gyrB for Fluoroquinolones, rrs(second line injectable) and eis(low level kanamycin resistance)for second line injectable).

Nucleic Acid Amplification Test (NAAT) provides accurate and rapid diagnosis of TB by detecting Mycobacterium tuberculosis (M. tuberculosis) and Rifampicin (Rif) resistance conferring mutations, in sputum specimen as well as specimen from extra-pulmonary sites. under the programme, its use is recommended for diagnosis of DR-TB in presumptive DR-TB patients and TB preferentially in key population such as children, PLHIV, Extra-pulmonary TB and in smear negative TB as per the diagnostic algorithm.

Diagnosis of TB by any microbiological tools and treatment for TB are available FREE of cost at all health facilities under RNTCP

Other diagnostic tools

Radiography

Chest X-Ray is to be used as a screening tool to increase sensitivity of the diagnostic algorithm. Any abnormality in chest radiograph should further be evaluated for TB including microbiological confirmation.

For the diagnosis in the absence of microbiological confirmation, X-ray can be used as a tool for supportive evidence. Though the inter and intra observer variability is high in X ray and no X ray shadow is specific for TB and 10-15% culture positive cases may remain undiagnosed (under reading) when x-ray alone is used as a diagnostic tool, careful clinical assessment and supportive X-ray findings can be used to diagnose TB and such cases will be considered as clinically diagnosed TB. It is also useful for diagnosing extra pulmonary TB like pleural effusion, pericardial effusion, mediastinal adenopathy and miliary TB.

Tuberculin Skin Test (TST) and Interferon Gamma Release Assay (IGRA) Are not to be used for diagnoseis of TB in adults as well as children. However, for LTBI these tests have a role which will be discussed latter.

Serological tests

The Government of India issued Gazette notification vide 433E 7th June 2012 has banned the manufacture, importation, distribution and use of currently available commercial serological tests for diagnosing TB. These tests are not recommended for diagnosis of TB (Annexure 3).

• Lateral flow urine lipoarabinomannan (LF-LAM) assay can only be used for diagnosis of TB in HIV positive patients with signs and symptoms of TB (pulmonary and/or extra-pulmonary) who have a CD4 cell count less than or equal to 100 cells/μL.

• C-Tb is the next-generation skin test for detection of Tuberculosis. It has high specificity and contains the same antigens used in IGRA i.e., ESTA 6 and CFP 10. It is unaffected by BCG vaccination status and hence can be used as a tool for latent TB diagnosis

Sputum Smear Microscopy

Sputum smear microscopy is the most widely used and acceptable testing tool for diagnosing smear positive pulmonary TB. Ziehl-Neelsen / Fluorescent staining technique is used under the programme. Sputum smear microscopy has the following advantages: -

A. Simple, inexpensive, requires minimum training
B. High specificity
C. High reliability with low inter-reader variation
D. Can be used for diagnosis, monitoring and defining cure
E. Results are available quickly
F. Feasible at peripheral health institutions
G. Correlates with infectivity in pulmonary TB

Therefore, this is the key diagnostic tool used for case detection under the programme..

Microscopy is more specific and has less inter and intra-reader variability than X-ray

The MO / health worker / laboratory technician (LT) should instruct the patient about proper sputum collection. If sputum collected is not of good quality and the patient has smear- positive pulmonary tuberculosis, the diagnosis may be missed, and the patient may continue to spread the infection to others. The LT should label the sputum container properly by writing the patient's laboratory serial number on the side of the sputum container and not on the lid.

Rapid diagnostic tools include:

The CB-NAAT system detects DNA sequences, specific for Mycobacterium tuberculosis complex and rifampicin resistance by polymerase chain reaction. It concentrates Mycobacterium tuberculosis bacilli from sputum samples, isolates genomic material from the captured bacteria by sonication and subsequently amplifies the genomic DNA by PCR. The process identifies clinically relevant, rifampicin resistance inducing mutations in the RNA polymerase beta (rpoB) gene in the Mycobacterium tuberculosis genome in a real time format using fluorescent probes called molecular beacons. Results are obtained from unprocessed sputum samples in 90 minutes.

Line Probe Assay (LPA)

Line Probe Assays detect DNA sequences specific for Mycobacterium tuberculosis complex as well as mutations conferring resistance. Sputum samples are decontaminated and the concentrated deposit subjected to smear microscopy. DNA is extracted from all smear positive samples and subjected to PCR; while all smear negative samples are inoculated in liquid culture and LPA performed using the culture isolate obtained upon growth of Mycobacteria. The PCR amplified products are reverse hybridized on nitrocellulose strips containing probes specific for detection of M.tb and mutations associated with drug resistance. First Line LPA detects resistance to Rifampicin (rpoB) and Isoniazid (katG , inhA), while Second Line LPA detects Fluoroquinolone class resistance (gyrA,gyrB) and Second line injectable class resistance (rrs ,eis)

Process of diagnosis of pulmonary TB

Medical Officers of the health care facilities (government medical college and non-government) should identify all presumptive pulmonary TB and refer for sputum examination using the Request form for examination of biological specimen for TB or by enrolling the patient in Nikshay and requesting the test on-line. Where the facilities are available, X-ray may be done simultaneously.

Add details of Enrolment details and screenshot

Patient may be given sputum containers for collecting early morning sputum and visit the laboratory if the health facility is a non-DMC. Patient should be educated about how to collect the sputum by the Health Worker or Medical Officer. If it is a DMC, LT will be educating, and giving sputum containers for collecting spot specimen and early morning sputum specimen on the next day. If, the health facility is transporting the sputum specimen, it should reach DMC as soon as possible. Two sputum samples are collected within a day or on two consecutive days.

Case Definitions:

Microbiologicallyc onfirmed TB	Microbiologically confirmed TB refers to apresumptive TB case from whom a biologicalspecimen is positive for acid fast bacilli, or positive forMycobacterium tuberculosis on culture, or positive fortuberculosis through Rapid Diagnostic molecular test
Clinically Diagnosed TB	A clinically diagnosed TB refers to apresumptive TB case who is not microbiologicallyconfirmed, but has been diagnosed with active TB bya clinician on the basis of X-ray abnormalities, histopathology or clinical signs with a decision totreat the patient with a full course of Anti-TBtreatment.

Classification based on anatomical site of disease

a) Pulmonary tuberculosis (PTB) refers to any microbiologically confirmed or clinically diagnosed TB involving the lung parenchyma or the tracheo-bronchial tree.

b) Extra Pulmonary tuberculosis (EPTB) refers to any microbiologically confirmed or clinically diagnosed TB involving organs other than the lungs such as pleura, lymph nodes, intestine, genitourinary tract, joint and bones, meninges of the brain etc.

Miliary TB is classified as PTB because there are lesions in the lungs. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of Pulmonary TB.

Classification based on history of previous TB treatment

a) New TB patient - A TB patient who has never had treatment for TB or has taken anti-TB drugs for less than one month is considered as a new TB patient.

b) Previously treated TB – A patient who has received one month or more of anti-TB drugs from any source in the past.

I. Recurrent TB patient - A TB Patient previously declared as successfully treated (cured/treatment completed) and is subsequently found to be microbiologically confirmed TB is a recurrent TB patient.

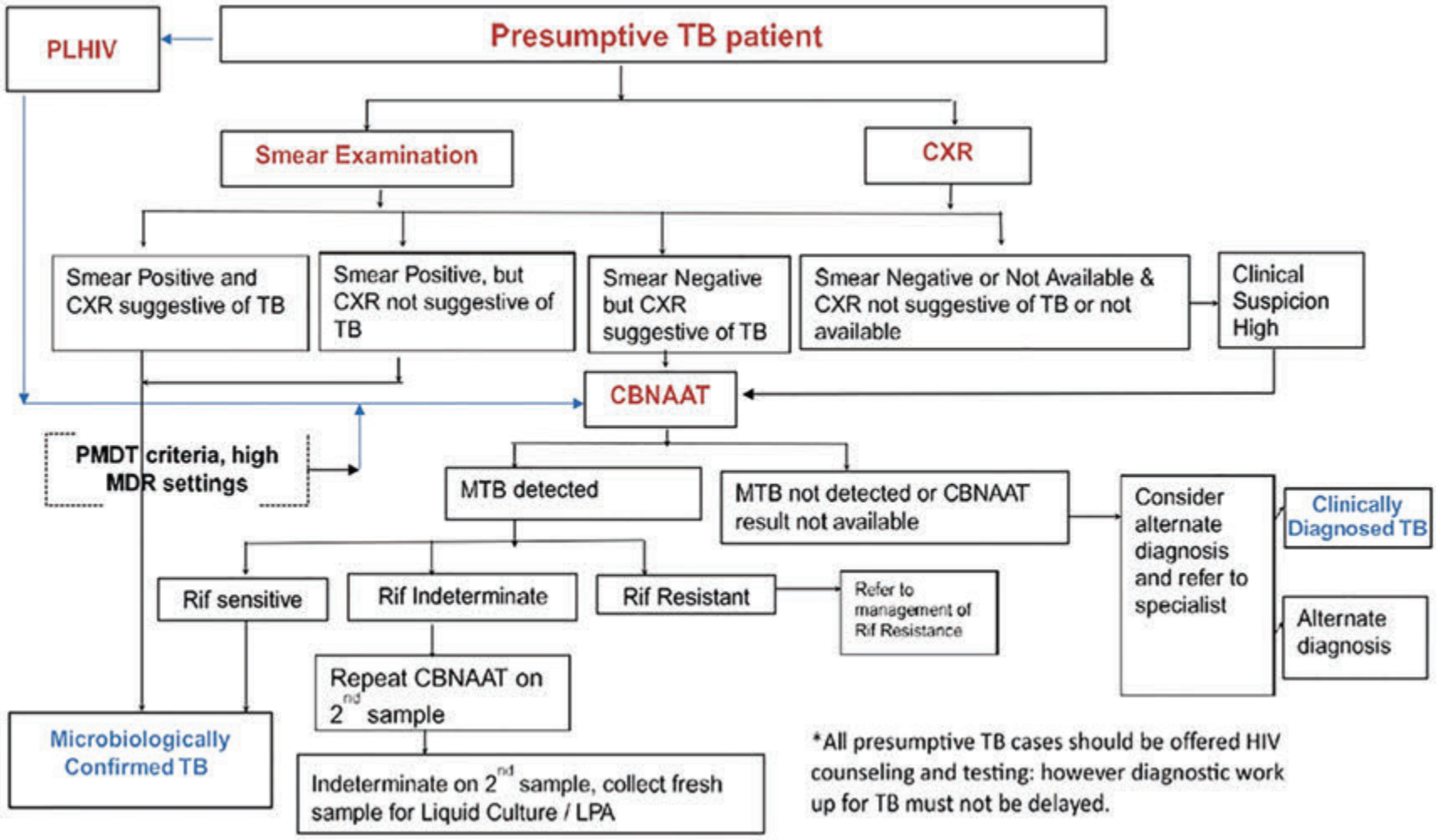
II. Treatment after failure patients are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.

III. Treatment after lost to follow-up A TB patient previously treated for TB for one month or more and was declared lost to follow-up (LFU) in their most recent course of treatment and subsequently found to be microbiologically confirmed TB

IV. Other previously treated patients are those who have previously been treated, who cannot be classified into any of the above.

c) Transfer in A TB patient who has been received for treatment in a Tuberculosis Unit, after starting treatment in another TB unit where s/he has been registered is considered as transferred in.

Diagnostic Algorithm for Drug Sensitive TB



***All TB patients have to be referred for UDST**

The diagnostic algorithm given above should be strictly followed. If not followed, patients may either be treated unnecessarily based only upon X-ray results or left untreated.

In any clinical settings presumptive PTB patients can be identified by screening for chest symptoms. Some of the patients may walk in with a chest X-ray, if there are some abnormality in chest X-ray those patients also will be identified as presumptive PTB.

A. These presumptive PTB patients should be subjected for sputum smear microscopy (ZN/FS). Two specimens will be collected (spot-early morning or two supervised spot specimen collected at least one hour apart and smears made from both the samples. If one or both of the smear is positive*, the patient is diagnosed as a microbiologically confirmed Pulmonary TB.

B. If both of the smears are negative, and the patient is already having a recent chest X-ray suggestive of TB; S/he should be referred for testing to the nearest CBNAAT laboratory.

C. If both smears are negative and the patient is not having a chest X-ray, s/he should be referred for chest X-Ray. If chest X-ray suggestive of TB, the patient should be referred for CBNAAT. If the first smear is negative and X-Ray is offered in parallel, the second specimen is sent to CBNAAT laboratory (if the X-ray is abnormal).

D. If both smears are negative and chest X-ray is NOT suggestive of TB and there is strong clinical suspicion of TB, then also the patient needs to be referred for CBNAAT testing.

Two sputum specimens are to be collected from the patient and sent to the CBNAAT site.. One specimen is tested using CBNAAT and if TB was detected, the other sample is used for further cascade testing

a. If CBNAAT result is MTB detected, the second sample need to be transported to C&DST Lab immediately
b. If CBNAAT result suggest rifampicin sensitive, second sample is sent for FL-LPA to look for H-mono/ poly resistance.
    i. If FL-LPA suggests H sensitive, then DSTB treatment is continued.
    ii. If FL-LPA suggests H resistance, then patient is managed as per Integrated diagnostic algorithm for DRTB (Fig on Page 31)
    iii. If MTB is not detected by CBNAAT, CXR is suggestive of TB or otherwise but the clinician considers TB as a probable clinical diagnosis requiring anti-TB treatment after ruling out other alternative diagnosis,the patient is labelled as Clinically diagnosed TB . In such cases alternative diagnosis should be actively ruled out.

E. If MTB is not detected by CBNAAT / CBNAAT result is not available and clinician does not consider TB as a probable diagnosis at this stage, the patient is not a TB case and needs to evaluated for other respiratory diseases.

F. All key population (PLHIV, Children, EPTB etc.) will be preferentially offered upfront CBNAAT.

G. The algorithm does not mandatorily decide the "order to DO" the tests / investigations. If multiple tests are available at a site, they may be offered to the patient to avoid diagnostic delay with a focus on microbiology confirmation.

H. If the clinician considers coexisting clinical conditions, along with TB, appropriate investigations must be done to diagnose those conditions.

Diagnosis of TB among children

The extent of TB in children is a reflection of the pool of infectious adult pulmonary tuberculosis cases in the community and their ability to transmit infection. All adolescents up to 18 years of age are to be treated using paediatric weight bands and those weighing more than 39 kg with adult weight bands.

Diagnosis

Early and prompt diagnosis of TB in children is often difficult. A battery of tests is required to arrive at accurate diagnosis of TB in children. Generally, diagnosis should be made by a Medical Officer and the existing NTEP case definitions are to be used for all cases diagnosed.

High index of suspicion of TB in a child is the first step in the diagnosis. Tuberculosis should be suspected among children presenting symptoms of prolonged / unexplained fever and / or cough for more than 2 weeks, with no weight gain or history of failure to thrive. It is to be remembered that cough may not be the predominant and constant symptom unlike in an adult. Children presenting neurological symptoms like irritability, refusal of feeds/failure to thrive, headache, vomiting or altered sensorium and convulsions, may be suspected to have TB meningitis.

History of contact with a Presumptive TB patient or a diagnosed patient of PTB within the last 2 years reinforces the suspicion of tuberculosis. Special efforts should be made to elicit the history of contact with tuberculosis patient.

Establishment of malnutrition on an objective basis is also helpful in reinforcing the diagnosis. (refer to CTD published guidelines on nutrition)

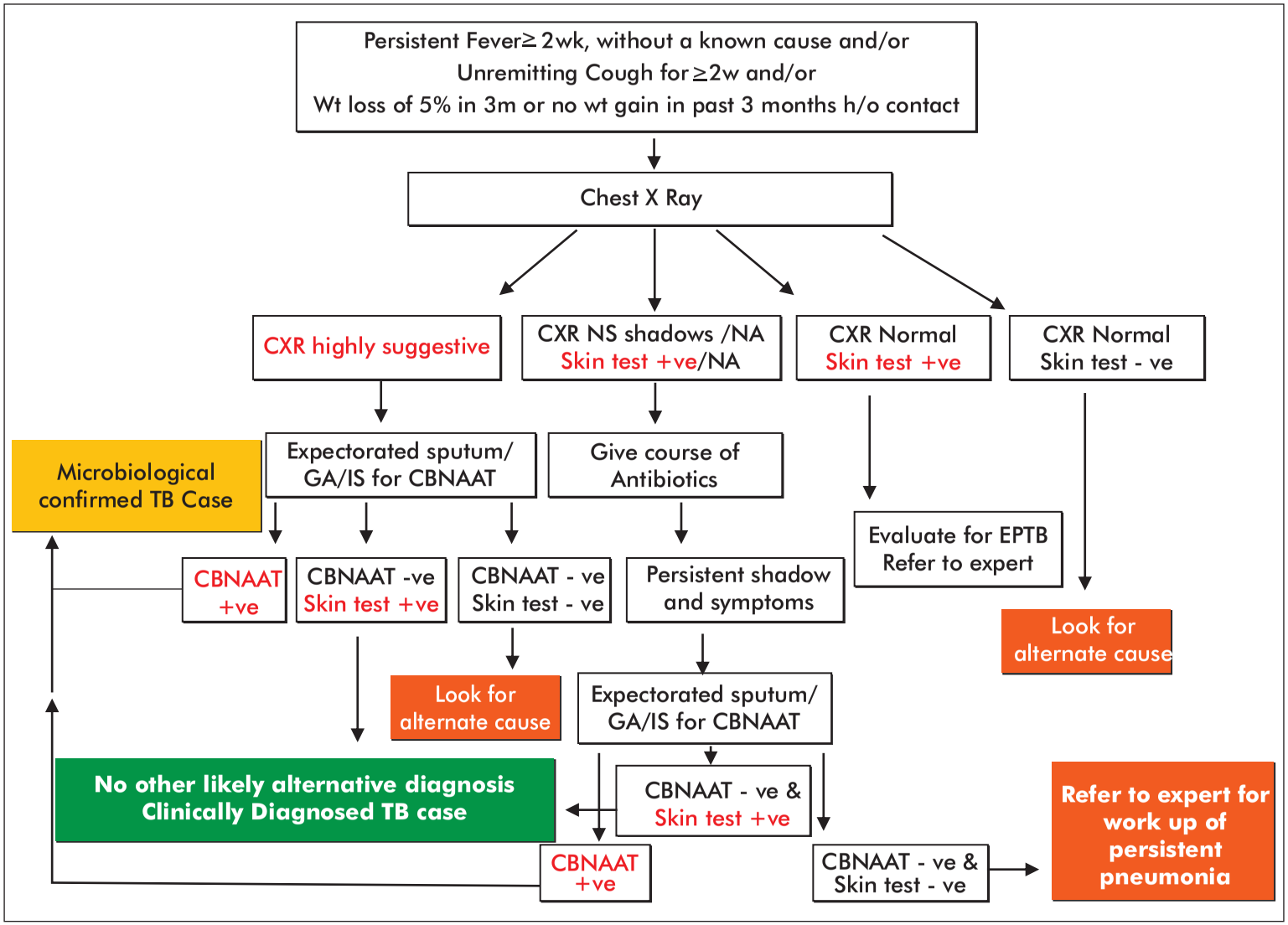
The diagnosis is further based on sputum examination wherever possible, Chest X-ray examination and Mantoux test (tuberculin skin test) using standard tuberculin.

Sputum examination, if feasible, is a very helpful tool in the diagnosis. It is pertinent to remember that pulmonary TB among children is most often pauci- bacillary and there are practical difficulties in obtaining good quality sputum. All attempts to be made to collect a good quality specimen. After X- Ray screening and sputum/gastric aspirate/gastric lavage, induced sputum etc., can be used for testing in CBNAAT.

Tuberculin skin test using standard tuberculin is an adjunct tool in the diagnosis of TB among children. While administering Tuberculin skin test it is to be ensured that a standard product - PPD RT23 with tween 80 is used and a dose of not more than two tuberculin units is given to elicit specific reaction to M.tb. Induration of 10mm and above read after 48-72 hours of properly administered tuberculin indicates that the child is infected. It may be noted that currently there is no standard PPD available in the country. A new skin test called C-Tb (which is equivalent to IGRA) is likely to be become available by mid- 2020.

Chest X-ray, also aids in the diagnosis of TB among children. Features in chest X-ray include hilar adenopathy infiltrations, pleural effusion etc., See paediatric pulmonary diagnostic algorithm given below.

Diagnostic algorithm for Paediatric Pulmonary Tuberculosis



The following foot notes to be included:

1. This algorithm is for children who are likely to have drug sensitive disease i.e., have not received ATT previously ever and are not presumptive drug resistant TB cases (lost to follow up, relapse, treatment failure, HIV).

2. Proper characterization of symptoms is a very important starting point. Weight loss or not gaining weight should always be documented with appropriate weighing.

3. Rapid molecular test (CBNAAT)

    a. Whenever Rif Resistant result is reported on Rapid molecular test (CBNAAT) further management should be carried out as per the guidelines on Drug Resistant TB.

    b. Rapid molecular test to be offered in non-specific symptoms with high index of suspicion. Rapid molecular test to be repeated for special situations including HIV, malnourished population. Where Rapid molecular test is not doable, smear examination may be done.

    c. A RIF indeterminate/Invalid/Error/No result will get an additional CBNAAT to get a valid result and in case of indeterminate on second occasion, an additional specimen will be collected and sent to the nearest Intermediate Reference Laboratory (IRL) or Culture & Drug Susceptibility Testing (C&DST) centre for LPA or Liquid Culture & DST as appropriate.

    d. If a specimen is positive by Rapid molecular test / Culture / smear examination, the disease is labelled as Microbiologically confirmed TB.

    e. Whenever indicated, alternative specimens (Gastric lavage/ Induced sputum/ broncho-alveolar lavage) should be collected by a skilled health care provider, depending upon available infrastructure and sample should be subjected to Rapid molecular test.

    f. A good sputum sample consists of recently discharged material from the bronchial tree with minimum amount of oral or nasopharyngeal material, presence of mucoid or mucopurulent material and should be 2-5 ml in volume. It should be collected in a sterile container after rinsing of the oral cavity with clean water.

The collected specimens should be transported to the laboratory as soon as possible after collection. If delay is unavoidable, the specimens should be refrigerated (maximum up to one week) to inhibit the growth of unwanted micro-organisms.

    g. Samples for culture should never be collected in formalin

    h. No preservative should be used for any extra-pulmonary specimen for culture. Necessary instructions are to be given to the concerned staff for sending the biopsy specimen in normal saline for culture and not in 'FORMALIN" as it kills bacilli.

4. Chest X Ray
   a. Chest X ray if available within 7 days, may be used.
   b. Highly suggestive Chest X-ray refers to skiagrams showing either Miliary or lymphadenopathy (hilar or mediastinal) or chronic fibro-cavitatory shadows. If the radiological picture is highly suggestive of TB, then proceed to do further investigations irrespective of the TST result as the sensitivity of the test is not 100%.
   c. Non-Specific Chest X-ray: Refer to patterns other than highly suggestive like consolidations, inhomogeneous shadows or bronchopneumonia, etc.
5. For Antibiotic trial, 7-10 days of broad-spectrum antibiotic - amoxicillin and Amoxyclav may be given. Antibiotics like linezolid or any quinolone should not be used as they have anti-TB action.
6. Skin test:
   a. Current recommendation is to use 2TU PPD RT23 for all diagnostic purposes
   b. Mantoux test or PPD skin test is considered positive if the induration is 10 mm or more, In HIV co-infected cases, 5mm may be taken as the cut off.
   c. Cut offs for higher strengths are not established. Higher strengths increase false positive reactions. The standard cut off of 10 mm can actually not be justified for any higher strength of PPD used
7. No role for inaccurate / inconsistent diagnostics like serology (IgM, IgG, IgA antibodies against MTB antigens), various in-house or non-validated commercial PCR tests and BCG test
8. Currently there is no role of IGRAs in clinical practice for the diagnosis of TB.
9. Children with persistent symptoms, non-specific shadows and negative smears and negative other samples (GA/IS) by Rapid molecular test should be referred to experts for further work up of persistent pneumonia.
10. All TB cases diagnosed must be offered testing for HIV.

There is no role for inaccurate / inconsistent diagnostics like serology (IgM, IgG, IgA antibodies against MTB antigens- these serological tests are banned in India), various in-house or non-validated commercial PCR tests and BCG test.

Currently there is no role of IGRAs in clinical practice for the diagnosis of TB.

Extra-pulmonary TB

15%-20% of the total TB cases comprise of Extra-pulmonary TB . Tuberculosis of organs other than the lungs such as pleura, lymph nodes, intestine, genito-urinary tract, joint and bones, meninges of the brain etc., is called as extra-pulmonary TB. Pleural tuberculosis is classified as extra-pulmonary. Tubercular lymphadenitis and pleural effusion are most common among extra-pulmonary TB.

Diagnosis of Extra-Pulmonary TB

Demonstration of AFB in a smear from extra-pulmonary site is often difficult because of low bacillary load. The clinical features pertaining to the system affected should be considered in the diagnosis of extra-pulmonary tuberculosis.

CBNAAT and Liquid Culture are the preferred diagnostic technologies for microbiological confirmation of Extra Pulmonary Tuberculosis.

However, the following are some of the special investigations which are helpful in diagnosing extra pulmonary tuberculosis. These may be radiological, cytological / pathological, biochemical and immunological.

(a) Fine Needle Aspiration Cytology (FNAC) and direct smear examination

(b) Excision / Biopsy of specimen for histopathological examination

(c) Fluid for cytology, biochemical analysis and smear examination

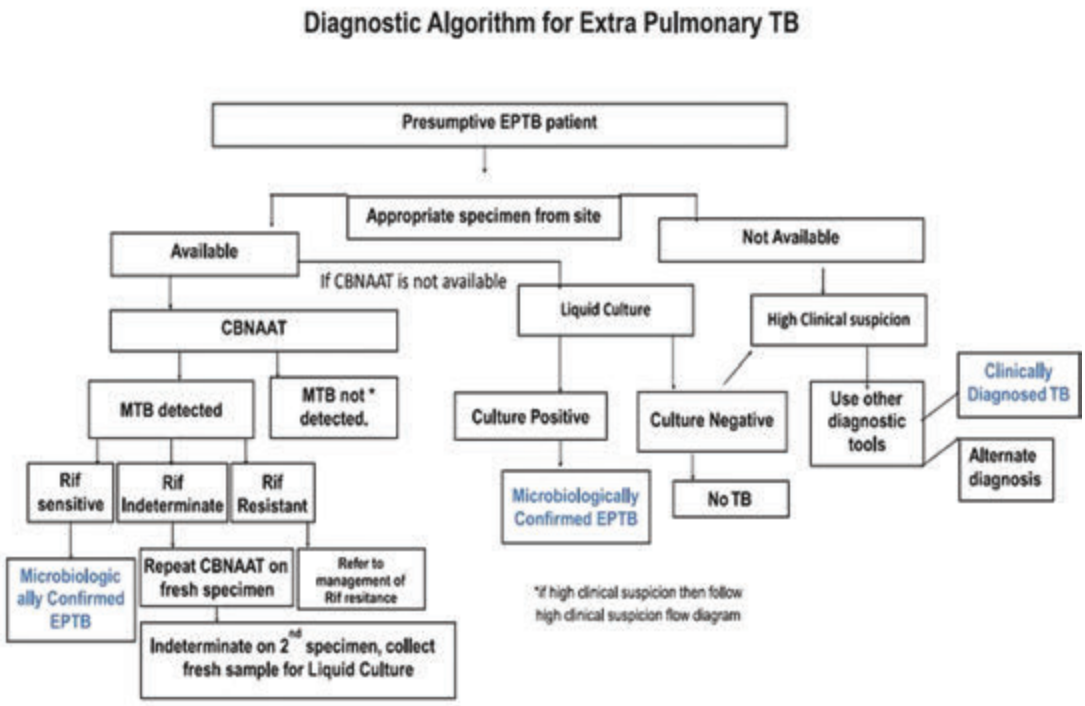
(d) X-ray of the involved region

(e) Ultra-Sonography for Abdominal Tuberculosis

Precise diagnosis of some forms of extra pulmonary tuberculosis is a challenge to the physicians as they present symptom complex with extraordinary diversity. Delay in the diagnosis can be fatal or result in life threatening sequelae as in the case of meningeal TB.

Patients with symptoms suggestive of extra pulmonary tuberculosis should be referred to the respective speciality for further investigations.

Diagnostic Algorithm for Extra Pulmonary TB



1. CBNAAT in specimen from extra-pulmonary sites provides the following results:

   a. M. tuberculosis detected, Rifampicin sensitive: Diagnosis of microbiologically confirmed EPTB is made.

   b. M. tuberculosis detected, Rifampicin indeterminate: a repeat CBNAAT test is performed on the 2nd specimen. If found to be indeterminate on the repeat test, an additional specimen should be collected and sent to the nearest NTEP certified lab for culture and DST.

   c. M. tuberculosis detected, Rifampicin resistance: patient should be treated as per PMDT guidelines;

   d. M. tuberculosis not detected: The patient should be evaluated for TB based on clinical, radiological findings and other investigations like histo-pathological examination, ultrasonogram etc.,. In the event of a decision to treat with anti TB drugs, of the patient will be classified as clinically diagnosed TB. Otherwise, an alternate diagnosis should be sought.

   e. Invalid test: a repeat CBNAAT test is performed on the 2nd specimen, if available.

   f. Error/No result: a repeat CBNAAT test is performed on the same sample/2nd specimen, if available.

Note: Second sample may not be available for most patients with extra-pulmonary TB.

1. In case CBNAAT is not available, liquid culture needs to be performed. If culture is positive, then diagnosis of microbiologically confirmed EPTB is made. Further work up may be done to evaluate Rifampicin and INH resistance.

2. If investigations like CBNAAT/smear microscopy/culture turn out to be negative or if appropriate specimen is not available for these investigations, consultation with a specialist followed by other tests such as histopathology, radiology, cytology, biochemical examinations, etc., may be undertaken. In the event of a decision to treat with a full course of anti-TB drugs, diagnosis of clinically diagnosed EPTB is made.

3. Depending on the site of EPTB accessibility of the sampling procedure and the amount of sample available, decision may be taken to do CBNAAT, Culture or both and the sample will be collected as per SOP. Sample should not be split in field conditions. Formalin should not be used for collecting the specimen.

Diagnosis of Drug Resistance TB (DR-TB):

Patients can have drug resistance tuberculosis through transmission from a drug resistant index case (Primary transmission) or develop resistance while on treatment (Acquired Resistance).

Emergence of Drug resistance is due to genetic mutation that makes a drug ineffective against the mutant bacilli. In clinical settings an inadequate or poorly administered treatment regimen allows drug-resistant mutants to become the dominant strain in a patient infected with TB.

Preventing emergence of drug resistance is of paramount importance. To prevent drug resistance, the Medical Officer has to ensure that the programme is implemented as per

Guidelines. All TB patients in his/her jurisdiction have to be diagnosed early, initiated promptly on treatment followed up correctly and supported well to complete the treatment successfully. MO should also help the Private health providers in his/her jurisdiction to diagnose ,manage, and notify TB as per National guidelines. When resistance has already occurred, it is important to diagnose it early prevent further transmission by following the Air borne infection control measure as well as to treat and cure the patient at the earliest.

The first step for detection of DR-TB cases is to identify presumptive DR-TB cases at the earliest.

Presumptive DR-TB: It refers to the following patients in order of their risk:

TB patients found positive on any follow-up sputum smear examination during treatment with first line drugs including treatment failures;

- paediatric TB non-responders;
- TB patients who are contacts of DR-TB;
- previously treated TB patients;
- new TB patients with HIV co-infection;
- all notified new TB patients*.

* *Under the Programme, all notified New Patients are offered CBNAAT to know if they are resistance to Rifampicin. This is termed as universal DST for Rifampicin. Efforts are to be made to collect specimen from all TB patients for CBNAAT at baseline.*

Integrated drug-resistant TB algorithm

The integrated DR TB algorithm clearly indicates the management strategies to be followed right from the day the result of NAAT test is available. The programme must strive to offer DST to all notified TB patients at diagnosis of TB or a maximum within 15 days of first line treatment initiation. The algorithm further offers FL LPA for the patients found R resistance not detected on NAAT. States must ensure availability of laboratory capacity to perform LPA (both SL and FL LPA) as per the estimated requirement including the patient notified from the private sector. Within the first 2 months of treatment initiation, patients would receive their LC DST results, their final classification will be arrived at and they will be treated with appropriate regimen. .

As per the algorithm, the TB patients with R resistance not detected will be initiated on first line treatment regimen while awaiting the results of FL LPA and continued on first line treatment if H resistance is not detected. These patients will be monitored closely and in patients with signs of non-response to treatment during follow up, another NAAT test will be offered. All follow up positive, failures and clinical non-responders of DS-TB treatment are also eligible for repeat NAAT irrespective of NAAT offered at the time of initiation of DS TB treatment.

If resistance to H is detected, the patient will be initiated on all oral H mono-poly DR TB regimen at the PHI level while awaiting the results of SL LPA and the regimen would be appropriately modified at the N/DDR TBC if Lfx/Mfx(h) resistance is detected on SL LPA. The patients with RR TB will be considered for shorter MDR TB regimen at N/DDR TBC after ruling out the exclusion criteria for shorter MDR TB regimen. Decision to start shorter MDR TB regimen will be based on

non-DST and DST based exclusion criteria(refer PMDT guidelines 2019 for details). The patients excluded from shorter MDR TB regimen would be initiated on all oral longer MDR TB regimen at N/DDR TBC. In case of additional resistance on LC DST, the all oral longer MDR TB regimen would be appropriately modified.

A patient is confirmed to have drug resistant TB, only when the results are from a NTEP quality-assured Culture & DST Laboratory and by a NTEP-endorsed testing method. Such patients are classified according to the following definition.

Classification based on drug resistance

a. Mono-resistance (MR): A TB patient, whose biological specimen is resistant to one first-line anti-TB drug only.

b. Poly-Drug Resistance (PDR): A TB patient, whose biological specimen is resistant to more than one first-line anti-TB drug, other than both isoniazid (INH) and Rifampicin (R).

c. Multi Drug Resistance (MDR): A TB patient, whose biological specimen is resistant to both isoniazid and rifampicin, with or without resistance to other first line drugs, based on the results from a quality assured laboratory.

d. Rifampicin Resistance (RR): resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs excluding INH. Patients, who have any Rifampicin resistance, should also be managed as if they are an MDR TB case.

e. Extensive Drug Resistance (XDR): A MDR TB case whose biological specimen is additionally resistant to a fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin) and a second-line injectable anti TB drug (kanamycin, amikacin, or capreomycin) from a quality assured laboratory.

So far, we have discussed on proper and early identification of Presumptive TB and Presumptive DR TB cases. Now we will shall discuss the process of diagnosis.

Collection of sputum from Presumptive Tuberculosis cases.

Presumptive Tuberculosis attending the DMC will be referred for sputum examination at the same facility. There are two options for patients attending PHI which is not a DMC.

- Either the patient may be referred to the nearest DMC for sputum examination or
- Sputum sample may be collected from such patients and transported to the DMC.

The above options may be left to the convenience of the patient in order to minimize the possible delay in diagnosis and initiation of treatment or avoid repeated visits by the patient. If sputum microscopy is not possible on the day the patient visits the PHI due to any unavoidable reason, his/her sputum sample should be collected on the same day and sputum microscopy may be done on the following day.

Guidelines for collecting sputum

The patients are given the sputum container with laboratory serial number written on its side. The person collecting the sputum demonstrates how to open and close the container, takes the patient to an open space away from other people and demonstrates how to bring out sputum from the depth of chest. The patient is instructed to inhale deeply 2–3 times with mouth open, cough out deeply from the chest, open the container and spit out the sputum into it, and close the

container. This is the spot specimen labelled as 'a'.

- Further, patient is given a labelled container with instructions to cough out sputum into the container early in the morning after rinsing the mouth with water. This is the early morning specimen. This is labelled as specimen 'b'.
- If the health facility is not a DMC, then the patient is given a sputum container with instructions to collect an early morning specimen and go with the sputum specimen to the DMC where the spot specimen can be collected. In case the patient is not able to travel to the DMC, then the spot specimen could be collected at the nearest health facility or sputum collection centre and transported to the DMC.
- These two samples should be collected within a day or two consecutive days.
- Two supervised spot samples may be collected one hour apart if patient is too sick, coming from a long distance or likelihood of not giving a second sample is significant.
- To obtain good quality sputum specimens and to prevent contamination, the staff must perform certain tasks:
    - Before sputum collection
    - During sputum collection and
    - After sputum collection.

The following are the details of the task to be performed:

1. Tasks performed before sputum collection

Before collecting the sputum specimen, the health worker should briefly explain to the patient the reasons for sputum collection. The NTEP request form for examination of biological specimens should be filled up completely, by the MO. This form is sent to the DMC along with the sputum specimens. Only one form needs to be filled for two sputum specimens collected from a patient. The form accompanies the patient's sputum specimens when they are transported from the peripheral health facility to the DMC for examination.

Request form for examination of biological specimens: (Annexure-2)

The request form is kept at all the PHIs. It is filled generally by the MO of the referring health facility. This form is used for microscopy or CBNAAT or culture DST or Chest X-Ray or TST. Only one form is filled for each patient. Patient will report to the diagnostic health facility along with the request form. In case PHI is a sputum collection centre, sputum samples are sent to the diagnostic facility along with the request form. It is essential to record patient details, reason for testing and type of test requested. The same form is sent back to the treating unit with the results. When this format is used for C&DST, a copy of this form will be sent electronically to lab and DTC. In turn, the laboratory will send the result in electronic copy back to district with copy to DR-TB centre.

Request form for examination of biological specimen has eleven parts to include all the possible relevant investigations in a single format. The same form is used to request test to diagnose TB, Drug susceptibility testing and follow up.

The first part contains details on general information like name of the referring health facility, name of the patient, complete address, age & gender of the patient and date of referral. The type of presumptive TB, the key population to which the patient belongs to, site of disease in terms of pulmonary and extra-pulmonary or disease in terms of pulmonary and extra-pulmonary has to be indicated. The upper half of this form is completed by the MO/ health care worker who requests a sputum examination.

Second part contains details of referring facilities and NIKSHAY ID for previously notified patient, the names of State, district and TB units.

The third and fourth portions contain reasons for testing. The third portion is for the diagnosis and follow up of TB and the fourth portion is for the diagnosis and follow up of Drug resistant TB.

The fifth portion is to indicate the required tests with the details of the person requesting the test.

Parts six to eleven are used for reporting test results.

Detailed description of completing the form is as follows:

Name of Referring Health Facility

Date

The date (day/month/year) on which the patient is examined and the form is filled up, is written in the space provided.

Patient Name

The patient's full name (also nickname, if any) is written in the space provided.

Age (in yrs.)

The age of the patient is written in the space provided.

Gender

The letter 'M' is ticked if the patient is a male, 'F' if female and 'TG' if Transgender.

Patient Mobile No. or other contact no.

More than one Mobile number available try to capture all. This will help to provide the information and communication technology (ICT) based treatment adherence support after diagnosis.

Specimen date of collection: To be given in a DD/MM/YY format

Tick the box for sputum or others according to the specimen: If the specimen is not sputum, specify that.

Patient address with Landmark:

Complete address of the patient with landmarks is written in the space provided. It is very important to write the complete address of the patients, so that they can be easily traced when they do not return to the laboratory or the outpatient department of the hospital for their results. The contact telephone number (landline or mobile) has to be obtained and recorded in the form.

HIV Status: Tick the status as 'Reactive' or 'Non-Reactive' if known and 'unknown' otherwise.

Key Population: Patients who belong to the key population are eligible for a direct CBNAAT test, for concurrent diagnosis of Rifampicin resistance if present. Appropriate boxes (more than one if required) to be ticked.

Name of reference health facility: The name of the referring facility (any health sector) from where the patient is being referred for sputum examination is written in the space provided.

Health establishment ID: Most of the health facilities might have been registered in Nikshay and hence having a health establishment ID, (if not available, the facility has to be registered in Nikshay).

Patient ID allotted by Nikshay:

When the patient is enrolled in Nikshay as a presumptive TB case, this ID (Nikshay ID/ Patient ID) will be generated.

If this ID is available write in the provided space.

Write the name of State, District and TB Unit to which the health facility referring the patient for test belongs to.

Reason for testing:

Diagnosis and follow up of TB:

Left portion of this segment is for 'diagnosis of TB' and the right portion is for the 'follow up of TB'.

Under the diagnosis section

Tick the appropriate box for H/o of treatment for more than one month. And tick the reason for requesting test as Presumptive TB, Repeat Examination, Private Referral and Presumptive NTM.

In case of any discordance, Error, Invalid results and indeterminate results and reconfirmation a repeat CBNAAT test will be done.

Predominant symptom of the patient and its duration are to be noted in the space provided Example Cough 35 days, fever, 15 days etc.

Under the Follow Up section: Follow up by microscopy will be required for all drug sensitive TB cases and TB cases with unknown sensitivity status. Follow up with microscopy and culture will be required for all drug resistant TB cases on treatment with H mono poly regime and shorter MDR regimen,

PMDT TB No: When a patient is registered in District DR TB centre or Nodal DR TB centre a PMDT No. is given. Write this number in the space provided for when the patient is referred for follow up.

The duration to which the patient has taken the treatment need to be mentioned as month and week.

Test Requested:

The appropriate test requested for diagnosis or follow up has to be marked by ticking the appropriate box.

All the columns have to be filled meticulously legibly, correctly and completely and signed with date by the medical officer.

The remaining portion is for the laboratory personnel to report the result of the test. The details of the Laboratory test and its procedures are given below.

Specimen Identification Number

If specimens are being transported to a DMC and CBNAAT site from another health facility, a Specimen Identification Number is given at the referring facility, because the Laboratory Serial Number can only be assigned at the DMC. Sputum specimens are assigned specific numbers to keep track of each patient's sputum results. After the request form for examination of biological specimens is filled up, this number is written on the side of the patient's sputum container (If a sputum specimen is separated from its request form for examination of biological specimens, a LT can find out whose specimen it is by using the Specimen IdentificationNumber on the sputum container. The laboratory technician can then locate the form by using the date and the identification number.) Each separate specimen will generally have its own unique Specimen Identification Number. If sputum is collected and transported to the DMC and CBNAAT site, the list of patients whose sputum is being sent should accompany the samples and laboratory forms for sputum examination. An example of such a list is given below

List of Patients whose sputum are sent to DMC

Health Facility: PHI 101 Sent on: 4/9/18 Health Worker who collected specimen: Raju				DMC: PHI 237	For DMC use Received on: 6/9/18 Examined on:_____ Result sent back on:
Specimen Identification No.	Name	Age	Sex	Address	Date of collection of sputum
C1, C2	Lakshmi Kumari	46	F	223 Gandhi Dham	3/9/18,4/9/18
D1, D2	Lakshmi Pati Rao	50	M	223 Gandhi Dham	3/9/18,4/9/18
E1, E2	Girija Devi	32	F	225 Gandhi Dham	3/9/18,4/9/18
F1, F2	Kailash Nath	35	M	225 Gandhi Dham	3/9/18,4/9/18

2. Tasks performed during sputum collection

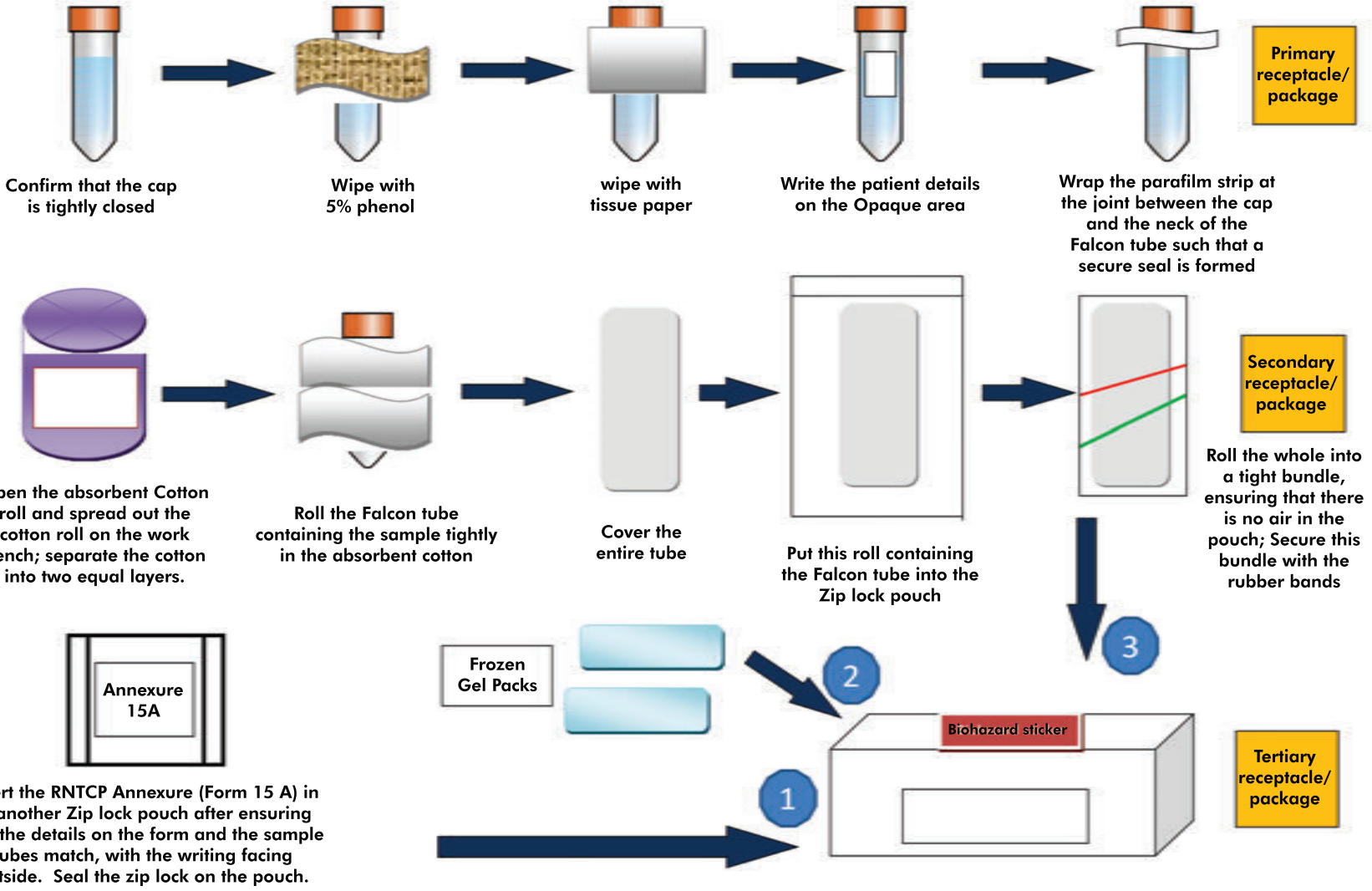
Person collecting the sputum specimen should follow the guidelines specified below:

- A specimen collected under supervision is likely to be of good quality and yield better results. The person guiding the patient for specimen collection should stand behind and encourage

him to cough from the depth of the chest and produce a quality specimen.

- Sputum should be collected in an open well ventilated space away from other crowded places in a health facility.
- The patient should be given a sputum container with the Laboratory Serial Number written on its side. If the sputum is being collected at a location other than the DMC, then the Specimen Identification Number (or patient's name with age) is written on the side of the container.
- For the diagnosis of tuberculosis, the two specimens of a patient i.e., one "SPOT-and the other an early MORNING " sample are collected. The spot sample is designated as 'A' and the early morning sample as 'B' adjacent to laboratory serial number. For follow-up sputum examination of patients, one specimen of sputum is collected. The specimen collected in the early morning is marked as 'B' and spot sample collected subsequently is marked as 'A'.
- The person collecting the specimen demonstrates how to open and close the container. The patient is instructed to inhale deeply (2–3 times), cough out sputum from the chest, spit into the container and close it.
- The person collecting the specimen should make sure that no one stands in front of the patient who is trying to collect sputum. Sputum should not be collected in closed rooms, toilets or ill-ventilated rooms.
- When a patient has only coughed up saliva or has not coughed up at least 2 l of sputum, the patient should be encouraged to give good specimen
- In case the container is soiled outside, it should be wiped dry using cotton swab and the same is disinfected in a bin containing 5% phenol solution.

Triple packaging system for sputum transportation



3. Tasks performed after sputum collection

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

- If the sputum specimens are to be sent immediately to the laboratory, the person should put the container into a special box meant for transport.
- If the sputum specimens are not being sent immediately to the laboratory, these should be refrigerated in the referring health facility.
- The person should wash hands thoroughly with soap and water whenever infectious material is handled.
- Patients should be instructed to collect the results of sputum examination. Alternatively, sputum results may be sent to the referring health facility by hand.

Transport of sputum specimens

Sputum collected in referring health facilities should be transported to the nearest DMC within 2 days. Once examined, the microscopy results should be reported on the same day. Arrangements should be made locally for transporting the specimens to the DMC and for sending the results to the referring health centres. The specimens should be packed carefully

Sputum specimens should be examined by microscopy on the same day and not later than 2 days after collection. The containers along with the sample MUST be disinfected with 5% phenol solution and disposed as per guidelines after the sputum smears results are recorded in the laboratory register.

Transportation of all specimens

Fresh sputum samples will need to be transported from the DMC to the CBNAAT laboratory in cool chain within 72 hours. Ideally an agency (courier/speed post) with a pan district presence should be identified by the DTO of every district for prompt transport of the specimen.

All States and districts should ensure that sample is always transported in cool chain The packaged box should be sent on the same day from the DMC to the courier / speed post office in the locality for onward transport to the CBNAAT/ Culture & DST laboratory assigned.

- The falcon tubes and the 3 layer packing materials like thermocol box, ice gel pack (pre-frozen at-20oC for 48 hours), request for C-DST forms, polythene bags, tissue paper roll for absorbent packing, parafilm tapes, brown tape for packing the thermocol box, permanent marker pen, labels, bio-hazard sticker, scissors, spirit swab etc. Should be supplied to the DMCs for collection of sputum through the DTO.
- The Lab technicians at DMCs should be trained to carefully pack the sputum samples in the cool box avoiding spillage of the samples.
- The LT of DMC issuing the falcon tubes, should also give clear instructions to the patients on correct technique of collection of the sputum. Also, the date of issue of the falcon tubes to the patient should be recorded.
- Two sputum samples are collected from each patient in a sterile 50ml falcon tube.

- At this point the lab number is written on the cap of the tube.
- The lab technician will perform surface disinfection of both the falcon tubes by placing the tubes in 5% Phenol for 20mins.
- After which the tubes will be wiped with tissue paper and left to air dry before packaging.
- After the tubes are completely dry, a label is affixed on the side of the tube indicating the date of collection of the samples and the patient's details like name, date of sample collection, name of DMC/DTC, Lab No., specimen A or B.
- Following this the cap tube interface is sealed using a small strip of parafilm.
- The tubes are then wrapped with absorbent cotton individually and is held in place with the help of a rubber band.
- Each tube is then placed inside a self-sealing cover/ ziplock pouch and wrapped around itself with a rubber band.
- The filled Annexure 15A should be folded and kept inside another self-sealing cover/ zip lock pouch.
- Both the falcon tubes along with the Annexure 15A is placed inside the thermacol box containing two frozen gel packs.
- The thermacol box is sealed using brown tape.
- "To" address and "from" address are affixed on the box. A biohazard symbol is also affixed on the box and is dispatched to the concerned lab for further testing.
- The LT of the DMC should promptly inform the sample transport agency like a courier/
- Speed post service, or a human carrier to collect and transport the samples.
- As per the national guidelines for BiomFedical waste management the containers used for transporting sputum samples to the NTEP-certified laboratory should be labelled with a "BIO-HAZARD" sticker.

EXERCISE 1 (Refer to annexure 2 –)

For this exercise assume that all patients are attending same health facility as the designated microscopy centre, called PHI 237. Complete annexure 15A NTEP request form for examination of biological specimen for TB and enrol in NIKSHAY for those where indicated. Date is 3rd September 2018. Referral is not indicated in all the patients. For patients in whom examination is necessary, specimen will be collected on 3rd September and 4th September. For ease of reference, each patient is given an alphabetic reference, which should be used for the specimen Identification Number wherever required.

1. Arun Kumar (Patient A) is 24-year-old male, labourer from 7 Institutional slum Area, Lodhi Road, 110006, weighing 40 kg with pain in the chest and cough for two weeks.
2. Raman Lamba (Patient B) of No. 18, Shalimar Bhagh, near sabji Mandi is a 24-year-old male labourer with pain in the chest for one week which increases on movement and cough/ sneeze.

3. Pooja Gupta (Patient C) is 13-year-old female student from 1064, Paranthe Wali Gali, Chandni Chowk – 110008, weighing 36 kgs with non-tender swelling of the lymph nodes in the interior and posterior areas of the left side of the neck for the last one month. She is also complaining of four days of cough.

4. Lakshmi Kumari (Patient D) is 46-year-old woman from 223 Gandhi Dham, Bapu Nagar - 110013 weighing 45 kg who has had cough for two months with fever, sweats at night, and occasional coughing up of blood.

5. Sita Devi (patient E) of 2586 Gali No. 3, Govind Puri, Near Gurudwara, is an eighty-year-old woman who complains that she feels tired. She does not have cough or any other symptoms. She has heard that people who are weak receive treatment at this centre and get better.

6. Narendra Kumar (Patient F) is 50-years known diabetic and alcoholic male from 223 Gandhi Dham, Bapu Nagar – 110013 weighing 40 kgs. He has had cough for a month. He gives no history of taking ATT in the past.

7. Ravindra Mehrothra (Patient G) of No. 70, Masjid ke pas, Sulthan Bazar, is a forty year old woman who complains of rash on her scalp and trouble sleeping at night.

8. Girija Devi (Patient H) is 50-year old female from 225 Gandhi Dham, Bapu Nagar- 110013 weighing 45 kgs. She has cough for a month. When asked about previous history of taking TB treatment, she remembers receiving multiple tablets taken for a few months once which made her urine turn orange. She recalls that these medicines helped her feel much better. She is a known HIV positive patient on ART and CPT.

9. Ashok kumar (patient I) of No. 55, Raja Garden, Near post office, is a 31 year old vendor who complains of cough and high fever for the past ten days. He is otherwise been healthy, but now feels very ill and short of breath when he walks. He remembers fever came suddenly.

10. Kailash Nath (Patient J) is 35-year-old, from 2586 Gali No. 3, Gobind Puri, Near Gurudwara 110036, weighing 60 kg. He is coughing and spitting blood. When asked, he reports that he has been coughing for several years. He has not taken any treatment before. He has two children aged 5 and 8 years at home who are asymptomatic.

TASKS PERFORMED AFTER SAMPLES ARE RECEIVED IN LABORATORY

The Tuberculosis Laboratory Register is a document maintained in a DMC for recording the details of the specimen smear examinations. The Laboratory Technician is responsible for maintaining and updating the laboratory register.

The TB Lab register (Annexure 3) captures all information of the patient who are being referred from referring health facility like PHI, ICTC, PHC CHC, ART centre, Medical college or even private health facilities

a. The left-hand portion of the TB lab register capture details of patient sample, his complete address, information on key population, the reasons for examination.

b. The right portion of the Lab register capture details of type of specimen, visual appearance results along with dates HIV and diabetics status, details of DST testing, Nikshay ID / Notification, Treatment initiation details and column for signature and remarks. of related top rapid DST results (Applicable for Dist. eg. CBNAAT), Culture results, DST results and reporting of the results.

1. Lab Serial no: A Laboratory Serial Number is assigned to each patient who has been referred for sputum examination.

2. Date of collection of first specimen: The date on which the first sample has been collected in the container.

Name

The patient's full name (also nickname, if any) is written in the space provided.

Age (in yrs)

The age of the patient is written in the space provided.

Gender

The letter 'M' is written for Male, 'F' for female and 'TG' for Transgender.

Complete Address (for diagnosis of patients)

Complete address with landmark. If more than one Mobile number available, try to capture all. This will help to provide the ICT based treatment adherence support after diagnosis.

Key Population: The numeric code for key populations given as foot note on the left side of the Lab register. The appropriate code for key population given in the request form need to be identified and recoded in this column.

Name and type of referring health facility: The name of referring health facility is as given in appropriately mentioned on Request form for examination of Biological specimen.

Reason for Examination:

In the first column under reason for examination, write whether patient is referred as presumptive TB, Repeat examination or Private. Presumptive NTM will be handled in the Culture & DST laboratory only.

Predominant symptoms and duration: Predominant symptom of the patient and its duration are to be noted in the space provided. Example, C 35 days, F 15 days etc. The coding is mentioned in the foot note in the Lab register.

Under Follow Up section: Follow up by microscopy will be required for all drug sensitive TB patients and TB patients with unknown sensitivity status. Follow up with microscopy and culture will be required for all drug resistant TB patients on treatment with H- mono/poly regimen and shorter MDR regimen,

History of 1 month of anti-TB treatment (ATT): Write Yes / No according to the history of treatment more than one month.

Follow up: for Follow Up patient Nikshay ID (Patient ID) will already available. Write that in the column for in the Nikshay ID.

Regimen: under the column regimen mention whether it is 1st tline ATT(Regimen for drug sensitive TB), or H-mono/poly or shorter MDR.

Month: Duration of treatment in completed month:

Post Treatment follow up month: After completion of treatment, the patients should be followed up at the end of 6, 12, 18 & 24 months. In presence of any clinical symptoms and/or cough, sputum microscopy and/or culture should be considered. This is important in detecting recurrence of TB at the earliest.

At the right side of the TB Lab register

Type of Specimen: Here mention whether the specimen is Sputum /Extra-pulmonary (CSF/Pleural Fluid, etc).

Visual Appearance: M- Mucopurulent, B- Blood Stained, S- Saliva.

A- For Supervised Spot,

B- Early Morning

Results: For sputum smear microscopy if the sputum is positive, write the exact grading in RED Ink, and for the Scanty mention the exact number of bacilli seene.g., Sc-5.

Date of Result: It is date on which the result is reported.

HIV Status (Reactive/ Non-Reactive/ Unknown): Mention whether Reactive or Non-Reactive or Unknown

Diabetic Status (Diabetic/ Non-Diabetic/ Unknown): Mention whether Diabetic/ Non-Diabetic/ Unknown

Sample for DST sent (Y/N) with date: Write Yes if the sample has been sent for CBNAAT or Culture Lab for Further diagnosis and No if not sent. All TB patients are expected to undergo DST for Rifampicin (Universal DST).

DST result (write the drugs to which resistance is demonstrated): Write the DST result obtained from CBNAAT or DST lab.

Patient ID (NIKSHAY ID): It is a Patient ID generated during enrolment in NIKSHAY.

Treatment Initiation Details: Name of PHI and TU in which the patient has been initiated on treatment or transferred to.

Signature: The Lab technician has to put his signature here.

Remarks: this is for additional comments if any e.g., Date of starting treatment, treatment regimen, referral details with date, remarks on unblinded rechecking

Laboratory procedures:

Ziehl–Neelsen staining:

1. A new unscratched slide is selected and Laboratory Serial Number is labelled on the slide using diamond marking pencil. New slide is selected in order to avoid deposition of carbol fuchsin which may result in false positive results.

2. Mucopurulent portion of the sputum is picked with a piece of clean broom stick and an oval shaped smear measuring 2 x 3 cm in size is prepared. The smear should neither be too thick nor too thin.

3. The optimum thickness smear of the smear can be assessed by placing the slide on printed matter .The print should be just readable through the smear.

4. Smears should be prepared near a flame as it sterilizes an area of six inches around the flame and disinfects the aerosols generated.

5. The slide is allowed to air dry for 15–30 minutes to clear air bubbles which would spurt while heating to fix the smear.

6. The smear is fixed by passing the slide over a flame 3–5 times for 3–4 seconds each time. Coagulation of the proteinaceous material in the sputum will facilitate fixing of the smear.

7. Carol fuchsin (1%, filtered) is poured to cover the entire slide and the slide is gently heated till vapour rises. The slide should not be heated to the extent of boiling. The carol fuchsin is kept on the slide for 5 minutes. Heating helps penetration of dye through the lipid wall of the bacilli.

8. The slide is gently washed using running water till free carol fuchsin stain is washed away. At this point, the smear on the slide looks red in colour.

9. 25% sulphuric acid is poured and allowed to stand for 2- 4 minutes. This will facilitate decolourisation of background except that of the bacilli.

10. The slide is gently rinsed under tap water and kept tilted to drain off the water.

11. A properly decolorized smear will appear light pink in colour. If the smear is still red, it is to be decolorized again using sulphuric acid for 1–3minutes. Slide is gently washed with tap water and the under surface of the slide is wiped clean with a swab dipped in sulphuric acid.

12. The smear is counterstained using methylene blue (0.1%) for 30 seconds. This renders the background blue and bacilli stained pink by ocarbon fuchsin, stand out in contrast. The slide is again rinsed gently with tap water and allowed to dry.

13. The slide is examined under the microscope using 40x lens to select the suitable area and then examined using 100x lens under of oil immersion (heavy liquid paraffin).

14. The results are recorded in the Laboratory Form and the Laboratory Register.

15. After the smear is read, the slide is inverted on a tissue paper till the immersion oil is completely absorbed. Xylene should not be used for cleaning the slides, as it may give false results upon repeat examination after storage.

16. All positive and negative slides are stored serially in the same slide-box until further instructions by the supervisor.

17. All contaminated material should be disinfected before discarding as per Bio-Medical Waste (management and handling) Rules 2016, using 5% phenol solution.

Importance of Grading of smears

- Grading of smears is a tool indicating the bacterial load in the patient. It is also used as a monitoring and supervisory tool under the program.
- This is meant to enhance the attention of the technician while reading the smears and facilitates supervision by STLS also.

The table below depicts information on grading and the number of fields to be examined in different situations:

Grading depends upon the number of Acid-Fast Bacilli (AFB) seen while examining the slides. Generally, laboratory technicians should have no difficulty in reading and grading the smear except in situations where the smears are scanty positive. The results should be reported to the treating physician after the examination of the specimen.

If the slide has:	No. of fields to be examined	Grading	Result
No AFB in 100 oil immersion fields	100	0	Negative
1-9 AFB per 100 oil immersion fields	100	Scanty*	Positive
10-99 AFB per 100 oil immersion fields	100	1+	Positive
1-10 AFB per oil immersion field	50	2+	Positive
More than 10 AFB per oil immersion field	20	3+	Positive

Fluorescent staining Procedures:

1. A new unscratched slide is selected and Laboratory Serial Number is labelled on the slide using diamond marking pencil. New slide is selected in order to avoid deposition of Auramine-O which may result in false positive results.
2. Mucopurulent portion of the sputum is picked with a piece of broom stick and an oval shaped smear measuring 2 x 3 cm in size is prepared. The smear should neither be too thick nor too thin.
3. The optimum thickness of the smear can be assessed by placing the smear on printed matter. The print should be just readable through the smear.
4. Smears should be prepared near a flame as it sterilizes an area of six inches around the flame and disinfects the aerosols generated.
5. The slide is allowed to air dry for 15–30 minutes to clear air bubbles which would spurt while heating to fix the smear.
6. The smear is fixed by passing the slide over a flame 3–5 times for 3–4 seconds each time. Coagulation of the proteinaceous material in the sputum will facilitate fixing of the smear.

7. Arrange slides in serial order on staining bridge, with smear side up, at a distance of at least one cm between every slide.

8. Flood the slide with filtered 0.1% Auramine solution. Do not heat

9. Keep the staining reagent for at least 20 minutes, make sure that the smear area is continuously covered with Auramine by adding more, if needed. Rinse with water and drain.

10. Apply decolourising solution, 0.5% acid alcohol for 3 minutes.

11. Gently rinse with water until the macroscopically visible stain has been washed away and drained

12. Flood smear with 0.5% potassium permanganate solution for 1 minute. Time is critical because counter staining for longer time may quench the acid-fast bacilli fluorescence. Gently rinse with water and drain.

13. Air dry on a slide rack away from sunlight. If they are not read immediately place them in slide box.

Grading scales for ZN/ FM

Grading scales for bright field (Ziehl-Neelsen) and fluorescence microscopy

Union / WHO scale 1000x field=HPF Result	Bright field (1000x magnification; 1 length=2cm= 100 HPF)	Fluorescence (200-250x magnification; 1 length=30 fields=300 HPF)	Fluorescence (400x magnification; 1 length=40 fields= 200 HPF)
Negative	Zero AFB / 1 length	Zero AFB / 1 length	Zero AFB / 1 length
Scanty	1-9 AFB / 1 length or 100 HPF	1-29 AFB / 1 length	1-19 AFB / 1 length
1+	10-99 AFB / 1 length or 100 HPF	30-299 AFB / 1 length	20-199 AFB / 1 length
2+	1-10 AFB / 1 HPF on average	10-100 AFB / 1 field	5-50 AFB / 1 field /10
3+	> 10 AFB / 1 HPF on average	>100 AFB / 1 field	>50 AFB / 1 field /8

HPF = high-power field; AFB = acid-fast bacilli.

Tubercle bacilli are quite variable in shape, from very short fragments to elongated types. They may be uniformly stained or with one or many gaps, or even granular. They occur singly or in small groups, are rarely in large lumps. The typical appearance is of bacilli that are rather long and slender slightly curved rods, with good staining (always check first a freshly stained positive control), there may still be fluorescing (sometimes green) artefacts which do not have a typical shape. Also, non-fluorescing bacillary shapes must be considered as artefacts.

Reasons for false-negative smear results

- Improper/Inadequate sputum collection

- Improper storage of sputum specimens
- Using saliva for smears
- Too thin or thick smears
- Over-heating / Insufficient heating of the slide while fixing
- Boiling carol fuchsin in ZN staining
- Over decolourization with sulphuric acid/ acid alcohol
- Improper storage of stained slides
- Inadequate examination
- Reading and reporting errors

Consequences

- Patients suffering TB may be missed and he/she may continue to spread the disease in the community.
- Wrong categorization
- Inadequate duration of treatment.
- Errors in declaring treatment outcome.
- Patients and the community may lose confidence in the programme
- Unnecessary repetition of investigations

Reasons for False-positive smear results

- Faulty sputum collection (presence of food particles)
- Using old scratched slides / already used slide
- Using unfiltered carbol fuschin in ZN staining
- Inadequate decolourization with sulphuric acid/ / inadequate exposure of acid alcohol resulting in inadequate decolourisation.
- Contamination due to transfer of bacilli from one smear to another
- Not wiping the oil immersion lens after examination of a positive slide
- Reading and reporting errors

Consequences

- Patients without TB may be put on anti-TB treatment unnecessarily
- Treatment may continue beyond the recommended duration
- Medicines are wasted
- Patients and the community may lose confidence in the programme

Preservation of slides:

Fluorescence fades with exposure to light and passage of time, thus it is important to store all the slides in slide storage box, immediately after smear microscopy.

Store all slides in slide boxes in the order they were recorded in the laboratory register. This will allow easy sampling of slides for external quality assessment using random blinded slide rechecking (RBRC)

Exercise 2:

Request form for examination of biological specimen for TB

Complete the Laboratory Form: Results Section

Start with Laboratory Serial Number 501. The appearance of the specimen is given in brackets. Specimens are examined on 4 September 2018. Sign your own name.

Patient		No. of AFB seen (visual appearance)
A. Arun Kumar	30	AFB are seen in 100 oil immersion fields (mucopurulent)
	6	AFB are seen in 100 oil, immersion fields (mucopurulent)
D. Lakshmi Kumari	150	AFB are seen in 50 oil immersion fields (bloody)
	80	AFB are seen in 50 oil immersion fields (mucopurulent)
F. Narendra Kumar	300	AFB are seen in 20 oil immersion fields (bloody)
	200	AFB are seen in 50 oil immersion fields (bloody)
J. Khaliah Nath	400	AFB are seen in 50 oil immersion fields (bloody)
	60	AFB are seen in 100 oil immersion fields (mucopurulent)
A. Pooja Guptas	0	per 100 oil immersion fields x 2 (saliva, mucopurulent)
	0	Per 100 oil immersion fields x 2 (saliva, mucopurulent)

Using the Tuberculosis Laboratory Register

- Every week the MO in Charge (or his designate) of the DMC should review the Tuberculosis Laboratory Register to ensure that correct numbers of sputum smear examinations (i.e., 2 per presumptive TB case) are being performed for diagnosis.
- Results recorded in the laboratory register, treatment cards and the TB Notification register are verified and ensured that they are consistent.
- It is the responsibility of the MO to ensure that all smear-positive patients diagnosed are started on treatment or are referred for treatment.
- If any smear-positive patients are not entered in the Tuberculosis Notification Register and are on treatment, they should be notified.
- For patients who have not been put on treatment it should be ensured that they are traced, put on treatment immediately and notified.

Accuracy of the Tuberculosis Laboratory Register

- The accuracy of recordings in the TB laboratory register should be checked by the laboratory technician (LT).
- All results of sputum smear examinations done in a Designated Microscopy Centre should be written only in Tuberculosis Laboratory Register, and not in any other register.
- Duplicate registers should not be maintained.
- LTs should ensure that correct laboratory serial number is recorded.
- Laboratory serial number is given to the patient and not to the sample.
- A new number should be assigned to every presumptive TB case whose sputum is to be examined.
- The Laboratory Serial Number should begin with a new serial (number 1) every calendar year.
- The Laboratory Serial Number is also written in the Tuberculosis Notification Register as well as the TB Treatment Card.
- It can be used as a cross-reference when the MO of the DMC cross-checks the results of the sputum examination in the Tuberculosis Register with that of Tuberculosis Laboratory Register and the TB Treatment Card.
- By using the name of the patient and his Laboratory Serial Number from the Tuberculosis Register, the MO of the DMC can easily locate the results of sputum examinations in the Tuberculosis Laboratory Register.
- Without this Laboratory Serial Number, it would be tedious to go through many pages of the Tuberculosis Laboratory Register for sputum results.
- The MO of DMC should check the Tuberculosis Laboratory Register and make sure all the columns have been completed. For example, it may be found that a patient's address or name of referring health facility is missing or incomplete in the Tuberculosis Laboratory Register.

The MO should emphasize on laboratory technicians, the importance of recording the complete addresses of patients examined for diagnosis. This facilitates tracing and initiation of treatment.

If the sputum smear examination is intended for diagnosis, the name of the health facility referring the patient should be written in the column meant for name of referring health facility (e.g. Dr CU Shah, Private Practitioner, or XYZ Hospital). If the presumptive TB case has attended the OPD of the DMC on his own, the name of the DMC should be mentioned in this column. If the patient has been referred from ICTC or ART centre, the same should be mentioned in this column. If the sputum smear examination is for follow-up examination, the name of the health facility where the patient is undergoing the treatment should be written in the Name of Referring Health Facility column.

The patient ID generated by Nikshay for all presumptive TB patients and the treatment initiation status of all diagnosed TB patients should be recorded in the columns meant for it. For patients whose sputum is examined for follow-up, patient ID, treatment regimen and month of follow-up should also be mentioned in the designated columns.

Recording of results of sputum smear examinations

- LTs should understand the importance of accurate recording of results of sputum smear examinations on the Request Form for examination of biological specimen for Sputum Examination.
- The Lab Technician should be informed that patients are put on appropriate regimen based on the results of the sputum examinations and further management of patients also depends upon the results of the follow-up sputum examination and at the end of the treatment.

Limiting administrative errors

- If the patient's sputum specimens are not labelled properly at the health facility or if the Request Form for examination of biological specimen gets separated from the specimens, the laboratory technician may not know whose sputum specimens are in the containers when they reach the laboratory.
- The LTs should ensure that the Laboratory Serial Number on the Request Form for examination of biological specimen matches with what is written on the side of the sputum container and on the slide used for smear preparation. Other health facilities which collect specimens and transport them to the DMC should assign Specimen Identification Numbers and write it on the side of the containers.

Results: The lower portion of the request form for examination of biological specimen of TB is to record the result of sputum smear microscopy. The Lab technician has to report the lab serial number, visual appearance and results of sample A and sample B correctly in this portion. The date tested, the date reported and the Laboratory name also have to be mentioned with the name and signature of the lab technician.

The visual appearance of the sputum specimen is to be entered in the relevant column. Results declared are to be entered in the column as either positive or negative and if positive, the appropriate grading is to be entered. This portion of the form should be duly signed by the laboratory technician of the DMC with date before dispatching the same to the Medical officer.

After receiving the sputum results

When the referring health facility receives the sputum results from the DMC, MO reviews the patients and based on the results of sputum smear examination, classifies the patient accordingly (as shown in the "diagnostic algorithm" earlier).

Monthly Abstract

The laboratory technician should summarize the information on sputum smear examinations done during that month. This information should be summarized in the prescribed format, printed in the Laboratory Register, at the end of each month . The STLS should write the monthly supervisory abstract after the last entry of the month. A new page is used every month for recording the sputum examination undertaken.

If only one sputum specimen was examined for diagnosis, patient should be traced and second sample should be examined. MOs are responsible for ensuring that the patient is traced. A smear- positive patient may be missed if the second sputum is not collected and examined. To minimize the proportion of 'false' smear-negative patients, at least 2 smear-negative sputum specimens should be available.

Accuracy of the results of follow-up sputum smear examinations recorded in the Tuberculosis Register, should be ensured by comparing with those in the TB Lab Register. Such comparisons especially for patients who were smear-positive at the beginning of treatment should be made.

Annexure 15 K

TB Laboratory Register

Lab. Serial No.	Date of collection of first specimen	Name (in full)	Age	Sex M/ F/TG	Complete address (for diagnosis patients) & Phone No.	Key Population [1]	Name and type of referring health facility[2]	Reasons for Examination				Follow-up			
								Presumptive TB / RE / Presumptive NTM	Predominant symptom[3] & its duration[4]	History of >1 month ATT (Yes/No)	Patient ID	Regimen New / H mono/ Shorter	Month	Post Treatment follow up month

[1] Key population – 1. Contact of TB/DRTB case, 2. Tobacco, 3. Prison inmates, 4. Miner, 5. Migrant, 6. Refugee, 7. Urban slum, 8. Health-care worker, 9. Other vulnerable population (specify)
[2] Name of referring health facility-PHI/DMC/TB/DTC/ICTC/ART/Medical College/DR-TB centre / Private/ Others, specify
[3] Predominant symptoms: Cough-C, Fever-F, Haemoptysis-H, Weight loss-W, Night Sweat - N Others-O, No symptoms - NS
[4] Duration of predominant symptoms should be recorded in days

Type of specimen	Visual appearance[5]		Results		Date of Result	HIV status (Reactive/ Non Reactive/ Unknown)	Diabetic status (Diabetic/ Non Diabetic/ Unknown)	Sample for DST sent (Y/N) with date	DST result[7] (write the drugs to which resistance is demonstrated)	Patient ID (notification no.)	Treatment initiation details (TB No. & TU details) / Referral for treatment	Signature	Remarks[8]
	a[6]	b[6]	a[6]	b[6]									

[5]Visual appearance- mention M, B, or S., Mucopurulent, Blood stained or Saliva

[6]a- stands for supervised spot sample, b- stands for early morning sample

[7] Sensitive= if sensitive to tested drugs, Name of drug if resistant to any – R= Rifampicin, H=Isoniazide, E=Ethambutol, Z=Pyrazinamide, SM=Streptomycin Lx=Levofloxacin, Mx (0.5) or (1) =Moxifloxacin, Km=Kanamycin, Cm=Capreomycin, Am=Amikacin, Eto=Ethionamide, Lzd=Linezolid, Cfz=Clofazimine

[8] Remarks column can include date of starting treatment, treatment regimen, TB no., referral details with date, remarks on un blinded rechecking, etc.

Exercise 3:

Complete the pages of the Laboratory Register using the laboratory form you have completed in Exercise 1 & 2

Processing of Sputum specimens using CBNAAT Preparation directly from sample:

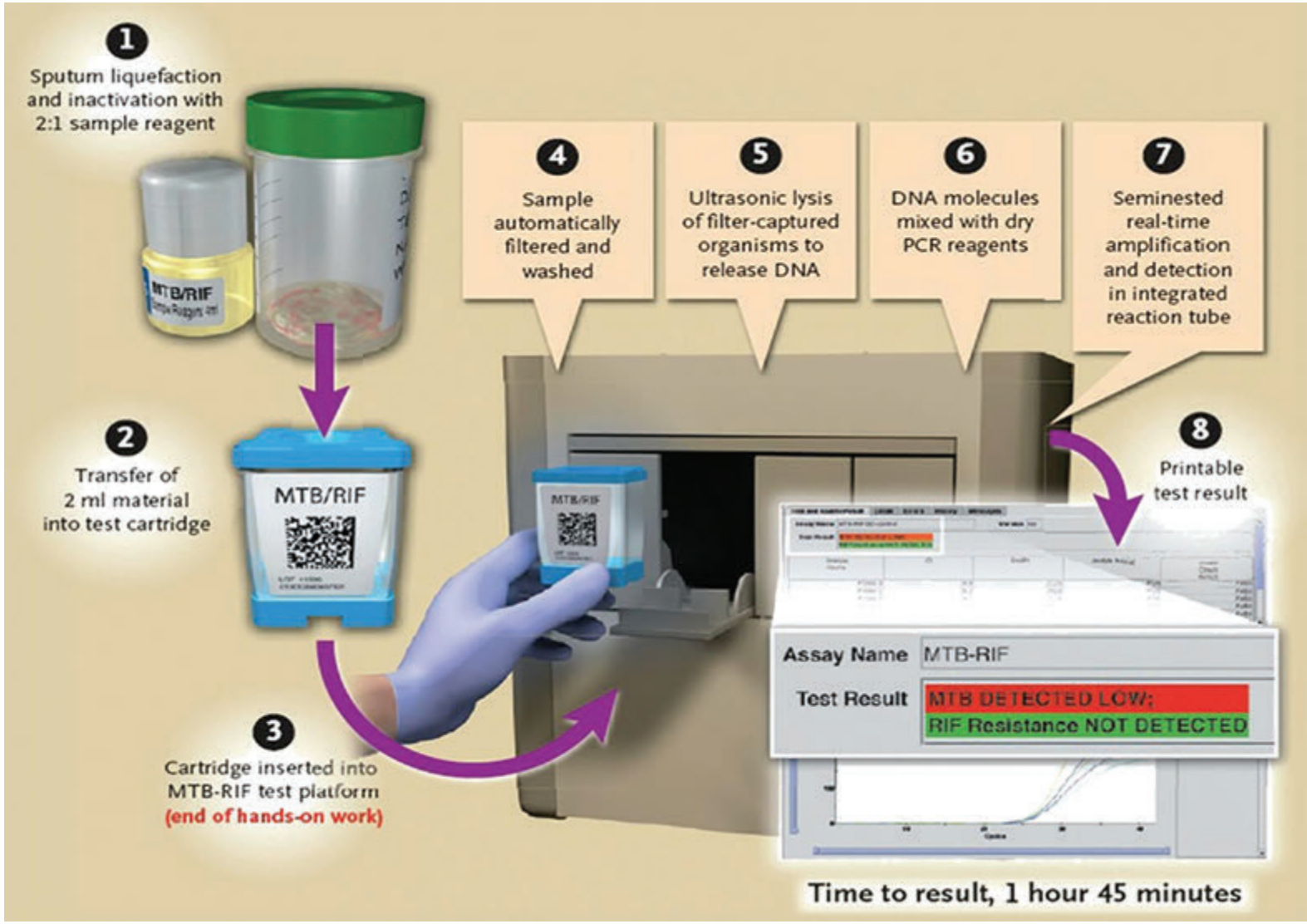
- For each of the sample: unscrew the lid of sputum collection container.
- Add directly in the collection container, 2 volumes of sample reagent to 1 volume of sample
- Replace the lid, and shake vigorously 10-20 times. (Note: one back and forth movement is a single shake.)
- Incubate at room temperature. After 10 min. of incubation, shake (or vortex) the specimen vigorously 10-20 times.
- Specimen should now stand for 5 minutes
- Sample should be perfectly fluid before being processed, with no visible clumps of sputum.

Prepare your cartridge

- Label the cartridge with the sample ID by writing on the left or right side of the cartridge or affix ID label.
- Transfer 2 ml of processed sample to cartridge.
- Begin test by loading the cartridge into the Gene X-pert Machine.

Note: do not put the label on the lid of the cartridge or obstruct the existing 2D barcode on the Cartridge. Do not touch 2D barcode on the cartridge.

- CBNAAT results are available within two hours from the time of loading the cartridge into the machine. The different type of results available are;
    a. MTB Detected High; RIF Resistance Detected
    b. MTB Detected Medium; RIF Resistance Detected
    c. MTB Detected Low; RIF Resistance Detected
    d. MTB Detected Very Low; RIF Resistance Detected
    e. MTB Detected High; RIF Resistance Not Detected
    f. MTB Detected Medium; RIF Resistance Not Detected
    g. MTB Detected Low; RIF Resistance Not Detected
    h. MTB Detected Very Low; RIF Resistance Not Detected
    i. MTB Not Detected
    j. MTB Detected Very Low; RIF Resistance Indeterminate
    k. Error
    l. Invalid


1
Sputum liquefaction and inactivation with 2:1 sample reagent
2
Transfer of 2 ml material into test cartridge
MTB/RIF
3
Cartridge inserted into MTB-RIF test platform
(end of hands-on work)
4
Sample automatically filtered and washed
5
Ultrasonic lysis of filter-captured organisms to release DNA
6
DNA molecules mixed with dry PCR reagents
7
Seminested real-time amplification and detection in integrated reaction tube
8
Printable test result
Assay Name
MTB-RIF
Test Result
MTB DETECTED LOW;
RIF Resistance NOT DETECTED
Time to result, 1 hour 45 minutes

Points to be remembered

- Undiagnosed and untreated pulmonary sputum smear-positive TB patients are the source of infection in the community and have the potential to transmit infection to others.
- The most common symptom of pulmonary TB is a persistent cough for 2 weeks or more.
- Under the programme, sputum smear microscopy, x-ray and molecular diagnostic tests are the main tools for the diagnosis of TB patients.
- Two sputum smears should be examined (Spot—Early morning) for diagnosis.
- Sputum should be examined within 2 days of collection and the results should be reported on the same day.
- It is important to elicit past history of anti-TB treatment from the patient.
- Extra-pulmonary TB patients, contacts of all smear-positive cases and PLHIV with cough should be subjected for sputum examination irrespective of the duration of cough.
- On an average, about 2–3% of new adult out-patients in a general clinic (in rural PHC settings) will be presumptive TB cases and should be referred for sputum examination.
- On an average, 10% of the presumptive TB cases, subjected for sputum examination (SOP) are found to be smear positive pulmonary tuberculosis.
- Grading of smears is helpful as a quality assurance tool

Universal drug susceptibility testing

The programme is committed to providing Universal Drug Susceptibility Testing (UDST) for all notified TB patients (bacteriologically confirmed and clinically diagnosed). All TB patients are offered DST to at least the Rifampicin through rapid molecular test. Cascading DST for Fluoroquinolones and second line injectable are offered through LPA.

Section B: Quality Assured Laboratory Services

Introduction:

An effective quality assurance (QA) system of sputum smear microscopy network is crucial for reliability of data generated under NTEP. QA is a system consisting of internal quality control (QC), external quality assessment (EQA), and continuous efforts for quality improvement (QI) of laboratory services. The system also provides credibility of laboratory results and motivation of staff for further improvement of their efficiency.

A nation-wide network of designated microscopy laboratories provide appropriate, accessible and quality assured laboratory services.

NTEP has established a three tier Quality Assurance system to monitor laboratory activities based on international guidelines which includes NRLs at the national level, STDCs / IRLs at the State level & DTC / TU at the District level.

In this section of the module the participants will learn about

- Structure of NTEP laboratory network
- Quality assurance for smear microscopy
- Maintenance of adequate supply of quality laboratory consumables
- Supervisory visit to DMC
- Infection control: Safe disposal of contaminated materials
- Annexures, Checklist and IQC documents

Structure of NTEP laboratory network

A wide national network of Designated Microscopy Centres (DMCs) with competency in smear microscopy has been established, to provide diagnostic services with an "easy access for the entire population" under the programme. The network of DMCs is supported by larger State TB Training and Demonstration Centres (STDCs), also referred to as Intermediate Reference Laboratories (IRLs), and overseen by six National Reference Laboratories (NRLs), viz., National Tuberculosis Institute (NTI), Bangalore, National Institute of Research in Tuberculosis (NIRT) Chennai, (SNRL), National Institute of Tuberculosis and Respiratory Diseases (NITRD) New Delhi, National JALMA Institute for Leprosy and Other Mycobacterial Diseases Agra, Bhopal Memorial Research Centre (BMRC) Bhopal and Regional Medical Research Centre (RMRC), Bhubaneswar.

The Central TB division is advised on all technical issues by the National Reference Laboratory Coordination Committee which includes members from all the six NRLs and representatives from WHO & CTD.

Levels of laboratories under NTEP

National Reference Laboratory: Each NRL will supervise sputum microscopy EQA of states designated to them. The NRL will ensure proficiency of NTEP staff for carrying out good quality diagnosis by providing technical training to the STOs, STDC Directors, Microbiologists and Lab Technicians of States.

Intermediate Reference Laboratory: The states will designate one Intermediate Reference Laboratories in the STDC or Medical College or in any Public Health Laboratory of the state. The IRL should be a facility deemed fit for certification by the respective NRL supervising the State. The designated IRL will conduct sputum microscopy EQA for the state and occasionally for a

neighbouring state or union territory. The IRL will provide technical training to district and sub-district technicians and STLS.

Designated Microscopy Centre: Sputum microscopy diagnostic services under NTEP are provided by Designated Microscopy centres (DMC) established for every laboratory where Binocular microscope and trained Lab Technician is available. LED Fluorescent microscopes are provided to DMCs of medical colleges and other DMCs with high work load.

Section B: Quality Assurance (QA) for smear microscopy

Quality assurance system includes

A. Internal Quality Control (IQC)

B. External Quality Assessment (EQA)

C. Quality Improvement (QI)

A. Internal Quality Control (IQC)

- It's a systematic internal monitoring of working practices.
- It includes technical procedures, checking instruments, quality of new batches of staining solution, smear preparation, grading, equipment infection control measures, waste management etc.

a. Staining reagents:

Preparation of 1% carbol Fuchsin:

- Ensure dye content is mentioned on the bottle while procurement
- Potency to be corrected before preparing the stain
- Stain should be filtered (Whatmann Filter No 1) before use

Preparation of 25% Sulphuric Acid

- Concentrated acid to be stored separately (away from other chemicals) to avoid accidental spillage.
- The required quantity of acid may be transferred into a small glass container (Borosil Glass). The accurately measured quantity of acid (using a measuring cylinder) is slowly transferred along the walls of the container into a round bottom flask containing the required quantity of distilled water. The reaction is exothermic (generates heat) and hence the flask (Borosil) should be kept in a cold-water bath/ice bath during preparation.
- Utmost care to be taken while transportation

Preparation of 0.1 % Methylene Blue

1. Ensure dye content is mentioned on the bottle while procurement
2. Potency to be corrected before preparing the stain

b. Manufacturing QCP and QCN by STLS:

- QCP & QCN slides to be prepared by the STLS only.
- QCP slides may be prepared by pooling 3+ grade sputum samples.
- QCN slides may be prepared by pooling Negative sputum samples with adequate number of pus cells (approximately 20 cells /field).
- One set of QCP & QCN to be used by the STLS while preparing each new batch of Staining reagent and entry made in the batch register (IQC document).

- One set of QCP & QCN to be supplied to the DMC LT by the STLS along with each batch of reagent. The DMC LT to stain and examine the QCP & QCN slides and enter the results in the IQC document.
- All Quality control slides should be stored for a maximum period of three months.

c. General maintenance of Binocular Microscope

- Oil to be removed from the objective lens using a soft lens cleaning tissue paper after examining each slide.
- The microscope to be stored inside a microscope box at the end of the day.
- The Microscope box should contain Silica Gel and an Electric Bulb of 10-15 Watt for desiccation to prevent fungal growth on the lens.
- The Silica Gel should be dehydrated periodically under direct sunlight and may be reused (Dehydrated gel looks blue in color).

All Microscopes should be under AMC with routine preventive maintenance.

External quality assessment for sputum smear microscopy

1. The activities of NRL:
   a. On-site evaluation of STDC/ IRL Labs
   b Manufacture of Panel testing slides and panel testing of STDC/ IRL Lab staff
   c. Training of STDC supervisory staff in:
   I. On site evaluation of STLS
   ii. Manufacture of panel slides
   iii. Assessment of blinded re-checking of DMC slides at DTC
   iv. Facilitating the training of STLS for External Quality Assessment (EQA)
   d. Re-training of STDC/ IRL supervisory staff, if required.
   e. Prompt reporting of the results of activities and feedback to STO/DDG TB.
   2. The activities of STDC/ IRL:
   a. Training of EQA for STLS, DTO, MO-TC
   b. On-site evaluation of DTC Labs and a sample DMCs
   c. Manufacture of Panel testing slides and panel testing of DTC Lab supervisors including all STLS of the district
   d. Assessment of blinded re-checking of DMC slides at DTC
   e. Re-training of DTC LT/ STLS, if required.
   f. Prompt reporting the results of activities by Director STDC/ IRL to STO, CTD & NRL.
   3. The activities of DTC/ TU:
   a. On-site evaluation of DMC Labs
   b. Unblinded re-checking of DMC slides at DMC
   c. Random Blinded re-checking (RBRC) of DMC slides at DTC
   d. Prompt reporting of the results of activities to LT and MO of DMC as well as STDC/ IRL.
   e. Panel testing and re-training of DMC LTs, if required.
   a. On-Site Evaluation (OSE)

A visit to STDCs/IRLs and DTC/DMCs is an essential component of a meaningful QA programme. As part of an ongoing EQA process, depending on the performance of the laboratory being visited, the frequency of on-site evaluation is decided. On-site evaluation is conducted at least once a month by STLS to the DMC, once a year by STDC/ IRL laboratory supervisors to District TB Centres (DTCs) and TB Units (TUs) and once a year by laboratory supervisors of NRLs to STDCs/ IRLs. This provides an opportunity for immediate problem solving, taking corrective action and on-site retraining.

When poor performance is identified through any of the above-mentioned activities, additional visits by trained laboratory personnel from the higher level laboratory (the STDC/ IRL or NRL laboratory Supervisors) are mandatory for evaluation of all laboratory procedures.

The visit includes a comprehensive assessment of laboratory safety procedure, conditions of equipment, adequacy of supplies as well as the technical components of AFB smear microscopy, which includes preparation, staining and reading of smears. Sufficient time must be allotted for the visit to include observation of all the work associated with AFB smear microscopy.

On-site evaluation at DMCs should also include examining five positive and five negative smears to observe the quality of smear and staining as well as condition of the microscope. At the DMC, the LT arranges all the slides in the slide box serially as per laboratory register and preserves all the slides after examination (LT has to preserve all the slides till RBRC process is complete and feed-back is given). The supervisor (STLS) re-checks monthly in an unblinded manner, on his onsite evaluation visits, 5 positive and 5 negative slides selected from the lab register by systematic random sampling procedure. STLS marks in the Laboratory register with a small 'x' sign and makes entries in his OSE-checklist and “remarks” column of the lab register. STLS should discuss discrepant slides with the LT, identify the cause of error, if any and provide specific corrective measures.

Checklists used during OSE (Annexure 5)

Checklists are developed to assist both laboratory and non-laboratory supervisors during the field visit and to allow for the collection and analysis of standard data for subsequent remedial action. Checklists may be refined to focus on problems that are frequently identified or most likely to occur, such as preparation of stains or errors in grading. Copies of the checklist should be left behind in the unit being evaluated. This will provide written documentation of the visit and findings and will also assist subsequent evaluations to monitor improvements. When poor performance is identified through any of the above-mentioned activities, additional visits are mandatory for evaluation of all laboratory procedures.

Comprehensive checklist for on-site evaluation of DMCs is provided in the annexure A. The checklist contains open, non-leading questions and recommended observations along with objective criteria for acceptable practices. Use of a simple standardized checklist even by well-trained district supervisors (e.g. DTO), can reduce the time necessary to evaluate a laboratory effectively.

Panel Testing

Panel testing is a method of EQA that is used to determine whether a laboratory technician can adequately perform AFB smear microscopy. This method evaluates individual performance in staining and reading, and not all the laboratory activities. Utilization of panel testing for EQA is considered to be less effective than random blinded re-checking of routine slides because it does not monitor routine performance.

Panel testing is a useful supplement to the system of re-checking of slides. It provides information on the capabilities of the peripheral laboratories prior to implementing a re-checking programme. It can also be used to assess the level of performance or to quickly detect problems associated with very poor performance. The proficiency of laboratory technicians after training can be evaluated.

Panel testing is used for supervisory lab staff of STDCs/ IRLs and DTCs, and will be conducted under the supervision of the visiting lab team during their annual on- site evaluation visit. A panel will consist of 5 unstained smears per laboratory personnel. Panel testing is not performed as a routine in the DMCs, as they will have regular on-site evaluation and blinded re-checking.

Random Blinded Re-Checking of Routine Slides (RBRC)

Blinded rechecking is a process of rereading a statistically valid sample of slides from a laboratory to assess whether that laboratory has an acceptable level of performance. This activity is performed once a month for every DMC.

Random blinded re-checking must ensure that:

- The sample contains a sufficient number of randomly selected slides to be representative of all slides of the DMC,
- The supervisor (STLS) of the laboratory (first controller), must not be aware of the original result of peripheral laboratory technician to prevent bias, i.e. results are "blinded",
- Minor false errors are included with major errors for the purpose of obtaining a smaller sample size. The smaller sample size facilitates implementation and sustainability of rechecking
- Discrepant results are resolved by a second controller (umpire).
- There must be a system to provide timely periodic feedback and improvements to the laboratories that are supervised.

Random blinded re-checking of routine slides from the DMCs is implemented throughout the laboratory network. A system utilizing Lot Quality Assurance Sampling (LQAS) method is used to calculate the sample size (LQAS Table)

Sample Size based on LQAS

(90% sensitivity, 100% specificity and '0' Acceptance number)

Number of negative slides in the DMC in a year (ANSV)	Slide positivity rate (SPR %)						
	2.5-4.99	5.0-7.49	7.5-9.99	10.0-12.99	13.0-14.99	15.0-17.99	≥ 18
	Annual sample size of both positive and negative slides (monthly sample size in parenthesis)						
301-500	330 (28)	249 (21)	202 (17)	172 (15)	138 (12)	124 (11)	111 (10)
501-700	404 (34)	288 (24)	227 (19)	189 (16)	148 (13)	132 (11)	117 (10)
701-1000	486 (41)	326 (28)	249 (21)	203 (17)	156 (13)	139 (12)	122 (11)
1001-2000	637 (54)	386 (33)	281 (24)	223 (19)	168 (14)	147 (13)	128 (11)
>2001	907 (76)	468 (39)	321 (27)	247 (21)	179 (15)	156 (13)	134 (11)

Note:

- The monthly sample size has been rounded off to the next higher number. It adds up to equal or more than annual sample size.
- If the number of slides available in the DMC is less than the monthly sample size, the same needs to be compensated in the forthcoming month/s.
- For the DMCs with ANSV <300 the sample size in the row 301-500 should be used as applicable with the respective SPR range. If the ANSV is less than the indicated annual sample size, the respective DMC should submit all their slides for blinded re-checking.

- The STLS selects from lab register RBRC sample slides for random blinded rechecking (RBRC) on the advice of the DTO
- These slides are selected using a systematic random blinded sampling procedure and the results of the slides selected are circled in the Lab register by STLS.
- The LT will enter the slide numbers that are selected by STLS in 'Annexure B' along with results;
- Encloses the annexure B in a sealed envelope;
- Arranges the slides in a separate box supplied by DTO and marks on the top of box as well as envelope with the title: RBRC slides, Name of DMC, TU and the month & year.
- STLS picks up the box and sealed envelope and hands them over to DTO.
- DTO conducts RBRC and gives feedback and corrective actions to LT through MO- DMC.

The activities to be performed by DTO at DTC are briefly given below.

Every calendar month, DTO instructs all STLS to collect appropriate number of slides from LTs of DMC as per LQAS method.

1. DTO receives sealed envelopes with Annexure B and slide boxes from the respective STLS.

2. DTO will code the boxes ensuring that the DMC does not get same code every month. Coding of boxes is an important activity of DTO and blinding of slides must be ensured by DTO.

3. DTO should maintain a register where he would enlist the codes given to each DMC for each of their RBRC months. The register should also show how DTO has allotted the codes to the STLSs. STLSs should be allotted the coded DMC boxes taking care that DMC allocation is not repeated to the same STLS who is supervisor of that DMC. Rotation of DMCs amongst different STLSs should also be ensured over consecutive RBRC monthly cycles.

4. DTO retains sealed Annexure B in his possession. (Annexure 6)

5. DTO will make a roster from 11th of the calender month onwards giving one or two or three days (based on no. of samples to be re-checked) for each STLS to come to DTC for the re-checking. No two STLS should come for re-checking at the same time. All STLSs are informed of the month's Blinded re-checking roster. STLS to read and record results for slides as per Annexure C - one slide box at a time.

6. After getting results from STLS, DTO transfers the results of LT from Annexure-B to Annexure-C (for each DMC).

7. DTO identifies the discordant slides for re-checking by second controller (called Umpire reader). Discordance is any slide with 'positive' smear result of LT (of any grade) being read as 'negative' by STLS and vice- versa and for 'positive' slides having a difference of more than one grade between LT and first controller.

DTO takes out the discordant slides in a separate box and gives it to an Umpire reader who could be any STLS.

Umpire has to de-stain and re-stain the slides before reading. De-staining is performed by dipping the slides in absolute alcohol for 5 mins. These are re-stained by ZN staining method. The format for giving these results to Umpire reading is as follows, which is maintained in a separate note book with DTO. Results 1 and 2 should not indicate the identity of the either LT or STLS and are interchanged frequently to maintain the confidentiality of the original readers.

RBRC		DMC Code	Discordant slide number	Result 1	Result 2	Umpire reading	Signature
Slide No.	Month						

10. STLS/DTO/MO-TC to evaluate results and give feedback to each DMC (MO and LT) as per annexure D, with information to the CMO/Civil Surgeon.

11. DTO receives a copy of the monthly on-site supervision report from STLS through MO- TC and decides on the next course of action in consultation with MO-TCs.

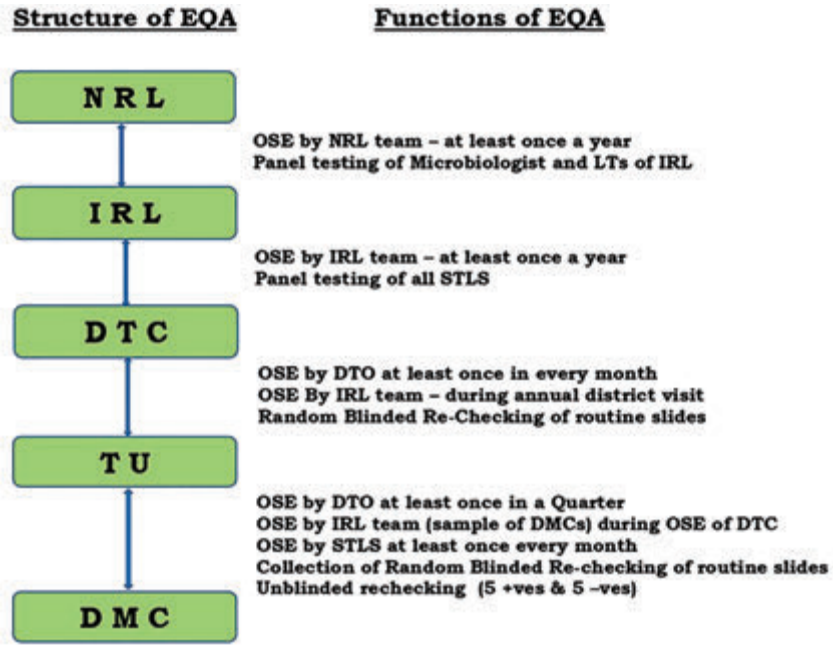
12. DTO sends a copy of the monthly report on random blinded rechecking to STDC/ IRL/STO every month (as per annexure E), Monthly lab abstract of district, DMC-wise (Annex M for district) and a copy of OSE summary report of EQA (Annex F) to STDC/ IRL every quarter and percentage of DMCs with high false error in the district, in district PMR report to STO/Central TB Division every quarter.

13. The pattern of errors that are likely to occur, possible causes for these errors and suggested investigation steps to be taken by the Lab supervisors including DTOs/ MO-TCs/ STLS are given in Annexure K.

14. DTOs and MO-TCs should familiarize themselves with these in order to effectively supervise the DMCs under their area.

15. The DTOs and MO-TCs have to report the EQA activities in their respective Quarterly report on Programme Management.

Structure & Functions of EQA



Quality improvement (QI):

- A process by which all components of smear microscopy diagnostic services are carefully analyzed with the aim of looking for ways to permanently remove obstacles to success.
- Appropriate data collection, data analysis, correct interpretation of the results and creative problem solving are the key components of this process.
- Involves continued monitoring, identifying defects, followed by remedial action including retraining when needed, to prevent recurrence of problems.
- Relies on effective on-site evaluation

Maintenance of adequate supply of quality consumables

The MO of DMC is responsible for determining the amount of reagents and other materials the DMC needs every month. The STLS will make sure these supplies are distributed in a timely manner, usually on a monthly basis or as and when required.

It is made sure that there is an adequate stock of reagents and other materials in the at all levels.

It is very important for the laboratory to maintain an adequate stock of reagents and other laboratory materials. If the laboratory has less stock of any items, it is ensured that supplies are provided to the laboratory from the district or sub-district stock. LTs are reminded to exhaust the old supplies before starting to use the new supplies. Old reagents should not be mixed with the new supplies. They should be kept in separate containers.

It is ensured that the reagents are of good quality. It should be freshly prepared at the DTC and supplied to the DMCs on monthly basis. In case the TU has adequate infrastructure and

equipment (Weighing balance, water bath, round bottom flasks etc.,), the reagents may be prepared at TU level as well. The LT himself should stain and examine the Quality Control slides supplied to him by STLS after receiving the fresh batch of reagents.

Reagents should not be used beyond 3 months from the date of its preparation. Commercially available 'readymade' laboratory reagents should not be used. It is ensured that the binocular microscope is in good working condition. Regular arrangements have to be made by the DTO for maintenance of the microscope through Annual Maintenance Contract. In case the microscope is under warranty, the supplier may be contacted for undertaking its repair. The following laboratory materials should always be available in the laboratory.

Chemical & Reagents • Carbol fuchsin (1%) • Sulphuric acid (25%) • Methylene blue (0.1%) • Auramine O (0.1%) • Acid Alcohol (0.5%) • Potassium Permanganate (0.5%) • Synthetic immersion oil • Methylated spirit	**Consumables** • Glass slides for microscopy, and slide-boxes for storing slides • Diamond markers (for marking the slides) and marking pens or grease pencils (for making the sputum containers) • Broom sticks (thick enough to make good smears)
• 5% phenol / 40% phenolic compound (proprietary Phenyl) diluted to 5% • Absolute alcohol to be available at the DTC only for de-staining discrepant slides during umpire reading • Silica gel (hygroscopic agent) to maintain the microscope in moisture free environment (to be placed in the cabinet for Binocular Microscope)	• Transparent glass bottles (1000 ml) for storage of reagents (with self-adhesive labels stating date of preparation of reagents) and dropper bottles (100 ml) • Plastic tumblers / mugs • Glass (or metal) rods (or holding slides during the staining process) • Staining racks (for drying the slides) • Sputum containers • Spirit lamp or Bunsen burner • Foot-operated bin (for disposal of contaminated materials) • Time (stop-watch) • Fine Silk and Lint cloth • Lens paper (for wiping the oil immersion lens after examination of each slide) • Whatmann filter paper No. 1 • Filter paper (to drain the oil from the slides)
Consumables Stationery • Request form for examination of biological specimen for sputum examination • TB Laboratory Register • Referral / Transfer form for treatment • Stock register - laboratory	

* These items are reusable

** If cut discs are not available, roll sheets can be procured

Calculation of consumables required for examination of 3000 smears

Reagents/ Equipment for staining	Quantity
Binocular microscope with 10x, 40x and oil immersion objective (100x) eyepieces (10x) and spare bulbs and fuses	At least 1 per DMC
Plastic disposable sputum containers	3,300
Slides for microscope, 25*75 mm, 1.1 mm-1.3 mm Thick	3,300
Broom stick 10 cms length	3,300
Diamond marker pencil	3 number
Timer, 30 or 60 minutes	1 number
Forceps, Chitel forceps stainless steel for slides 15 cm	1 number
Scissors, 25 cm stainless steel	1 number
Slide rack, Staining slide rod of metal or plastic or glass for 12 slides	2 numbers
Slide boxes, For 100 slides	33 boxes + 2 per DMC for RBRC
Tissue rolls	4 numbers
Marker pen	12
Absorbent cotton, 500 gms/ roll	4 numbers (2 k.g)
Pressure cooker, For disposal by autoclaving	Optional
Phenol with concentration mentioned on the bottle	80 litres
Methylated spirit	3 litres
Cotton, full sleeves Aprons	2
Disposable gloves, 6 and 8 inches (box of 25 pairs)	12 boxes
Spirit lamp with wicks	1 number
Metal wire, For swab for heating of Carbol fuchsin	1 number
Sputum specimen transport box, Insulated box, made of plastic 10" x 10" x 10", thickness 1" with lid, handle and nylon belt 1" width 2.5 feet length, nylon strap of 1" width 2 feet length with Velcro to strap the lid of the box from side to side.	2 numbers

For preparation of reagents at DTC/TU

Reagents/ Equipment for staining	Quantity
Reagents for ZN staining	
Basic fuchsin, Pararosaniline hydrochloride, C19 H18 N3 Cl, molecular wt: 323.8, Colour: Metallic green, Dye content: Should be available on the container. Approximately 85%-88%	250 gms
Carbolic acid (Phenol), C6H5OH, and molecular wt: 94.11, Melting point: 400C, Solidification point: 40.50C, Purity: 99.5%	850 gms
Sulphuric acid: H2SO4, molecular wt: 98.08, Purity: 95-97%, Colour: Clear (potency correction should not be made)	6 ltrs
Methylene blue, (Methylthioninechloride), C16H18CIN3S, molecular Wt: 319.9 Dye content: Should be available on the container. Approximately 82%	25 gms
Alcohol (absolute)	2.5 ltrs
Distilled water (instead of distillation apparatus)	50 ltrs
Reagents for FM	
AuramineO Dye powder	20 gm
Carbolic acid (Phenol), C6H5OH, and molecular wt: 94.11, Melting point: 400C, Solidification point: 40.50C, Purity: 99.5%	400 gm
Alcohol (absolute)	20 ltrs
Concentrated Hydrochloric acid (HCl)	200 ml
Potassium Permanganate KMnO4	100 gm
Distilled water (instead of distillation apparatus)	35 ltrs
Equipment required	
Funnel, 7" dia 7" height and 5" stem height	4 nos.
Funnel, 3" dia 4" height and 5" stem height	4 nos.
Drop bottles, Glass/ plastic 100 ml capacity	8 nos.
Bottles for storage of stock solutions, Brown bottles 2 litre capacity	2 nos.
Bottles for storage of stock solutions, 2 litre capacity	10nos
Flat bottom round flask, Capacity 5 litres of borosil Glass	5 nos.
Wash bottle, Plastic 500 ml	6 nos.
Drop plastic bottle for immersion oil, 10 ml capacity	2 nos.
Disposable bucket, Plastic foot operated 12 litres	2 nos.
Measuring cylinder, 1000 ml capacity plastic or glass	6 nos.
Measuring cylinder, 100 ml capacity plastic or glass	4 nos.

Water tanks, Plastic with tap, 100 litres where there is no running water facility.	1 no
Filter paper, Whatman no. 1 packs of 100 2″ * 2	3 box
Adhesive labels for sputum containers	6 rolls
Soap, soap box, towel and clean rags as needed	As per requirement
Aluminium vessel, for the purpose of carbol fuchsin solution preparation 16″ diameter 9″ height	1 no.
Water bath, for the preparation of carbol fuchsin (to fit 5 lit round bottom flask)	1
5 lit round bottom flask)	
Beaker, 250 ml with spout	1 no.
Display board	1 no.
Stove wick type/ Bunsen burner with butane gas cylinder/ burner with gas cylinder	1

Supervisory visits to designated microscopy centres

Designated microscopy centres are supervised by STLS from the sub-district. The DTO/MO-TC/MO will coordinate with the STLS to ensure that tuberculosis-related laboratory services are properly performed and recorded by the laboratory technician. Prior to the visit to the designated microscopy centre, one has to plan thoroughly.

In this section, DTO/MO-TC/MO will learn how to prepare for visits to designated microscopy centre, review the items to be checked during the visit to a laboratory and will develop a checklist to use the same during supervision visit.

Preparation for visits to designated microscopy centre

1. The DTO/MO-TC has to decide when to visit each designated microscopy centre in the TU/district. The visit is planned in advance so that a DTO can visit all DMCs in his/her district at least every quarter and a MO-TC can visit all DMCs in his TU at least every month.

2. Decide what to check. Some important items to check are listed under point 4 (below). Review the recommendations made during previous visits and the actions taken.

3. Decide when to check each item. Some items, such as the Tuberculosis Laboratory Register, should be checked during each visit. Other items including stocks of sputum containers, slides and reagents may be checked periodically.

4. Decide how to check each item. Depending on the time available for the visit, decide the best ways to collect information:

   (I) Review the Tuberculosis Laboratory Register. Check the Tuberculosis Laboratory Register to make sure it is filled completely and accurately. Make sure that all smear-positive patients in the Tuberculosis Laboratory Register have undergone Universal DST. Look for the name of the PHI/TU/District in the remarks column if the patient is referred for treatment. Verify that patients who were examined for diagnosis had correct number of

sputum specimens examined. Also verify that the details of follow up examination (Patient ID., regimen and month) have been entered in the reasons for examination column. Make sure that LT is writing the monthly summary correctly. Lastly verify whether in the remarks column there are any entries mentioning about DR TB suspects and sample sent for C & DST.

(ii) Talk with the laboratory technicians. Make sure that they understand the importance of examining the correct number of sputum specimens. Also, make sure that they understand the importance of limiting administrative errors and accurately recording the results of sputum smear examinations on the Laboratory Form for Sputum Examination. In addition, make sure that the laboratory technicians keep the examined sputum smear slides of all patients until the EQA procedure is completed. Reiterate that LT should immediately inform the treating physician regarding every follow up positive patient., .

(iii) Examine supplies. Check to see if there are adequate numbers of sputum containers, slides, reagents, forms and other laboratory supplies.

5. Develop a checklist. Once it is decided what to look for when one goes to the designated microscopy centre and how to check each item, it will be helpful to organize the information into a 'checklist'. In general, the checklist should be just long enough to remind the supervisor about the important items/activities that needs to be checked. It should be easy to use. Include important general information, such as the name of the centre and supervisor, and date of the visit. A more comprehensive checklist is given below. Review it now. This checklist is longer than the one that should be used during supervisory visits, but is provided for reference. You should develop your own checklist based on this.

Conduct the visit- Information should be given to the Medical Officer/ BMO/ In-charge and STS and STLS in advance about the visit to the designated microscopy centre. In the DMC, the checklist that you have prepared should be used.

Checklist for laboratory supervision

Review of resources

Please write Yes/No in the column "Observation"

No	Check-points	Observations	
1	Is at least one trained Medical Officer available in the health facility?	Yes	No.
2	Is a full-time trained Laboratory Technician (LT) available for sputum microscopy?		
3	Have provisions been made for sputum collection when LT is absent?		
4	Is a functional binocular microscope available?		
5	Has the binocular microscope undergone any servicing during last12 months?		
6	Are all essential lab consumables available adequately, enough to last at least for one month?		

7	Is running water available for sputum microscopy**?**		
8	Is electricity available for the binocular microscope**?**		
9	Have civil works been done in the Lab as per NTEP guidelines**?**		
10	Are printed reference materials on standard operating procedures available**?**		
11	Are all the samples collected at collection centre and transported to the DMC are documented and examined**?**		
12	Are all SOPs displayed at the place where LT prepares the slides (staining charts, grading charts, BMW material etc.,)		

Review of forms, registers, records and reports

1	Are the request forms for examination of biological specimens Forms for Sputum Exams filled correctly, completely and legibly?	
2	Is the TB Laboratory Register filled correctly, completely and legibly?	
3	Is the Lab Serial Number entered correctly, starting with 1 on 1stJanuary of the year and continuing until 31 December?	
4	Are results correctly recorded?	
5	Are there 2 sputum smears for diagnosis?	
6		
7	Are positive results written as scanty, 1+, 2+ or 3+in red and negative in black/blue?	
8	Are results up-to-date?	
9	Does the Lab register have the summary abstract completed at the end of each month?	
10	Is there a duplicate Lab Register?	
11	Are copies of supervisory reports of Senior TB Lab Supervisor available with LT?	
12	Is there evidence of supervision by STLS on lab register?	
13	Is monthly PHI-level report on sputum microscopy and logistics being submitted by the health facility?	
14	Is there a TB notification register available in DMC? Are the names of all the smear positive patients recorded in the notification register with all relevant details?	
15	Are all smear positive patients notified in NIKSHAY? Log on to NIKSHAY and verify.	

16	Is the Lab register consistent with the treatment cards and TB notification register? (Check information for at least 4-6 randomly selected new smear -positive patients.)	
17	Review the OSE reports and Annexure D kept at the laboratory	
18	Review whether all patients smear positive on follow up were identified as presumptive DR TB patients.(Remark column)	
19	Review whether the sputum sample collection was done from all identified DR-TB suspects?	
20	Review whether the QC usage register is being maintained?	

Observe the Lab Technician during the sputum-collection procedure

1	Did the LT check to ensure that the Lab Form was complete and correct?	
2	Is the sputum container clearly labelled on the side and not on the lid?	
3	Are each set of sputum samples from a single patient given a single Lab Serial Number?	
4	Is the Patient ID written in the space provided for all patients whose reason for examination is "follow-up" of treatment?	
5	Does the LT demonstrate to patients how to bring up sputum?	
6	Does the LT supervise patients when they provide spot sputum specimens?	
7	Does the LT visually examine the sputum provided to determine if it is sputum or saliva only?	

Observe the Lab Technician preparing smears for examination

1	Does the LT use only new slides?	
2	Does the LT engrave the Lab Serial Number on each slide with a diamond marker?	
3	Does the LT use a different broom stick for each sputum smear?	

4	Are the sputum smears made on the slide of the correct size(2cmX3cm) and thickness?	
5	Does the LT wait for the slide to dry before heating the slide to fix it?	
6	When the Lab technician fixes the slide by heating, does s/he do it for the proper duration of time?	
7	Is only "freshly prepared" carbol fuchsin being used, instead of ready-made commercially-available solutions?	
8	Is the carbol fuchsin free of particles and properly filtered before use?	
9	When the LT heats the carbol fuchsin, does s/he do it properly, avoiding boiling and allowing the slides to stand for 5 minutes after heating?	
10	Does the LT tilt the slides after rinsing with water to remove excess water?	
11	Is the sulphuric acid allowed to stand on the slide for the appropriate time period (2–4minutes)?	
12	Is the methylene blue allowed to stand on the slide for the appropriate time period (30 seconds)?	

Observe the Lab Technician examining slides under the microscope

1	While placing immersion oil on the slide, does the LT take care to avoid touching the slide with the applicator?	
2	While examining the slide with the X100 lens, does the LT take care to make sure that the lens does not touch the slide?	
3	Does the LT examine negative sputum smear slides for at least 5 minutes?	
4	Does the LT have correct knowledge about grading?	
5	Does the LT see 100 fields before declaring the smear as negative?	
6	Does the LT correctly complete the Lab Form for Sputum Examination and Lab Register?	
7	Does the LT clean the X100 lens with lens paper/fine silk after completing the examination?	
8	Are slides correctly cleaned and maintained serially in slide boxes for review by the supervisor?	
9	Are all smear-positive results recorded in red ink in the Lab Register?	

10	After examining the slides, does the LT put the sputum containers and lids (with lids removed) along with the broom sticks, into a foot-operated bucket containing 5% phenol?	
11	Does the LT break all the remaining slides of the previous month after The EQA procedure is completed?	
12	Does the LT ensure that smear-positive as well as smear-negative slides are not being re-used for AFB microscopy?	

Exit-interviews of atleast 2 patients undergoing sputum microscopy

1	Do the patients know how to cough out good quality sputum properly?	
2	Do the patients know when they should return for the next sputum exams?	
3	Do the patients find the timings and location of the Lab convenient?	
4	Do the patients face any difficulties for undergoing sputum microscopy?	

Quality assurance for CBNAAT

Internal Quality Control:

Each CBNAAT cartridge contains internal controls, Specimen Processing Control (SPC) and Probe Check Control.

If the probe check fails, then the test is stopped and an error result is obtained. Troubleshooting is required based on the error code generated. Error rates higher than 5% should be investigated.

SPC must be positive when the result is MTB not detected. It can be negative/positive when the result is MTB detected. The test result is considered invalid if the SPC is negative when the test result is found negative.

External Quality Assurance (Proficiency Testing) for CBNAAT:

EQA is a specialized form of assessment focused on assuring accuracy and reliability of examination methods.

EQA /PT is an effective tool to promote continual improvement which can identify occurrences/nonconforming events and offers external assessment of process output.

Importance:

- Gives assurance to users that the CBNAAT instrument is functioning properly at the time of installation.
- Checks to verify that users can correctly interpret and report results.
- Verifies that there are no major errors in the process control system and that samples are identified correctly, tested correctly and reported correctly.
- Quickly recognizes major problems with an instrument or user at installation.

Dried tube specimens (DTS) PT panels are used for testing the efficiency of laboratories. Panel consists of inactivated non-infectious dried culture of M.tb with RIF sensitive and resistant and negative / NTM. Procedure are safe and compatible with testing protocol.

PT panel of 5 DTS samples are provided for testing to the laboratories to check pre-analytical, analytical and post-analytical processes, and the results of all laboratories are analyzed, compared, and reported to the laboratories.

To enable prompt initiation of corrective actions, feedback regarding PT results is provided in a timely manner to the testing sites and to supervisory staff. PT will help to identify major non-conformities, allowing supervisors to target the most poorly performing laboratories for on-site supervision.

Quality assured CBNAAT test results are essential to ensure patients are correctly diagnosed early and initiated on an appropriate treatment regimen.

Infection Control

There is the risk of transmission of tuberculosis infection occurring in health care facilities including the laboratory when patients remain undiagnosed and untreated for tuberculosis. This may be curtailed by early diagnosis and immediate initiation and adherence to NTEP treatment regimens. This prompt and timely action will make infectious TB patients rapidly non-infectious.

It is now mandatory that any Infection Control plan of the facility should include infection control for TB and TB/ HIV. Broadly, infection control needs to be addressed at three different levels: administrative, environmental and personal.

Administrative control relies on the extent of complete implementation of diagnostic and treatment guidelines in the health care facility. TB infection control plan includes the following:

- Giving priority for patients with cough for clinical and laboratory investigations for early detection of smear-positive pulmonary tuberculosis patients
- Reducing delay in starting appropriate treatment once diagnosed
- Avoiding unnecessary admission for inpatient care
- Assessment of health care workers training needs

Sputum collection should ideally be done outside the facility and away from the people. It should not be done in closed areas such as toilets and in ill-ventilated rooms. Processing specimens for smear microscopy (after sputum collection) has not been documented to cause any increased risk to laboratory personnel. However, TB suspects amongst health care workers should be subjected to screening procedures.

Second priority is environmental control, which is used to reduce the generation and concentration of droplet nuclei in the air in high-risk areas. High-risk areas that increase transmission include exposure in relatively small, enclosed rooms in health facilities, which lack adequate cross ventilation in the form of open windows and doors to "clean" the environment through dilution or removal of infectious droplet nuclei. Hence, the TB IC plan should also include educating the patients regarding cough hygiene (covering the face while coughing and avoiding indiscriminate spitting), frequent identification of risk areas within the facility and providing good cross-ventilation to the area.

Wearing of surgical masks made of cotton wool/ gauze/ paper for personal protection does not protect the person who is wearing the mask from inhaling the droplet aerosols and hence is not recommended as a means to prevent hospital infection. However, masks are useful in preventing droplets when worn by the patient.

The key to reducing the risk of tuberculosis transmission at health facilities is early diagnosis and prompt initiation of treatment regimens. Infectious TB patients become rapidly non-infectious once they are started on treatment.

All health care workers at the district level should receive onsite training at least once in two-years regarding M. tuberculosis transmission and airborne infection control. Training should include Signs and symptoms of TB, increased risk of TB disease in persons who have HIV infection and other immunosuppressive conditions and prevention of airborne infection with M. tuberculosis.

An Infection control plan for TB-HIV may include precautions to be observed for HIV, in addition to that observed for TB, especially when streptomycin injections are being provided. The risk of acquiring HIV following percutaneous exposure (needle stick/ needle prick with inoculation) from an HIV-positive source is extremely low: 0.25- 0.3%. This is because the concentration of HIV in peripheral blood is extremely low (104 infectious virions /ml). On the other hand, the risk of acquiring hepatitis virus (HBV) following similar exposure ranges from 9-30% because the concentration of HBV in blood is high (>10,000,000 infectious doses /ml). The chance of acquiring Hepatitis C is approximately 3-10%. Disposable needles and syringes should be used for injections. Needles and syringes should be disposed as per the Bio Medical waste management guidelines.

Health care workers can effectively prevent infections acquired through contaminated blood by the adoption of "Universal Precautions" or "Bio-safety Precautions"

Bio-Medical Waste Management under NTEP at PHIs:

The Government of India (GoI) under its Environment Protection Act (1986), passed the Biomedical Waste (Management and Handling) Rules in 1998 and a subsequent amendment followed in 2000. The rules form the legal framework for the collection, segregation, transportation, treatment and disposal of biomedical waste throughout the country. The State Pollution Control Boards (SPCBs) in the states and the Pollution Control Committees (PCCs) in the Union Territories are monitoring the compliance to the rules in the respective states.

BMW is integrated into the general health system of the states. Waste management is a component of overall facility management of the respective state health system institutions where TB centres are located. Accordingly, the waste generated by PHIs, DMCs should not be viewed in isolation, but is to be integrated in the broad framework of the peripheral institutions' waste management practices. The peripheral health institutions would be responsible for disposal of the wastes and reporting to their respective PCBs.

Types of wastes generated by the PHIs

- Human/biological waste (sputum);
- Sharp waste (needles, glass slides etc.);
- Used blister packs, drug packaging material;
- Plastic waste (waste generated from disposable syringes, cups and glasses); and
- Laboratory and general waste such as liquid waste, broomsticks, and paper waste; and
- Construction waste (waste generated from civil work activities).

Waste Management at Phis

Waste generated by TB laboratories will be discarded with the overall waste of the health facility in which TB services are provided. The staff carrying out TB services like LTs and DOT providers in PHIs will adopt infection control techniques as detailed in the guidelines and will take action to integrate waste generated by the TB laboratory into the waste management activities of the

concerned PHI. The activities by the PHIs will include organized waste collection, information dissemination, reporting and monitoring of disposal of the waste.

Disposal of sputum container with specimen and wooden sticks

Step 1: After the smears are examined, remove the lids from all the sputum cups.

Step 2: Put the sputum cups, left over specimen, lids and wooden sticks in foot operated plastic bucket/bin with 5% phenol or phenolic compound diluted to 5%. The cups and lids should be fully immersed in the solution. Keep it overnight/ for about 12 hours.

Step 3: Next day/ at the end of the day, drain off the phenol solution in to the drain.

Step 4: Take out the sputum cup/lid/wooden sticks and put into a reusable metal or autoclaveable plastic container or red bag. The red bag should have a biohazard symbol and adequate strength so that it can withstand the load of waste and be made of non-PVC plastic material.

Step 5: Put this container/bag into the autoclave with other autoclavable BMW and the contents should be autoclaved at 121°C at 15 psi pressure for 15 – 20 minutes. The autoclave shall comply with the standards stipulated in the rules. Under certain circumstances, if autoclaving is not possible, boil such waste in a pressure cooker of approximately 7 litre capacity containing adequate amount of water to submerge the contents and boiled for at least 20 minutes using any heating source, electrical or non-electrical. However, the District Hospital/CHC/PHC etc. shall ultimately be expected to make the necessary arrangements to impart autoclaving treatment on regular basis.

Step 6: After adequate cooling, the material can be safely transported to a common waste treatment facility for mutilation / shredding / disposal.

If a common waste treatment facility is not available in the area, the sputum cups/lids/ wooden sticks after autoclaving, can be buried in a deep burial pit.

LTs and support staff handling biological waste should wear gloves.

Disposal of stained slides

Step 1: The slides should be put into a puncture proof container and red bag. The red bag should have a biohazard symbol and should be made of non-PVC plastic material. This bag/sharp container should then be put in to an autoclave or pressure cooker for autoclaving/boiling.

Step 2 : Dispose off the autoclaved/ pressure boiled slides into a pit for sharps.

Under no circumstances should the slides should be broken.

Points to remember

- DTO and MO-TC are responsible for supporting laboratory services.
- STLS is responsible for supervisory activities of all the designated microscopy centres in the sub-district.
- Only Tuberculosis Laboratory Register should be used to record information about sputum smear results.
- All smear-positive (including scanty) results should be recorded in red ink in the Tuberculosis Laboratory Register.
- Slides once used should not be reused.
- Contaminated materials should be disinfected and disposed safely.
- Only one Laboratory Form for Sputum Examination is used for one patient and only one Laboratory Number is given for 2 sputum examinations for diagnosis.
- Grading of smears increases the accuracy of results and helps in quality control measures. Grading is resorted to enhance the concentration of the laboratory technician while reading the smears.
- Follow-up sputum smears done at scheduled time help in monitoring treatment.
- Accurate recording of results of sputum smear examinations on the Laboratory Form for Sputum Examination ensures correct diagnosis and appropriate treatment.
- Ensuring quality of each and every designated microscopy centre is an essential feature under the programme.ach and every designated microscopy centre is an essential feature under the programme.

MODULE 3

TREATMENT SERVICES

Learning objectives

In this module, the participants will learn about the following:

- Goal and objectives of treatment
- Scientific basis of treatment
- Case definitions
- Fixed Dose Combinations (FDC)
- Treatment Regimen and drug dosages
- Operational guidelines for treatment initiation
- Treatment support systems
- Follow-up of treatment
- Contacts
- TB Preventive Therapy
- Flow of patients
- Treatment outcomes
- Prevention and management of Adverse reactions to drugs
- Management of Special situations and comorbid conditions
- Hospitalization
- Extrapulmonary TB
- Drug-Resistant TB
- Nikshay entries- Transfer, Initiation, Prescription, Comorbidity, Refill, follow ups, adherence, and outcome
- Organization of DOT and flow of patients for treatment

Introduction

The previous module has dealt with the provision of quality assured laboratory services. This module deals with the technical and operational aspects of the treatment services provided by the programme.

Goal and Objectives of treatment

- Render patient non-infectious, break the chain of transmission and decrease pool of infection
- Decrease case fatality & morbidity by ensuring relapse free cure
- Minimize & prevent development of drug resistance

Scientific basis of treatment of TB

The strategies adopted in the treatment of TB are based on both scientific and operational research.

The following four components are discussed in brief

- Domiciliary treatment
- Short course chemotherapy
- Treatment regimen
- Direct observation of treatment

Domiciliary treatment

Domiciliary chemotherapy has been proved to be as effective as sanatoria treatment. Studies in India have shown that smear positive TB patients treated on a domiciliary basis have achieved high cure rates as good as those when treated at sanatorium besides having other social benefits of being at home. The patients after the initiation of treatment on domiciliary basis also did not pose extra risk as a source of infection among contacts at home.

Short course chemotherapy

Short course chemotherapy regimens have made it possible to treat and cure TB patients in as short a period as six months. Reduction in the duration of treatment regimens was possible because of the introduction of Rifampicin and Pyrazinamide. Treatment regimens of six months duration given daily have been found to be effective and achieve high cure rates, prevent emergence of drug resistance and minimize relapses. The shorter duration has contributed to improvement in the treatment adherence. Short course chemotherapy regimens of 6 months are recommended internationally for most forms of extra-pulmonary TB.

Basis of chemotherapy

(a) Bacteriological basis

i. Existence of naturally occurring drug resistant mutants

- In an untreated smear positive pulmonary tuberculosis patient, there are naturally occurring drug resistant mutants to different drugs at different frequencies. The larger the bacterial population higher is the probability that resistant mutant strains are present. The number of bacilli is lower in smear negative and extra pulmonary lesions. The number of viable bacilli commonly found inside the cavities sized about 2 centimetres in diameter on an average is likely to be in excess of 100 million (108). As a thumb rule the frequency of occurrence of drug resistant mutants would be roughly ~1 in 106 to isoniazid (H), ~1 in 106 to streptomycin (S) and ~1 in 108 to

rifampicin (R). Based on these frequencies, the chances of naturally occurring organisms that is resistant to both H and R would be roughly ~1 in 1014, which is virtually negligible.

There would be appreciable numbers of mutant resistant to any single drug before the start of the treatment that are capable of multiplying and will not be affected by a single drug, e.g. isoniazid. This accounts for frequent failures observed with monotherapy of patients harbouring large number of bacilli. Thus, if two or more drugs are given concurrently, in the initial Intensive Phase when the bacterial load is high the chances of survival and selection of drug resistant organism to any drug would be very small as mutants resistant to one drug are as a rule susceptible to other and vice versa. This is the basis for the use of multi-drug therapy in the treatment of tuberculosis.

Role of intensive phase

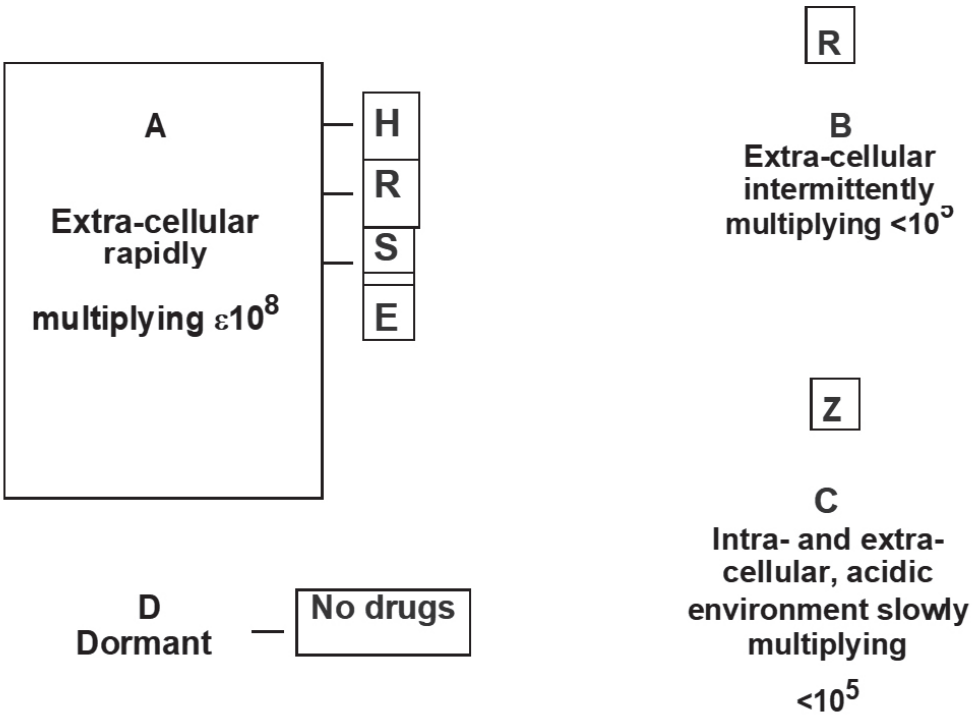
The objective of combining four drugs in the intensive phase (IP) is to achieve rapid killing of actively multiplying bacillary population. This phase will eliminate naturally occurring drug resistant mutants and prevent the further emergence of drug resistant mutants.

Role of continuation phase

Continuation phase (CP) with fewer drugs for a comparatively longer time will ensure elimination of persisters which are responsible for relapses.

Existence of sub-bacillary population

In a given lesion of TB, there are 4 bacterial sub-populations having different metabolic rates depending on their surrounding environment. They are acted upon with different intensity by the different anti-TB drugs. The bacillary population and different drugs acting on them are shown in the figure below.



The bacillary sub populations B and C are referred as semi-dormant or persisters which are difficult to eliminate and are the source of relapse.

Anti-TB drugs have the following three actions:

a. Early bactericidal activity
b. Sterilizing activity
c. Ability to prevent emergence of drug resistance

Isoniazid (H): Isoniazid is a potent drug exerting early bactericidal activity, prevents emergence of drug resistant mutants to any companion drug and has low rates of adverse drug reactions.

Rifampicin ®: Rifampicin is a potent bactericidal and sterilizing drug acting on semi- dormant bacilli which multiply intermittently and causing relapse.

Pyrazinamide (Z): Pyrazinamide is a bactericidal and sterilizing drug effective in eliminating the semi dormant bacilli multiplying slowly in an acidic environment.

Ethambutol (E): Ethambutol is an effective bacteriostatic drug helpful in preventing emergence of resistance to other companion drugs.

Streptomycin (S): Streptomycin is a bactericidal drug known to reduce septicaemia and toxicity.

The ranking of the drugs with respect to their type of activity is indicated in the following table.

Drugs	Early bactericidal	Sterilizing activity	Prevention of emergence of drug resistance
Isoniazid	++++	++	++++
Rifampicin	+++	++++	+++
Streptomycin	+++	-	++
Pyrazinamide	++	+++	+
Ethambutol	+	-	++

Pharmacological basis of treatment

It is established that in the treatment of tuberculosis it is of importance to achieve peak serum levels of all the drugs simultaneously, so that maximum bactericidal effect is obtained. This is achieved by administration of all the drugs at the same time. This also renders operational convenience of advising the patients to consume all the drugs at the same time.

Daily Regimen

The NTEP had adopted thrice weekly regimen for treatment of drug sensitive TB until the year 2016. Various research studies have shown that relapse rates were higher with intermittent regimen. Hence the programme has now shifted to daily regimen for treatment of all drug sensitive TB patients. The adverse drug reactions with daily regimen may be higher compared to intermittent regimen, therefore, it is necessary to clinically monitor the patients on treatment.

Directly Observed treatment (DOT):

Studies in India and many other countries have consistently shown that at least one third of patients do not consume medicines regularly. DOT is a supportive mechanism that ensures the best possible results in treatment of TB. Here a treatment supporter helps the patient in taking the treatment, thereby ensuring adherence. Many patients who do not receive directly observed treatment stop taking drugs once they feel better. It is neither possible to predict who these patients will be nor to prevent non-adherence through health education. Studies have shown that there will be poor treatment outcome and high death rates in the absence of DOT, even when regular supply of drugs is ensured. Hence, by providing DOT, NTEP ensures that patients receive the right drugs, in the right doses, at the right intervals and for the right duration.

CASE DEFINITIONS

- **Microbiologically confirmed TB:**
  - presumptive TB patient with biological specimen positive for AFB, or positive for MTB on culture, or positive for TB through Quality Assured Rapid Diagnostic molecular test.
- **Clinically diagnosed TB case:**
  - A presumptive TB patient who is not microbiologically confirmed, but diagnosed with active TB by a clinician on the basis of X-ray, histopathology or clinical signs with a decision to treat the patient with a full course of Anti-TB treatment.
  - In children, this is based on the presence of abnormalities consistent with TB on radiography, history of exposure to an infectious case, evidence of TB infection (positive TST) & clinical findings suggestive of TB in the event of negative or unavailable microbiological results

TB cases are also classified according to:

- anatomical site of disease
- history of previous treatment
- drug resistance

Classification by anatomical site of disease

- **Pulmonary tuberculosis (PTB):** any microbiologically confirmed or clinically diagnosed case of TB involving lung parenchyma or tracheo-bronchial tree.
- **Extra Pulmonary tuberculosis (EPTB):** any microbiologically confirmed or clinically diagnosed case of TB involving organs other than lungs e.g. pleura, lymph nodes, intestine, genitourinary tract, joint and bones, meninges of the brain etc.

Miliary TB classified as PTB because there are lesions in the lungs.

A patient with both pulmonary and extra-pulmonary TB should be classified as a case of PTB.

Classification by H/O previous TB treatment

- **New case -** A TB patient who has never had treatment for TB or has taken anti-TB drugs for less than one month.
- **Previously treated patients have received 1 month or more of anti**-TB drugs from any source in the past.
  - **Recurrent TB case -** A TB Patient previously declared as successfully treated (cured/treatment completed) and is subsequently found to be microbiologically confirmed TB case.

- Treatment After failure- those patients who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.
- Treatment after lost to follow-up A TB patient previously treated for TB for 1 month or more and was declared lost to follow-up in their most recent course of treatment and subsequently found microbiologically confirmed TB case.
- Other previously treated patients are those who have previously been treated for TB but who cannot be classified into any of the above classification.

Classification based on drug resistance

- **Mono-resistant (MR):** A TB patient, whose biological specimen is resistant to one first-line anti-TB drug only.
- **Poly-Drug Resistant (PDR):** A TB patient, whose biological specimen is resistant to more than one first-line anti-TB drug, other than both INH and Rifampicin.
- **Multi Drug Resistant (MDR):** A TB patient, whose biological specimen is resistant to both isoniazid and rifampicin with or without resistance to other first line drugs, based on the results from a quality assured laboratory.
- **Rifampicin Resistant (RR):** resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs excluding INH. Patients, who have any Rifampicin resistance, should also be managed as if they are an MDR TB case.
- **Extensively Drug Resistant (XDR):** A MDR TB case whose biological specimen is additionally resistant to a fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin) and a second-line injectable anti TB drug (kanamycin, amikacin, or capreomycin) from a quality assured laboratory.

Treatment regimen

For all TB patients whether being treated in public or private sector, clinicians should follow Standards for TB care in India (STCI) guidelines. In NTEP, the principle of treatment for tuberculosis (other than confirmed Drug Resistant forms of TB) is to administer daily fixed dose combinations of first – line anti-tuberculosis drugs in appropriate weight bands. For patients being treated in private sector, FDCs may be provided by NTEP whenever requested.

Regimen for Drug-Sensitive TB (DSTB) cases: 2HRZE/4HRE

This regimen is for H & R sensitive TB cases and cases with unknown sensitivity pattern.

Treatment is given in two phases:

- Intensive phase (IP) consists of 8 weeks (56 doses) of isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) given under direct observation in daily dosages as per weight band categories.
- Continuation phase (CP), consists of 16 weeks (112 doses) of isoniazid, rifampicin and ethambutol in daily dosages. Only pyrazinamide will be stopped in the continuation phase. The CP may be extended by 12-24 weeks in certain forms of TB like CNS TB, Skeletal TB, Disseminated TB etc. based on clinical decision of the treating physician on case to case basis. Extension beyond 12 weeks should only be on recommendation of specialists.

Regimen for	IP*	CP
	Doses	Doses
Drug Sensitive TB	56	112

Loose Drugs could be used as substitutions in case of adverse drug reaction or with comorbid conditions.

Steroids as an adjunctive therapy is useful in patients with TB pericarditis and meningeal TB, with an initial high dose tapered downwards gradually over 6 - 8 weeks.

Type of TB case	Treatment Regimen in IP	Treatment regimen in CP
New and previously treated cases (H and R Sensitive / unknown)	2 HRZE	4 HRE

Prefix to the drugs stands for number of months

Fixed Dose Combinations (FDCs)

Fixed Dose Combinations (FDCs) refer to products containing two or more active ingredients in fixed doses, used for a particular indication(s).

IN NTEP, for Adults - 4-FDC (given in IP) consists of HRZE and 3-FDC (given in CP) consists of HRE

For paediatric patients -Dispersible 3 FDC consists of HRZ and Dispersible 2 FDC consists of HR.

Advantages of FDCs

- Simplicity of treatment
- Increased patient acceptance
  - Fewer tablets to swallow
  - Prevents 'concealed' irregularity
- Increased health worker compliance
  - Fewer tablets to handle, hence quicker supervision of DOT
- Easier drug management
- Reduced use of monotherapy
  - Lower risk of misuse of single drugs
- Lower risk of emergence of drug resistance
- Easier to adjust dosages by body weight

Drug dosages for first line anti- TB drugs

Drugs	Adult	Children	Maximum in children
Isoniazid	5 mg/kg daily (4 to 6 mg/kg)	10 mg/kg daily (7-15 mg/kg)	300 mg
Rifampicin	10 mg/kg daily (8-12 mg/kg)	15 mg/kg daily (10-20 mg/kg)	600 mg
Pyrazinamide	25 mg/kg daily (20- 30 mg)	35 mg/kg daily (30-40 mg/kg)	2000 mg
Ethambutol**	15 mg/kg daily (12-18 mg/kg)	20 mg/kg daily (15-25 mg/kg)	1500 mg
Streptomycin*	15 mg/kg daily (15-20 mg/kg)	20 mg/kg daily (15-20 mg/kg)	1000 mg

*Streptomycin is administered only in certain situations, likeTB meningitis or if any first line drug need to be replaced due to ADR as per weight of the patient

** Ethambutol is given separately for children to monitor ophthalmic ADR.

Daily Dose Schedule for Adults (as per weight bands)

Weight category	**Number of tablets (FDCs)**		
	Intensive phase HRZE	**Continuation phase HRE**	
	75/150/400/275	**75/150/275**	
25-34 kg	2	2	
35-49 kg	3	3	
50-64 kg	4	4	
65-75 kg	5	5	
>75 kg	6	6	

During treatment if the weight of the patient increases by more than 5 kg and crosses the next weight band category then patient should be given the next higher weight band FDC drugs.

Treatment of Paediatric TB

Paediatric cases are to be treated under NTEP in daily dosages as per 6 weight band categories. All adolescents up to 18 years of age and weighing less than 39 kg, are to be treated using paediatric weight bands and children weighing more than 39 kg with adult weight bands.

Key Product Information (for Paediatric)

1. **Dispersible FDC, flavoured**
   Rifampicin 75 mg + Isoniazid 50 mg + Pyrazinamide 150 mg
   Rifampicin 75 mg + Isoniazid 50 mg

2. **Dispersible Loose drugs**
   Ethambutol 100 mg
   Isoniazid 100 mg

Drug Dosage for Paediatric TB

Weight category	Number of tablets (dispersible FDCs)			
	Intensive phase		Continuation phase	
	HRZ	E	HR	E
	50/75/150	100	50/75	100
4-7 kg	1	1	1	1
8-11 kg	2	2	2	2
12-15 kg	3	3	3	3
16-24 kg	4	4	4	4
25-29 kg	3 + 1A*	3	3 + 1A*	3
30-39 kg	2 + 2A*	2	2 + 2A*	2

A=Adult FDC (HRZE = 75/150/400/275; HRE = 75/150/275). It is added in higher weight band categories i.e. > 25 kg as these children may be able to swallow tablets.

- Change in weight bands to be effective upon crossing of weight bands irrespective of the quantum of weight gain/loss
- Pyridoxine may be given at a dosage of 10 mg per day to all children receiving INH containing therapy irrespective of age group

Operational Guidelines for treatment initiation

After receipt of the diagnostic test results, the MO of the Peripheral Health Institution (PHI) should take the following measures:

1. Initiation of appropriate regimen- Establishment of diagnosis of tuberculosis and decision on type of patient and treatment regimen (based on drug sensitivity pattern, i.e., DSTB or H-mono/ poly resistance, history of ADR to ATT). Initiation of appropriate regimen and ensures completion of treatment. All diagnosed patient should be initiated on treatment at the diagnosing PHI

Counselling: MO-PHI should counsel all TB patients before initiating treatment. It is advisable to involve close family members during the counselling. Counselling should include education of patient and family members about type, and mode of spread of disease and dosage schedule,

duration, common side-effects of treatment & methods to prevent them. Counselling regarding importance of need for regular treatment and consequences of irregular treatment or premature cessation of treatment should be given. Treatment adherence monitoring methods as in DOT manually, other ICT methods should be explained.

Cough etiquette Patient should also be explained about cough etiquette and proper disposal of sputum for prevention of transmission of disease and encourage him to get all his close contacts (especially household contacts) screened at the earliest.

Assure the patients that h/she will be supported during the entire course of treatment by the MO and peripheral health workers.

2. Clinical evaluation:

- Record weight of the patient and also height to assess Body Mass Index (BMI), which would provide a good indicator for prognosis of disease and also for initiating treatment regimen based on weight bands.
- Assess nutritional status of patient and link the patient for extra nutritional support.
- Assess general condition to identify patients who may need hospitalization.
- Assess for comorbidities like HIV, diabetes, liver or renal diseases, neurological disorders etc so that appropriate management measures can be taken.
- Assess for substance abuse especially tobacco (in any form) & alcohol and link him/her to respective TCC (Tobacco Cessation Clinic)/ de-addiction centre.

3. HIV Testing

All presumptive TB patients should be offered HIV testing. For all diagnosed TB patients, MO should make efforts to get HIV testing done. All HIV positive TB patients must be referred to ART centre for initiation of ART and CPT.

4. **Assess the socioeconomic status** of the patient and link him/her with appropriate treatment support schemes.

5. Open a treatment card (in duplicate when required) (Annexure 5) for each patient at the time of initiation of treatment. Each patient must be given TB Identity Card. (Annexure 6)

6. Plan appropriate treatment adherence and monitoring mechanisms at the time of treatment initiation in consultation with the patient, his/her family members and the peripheral health worker who is responsible for monitoring treatment adherence

7. Drugs should be made available at the treatment centre along with the TB treatment card and arrange for sputum containers for collection of early morning samples for follow-up examinations.

8. Arrange for follow up during treatment and long term follow up of TB cases.

9. MO should maintain TB Notification register (Annexure 7) for patients diagnosed in PHI and transferred in PHI and also ensures updating of notification register and NIKSHAY.

10. Arrange for Public Health Action for all notified TB patients including those notified from private sector.

11. Clinical examination of all TB cases should be done by MO and clinically follow up the patient once in a month to early identify any adverse drug reaction and also to assess clinical improvement. Follow up should be supported by laboratory investigations whenever necessary.

Nikshay entry- Once the treatment regimen is finalized, all patients will be initiated on treatment after opening of the treatment card and entries are done in Nikshay. MO-PHI should ensure that the treatment details are entered in Nikshay immediately, by the PHI staff designated by him. Nikshay entry should not be a separate activity, all events starting from notification to treatment outcome are from Nikshay only and its integrated part of documentation

Patient flow in Nikshay

a. Nikshay 1- Initiating the patient on appropriate treatment regimen
b. Nikshay 2- Transfer / referral flow after initiation of treatment
c. Nikshay 3- Nikshay Aushadhi

Treatment support program

Adherence to regular and complete treatment is the key to relapse free cure from TB. To assess and foster adherence, a patient-centred approach to administration of drug treatment, based on the patient's needs and mutual respect between the patient and the provider, should be developed for all patients.

The treatment support plan should include initial and frequent follow-up counselling of the patient and family members, supervision of treatment by a trained treatment supporter (a health worker, family member or community volunteer), locally managed additional nutritional support, retrieval of treatment interrupters, screening for adverse reactions, psycho-social support, co-morbidity management and follow up laboratory investigations. Considering patient as a VIP, the treatment support plan need to be tailored as per patient's need.

Direct observation of treatment (DOT) is one of the best practices to promote adherence. It ensures patient consumes every dose of the treatment before a trained treatment supporter and provides additional opportunity to support treatment. Government health staff (Eg. Pharmacist, ANM, MPW, Staff nurse, nursing assistants etc.), health volunteers from the community (ASHA, AWW, NGO volunteer, shop keeper, TB survivors etc.) can act as a treatment supporter and provide directly observed treatment (DOT). The treatment supporter should be accessible and acceptable to the patient and accountable to health system. All efforts must be put in to find a treatment supporter close to the patient's residence.

- It must be ensured that each and every dose taken by the patient should be supervised in IP and at-least twice in a week in CP by a trained treatment provider.
- The record of the supervision during IP & CP need to be maintained.
- Only in exceptional circumstances, like sick and bedridden patients & children, a trained family member can be assigned with the responsibility of observing treatment and the decisions in such situations, will be taken by the DTO/MO.
- These patient's adherence need to be supervised by the programme staff and documented.
- Such exceptions should be restricted to less than 5% of all TB patients in the district including private sector.
- Each patient and his/her treatment supporter should be supervised by a health worker.

- It may be a peripheral health worker in the public health system.
- For patient initiated on treatment by a private health care provider, public health support needs to be provided to the patients on treatment.
- It is the responsibility of MO to sensitize nearby private practitioners about the services provided under public health action (PHA).

- Digital Adherence Technology (DAT) like intelligent deployment of information communication technology (ICT) like frequent calls, SMS reminders, IVRS, etc also may be deployed to further enhance adherence to treatment

For the purpose of identifying an ideal treatment supporter and an appropriate DOT Centre, a DOT Directory should be maintained at PHI level. This directory should contain a locality- wise list of DOT Centres / treatment supporter in the area. It should be updated regularly. It is the responsibility of the Government field staff (PHWs / MPWs / TBHV) in coordination with treating physician (private/public) to organize and ensure DOT for the patient. They would also monitor and supervise the community treatment supporter in their respective sub centres.

If the patient is to be given DOT by treatment supporter, a duplicate treatment card will be prepared and given. The MO of the PHI will ensure uninterrupted supply of drugs. MO PHI should monitor monthly replenishment of stock to treatment supporter if drugs are not already given and update in drug stock register maintained at the PHI and in NIKSHAY Aushadhi.

The PHW visits the house of the patient within a week of diagnosis. During this visit, he/she should give counselling to patient and family members regarding disease, treatment and its adherence and ensures treatment support to the patient. Patient should be started on treatment as early as possible after diagnosis. Emphasis is given to the points similar to the ones mentioned above for the MO-PHI. This opportunity should also be used for screening of contacts. Residential address is also verified so that in case of interruption, retrieval action can be taken. The initial home visit should be recorded in treatment card in the space provided. A convenient location for drug administration and a suitable treatment supporter is decided mutually by the PHW and the patient.

Tasks performed by the health worker on home visit:

1) Address verification
2) Screening of all contacts (close and household contacts, reverse contact tracing in case of children)
3) Facilitating diagnostic testing of all symptomatics irrespective of duration of symptoms
4) TB Preventive Therapy(TPT) to all eligible
5) Collection of the address and phone number of the contact person outside the household
6) Collection of Bank account number of the patient/ or one of the households and the phone number. Facilitate getting the bank account opened if not having one.
7) Health education and Counselling of patient and family members

A community treatment supporter is a person who has volunteered to administer DOT as per the programme guidelines and is:

- from the community where patient resides/works,
- other than Government salaried staff

For example, a shopkeeper, NGO volunteer, priest, ASHA could be the treatment supporter.

In case, the DOT is organized through a community treatment supporter, then duplicate TB treatment card, TB identity card and anti TB medicines are handed over to the patient by the PHW. Sputum container for collection of morning samples for follow-up sputum examinations is also provided. The name of the DOT centre and name and designation of the treatment supporter should be entered in treatment card in the space provided. Before starting treatment, Onsite training is to be provided for the community treatment supporter, by the PHW, focussing on directly observed treatment, adherence, contact tracing, identification of adverse reactions, follow-up sputum examination and recording of drug intake. The treatment supporter should also be trained to impart health education to the patient. The PHW is responsible for supervising and ensuring DOT and updating of the original treatment card at the PHI on a fortnightly basis. In case the patient interrupts treatment, PHW will help the community DOT worker in retrieving the patients. The MO of the PHI (where treatment card was opened) and the STS should also supervise DOT on a regular basis. DTO and MO-TC should support them in their efforts through field- visits.

During TB treatment, each and every dose is taken under direct observation of the treatment supporter. DOT is administered at a place which is convenient to both patient and treatment supporter. This place is designated as DOT centre. However, in situations where patient is bedridden, children, long day workers etc. DOT should be administered under supervision at the patient's home by the family member who will be treatment supporter.

Only under exceptional circumstances, unsupervised drug administration can be allowed for a limited number of doses. For instance, if a patient is being discharged from hospital after initiation of treatment, s/he will have to be provided with one week doses of treatment so that the treatment is not interrupted during transfer to a nearby PHI. A home visit should also be made for these patients by health worker of the receiving unit preferably within a week of receiving the patient.

The treatment supporter indicates the drug administration by a tick mark against the days in the appropriate box on the tuberculosis treatment card. Patient is also asked about adverse drug reactions and, if necessary, referred to the MO. Patient is referred to the Designated Microscopy Centre (DMC) for follow-up sputum examinations. When patient reports to the DMC along with an early morning sputum sample on the scheduled day.

Patient should be referred for follow-up sputum examinations at the prescribed intervals at the end of IP, end of CP and long term follow up from outcome/last dose of the treatment up to 2 years (at 6 months, 12, 18, 24 months).

Other modalities for treatment adherence, Digital Adherence Technology (DAT) While observing treatment is one of the best modalities of promoting treatment, other modalities like intelligent deployment of information communication technology (ICT) like frequent calls, SMS reminders, IVRS, etc also may be deployed to further enhance adherence to treatment for patient who is unable to undergo supervised treatment for e.g. frequent on job travellers, truck drivers, sailor etc. This decision is taken by the MO/ DTO after exploring the possibility of making a co-worker, for example, Cleaner for the truck driver etc., We should remember that this option when opted, there is always a possibility of the patient stopping the treatment before completion thereby increasing the possibility of development of drug resistance. Hence, good quality of programme

will have no patient on self-administered treatment and reflects on the efficiency of the program manager in convincing the patient for direct observation, along with other modalities of monitoring adherence of treatment as only adjunctive to DOT.

Patient support systems:

1. Mobility support for patients in situations like patients visit to ART centre, DRTB centre, DMC for collection of sputum for follow up visits for DRTB patients.

2. Counselling may be required to quit substance abuse.

3. Nutritional assessment & support
   a. Nutritional support to TB patients (NIKSHAY Poshan Yojana): Under this scheme all notified TB patients are provided incentive of Rs 500 per month during anti-TB treatment for Nutritional support in cash or in-kind support through Direct benefit transfer (DBT).
   b. All individuals with active TB should receive assessment of nutritional status, appropriate counselling based on nutritional status at diagnosis and throughout their treatment. If malnutrition is identified, it should be managed according to 'Guidance Document- Nutritional care and support for TB patients in India'.
   c. Linkages for extra nutritional support for TB patients or of his/her contacts on IPT may be explored with existing Govt. schemes like public distribution system (PDS) or Food security act.

4. Ancillary drugs for management of ADR, comorbidities etc.

5. Comorbidity management

   To avail above, synergy between social welfare support systems like RSBY, TB pension schemes, national rural employment guarantee scheme, corporate social responsibility (CSR) initiatives, counselling centres etc. to mitigate out of pocket expenses such as transport and wage loss incurred by TB patients should be established.

6. Under the programme, compensation is provided for transport costs incurred by DR TB patient for sending specimen for follow up or for travel to DR-TB centre. TB patients in tribal and difficult areas get Rs. 750.

Contact investigations

'Close contacts' are those individuals who share a common air space with the patient.

All close contacts, especially household contacts should be screened for TB. In case of paediatric TB patients, reverse contact tracing for search of any active TB case in the household of the child must be undertaken. All close contacts of DR-TB cases should be identified through contact tracing and evaluated for active TB disease as per NTEP guidelines. This information has to be entered in Nikshay by the PHI staff

Insert Nikshay screen shot / flow

TB Preventive Therapy (TPT)

TPT is given to prevent breakdown of TB infection to TB disease.

Isoniazid Preventive Therapy (IPT)

INH is the drug currently used for TPT to prevent breakdown of TB infection to TB disease. Currently IPT should be given after ruling out active TB disease in contacts of drug sensitive TB patients who are aged 5 years or less and PLHIV (IPT in PLHIV is dealt in detail in TB and HIV section of this module).

IPT in children:

Children are more susceptible to TB infection, more likely to develop active TB disease soon after infection and are more likely to develop severe forms of disseminated TB. Children <6 years of age, who are close contacts of a TB patient, should be evaluated for active TB by a medical officer/ paediatrician. After excluding active TB, he/she should be given INH preventive therapy irrespective of their BCG or nutritional status.

The dose of INH for preventive therapy is 10 mg/kg body weight administered daily for a minimum period of six months. The INH tablets should be collected on monthly basis. During the monthly collections, child should be closely monitored for TB symptoms to rule out active TB and also assess for any INH related adverse effects.

INH preventive therapy should also be considered in following situations: -

- For all HIV infected children who either had a known exposure to an infectious TB case or are Tuberculin skin test (TST) positive (>=5mm induration) but have no active TB disease
- All TST positive children who are receiving immunosuppressive therapy (e.g. Children with nephrotic syndrome, acute leukaemia, etc.).
- A child born to mother who was diagnosed to have TB in pregnancy should receive prophylaxis for 6 months, provided congenital TB has been ruled out. BCG vaccination can be given at birth even if INH preventive therapy is planned.

Asymptomatic Close contacts of DR-TB patients should be closely monitored for signs and symptoms of active TB as isoniazid may not be prophylactic in them. Alternative prophylaxis treatments have been suggested but there is no consensus regarding the choice of the drug(s) and the duration of treatment. Prompt treatment of DR-TB in index case is the most effective way of preventing the spread of infection to others.

Follow up of treatment

Patient should be closely monitored for treatment progress and disease response. There are two components of follow up: Clinical follow up and Laboratory follow up

Clinical follow up

MO should clinically follow up for every patient at least monthly (patient visits the clinical facility or the MO reviews during home visit). Improvement on clinical symptoms, increase in weight etc. may indicate good prognosis. Control of comorbid conditions like HIV and diabetes by appropriate treatment is essential for getting a better prognosis to TB treatment. Symptoms and signs of adverse reactions to drugs should be specifically asked for. Detailed description of symptoms and signs of adverse reactions to anti-TB drug should be recorded in TB treatment card.

Laboratory investigations for:

- assessing the prognosis of disease, monitoring the treatment and
- managing comorbidities or adverse reaction whenever needed.

In case of pulmonary tuberculosis, sputum smear microscopy should be done at the end of IP (56th dose) and end of treatment (preferably when collecting the 108th dose of the CP, Patient is given the sputum container for collecting the early morning sputum of the next day for the end of treatment follow up sputum test or i.e., four doses before the last dose). CP will be initiated and continued till completion. A negative sputum smear microscopy result at the end of IP may indicate good prognosis. If Sputum result is positive at the end of IP, then CP will be initiated and continued till the DST results are available and modified if warranted after the results of DST.

At completion of treatment, a sputum smear and/or culture should be done for every patient. The follow-up sputum smear examination at the end of treatment is very important for evaluating the results of treatment. However, in the presence of clinical deterioration, the medical officer may consider repeating sputum smear microscopy even during CP. This will provide the patient an additional opportunity to undergo drug susceptibility testing if s/he is found to be sputum smear positive.

One sputum sample is to be collected, preferably early morning. If not available, supervised spot sample can be collected. It must be ensured that the patients undergo the follow-up sputum smear examination as scheduled and the last follow-up sputum examination is done before the completion of the last dose of treatment.

The results of follow up sputum collected not later than two weeks of completion of treatment, should be available as early as possible so that appropriate outcome for the patient can be given in the TB Treatment Card.

Chest X-ray may be a good tool to assess the progress of clinically diagnosed TB case and it is to be offered whenever required and available. For drug resistant TB, it may be carried out at end of IP, end of treatment, and whenever required.

Response to treatment in extra-pulmonary TB may be best assessed clinically. Help of radiological and other relevant investigations may be taken.

CBNAAT should not be done as a follow-up sputum examination

Discuss Nikshay flow

Response to treatment in children:

In children in their early ages are unable to produce sputum, the response to treatment among them may be assessed clinically. Improvement should be judged by absence of fever or cough, weight gain, etc. Clinical or symptomatic improvement is to be assessed at the end of the intensive phase and at the end of treatment. The help of radiological and other relevant investigations may be taken. Radiological changes may persist and may not correlate with clinical improvement and hence should not cause concern.

For the monitoring of treatment in children who can produce sputum, follow-up sputum examinations are to be performed with the same frequency as in adults. CBNAAT is not appropriate follow up tool for monitoring the progress of the disease. Hence it should not be used as a follow up test.

Long term follow-up:

After completion of treatment, the patients should be followed up clinically at the end of 6, 12, 18 & 24 months. In the presence of any clinical symptom, (e.g., cough) sputum microscopy and/or culture of the biological specimen should be considered. This is important in detecting recurrence of TB at the earliest.

Patient Provider Interaction

The following information regarding the disease and treatment should be provided to the patient: -

- Diagnosis
- Cause and spread of disease
- Treatment related information
  - Reassuring that TB is curable
  - Importance of regular and complete treatment
  - Importance of treatment being given under DOT.
  - Duration of treatment, Intensive phase & Continuation Phase
  - Adherence to follow-up schedules
  - Early disappearance of symptoms is not a sign of cure, treatment to be stopped only when advised by the treating physician.
  - Treatment is available free of cost.

Other important issues:

- Diet/ DBT
- Cough hygiene and sputum disposal
- Provision of transfer facility during treatment
- Referral for HIV counselling and testing
- Smoking / alcohol abuse
- Comorbid conditions for example diabetes, renal failure, patient on immunosuppressive drugs
- Sensitization on adverse reactions
- Importance of screening of close contacts and children aged5 years or less and chemoprophylaxis

Information is to be provided at the treatment initiation and periodically during the treatment. Patients are reassured that they are being provided effective, high-quality curative care. Patients are encouraged to continue their treatment by drawing their attention to the gain in weight and relief of symptoms. In NTEP, the patient is the VIP and should be treated accordingly.

Divulgence of TB diagnosis: Diagnosis should be revealed in such a way that patient neither gets unduly perturbed nor takes it very casually. Patient should be reassured that TB is completely curable provided the drugs are taken regularly as prescribed for the entire duration. Patients will be informed that they continue to spread TB if they do not take treatment as prescribed. Reassure them frequently that TB is curable.

Cause and spread of disease: Efforts should be made to clear the taboos associated with the disease. It should be explained to the patient that TB is caused by Mycobacterium tuberculosis

through droplet infection from patient suffering from pulmonary tuberculosis. The disease neither runs in the family (hereditary) nor is a curse.

Treatment related information:

DOT and its necessity: It is important for the patient to take the drugs under observation. The real purpose of direct observation is to develop a human bond with the patient and not to mechanically watch the patient swallow the drugs. Patients if given self-administered treatment are likely to take it irregularly or discontinue the treatment upon relief of symptoms. DOT is not because of suspicion about the patient but it is an expression of compassion and care for the patient so that s/he completes the treatment, comes out of their own suffering and will not be source of infection to the community. Early Disappearance of symptoms is not a sign of cure. It is very important for the patient to know the duration of treatment and understand the necessity of taking all prescribed drugs regularly.

Patient is also explained about the importance of sputum smear conversion at the end of two months and at the completion of treatment and also about long-term follow up. Patient should be made aware that treatment services are provided free of cost.

Diet: Health staff should advise patient on balanced diet and they can be told to take the food they can afford and also about nutritional support systems available for the eligible patients.

Role of isolation and rest: Patient and family members are made to understand that once the treatment is started, patient ceases to spread the infection and there is no need to isolate him in terms of accommodation, use of utensils and clothes. However, patient should be advised to use appropriate air-borne infection control measures and rest is required only if constrained by physical weakness. Patient should be impressed that it is the treatment alone which cures.

Cough hygiene and sputum disposal: Patient should be educated in exercising the cough hygiene- not resorting to indiscriminate coughing and spitting, and covering nose and mouth while coughing or sneezing.

Provision of transfer facility during treatment: In case the patient wishes to shift or migrate to other TU / district / state after the initiation of the treatment, patient should be informed that there is a provision of transfer facility for treatment. Any such event should be duly informed to the treating medical officer for completing the formalities for transfer and necessary arrangement for further treatment.

Referral for HIV counselling and testing: All the patients diagnosed as TB cases should be encouraged and referred to the nearest ICTC for HIV testing.

Comorbid conditions for example diabetes, renal failure, patient on immunosuppressive drugs: History regarding the conditions mentioned above and any treatment for the same has to be elicited as these conditions and treatment for the same may adversely interfere with the TB Treatment. Patients are to be referred to the respective speciality and managed appropriately depending upon the co-morbid conditions.

Adherence to follow-up schedules: The patients should be impressed upon the necessity of complying with periodic follow-up sputum examination schedule as advised. This will help in objective assessment of response to the treatment. Conversion to smear negativity is a forerunner of successful treatment.

Sensitization on Adverse reactions: In case patients experience any unusual symptoms after initiation / during treatment, they should be instructed to approach the medical officer and report the same. On their own they should not take a decision either to stop or to continue the drugs.

Smoking: It should be impressed upon the patient that smoking of tobacco will adversely affect the treatment outcome. The patients should be protected from passive smoking. The environment of the patient has to be smoke free at home / office and at clinic. Smoking status of the TB patient should be checked at every interaction. The Medical Officer has to help the patient with simple tips to quit smoking. However, if this does not yield any positive result, he should be referred to the Tobacco cessation Clinic (TCC).

Alcohol abuse: History of addiction to alcohol should be elicited. If found alcoholic, the patient should be advised to strictly refrain from alcohol as it would increase the chances of patient developing hepatitis (Jaundice), irregularity in drug intake and adverse treatment outcome. The patients should be encouraged to give up alcohol with the help of frequent motivation, family and social support.

Importance of screening close contacts: Patients should be encouraged to bring symptomatic adult contacts and all children aged five years and below for screening at health facility. This will facilitate early detection of cases among them and appropriate treatment. Eligible children will be administered chemoprophylaxis.

Use the following documents as per the flow of the patients:

Maintenance of accurate records and registers of patients and programme activities; and reporting data to the state/central unit, is essential for proper monitoring and management of Revised National Tuberculosis Control Programme (NTEP). NTEP records and reports are standardized and provide the required information for managing the programme effectively

Standardized Records

The following standardized records are used in the NTEP:

Forms	Registers
• Referral Slip • NTEP Request form for examination of biological specimen for TB Examination • Tuberculosis Treatment Card • NTEP PMDT Treatment Card • NTEP TB Identity Card • NTEP PMDT Treatment Book • NTEP Referral/ Transfer form • NTEP PMDT Referral for treatment form • aDSM treatment initiation form • aDSM treatment review form • TB Preventive Treatment Card	• Tuberculosis Laboratory Register • NTEP Laboratory Register for CBNAAT and CDST • Tuberculosis Notification Register • NTEP PMDT notification register • Stock Register • Reconstitution Register

1. **Referral slip** This is used b peripheral health workers to refer patients to health facilities where specimen is collected either for examination or transportation

2. **NTEP Request form for examination of biological specimen for TB**

The request form is kept at all the PHIs. It is filled generally by the MO of the referring health facility. This form is used for microscopy or CBNAAT or culture DST or Chest X-Ray or TST. Only one form is filled for each patient. Patient will report to the diagnostic health facility along with the request form. In case PHI is a sputum collection centre, sputum samples are sent to the diagnostic facility along with the request form. It is essential to record patient details, reason for testing and type of test requested. The same form is sent back to the treating unit with the results. When this format is used for C&DST, a copy of this form will be sent electronically to lab and DTC. In turn, the laboratory will send the result in electronic copy back to district with copy to DR-TB centre.

3. **Tuberculosis Treatment card**

Treatment card is filled at the PHI when patient is initiated on treatment. This card contains important information about a patient, such as: Name, age, sex and address of the patient; Type of disease; history of anti-TB treatment; Regimen prescribed; Duration of treatment; Amount of drugs to be given; Results of investigation before and during treatment; Drugs administered during the intensive and continuation phases of treatment; Treatment outcome of the patient; Retrieval actions for missing doses; Adverse event, Preventive treatment for children; details of X-ray or other tests for diagnosis of EP TB; information on TB comorbidity and Remarks. It also has information on the treatment supporter, person conducting the initial home visit and the signature of the MO. An additional treatment card should be kept, if treatment supporter is not at health facility. In such cases, treatment supporter should be trained on recording treatment card.

4. **NTEP TB Identity Card**

Identity card is completed for each patient who has a Tuberculosis Treatment Card. It is kept with the patient. Information from the Tuberculosis Treatment Card is used to complete the identity card. The front part of the ID card has patient information, name and address of the TU/ district and treatment details of patient including disease classification, type of patient, weight bands, smear results and information on the date of starting treatment. The back portion of the ID card has the results of follow-up smear examination, appointment dates for visits for drug administration and treatment outcome. This information will help to continue treatment in case the patient is transferred, or admitted to any other health facility anytime during the treatment period

5. **NTEP PMDT notification Register**

This register is maintained at each Nodal and District DR TB Centres level. Additionally, DTC is expected to maintain an aggregate register only in those districts where more than one nodal or district DR TBCs are functional. At each DR TB site working as District DR TB centre, all diagnosed DR TB patients (H mono/poly, MDR/RR or XDR TB) from both public and private sector for which the specimen was collected within the district should be entered in the list irrespective of location of diagnosing facility (within or outside the district). Each episode based on diagnosis of additional resistance requires a change in the regimen is entered in separate row against a new episode ID with patient ID in remarks column. Senior DR TB and TB HIV supervisor of the respective district is expected to coordinate with all NAAT sites, CDST labs and compile all the DR

TB patients diagnosed to enter it in PMDT notification register maintained at district level. Information about DR TB patients notified from private sector can be extracted from Nikshay. NDR TBC are also expected to update this register for the patients initiated on treatment at the centre. As far as possible, patients should be entered consecutively by their date of diagnosis. The following is recorded in the PMDT notification register

6. TB Notification register

A TB notification register is maintained at each peripheral health facility. This register contains records of all patients diagnosed with TB and eligible for TB treatment, regardless of initiation of treatment. It will also incorporate those cases initiated on first line treatment and offered drug susceptibility testing and results are awaited. The registration data is based on the date on which a TB patient is diagnosed.

If patient is put on treatment in area of facility where s/he is diagnosed then information on treatment and follow up is recorded in the same TB notification register. If patient is treated in area other than where h/she is diagnosed then information on treatment and follow up is recorded in TB notification register of health facility where patients is residing.

In each health facility, TB notification register is maintained by its staff. STS of the respective TB units will support updation and coordination for completing the information.

For every patient, status of treatment should be recorded. The status of treatment for any patient would be one of the following:

1. Initiated on First line treatment in the same Health Facility
2. Initiated on treatment outside Health Facility
3. Initiated on second line treatment in the same Health Facility
4. Treatment initiated outside NTEP
5. Incomplete/ incorrect address
6. Died
7. Migrated & untraceable
8. Refusal of treatment
9. Repeat diagnosis
10. Patient already on treatment/ Follow up patient
11. Wrong diagnosis
12. Referred for treatment with pending feedback
13. Other

7. Transfer form for treatment

It is to be used while transferring notified patients for treatment from one PHI to another. If a patient is "transferred out", this form needs to be filled and given to patient. If patient is already on treatment, a copy of TB treatment card also is given.

The first part of the form contains information about the patient, her/his disease, treatment details and address of the transferring unit and his/her NIKSHAY ID. This information should be used to complete a new TB treatment card for the patient.

When the patient has reported to the receiving unit, the bottom part of the form is completed by the receiving unit and returned to the transferring unit. Patients follow up examination results at

the end of intensive phase and treatment outcome should be communicated to the transferring unit.

8. IPT Card

IPT is given for a period of 6 months after ruling out TB.

IPT card need to be filled up in a manner the TB treatment card is filled up.

It has 5 sections, viz., demographic details of the patient and his treatment provider, treatment section, details on drug adverse reaction including follow up and clinical details and findings on CXR and remarks section.

IPT Card can be utilised both for children and adults who receive IPT for any indication. Mark ticke (0) similar to the way we tick for adult treatment and Zero (0) mark for the day the IPT is missed. If the there is a missed dose/doses, missing doses should be made up at the end and the total doses of IPT should be completed. Every time when there is a irregular intake and when restart of IPT is planned and whenever clinically indicated the child/ patient should be reassessed for active TB before restarting the IPT.

For every eligible patient for IPT, two cards will be opened by the treatment provider. One card will be with the treatment provider and the other will be with the person identified in the family (preferably, mother or father in case of child). The drugs for IPT will be provided on monthly basis. The card at the centre will be updated by the treatment provider on a monthly basis

The IPT Card

TB Notification No. of the patient* _____State_____
City / District _____ TB Unit _____ PHI _____
Name of the contact/ HIV patient on IPT_____
Sex ☐ M ☐ F ☐ TG ☐ Age: _____ Mobile No. Patient_____
Name of personnel issuing the IPT: _____ Designation _____
Mobile No.: _____ Name of the family member giving DOT:_____
Initial home visit by _____ Date _____ investigations done to rule out active TB: _____

Month/ year	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

* May not be available for HIV patients put on IPT

Details of Adverse events

Date of adverse event	Details of symptoms	Action taken	Duration of management for adverse event	Outcome of adverse event

Follow up clinical & sputum (Results with date)

Follow up date	Clinical	CXR	Smear	Culture	Impression

Findings_____
_____

Remarks / interruptions
_____
_____
_____

Signature of the MO with date:_____

Date of completion of IPT / Breakthrough disease_____

Filling up of the treatment card

Treatment Card

Each patient who begins treatment for TB must have a tuberculosis treatment card. Original TB treatment card should be kept at PHI and duplicate treatment card is to be given to the treatment supporter for documentation of daily events. Information in the original TB treatment card is to be updated fortnightly.

The information on the patient's treatment card should be accurate, reliable, relevant, up to date and legible as this would be the source of information for updating the TB notification register and NIKSHAY. This card contains TB Notification No., Nikshay ID and name of State, city/district/TB Unit where he/she belongs to.

This card contains other important information about patient, including the following details:

General information about patient	Data related to treatment support	Treatment related information
• Name, Age, sex of the patient • Complete address and phone number of the patient with important landmark • Occupation & Socioeconomic status c Name, address and phone number of the contact person	• TB unit with code • Name of the PHI • Name, designation, contact no. of treatment supporter • DOT centre • Initial home visit by whom (Name and Designation) with date • Type of treatment adherence	• Disease classification and site • Type of patient • Basis of diagnosis • Details of Investigations for diagnosis and follow up (ZN/FM/CBNAAT/Culture) • other investigations for diagnosis if any • Source of treatment • Contact investigations • HIV, Diabetes and other comorbidities related data • Addiction related information • Chemoprophylaxis for less than years children Treatment regimen • Drug intake in intensive and continuation phase • Retrieval actions for missed doses • Adverse drug reactions • Post treatment follow up • Details of X Ray • Nutritional support • Treatment outcome with date • Remarks

The Tuberculosis Treatment Card is maintained at health facility where the patient is initiated on treatment. For patients receiving treatment in a DOT centre other than the place of treatment initiation, a duplicate treatment card is prepared and maintained at the DOT centre by the DOT provider. The original treatment card at the PHI is to be updated at least once in a fortnight.

General information of patient

Name: Full name of the patient with father/husband name is recorded (Id card/relevant document may be referred to where available for correct spelling of the name)

Age and Gender: Age and sex of the patient is recorded. Estimated age is recorded if actual age is not known.

Complete address and phone number of the patient: Complete address with land marks is recorded which will facilitate in locating patient's residence in case of interruption of treatment. The same has to be verified at the time of initial home visit by the health worker. The telephone numbers both landline and mobile of the patient, if available, are also to be recorded along with the address.

Occupation of the patient: Occupation may be specified. If unemployed, the same may be stated. Nature of occupation will help in arranging suitable DOT facility. For example, a truck driver who needs to travel out for a long time, one of his colleagues can be made treatment supporter.

Name, address and phone number of the contact person: Name and address of a person, identified by the patient through whom patient can be contacted. A relative not from the same household, community/tribal leader, village doctor, community volunteer, employer could be contact persons. This person can be contacted in case the patient is not traceable following interruption of treatment. Relationship of the contact person to the patient may be specified.

Data related to Treatment support

TB unit with code: Name of the TB unit and code allotted are recorded

TB Notification number: TB notification number generated in NIKSHAY at the time of notification needs to be filled in treatment card.

Name of the PHI: Name of the PHI where the treatment is initiated is recorded.

Name, designation and contact number of treatment supporter: Designation of the treatment supporter namely Anganwadi worker /staff nurse/ ANM/ Health Inspector / ASHA / NGO /Health Visitor/ Laboratory technician/ Pharmacist / is indicated.

DOT centre: A place which is mutually convenient for the patient and treatment supporter where Directly Observed Treatment can be administered is identified and the same is recorded. For example, a PHI, sub-centre, shop, etc.

Initial home visit: Name and designation of the person undertaking the initial home visit. This will ensure accountability and authenticity. Initial home visit will ascertain the reliability, completeness of address and changes if any. It is necessary to confirm the residential status of the patient from the neighbourhood. The details regarding the work place will also benefit in retrieving patient in case of interruption of treatment. During initial home visit, patient and family members should be counselled and contact investigation should be carried out after diagnosis and not later than a week of initiation of the treatment.

Type of treatment adherence – DOT / Family DOT with or without ICT: Treatment adherence to regular and complete treatment is important for successful treatment outcome and relapse free cure from TB. DOT is one of the best practices to promote adherence. For patients who are unable to undergo supervised treatment, other ICT modalities can be utilized in that district. Family members can be assigned role of treatment supporter can be instituted in case of children, sick and bedridden patients etc.

Treatment related information

Disease classification: Box provided for pulmonary or extrapulmonary TB is ticked as the case may be. If extra pulmonary, the site is specified. In patients having both pulmonary and extrapulmonary TB, the box for the pulmonary is ticked and site of extrapulmonary is specified.

Type of patient- Box provided for new, Treatment after lost to follow up (LTFU), recurrent, treatment after failure, others, previously treated, is ticked as the case may be.

Basis of diagnosis - Microbiologically confirmed or clinical TB may be ticked as appropriate.

Recording

Results of Investigation before and during treatment (ZN/FM/CBNAAT/culture): Date of examination, DMC/lab conducting the bacteriological examination, Laboratory serial number allotted, test results are recorded in the rows meant for pre-treatment, end of IP and at the end of the treatment. Date of sample sent to culture & DST lab and DST results are to be entered in appropriate row. Other investigations if any to be entered with date in the box provided.

This information is to be transferred from NTEP request form for examination of biological specimen for TB to the treatment card.

History of previous anti TB treatment: Previously treated patients may require close monitoring compared to new patients due to high risk for resistance. However, this information is not used to decide the treatment regimen. Patients should be assured that revealing of facts about previous history of treatment for TB is in their best interest. The medical officers should impress upon the patients the importance of providing the complete facts, without any apprehension of discrimination with regard to subsequent treatment. While eliciting the history, emphasis should be given for ascertaining the following:

Previous history from patients	Review of available record / documents
• Cough with expectoration • Blood in the sputum • Sputum examination/chest X-ray examination • Consuming drugs which turned urine red/taken injections for >1 month • Injections taken for a long duration e.g. two months.	• Sputum examination/Bacteriological examination reports • Chest X-ray reports / any other relevant reports / • Drug prescriptions • Empty blister packs/strips of anti TB drugs

Source of treatment: Public or private box may be ticked as appropriate.
The previous regimen should also be mentioned.

HIV related data

This box is meant for recording information regarding the HIV status of the patient, and if positive, details of CPT and ART being administered to be given.

Information on HIV status, CPT delivery and ART referral and initiation of the TB patient is to be documented only in the original TB treatment card and must be kept confidential within health system. This should not be disclosed to the community treatment supporter.

1. HIV Status:

i. HIV testing is a voluntary procedure and not mandatory. Patients not willing for HIV testing or sharing their HIV test result should not be forced to undergo testing or disclose their HIV status.

ii. If HIV status of the patient is known, tick the appropriate box ('Reactive or 'Non-Reactive {NR}) and record the date of test along with PID Number. If the HIV status is not known, don't tick any box initially.

iii. Patients already on HIV care should not be required to show proof of HIV test result

iv. If the HIV status is ascertained during the course of TB treatment, the latest information should be updated on the card.

v. If HIV status of the patient remains unknown at the end of the treatment, tick the appropriate box ('unknown'), at the time of declaring treatment outcome for the patient.

2. CPT (Cotrimoxazole Prophylactic therapy) delivery

i. All known HIV-infected TB patients are to be provided access to CPT.

ii. Record dates of each monthly CPT delivery in the space provided.

iii. In case the TB patient is already on CPT before the initiation of TB treatment, record most recent date of CPT pickup.

3. Referral and initiation on ART

1. All known HIV-infected TB patients are to be referred for ART to the nearest ART Centre.
2. If patient initiated on ART, tick the "yes" box, and the date of initiation of ART and ART Registration Number should be recorded on the treatment card.
3. In case the TB patient is already on ART before the initiation of TB treatment, tick yes, and record approximate date of initiation.

Diabetes related information

This box is meant for recording information regarding the Diabetes status of the patient (unknown/Diabetic/Non-Diabetic). RBS and FBS value to be given. If patient initiated on Anti-diabetic treatment (ADT), tick the "yes" box, and the date of initiation of ADT and ADT Number should be recorded.

Other comorbidities if any should be mentioned.

Contact Investigation-

Record the number of household contacts less than 6 years age. Among these recorded contacts, document the number of contacts screened, contacts with symptoms, contacts evaluated, contacts diagnosed, and contacts put on treatment.

Chemoprophylaxis

Preventive chemotherapy with isoniazid (H) is administered to all the children aged 5 years and below who are in contact with all forms of Drug sensitive TB case. The number of such children residing in the household should be enquired during the initial home visit. The parents are advised to bring children to the Health Centre for screening for the evidence of TB. They are examined and investigated to rule out active TB disease. If found to be suffering from disease, they should be treated appropriately. Children found eligible for chemoprophylaxis after ruling out the TB are to be administered preventive chemotherapy with INH 10 mg/kg body weight daily for 6 months.

The number of children aged5 years or less put on chemoprophylaxis should be mentioned. Name, weight of the child and dose of INH should be recorded with tick mark in the appropriate column for monthly delivery of INH.

Addiction related information

Details regarding tobacco and alcohol intake are recorded here. If current tobacco user, mention whether smoking or smokeless and also link him/her to district tobacco control centre.

At the end of treatment, status of tobacco use should be documented.

If patient has history of chronic alcohol intake, whether linked to de-addiction centre.

Treatment Regimen

The MO of the PHI will initiate all patients who are sensitive to H & R and all patients whose H & R status is not known on first line anti-TB treatment. Date of initiation of IP and CP should be recorded. Dosage frequency, drug formulations and drug packaging should be tick marked appropriately. Relevant weight bands are to be tick marked in the boxes provided. Number of FDC tablets to be taken per day needs to be mentioned. If patient is on loose drugs, the dosages and pills against each drug needs to be mentioned in the box provided.

Administration and monitoring of treatment

Recording of drug administration and monitoring

The month and the year during which the patient is undergoing treatment are written under the month and year column in the table. Last column is for recording weight of the patient each month.

A tick mark '(√)' is recorded in the appropriate box (according to the dates of the month 1 – 31 as the case may be) to indicate the day the drugs were consumed under direct observation.

Missed dose, is denoted by a circle (0) in the appropriate box.The entry for unsupervised doses should be recorded by encircling the tick mark on the TB Treatment Card

Each row is for recording whether dosages taken under observation or not, and also the interrupted doses against each month.

The continuation phase should always start from fresh row.

Intensive phase

Month and year

Month and year of initiating the intensive phase is recorded.

Date of initiation of treatment- The date of initiation of IP of treatment regimen prescribed is ticked () on the appropriate box under the date against the month. Then with every daily dose consumed a tick mark is placed in the against that date.

The date/day (for example on 10thApril) on which patient fails to attend for DOT, and interrupts the dose, is denoted by a circle (0) in the appropriate box and effort should be made to retrieve the patient. In case, the patient visits the health facility the next day (for example on 11th April), the drugs interrupted are administered on that day and continues the treatment as scheduled, however, it should be ensured that patient completes 56 doses of IP before transiting into CP.

Month / year	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
April 17	✓	✓	✓	✓	✓	✓	✓	✓	✓	0	✓	✓	✓	✓	✓

On Sunday, treatment will be unsupervised and marked as tick with in the circle

Only under exceptional circumstances unsupervised drug administration can be allowed for a limited number of doses. For instance, if a patient is being discharged from hospital after initiation of treatment, s/he will have to be provided with maximum 7 doses of treatment so that her/his treatment does not get interrupted during her/his transfer to a nearby PHI. In such circumstances, the entry for unsupervised doses should be recorded by encircling the tick mark on the TB Treatment Card and the reason for the same should be stated in the Remarks column of the treatment card.

Month / year	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**
April 10	✓	✓	✓	✓	✓	✓	(✓)	(✓)	(✓)	✓	✓	✓	✓	✓	✓	✓	

Continuation phase

Month and year

Month and year of initiating the continuation phase is recorded.

The date of initiation of CP of treatment regimen prescribed is ticked (√) on the appropriate box under the date against the month in the fresh row of the box provided in treatment card, as given below.

Month / year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
April 17	✓	✓	✓	✓	✓	✓	✓								
April 17								✓	✓	✓	✓	✓	✓	✓	✓

During the continuation phase of treatment, patient is administered the drugs on daily basis under direct observation.

The recording of doses taken is similar to as in IP. The total of 112 doses of CP should be completed before declaring treatment outcome. In some circumstances where CP is extended by 12 to 24 weeks, the treatment outcome should be declared after completion of all the prescribed doses.

Monitoring of drug administration can be done by comparing the stock of drugs available in the strips with the dosages given and marked in the Tuberculosis Treatment Card. Any observed variation should be looked into and remedial measures taken.

Retrieval actions in interruptions of treatment

In case of interruption of treatment, health staff should visit the patient at his home. Reason for interruptions should be reviewed carefully and efforts made to bring the patient back for treatment. This should be done by the treatment supporter not later than the day after the patient was due to come for treatment irrespective of whether the patient is in IP or CP. It is very important to take prompt action after knowing that the patient has missed the dose. Delays in retrieval actions can lead to irretrievable loss of the patient for treatment.

If a patient does not take medication as scheduled in IP or CP, s/he should be traced and given the medication as per regular schedule and complete total of 56 doses of IP/112 doses of CP.

If the treatment supporter is not successful in retrieving such patients, it should be reported to next higher level of supervisors (e.g. MPW, STS, etc.) and take all efforts to retrieve the patient. If the patient interrupts treatment on two occasions, MO-PHI should visit the patient's home. The MO-PHI can review the reasons for the same, give intensive counselling to the patient and may provide additional support to continue the treatment without interruption.

Despite all efforts, if the patient does not return for treatment after interrupting the treatment for continuous 1 month or more, the outcome of treatment should be recorded as "Lost to follow up" and the reason should be mentioned in the "remarks" column of the treatment card and the drugs should be returned to the PHI.

Recording of Retrieval actions

Action taken to retrieve patients interrupting treatment has to be recorded in the space provided on the reverse of the treatment card with details of date, name of the health staff taking retrieval action, person contacted, reasons for interruption and the outcome of such efforts.

The number of doses to be administered must be strictly adhered to.

In DOT centres with large numbers of patients, Tuberculosis Treatment Cards should be organized according to the day of scheduled drug administration and the phase of treatment. After the patient consumes the medication under direct observation, the Tuberculosis Treatment Card should be updated and placed behind the divider for the next observation. In this manner, the Tuberculosis Treatment Cards of patients who do not present for treatment will be apparent on the same day, facilitating appropriate retrieval action of patients.

Recording of Adverse events

Adverse events must be recorded in the space provided on the reverse of the treatment card with details of date of event, symptoms of event, action taken, duration of management of adverse event and outcome of adverse event.

Post-treatment Follow-up for clinical & sputum examination

Clinical, sputum examination and chest X ray findings with impression should be recorded against each scheduled follow up at 6, 12, 18- and 24-months post treatment.

Details of Chest X-ray:

This space is provided on the bottom of reverse side of the treatment card for recording chest x-ray findings.

Nutritional support

Details of nutritional support given to the patient needs to be recorded in the space provided.

Bank Details

Information regarding bank details entered in Nikshay should be mentioned as 'Yes' or 'No'

Remarks

The following information has to be recorded in the remarks box on the bottom of reverse side of treatment card:

- Reasons for unsupervised dose(s)
- Reason for interruption (e.g. Migrated, patient transferred to another district, etc.)
- Details of hospitalization if any during the treatment
- Information on dispatch of sputum for culture & drug sensitivity test
- Any other relevant information about the patient such as pregnancy status, cause of death in case the outcome is "died" etc.

Determination of treatment outcome with date

There are seven possible treatment outcomes –viz., Cured, treatment Completed, Lost to follow-up, Failure, Died, Not evaluated and Treatment regimen changed. Determination of treatment outcome depends upon:

- Type of patient
- Recording of drug administration
- Follow up sputum smear results
- DST Reports
- Recording in remarks column

The relevant outcome along with the date is recorded in the line provided for this on the reverse of the treatment card. A patient will have only one outcome at a time.

For determination of 'Cure' and 'Treatment completed', the date of outcome is the date on which the last dose was taken in the CP.

For the determination of date of outcome in cases of Failure, the date on which the sputum was found to be positive at the end of treatment is taken as date of outcome.

For 'Lost to follow-up, 'the date of interrupting treatment is taken as a date of outcome. For 'Died' on which the event occurred is taken as a date of outcome.

If patient on treatment cannot be given any of these outcomes, he is considered as 'Not Evaluated'.

The treatment outcome has to be recorded on the Treatment Card, NIKSHAY and in the TB Notification register within one month of the event. Declaration of the treatment outcome has to be decided upon and signed with date by the MO.

Treatment outcomes for drug susceptible TB Patients

1. Cured: Microbiologically confirmed TB patients at the beginning of treatment who was smear or culture negative at the end of the complete treatment

2. Treatment completed: A TB patient who has completed treatment without evidence of failure or clinical deterioration BUT with no record to show that the smear or culture results of biological specimen in the last month of treatment was negative, either because test was not done or because result is unavailable.

E.g. A microbiologically confirmed patient who has completed treatment with positive smear at the end of IP but no resistance to H and R detected or with negative smears at end of the intensive phase, but none at the end of treatment, the outcome is declared as treatment completed.

or

A clinically diagnosed patient, pulmonary or EP, who has received full course of treatment with no positive smear or culture at the end of treatment.

3. Failure: A TB patient whose biological specimen is positive by smear or culture at end of treatment.

Failure to Respond: A case of paediatric TB who fails to have microbiological conversion to negative status or fails to respond clinically / or deteriorates after 12 weeks of compliant treatment shall be deemed to have failed response provided alternative diagnosis/ reasons for nonresponse have been ruled out.

4. Lost to follow up: A TB patient whose treatment was interrupted continuously for ONE month or more.

5. Not Evaluated - A TB Patient for whom no treatment outcome is assigned. This includes former "transfer-out"

6. Treatment Regimen Changed - A TB patient who is on first line regimen and has been diagnosed as having DRTB and switched to drug resistant TB regimen prior to being declared as failed.

7. Died: A patient who has died during the course of anti-TB treatment.

Treatment Success: TB patients either cured or treatment completed are accounted in treatment success. It is an indicator and not an outcome.

Determination of date of treatment outcome

Outcome	Date of determination	Illustrations
Cured or Treatment Completed	The last dose treatment (112th dose of CP)	Patient administered last DOT in continuation phase on 16-06-2017. then the outcome will be written as *Cured or treatment completed on 16-06-2017.*
Not evaluated (includes previous Transferred out)	Transferred out is the date on which the patient is supposed to have consumed the last dose of the drugs provided to him on transfer as recorded in the card. This is only an interim outcome. The actual outcome as reported from the unit where the patient was transferred will be updated in the card and in the TB Notification register.	If patient is transferred out on 26-06.2017, and no feedback has been received from receiving unit for **one month**, the actual date of 'not evaluated' is the day he was supposed to continue treatment in the new PHI/Treatment centre. It will be 27/06/2017 if the last dose from the transferring unit was consumed on 26/06/2017. ``
Lost to follow up	The scheduled date of administration of drug when patient interrupted treatment continuously for 1 month or more	Patient interrupted treatment on 16-9-2017 Record outcome as Lost to follow up *'on 16-9-2017'* on or after 17-10-2017 within one month
Failure	The date on which the sputum examination was found to be positive for AFB	If the smear result is positive on 18-05-2017, *Failure on 18-05-2017*
Died	The actual date of death	Patient died on 11-08-2017, *Died on 11-08-2017*
Treatment Regimen Changed	The date on which the patient is started on NTEP DR-TB treatment regimen.	Patient declared as DR-TB on 01-01-2017 and put on DR- TB treatment on 21-01-2017. the date for **Treatment Regimen Changed** would be 21-01-2017.

A patient will have only one outcome. The outcome which occurs first is considered and recorded in treatment card and subsequently in the TB notification register and NIKSHAY. Outcome should be declared within one month of the event.

Management of patients with treatment interruptions

The factors to be considered for the management of interruptions are

i. **Type of case** – Whether new, relapse or failure etc case
ii. **Duration of treatment taken**: Less than one month / more than one month. This helps in assessing the risk of presence of drug resistance.
iii. **Duration of Interruption:** Less than one month / more than a month.

If it is more than one month, patient is to be declared the outcome as 'lost to follow up'. If patient returns the health facility after interrupting treatment for more than one month, patient sample needs to be subjected for DST to determine resistance/sensitive status to anti TB drugs.

In case interruption is for less than one month, continue same treatment regimen to complete all doses.

Summary of Definitions

Case definitions	Type of case	Treatment outcome definitions
Microbiologically confirmed TB: presumptive TB patient with biological specimen positive for AFB, or positive for MTB on culture, or positive for TB through Quality Assured Rapid Diagnostic molecular test. **Clinically diagnosed TB case:** A presumptive TB patient who is not microbiologically confirmed, but diagnosed with active TB by a clinician on the basis of X-ray, histopathology or clinical signs with a decision to treat the patient with a full course of Anti-TB treatment In children, this is based on the presence of abnormalities consistent with TB on radiography, history of exposure to an infectious case, evidence of TB infection (positive TST) & clinical findings suggestive of TB in the event of negative or	**New case** - A TB patient who has never had treatment for TB or has taken anti-TB drugs for less than one month. **Previously treated patients** have received 1 month or more of anti-TB drugs in the past. **Recurrent TB case** - A TB Patient previously declared as successfully treated (cured/treatment completed) and is subsequently found to be microbiologically confirmed TB case. **Treatment After failure-** those patients who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment. **Treatment after loss to follow-up** A TB patient previously treated for TB for 1 month or more and was declared lost to follow-up in their most recent course of treatment and subsequently found microbiologically confirmed TB case. **Other previously treated patients** are those who have previously been treated for TB but who cannot be classified into any of the above classification.	**Cured:** Microbiologically confirmed TB patients at the beginning of treatment who was smear or culture negative at the end of the complete treatment **Treatment completed:** A TB patient who completed treatment without evidence of failure or clinical deterioration BUT with no record to show that the smear or culture results of biological specimen in the last month of treatment was negative, either because test was not done or because result is unavailable. **Eg.** A microbiologically confirmed patient who has completed treatment with negative smears at end of the intensive phase, but none at the end of treatment, the outcome is declared as treatment completed. or A clinically diagnosed patient who has received full course of treatment **Failure:** A TB patient whose biological specimen is positive by smear or culture at end of treatment. **Failure to Respond:** A case of

Case definitions	Type of case	Treatment outcome definitions
unavailable microbiological results **Extra Pulmonary tuberculosis (EPTB)**: any microbiologically confirmed or clinically diagnosed case of TB involving organs other than lungs e.g. pleura, lymph nodes, intestine, genitourinary tract, joint and bones, meninges of the brain etc. *Miliary TB classified as PTB because there are lesions in the lungs.* *A patient with both pulmonary and extra-pulmonary TB should be classified as a case of PTB*		paediatric TB who fails to have microbiological conversion to negative status or fails to respond clinically / or deteriorates after 12 weeks of compliant intensive phase shall be deemed to have failed response provided alternative diagnoses/ reasons for non- response have been ruled out. **Lost to follow up:** A TB patient whose treatment was interrupted for one month or more continuously **Not Evaluated** - A TB Patient for whom no treatment outcome is assigned. This includes former "transfer-out" **Treatment Regimen Changed** - A TB patient who is on first line regimen and has been diagnosed as having DRTB and switched to drug resistant TB regimen prior to being declared as failed **Died** A patient who has died during the course of anti-TB treatment

Death audit:

The medical officer should conduct an in-depth audit of all the deaths occurring amongst the TB patients irrespective of initiation of treatment. Similarly, DTO should conduct death review of all MDR-TB patients died. This would be beneficial in understanding the causes leading to the deaths and guide the programme in taking appropriate action to prevent them.

Prevention and management of Adverse Drug Reactions to Anti-TB drugs

Most TB patients on first line drugs complete their treatment without any significant adverse drug effects. However, a few patients do experience adverse effects and some of the drugs induced side effects can be prevented. Moreover, many second line drugs are associated with more side effects during long duration of treatment. It is therefore important that patients be clinically monitored during treatment so that adverse effects can be detected promptly and managed properly.

Treatment supporter should be aware of the commonly occurring adverse reactions so that they can identify it promptly and refer the patient to the medical officer for further management. Any adverse reactions reported during treatment is recorded in the space provided for ADR in the treatment card. Orange / red discoloration of the body fluids especially urine which is commonly encountered is not an adverse reaction and patient should be made aware of this.

All health personnel should monitor patients about adverse drug effects and inform patients to report to health system in case of any side effects. Health care workers need to be informed and trained about the methodology and channels for reporting ADRs

Adverse effects of Anti-TB drugs

Anti-TB treatment with first-line drugs is generally safe and well tolerated. Side effects to anti-TB drugs are common. Trivial side effects may lead to reduced compliance with treatment. These adverse effects must be recognized early, to reduce associated morbidity and mortality.

Side effects of first line anti-TB drugs:

Drug	Main effects	Rare effects
Isoniazid	Peripheral neuropathy Skin rash Hepatitis Sleepiness and lethargy	Convulsions Psychosis Arthralgia Anaemia
Rifampicin	Gastrointestinal: abdominal pain, nausea, vomiting Hepatitis Generalised cutaneous reactions Thrombocytopenic purpura	Osteomalacia Pseudomemberanous colitis Pseudoadrenal crisis Acute renal failure Haemolytic anaemia
Pyrazinamide	Arthralgia Hepatitis Gastrointestinal	Cutaneous reactions Sideroblastic anaemia
Ethambutol	Retrobulbar neuritis	Generalised cutaneous reactions Arthralgia Peripheral neuropathy Hepatitis (very rare)

Streptomycin	• Allergy –severe fever • Burning or tingling sensation • Vertigo • Nausea and vomiting • Difficult or painful urination • Blurred or double vision • Hearing impairment - SEVERE • Fast/irregular heart beat	

Management of ADRs:

What to do if symptoms of adverse effects occur? If symptoms of ADRs occur, the following should be done: -

- The dose of drugs should be checked
- All other causes of symptoms should be excluded
- The seriousness of the adverse effects should be estimated
- The adverse effects should be registered
- The drugs may need to be stopped and should eventually be reintroduced gradually when symptoms disappear
- Development of drug resistance should be avoided

A symptom-based approach to the management of the most common adverse effects is adopted. These side effects are classified as major or minor. In general, a patient who develops minor adverse effects should continue TB treatment and be given symptomatic treatment. If a patient develops a major side effect, the responsible drug or the entire regimen may need to be stopped and the patient should be urgently referred to a clinician or health care facility for further assessment and treatment. Patients with major adverse reactions should be Managed in a hospital with sufficient infection control measures and expertise. In DR TB patients, the DR TB committee needs to be involved in the management and modification of the regimen if required.

Symptom-based approach to evaluation of possible side effects of anti-TB drugs

Symptom	**Drug (abbreviation)**	**Action to be taken by HW**	**Action to be taken by MO**
Gastrointestinal (vomiting or epigastric discomfort)	Any oral medication	Reassure patient. Give drugs with less water and over a longer period of time (e.g. 20 minutes). Do not give drugs on an empty stomach If the above fails, refer to MO	Maintain hydration Consider treatment with anti-emetics (e.g. domperidone) and proton pump inhibitors (e.g. Omeprazole)

Itching/Rashes	Isoniazid (and other drugs also)	Reassure patient If severe, stop all drugs and refer patient to MO	Itching without rash or a mild rash • Continue treatment and give antihistamines Itching with moderate to severe rash • Stop all drugs till symptoms subside • Treat with antihistamines • Patients with mucosal involvement, fever and hypotension will require treatment with corticosteroids • When the reaction subsides reintroduce drugs one by one in this order INH. Rifampicin Pyrazinamide Ethambutol • Re-introduce each drug in a small dose and gradually increase over 3 days before introducing the next drug.

Tingling/burning /numbness in the hands and feet	Isoniazid	Refer to MO	• Give pyridoxine 100 mg/day orally or parenterally until symptoms subside. Patients not responding to pyridoxine will require treatment with amitryptiline
Joint pains	Pyrazinamide	Reassure that it is a self-limiting condition. Encourage patients to increase intake of liquids. If severe, refer patient to MO for evaluation	• Give NSAIDs like paracetamol, Aspirin or ibuprofen and in severe cases Indomethacin for a week to 10 days • In severe cases estimate serum uric acid levels - If uric acid levels are significantly raised treat with NSAIDs and colchicine. Allopurinol is not effective In severe cases with normal or slightly elevated uric acid consider reduction of the dose of Pyrazinamide.
Impaired vision	Ethambutol	STOP Ethambutol, refer patient for evaluation	• Refer to ophthalmologist for evaluation • Impaired vision may, within a few weeks, or may not return to normal after stopping ethambutol. Don't restart ethambutol.

Ringing in the ears Loss of hearing Dizziness and loss of balance	Streptomycin	STOP Streptomycin, refer patient for evaluation	• Refer to oto-rhino-laryngologist for opinion • As hearing loss is usually not reversible do not restart Streptomycin
Hepatitis: Anorexia / Nausea / vomiting / Jaundice	Isoniazid, Rifampicin or Pyrazinamide	STOP all anti TB drugs, Refer patient for evaluation	• Rule out other causes of hepatitis • Do not restart treatment till symptoms resolve and liver enzymes return to baseline levels • If liver enzymes cannot be performed wait for 2 weeks after jaundice has disappeared to restart treatment • Restart treatment with one drug at a time starting with Rifampicin INH Pyrazinamide. • In patients with severe disease in whom treatment cannot be stopped use a non-hepatotoxic regimen consisting of Streptomycin and Ethambutol

Pharmacovigilance in TB control Programme

Pharmacovigilance is defined by the WHO as the "Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem".

It is a fundamental activity to inform the management of patient safety measures in health care.

Pharmacovigilance is a public health surveillance activity. There are 3 methods for reporting on Pharmacovigilance activities: -

1. Spontaneous reporting
2. Targeted reporting
3. Active surveillance

- **Spontaneous reporting:** -Spontaneous (or Voluntary) reporting means that no active measures are taken to look for adverse effects other than encouragement of the health professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. This is the most common form of pharmacovigilance, sometimes termed passive reporting.

- **Targeted reporting:** -It focuses on capturing ADRs in a well-defined group of patients on treatment. Health professionals in charge of the patients are sensitized to report specific safety concerns.

- **Active surveillance:** - It is a pro-active effort made to elicit adverse events. Events detected by asking patients directly, screening patient record as, laboratory and clinical tests. It is best done prospectively.

Need for Pharmacovigilance

NTEP has a strong monitoring mechanism but information on ADRs is lacking (Indian database). There is minimal information from private sector. The mortality, morbidity and reduced quality of life associated with ADRs are poorly documented. Anti-TB drugs used for drug-resistant TB are commonly associated with ADRs. In TB-HIV patients, use of anti-retroviral drugs along with anti-TB drugs is associated with ADRs. Pharmacovigilance will help in understanding and detecting ADRs associated with newer drugs to treat TB (Bedaquiline, Delamanid). To strengthen patient safety, safeguard patient's interest and ensure adherence to prescribed drug regimens. Antimicrobial resistance

For details "A practical handbook on the pharmacovigilance of medicines used in the treatment of Tuberculosis" by WHO in 2012 may be referred. Under the Pharmacovigilance Programme of India (PvPI) set up by the Ministry of Health and Family Welfare, Govt. of India in July 2010 routine reporting and monitoring of ADRs will be continued.

Priority is given to establishing pharmacovigilance at DR-TB centres for drug resistant cases. The DR-TB centres would be linked with ADR monitoring centres established under PvPI in medical colleges to initiate reporting of ADR in systematic manner. With introduction of daily anti-TB treatment regimen priority will be given to establish Pharmacovigilance at ART centres for TB-HIV patients. The standardized suspected ADR reporting form (Annexure-11) and needs to be filled by the treating doctor.

Annexure 11

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by healthcare professionals

CDSCO
Central Drugs Standard Control Organization
Directorate General of Health Services,
Ministry of Health & Family Welfare, Government of India,
FDA Bhawan, ITO, Kotla Road, New Delhi
www.cdsco.nic.in

(AMC/ NCC Use only)
AMC Report No.
Worldwide Unique no.

A. Patient Information

1.Patient Initials _____

2.Age at time of Event or date of birth ----------

3. Sex ☐M ☐ F

4. Weight __ Kgs

12. Relevant tests / laboratory data with dates

B. Suspected Adverse Reaction

5. Date of reaction stated (dd/mm/yyyy)

6. Date of recovery (dd/mm/yyyy)

7. Describe reaction or problem

13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcoholuse, hepatic/ renal dysfunction etc)

14. Seriousness of the action

- ☐ Death (dd/mm/yyy)___
- ☐ Life threatening
- ☐ Hospitalization-initial or prolonged
- ☐ Disability
- ☐ Congenitial anomaly
- ☐ Required intervention to prevent permanent impairment / damage
- Other (specify)

15. Outcomes

- ☐ Fatal
- ☐ Continuing
- ☐ Recovering
- ☐ Recovered
- ☐ Unknown
- ☐ Other (specify)____

C.Suspected medication(s)

S.No	8. Name (brand and /or generic name)	Manufacturer (if known)	Batch No./ Lot No. (if known)	Exp. Date (if known)	Do used	Route used	Frequency	Therapy dates (if known give duration)		Reason for use of prescribed for
								Date started	Date stopped	
i.										
ii.										
iii.										
iv.										

Sl.No As per C	9. Reaction abated after drug stopped or dose reduced					10. Reaction reappeared after reintroduction				
	Yes	No	Unknown	NA	Reduced dose	Yes	No	Unknown	NA	If reintroduced dose
i.										
ii.										
iii.										
iv.										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (exclude those used to tre at reaction)

D. Reporter (see confidentiality section in first page)

16. Name and Professional Address _____

_____

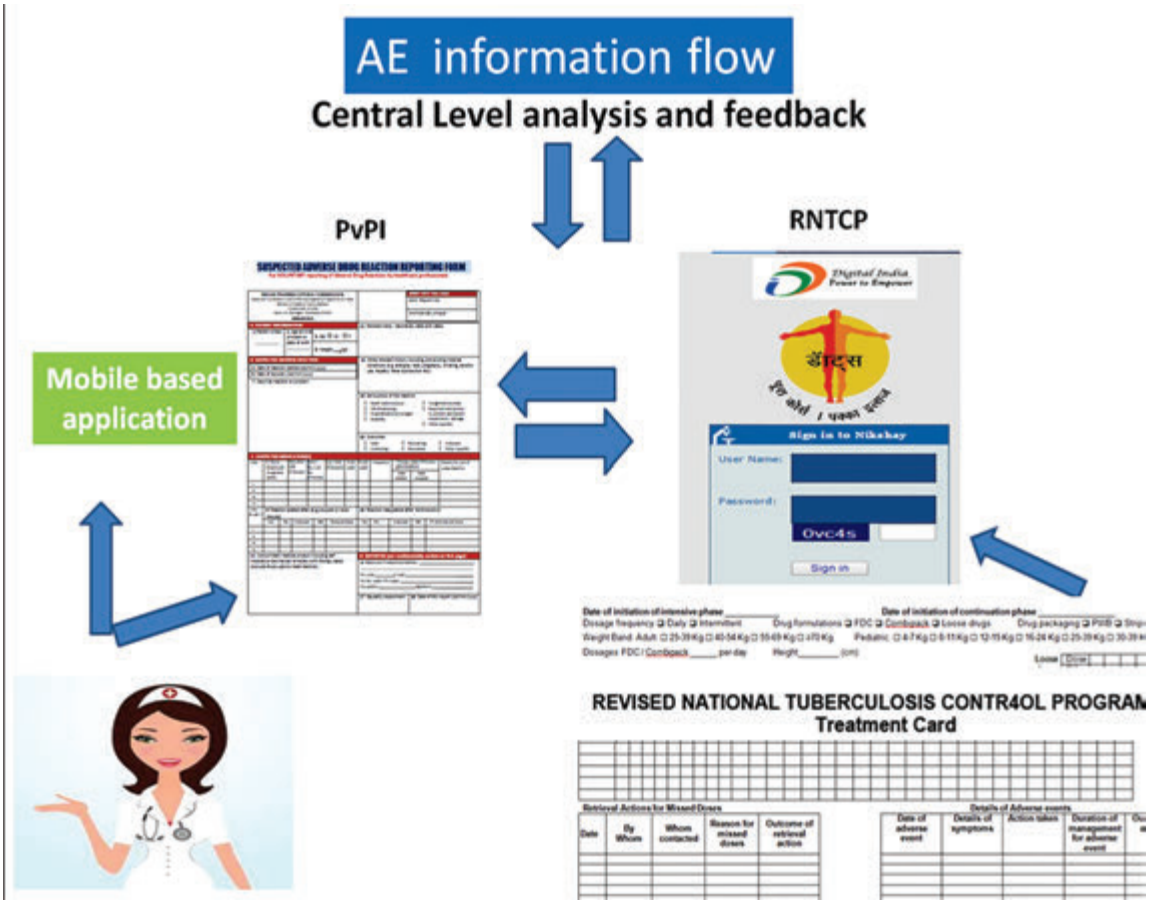
Pin code: _____E-mail _____

Tel. No. (with STD code):_____

Occupation _____Signature _____

17. Causality Assessment

18. Date of this report (dd/mm/yyyy)



Management of Hospitalized patients:

The usual mode of TB treatment is domiciliary, but patients require hospitalization in the following conditions:

- pneumothorax or
- large accumulations of pleural fluid leading to breathlessness
- massive hemoptysis etc. the patients might need hospitalization.
- In case of severe adverse reactions
- Severe malnutrition

These patients can be managed in general hospitals preferably in wards where adequate air borne infection control measures are taken to prevent the spread.

All indoor patients who are found to be suffering from TB are to be treated with same NTEP regimen. The DOTS Centre of the respective hospital/Medical College must be informed of the patient's admission at the earliest, to enable transfer out of the patient to their respective DOTS Centre on discharge.

If the hospitalized patient is newly diagnosed, he/she should be notified. Once these patients go back, the peripheral health workers and NTEP staff should conduct home visits within a week. If transferred for treatment, the follow up results and treatment outcome should be sent back to the referring PHI/TU and updated in Nikshay. On discharge, patients may be given a maximum of 1-week drug supply to cover the transit period prior to their resumption of treatment at their respective DOT Centre, ensuring uninterrupted treatment.

Management of Extrapulmonary TB patients

The burden of EPTB ranges from 15-20% of all TB cases in HIV-negative patients while among PLHIV, it accounts for 40-50% of new TB cases. Every attempt should be made to establish microbiological confirmation of EPTB wherever specimen is available. All EPTB patients should be offered CBNAAT upfront for diagnosis which will also help in detection of a greater number of drug-resistant EPTB cases in the country. All EPTB patients should be screened for HIV. All patients suspected of EPTB should have clinical assessment for active Pulmonary TB also.

The treatment regimen and schedule for EP TB cases will remain the same as for pulmonary TB. However, the duration of continuation phase in EPTB may be extended by 3 to 6 months in special situations like TB meningitis, Bone & Joint TB, Spinal TB with neurological involvement and neuro- tuberculosis. Unless drug resistance is suspected, adjuvant corticosteroid treatment is recommended for TB meningitis and pericarditis.

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

Same outcome definitions would be used as for drug sensitive /drug resistant Pulmonary TB patients, treatment outcome of treatment completed will be considered. Treatment outcome will depend on availability of culture reports of specimens, treatment completion and clinical improvement of the patient.

For further details on management of EPTB, refer to Index-TB guidelines on management of EPTB. There are 10 key principles for managing EPTB patients as described in Index-TB guidelines on management of EPTB.

Follow up

a. Clinical Follow up: it is the most important criteria for the follow up of patients with Extra-pulmonary TB. The follow up is mainly based on following clinical parameters. -

- Weight Gain
- Decrease or increase in symptoms (e.g. healing of ulcer/scrofuloderma)
- Increase or Regression in size of nodes {possibility of Immune Reconstitution Inflammatory Syndrome (IRIS) should be considered and differentiated from disease progression}
- Appearance of new nodes
- If chest symptomatic, monthly sputum for AFB and chest X-ray (to rule out pulmonary involvement)
- Other Extra-pulmonary sites should be monitored (USG abdomen if necessary)
- Serum Creatinine – monthly for the first three months of treatment and then quarterly till the patient receives Kanamycin and further when clinically indicated
- Liver function test – as clinically indicated
- USG-abdomen – if necessary
- Monitoring for drug adverse reactions

b. Bacteriological Follow up: it should be done as per schedule, whenever specimen is available.

Management of TB patients in special situations

TB in Pregnant and Lactating women

Before initiating treatment for tuberculosis, women of childbearing age should be asked about current or planned pregnancy and counselled appropriately. A successful treatment of TB is important for successful outcome of pregnancy. Except for streptomycin, the first line anti-TB drugs are safe for use in pregnancy. Streptomycin is ototoxic to the fetus and should not be used during pregnancy.

A breastfeeding woman should receive a full course of TB treatment. Correct chemotherapy is the best way to prevent transmission of TB to baby. Breast feeding must be continued. After ruling out active TB, the baby should be given 6 months of isoniazid preventive therapy, Breast feeding should not be discouraged. The mother should be advised about cough hygiene measures such as covering the nose and mouth while coughing, sneezing or any act which can produce sputum droplets.

Mothers receiving INH and their breastfed infants should be supplemented with vitamin B6 (pyridoxine), recommended dose of Pyridoxine in infants is 5 mg/day and for mother is 10mg/day

TB and Contraceptive pills usage

As Rifampicin is a potent inducer of hepatic enzymes, the protective efficacy of oral contraceptive pills may be decreased. Oral contraceptives might have decreased efficacy due to vomiting and drug interactions with second line anti-TB drugs. Hence, women suffering from TB and using contraceptive pills should be advised to use alternative contraception method.

Patients with mono- and poly-resistant TB who are susceptible to rifampicin, rifampicin interacts with the contraceptive drugs resulting in decreased efficacy of protection against pregnancy. A woman on oral contraception while receiving rifampicin treatment may choose between two options following consultation with the treating physician:

- Use of an oral contraceptive pill containing a higher dose of estrogen (50 /g)
- Use of another form of contraception.

Methods that can be used for contraception, based on individual preference and eligibility

- Barrier methods (Condoms/ diaphragms)
- IUDs (CuT)
- Depot medroxy-progesterone (Depo-provera)

Management of TB in patients with liver disorders

- Patients with hepatitis virus carriage, a past history of acute hepatitis, current excessive alcohol consumption can receive the usual TB regimens provided that there is no clinical evidence of chronic liver disease.
- Hepatotoxic reactions to anti-TB drugs may be more common
- In patients with unstable or advanced liver disease, liver function tests should be done at the start of treatment.
- If the liver disorder is severe, lesser hepatotoxic drugs have to be used.
  - Expert consultation is advisable in treating patients with advanced or unstable liver disease.

- Clinical monitoring (and liver function tests, if possible) of all patients with pre-existing liver disease should be performed during treatment.
- If the serum alanine aminotransferase level is more than 3 times normal before the initiation of treatment, the following regimens should be considered:
  – Containing two hepatotoxic drugs:

- 9 months of isoniazid and rifampicin, plus ethambutol (until or unless isoniazid susceptibility is documented)- 9HRE
- 2 months of isoniazid, rifampicin, streptomycin and ethambutol, followed by 7 months of isoniazid and rifampicin-2SHR/ 7HR
- 6–9 months of rifampicin, pyrazinamide and ethambutol-(6-9 RZE)
  – Containing one hepatotoxic drug:

- 2 months of isoniazid, ethambutol and streptomycin, followed by 10 months of isoniazid and ethambutol (2SHE/10 HE)
  – Containing no hepatotoxic drugs:

- 18–24 months of streptomycin, ethambutol and a fluoroquinolone. (18-24 SLE)

TB patient with renal failure and severe renal insufficiency

- Patients suffering from Chronic Kidney diseases (CKD) are at an increased risk of developing Tuberculosis.
- Active TB should be excluded in patients with CKD by appropriate investigations in patients who have an abnormal chest x-ray or a history of prior pulmonary or EPTB that has been either inadequately or not previously treated.
- TB should be considered in all patients with unexplained systemic or system-specific symptoms as EPTB is common, particularly in patients on dialysis, with peritoneal TB being common in patients on chronic ambulatory peritoneal dialysis.
- Any patient with active TB, either pulmonary or extrapulmonary, should receive standard chemotherapy agents, albeit with dose interval modifications where appropriate.
- 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

- For patients with stages 4 and 5 Chronic renal disease and on haemodialysis, dosing intervals should be increased to three times weekly for ethambutol, pyrazinamide and the aminoglycosides.
- Treatment can be given immediately after haemodialysis to avoid premature drug removal. With this strategy there is a possible risk of raised drug levels of ethambutol and pyrazinamide between dialysis sessions.

Alternatively, treatment can be given 4 to 6 hours before dialysis, increasing the possibility of premature drug removal but reducing possible ethambutol or pyrazinamide toxicity. Three times per week administration of these two drugs at the following doses is recommended: pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg). These doses are the ones used in daily regimens.

Estimated creatinine clearance calculations

- **Men:**
  - Ideal Body Weight (kg) X (140 – age) / 72 X serum creatinine (mg/dl)
- Women:
  - 0 85 X Ideal Body Weight (kg) X (140 – age) / 72 X serum creatinine (mg/dl))

Dose adjustment of anti-TB drugs in presence of renal impairment

Drug	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving haemodialysis (unless otherwise indicated dose after dialysis)
Isoniazid	No adjustment necessary
Rifampicin	No adjustment necessary
Pyrazinamide	25-35 mg/kg per dose three times per week (not daily)
Ethambutol	15-25 mg/kg per dose three times per week (not daily)
Rifabutin	Normal dose can be used, if possible monitor drug concentrations to avoid toxicity
Rifapentine	No adjustment necessary
Streptomycin	12-15 mg/kg per dose two or three times per week (not daily)
Capreomycin	12-15 mg/kg per dose two or three times per week (not daily)
Kanamycin	12-15 mg/kg per dose two or three times per week (not daily)
Amikacin	12-15mg/kg per dose two or three times per week (not daily)
Ofloxacin	600-800 mg per dose three times per week (not daily)
Levofloxacin	750-1000 mg per dose three times per week (not daily)
Moxifloxacin	No adjustment necessary
Cycloserine	250mg once daily, or 500mg / dose three times per week*
Terizidone	Recommendations not available
Prothinamide	No adjustment necessary
Ethionamide	No adjustment necessary
PAS	4g/dose, twice daily maximum dose
Bedaquiline	No dosage adjustments required in patients with mild to moderate renal impairment (dosing not established in severe renal impairment, use with caution)
Linezolid	No adjustment necessary
Clofazimine	No adjustment necessary
Amoxicillin / clavulanate	For creatinine clearance 10-30 ml/min dose 1000 mg as amoxicillin component twice daily; For creatinine clearance <10 ml/min dose 1000 mg as amoxicillin component once daily
Imipenem / cilastin	For creatinine clearance 20-40 ml/min dose 500 mg every 8 hours; For creatinine clearance <20 ml/min dose 500 mg every 12 hours
Meropenem	For creatine clearance 20-40 ml/min dose 750 mg every 12 hours; For creatine clearance <20 ml/min dose 500 mg every 12 hours

*Companion Handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis 2014. (30)

Estimated creatine calculations:

Men: Ideal body weight (kg) x 140-age) / 72 x serum creatinine (mg/dl)

Women: 0.85 x ideal Body Weight (kg) x (140-age) / 72 x serum creatine (mg/dl)

TB in patients with seizure disorders

- The use of isoniazid and rifampicin may interfere with many of the antiseizure medications.
- High dose isoniazid also carries a high risk of seizure and should be avoided in patients with active seizure disorders.
- The prophylactic use of oral pyridoxine (vitamin B6) can be used in patients with seizure disorders to protect against the neurological adverse effects of isoniazid or cycloserine.
- Suggested prophylactic dose
  - for at-risk patients on isoniazid is 10 to 25 mg/day
  - for patients on cycloserine is 25 mg of pyridoxine for every 250 mg of cycloserine daily.
- The optimal prophylactic dose of pyridoxine for children has not been established,
  - 1–2 mg/kg/day has been recommended with a usual range of 10–50 mg/day for paediatric patients at risk for neurological sequel.

Latent Tuberculosis Infection (LTBI)

- Latent tuberculosis infection (LTBI) is the presence of Mycobacterium tuberculosis in the body without signs and symptoms, or radiographic or bacteriologic evidence of tuberculosis (TB) disease. Studies have demonstrated that Isoniazid (INH) taken for at least 6 months in persons with LTBI reduced subsequent TB incidence by 25 to 92 per cent, the differences in effectiveness largely explained by differences in treatment completion. Refer to the recently updated WHO guidelines for management of LTBI in the year 2018. (Latent TB infection: updated and consolidated guidelines for programmatic management).

- India, with one-fourth of the global burden of TB, has 40 per cent of the population infected with M.TB. Treating 40 per cent of the population for LTBI based on Tuberculin Skin Test (TST) positivity or Interferon Gamma Release Assay is neither rational nor practicable, thus emphasizing the need for a focussed approach. In clinical situations, the most obvious group for LTBI treatment would include high-risk patients such as those receiving long term corticosteroids, immunosuppressants, HIV-infected and juvenile contacts of sputum-positive index cases.

Differentiating Between Latent TB Infection and TB Disease

LTBI	TB Disease
• No symptoms or physical findings suggestive of TB disease. • TST or IGRA result usually positive. • Chest radiograph is typically normal. • If done, respiratory specimens are smear and culture negative. • Cannot spread TB bacteria to others. • Should consider treatment for LTBI to prevent TB disease.	• Symptoms may include one or more of the following: fever, cough, chest pain, weight loss, night sweats, haemoptysis, fatigue, and decreased appetite. • TST or IGRA result usually positive. • Chest radiograph is usually abnormal. However, may be normal in persons with advanced immunosuppression or extrapulmonary disease. • Respiratory specimens are usually smear or culture positive. However, may be negative in persons with extrapulmonary disease or minimal or early pulmonary disease. • May spread TB bacteria to others. • Needs treatment for TB disease.

TB Comorbidities

Several medical conditions are risk factors for TB and poor TB outcomes. Similarly, TB can complicate course of some diseases. It is therefore important to identify these comorbidities in people diagnosed with TB and manage both the conditions in order to ensure early diagnosis and improved outcome.

TB and HIV

The primary impact of HIV on TB is that the risk of developing TB becomes higher in patients with HIV. Overall, HIV-infected persons have approximately an 8-times greater risk of TB than persons without HIV infection. The risk of TB in HIV-infected persons continues to increase as HIV disease progresses and CD4 cell count decreases. While anti-retroviral treatment can substantially decrease the risk of TB, this risk always remains higher than that in HIV negative individuals. Furthermore, among cured TB survivors with HIV infection, the risk of recurrent TB is also quite high.

Similarly, Tuberculosis is the most common opportunistic infection amongst HIV-infected individuals. It is a major cause of mortality among patients with HIV and poses a risk throughout the course of HIV disease.

The presentation of TB in the HIV-infected patient may vary with degree of immune suppression. The diagnosis of TB in PLHIV can be more difficult and may be confused with other pulmonary or systemic infections. As the HIV disease progresses and the individual become more immune-compromised, the clinical presentation is proportionately more likely to be extra-pulmonary or smear-negative than in HIV-uninfected TB patients. This can result in misdiagnosis or delays in diagnosis, and in turn, higher morbidity and mortality.

It is estimated that there are 2.14 million people living with HIV in India with an estimated (2017 report)Adult, 15-49 years, HIV prevalence in India of 0.22% (0.16% – 0.30%).TB accounts for 25% of deaths among People Living with HIV and AIDS (PLHIV) in India. Although only 5% of incident TB patients are HIV-infected, in absolute terms it means more than 100,000 cases annually, ranks second in the world and accounts for about 10% of the global burden of HIV-associated TB. HIV positivity among PLHIV varies from states /districts in the country, the proportion of HIV positive among TB patients over 10% in high HIV burden states to up to 40% in some high burden districts.

HIV Testing for TB Patients / Presumptive TB Cases

1. National HIV counselling testing services guidelines (HCTS), 2016 and WHO consolidated guidelines on HIV, 2015 recommend offering routine HIV testing to all presumptive and diagnosed TB cases, partners of known HIV positive TB patients, decentralization of HIV testing facilities, task sharing & multitasking of HIV testing responsibilities in order to reduce coverage gaps and improve access to HIV prevention, treatment, care and support.

2. Presumptive / Diagnosed TB patients coming to the health facilities will be referred to Stand Alone-Integrated Counselling & Testing Centre (SA-ICTC) by health care workers, called provider-initiated testing & counselling (PITC), where they will be offered counselling & testing as per the norms and standard operating procedures of the National AIDS Control Programme (NACP).

3. In PITC, health care worker or counsellor provides basic information on HIV, the testing process, clinical and prevention benefits of testing and potential risk of discrimination. The clients are also informed about their "right to refuse" the offer of HIV testing and that declining the test will not affect their access to other services.

4. At many health facilities where infrastructure of ICTC is not available, Facility Integrated Counselling & Testing Centres (F-ICTC) have been established by State AIDS Control Societies (SACS) under NACP. At F-ICTCs, Presumptive / Diagnosed TB patients are screened for HIV by whole blood finger prick test (WBFPT) kits. It is easy to perform and provides results within 30 minutes.

5. If the test result on the initial screening test is negative then the LT will hand over report of HIV screening test to presumptive TB patient/ diagnosed TB case provided with the serial number of tests in counselling register & date and signature of a Medical officer.

6. If test result is found 'Reactive' for HIV at screening, no report is given to the presumptive TB patient/ diagnosed TB case. They are further referred to nearest SA-ICTC for confirmation of the HIV diagnosis

7. NACP also recommends the establishment of provider-initiated HIV screening at all DMCs under the NTEP.

8. HIV screening at all F-ICTCs will be implemented through their existing staff with due sensitization, orientation, guidance, monitoring and supervision by the linked SA-ICTC. The WBFPT kits need to be stored between 2°C and 8 °C in the refrigerator available at the health facility.

9. For patients with HIV positive results at confirmatory site (SA-ICTC), the counsellor will link the patient to the nearest ART centre available in the district/state. This will be done by giving a referral form and explaining the patient on how to access the centre. The patient will be given the contact details of the district programme managers for any assistance needed.

10. The counsellor will document the HIV status, date of HIV testing and Patient ID number in the 'NTEP Request form for examination of biological specimen for TB' as a feedback to LT of DMC. The counsellor will also assist the DMC LT to update the laboratory register with information on HIV status (Reactive /Non-reactive).

TB Screening among HIV patients

Intensified TB case finding (ICF) at ICTCs, ART and Community Support Centres (CSCs)

Intensified TB case finding at HIV care settings is an important strategy for early diagnosis of TB among PLHIV.

Three "I" s to reduce burden of TB among PLHIV

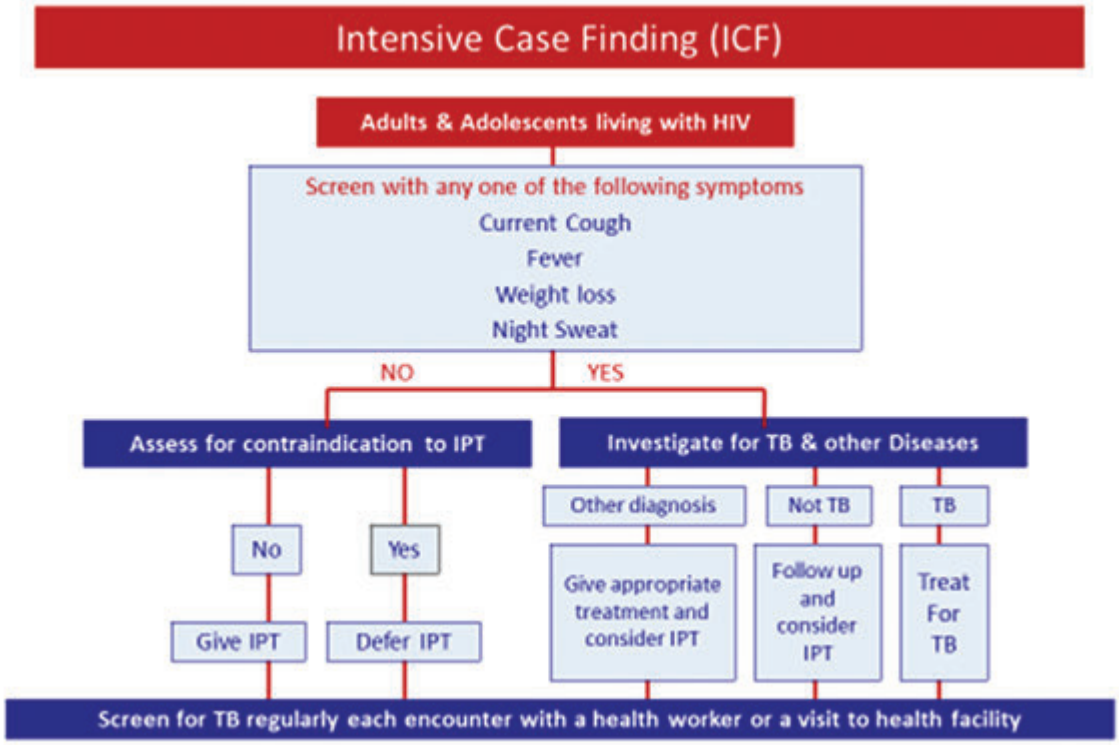
- **ICF:** Intensified (TB) case finding (ICF) at ICTC, ART centres and Link ART Centres (LAC)
- **IC-AIC:** Air-borne infection control measures for prevention of TB transmission at HIV care settings
- **IPT:** Implementation of Isoniazid preventive treatment (IPT) for all PLHIV (On ART + Pre-ART)
- Provision of ART for HIV infected TB patients

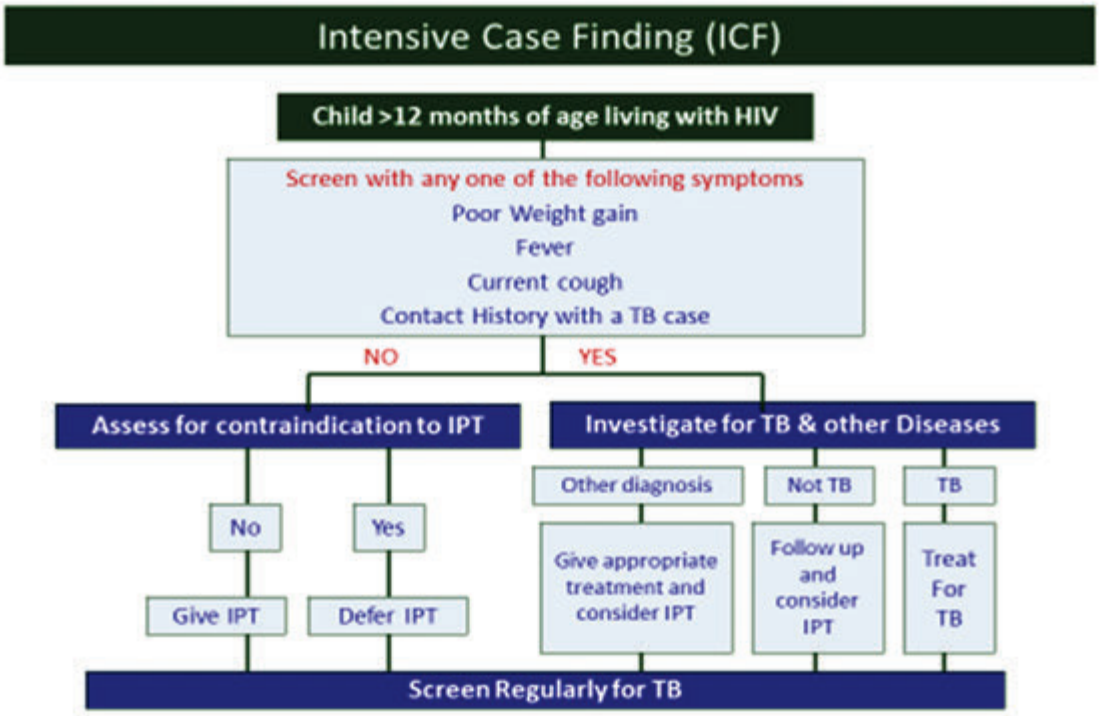
Intensified TB Case Finding (ICF)

- Actively looking for signs and symptoms of TB disease
  - Symptom screening and then follow-up evaluation as indicated
  - Can be in settings (clinic, prison, etc.) or community-based
- Goals of ICF for PLHIV
  - Earlier diagnosis and treatment of TB to reduce mortality
  - Prevent ongoing transmission
  - Initial step in ICF-IPT cascade for excluding disease to provide TB preventive therapy
- Steps for ICF
  - Screening for TB using 4 symptom complex
  - Fast tracking
  - Early diagnosis

4. symptom complex for TB screening among PLHIV

Adult	Children
• Current cough	• Current cough
• Fever	• Fever
• Weight loss	• Poor weight gain
• Night Sweats	• Contact with TB case





ICF at ICTC

All ICTC clients should be screened by ICTC counsellors for presence of TB symptoms at every encounter (pre, post or follow-up counselling). Clients who have symptoms or signs, irrespective of their HIV status, should be referred to NTEP diagnostic and treatment facility located in same institution. Therefore, NACP and NTEP promote establishing co-located facilities, for better coordination between the two programmes. Hence, as network of HIV testing facilities is being expanded, consideration should be given to establish them at sites, which already have NTEP, designated microscopy centres (DMC).

The referrals of presumptive TB cases from ICTCs to TB diagnosis facility should be recorded on a line list to facilitate exchange of information with NTEP and track the client through the process of TB diagnosis and initiation of TB treatment. To streamline this process further NTEP programme staff should stay in touch with ICTC counsellors to complete the exchange of information in time. In addition, ICTC counsellors and NTEP programme staff participate in monthly HIV/TB coordination meeting at district level to validate line-lists and Monthly HIV/TB reports and resolve operational issues if any.

ICF at ART Centres

HIV-infected persons attending ART centres for pre-ART registration have a high prevalence of TB disease (6 to 8%). The incidence of TB among ART clients is also very high, even when on ART. Although ART reduces risk of incident TB, it remains many times higher compared to general population. In addition, HIV-infected clients having undiagnosed or untreated TB may seek care at ART centres and thus exposing other HIV-infected persons to the risk of acquiring TB. Therefore, active efforts for intensified TB case finding (ICF) at ART centres is critical for early suspicion and detection of TB, linkage to treatment and thus for prevention of transmission of infection to other clients. The national ART guidelines clearly state that all patients coming to ART centres should be actively screened for opportunistic infections, particularly tuberculosis. All

people living with HIV should be regularly screened for four symptoms viz., current cough of any duration, fever of any duration, significant weight loss or drenching night sweats, during every visit to a health facility and every contact with a health-care provider. Those with history of coughing blood and sputum and with any pulmonary abnormality in chest X-ray should also be evaluated for TB. Similarly, children living with HIV who have one or more of the following symptoms – failure to thrive, fever or cough of any duration or history of contact with a TB patient should be evaluated for TB.

Screening for TB is important regardless of whether the PLHIV is receiving IPT or ART. The presumptive TB cases identified at ART centres or Link ART centres should be prioritized and "fast-tracked" for evaluation by SMO/MO to minimize opportunities for airborne transmission of infection to other PLHIV.

PLHIVs suspected to have TB by MO, should be subjected to testing of sputum / appropriate specimen from a relevant extra-pulmonary site by CBNAAT at the nearest facility. CBNAAT is the frontline test for diagnosis of TB among PLHIV. If CBNAAT is not available, arrangements have to be made for collection and transportation of sputum specimen to the nearest CBNAAT site. If CBNAAT linkage is not available, then the patient should be evaluated with microscopy and Chest-X ray on the same day.

Smear negative TB and extra pulmonary TB is more common among people living with HIV and therefore a high level of suspicion is required. In the event of suspicion of Extra Pulmonary TB, the diagnostic algorithm as for HIV negative presumptive EPTB patients may be followed. Similarly, refer to diagnostic algorithm for paediatric pulmonary TB.

Preferably, PLHIVs should be offered TB and HIV diagnostic facility at the same premises as a "one-stop service" in order to reduce diagnostic delay and to link those not having any of the four symptom complex to IPT services.
In addition, the referrals presumptive TB cases should be recorded on an ART centre TB-HIV line list to facilitate coordination with NTEP programme staff and to track the patient closely through the process of TB diagnosis and TB treatment initiation. It is also crucial that ART Centre staff members attend monthly HIV/TB coordination meeting. The HIV/TB monthly reporting format to be generated at ART centres is incorporated into the ART centre monthly report (CMIS).

Information of all HIV infected TB patients in HIV care should be recorded in the ART centre HIV/TB register. These include TB patients detected by ART centre staff as well as those TB patients found HIV infected while on TB treatment and referred to ART centre by the NTEP. TB-HIV register is an important monitoring tool to track timeliness of initiation of CPT and ART the TB treatment outcome to modify ARV regimens as per guidelines. It is also important that ART centre staff carry this register when they attend monthly HIV/TB coordination meeting to update information on TB treatment outcome from NTEP staff and share information pertaining to CPT and ART with them for recording into NTEP TB Notification registers.

PLHIV diagnosed to be suffering from TB are presumptive MDR cases and need to follow the algorithm for diagnosis of drug resistant TB.

ICF at Link ART Centres (LAC)

The ICF activity is also implemented at all Link ART plus and Link ART centres in the country. As in ART centres LAC-Plus and LAC should 1) implement ICF using symptom screening on every encounter 2) promptly refer presumptive TB case to NTEP diagnostic facilities, and 3) refer the

patient to ART centre promptly if TB is detected for initiation of ART or modify current ARV regimen. Similar to ART centre, the LAC staff nurse /counsellor should maintain line-list, exchange with local NTEP staff to seek information on TB diagnosis and treatment and complete the line-list.

The LAC Plus use same line-list format as the ART centre while at LAC the ICTC line-list format is used (since ICTC counsellor runs the LAC). The completed line-list from LAC-plus is merged with ART centre line-list whereas that from LAC is merged into ICTC line-list for the same period and monthly report is generated accordingly.

These mechanisms are designed considering operational feasibility but key point is if TB is detected among patients at LAC plus of LAC, they must be promptly referred to ART centre for further management.

ICF among HIV high risk groups (HRG)

Operational research conducted in high HIV prevalent states have shown that HRG's like female sex workers (FSW), men having sex with men (MSM), injection drug users (IDU) etc. are more likely to have tuberculosis compared to general population. In addition, it is known that HIV prevalence among the HRG is several times higher than general population. While NACP provides HIV prevention interventions for the HRG through its targeted interventions, the ICF provides an opportunity to provide additional services to this population. This intervention is likely to help in detection HIV/TB cases early and link to care support and treatment. Among the HRG's, IDU have highest HIV prevalence therefore the programmes aim to provide ICF services and prompt linkage to care support and treatment to IDU as a priority.

Care and support centres:

TB symptom screening based on 4 symptom complex should also be done by counsellors and outreach workers at Care and support centre in collaboration with SACS.

Treatment of HIV-infected TB

Early diagnosis and effective treatment of TB among HIV-infected patients are critical for controlling the disease and minimizing the adverse impact of TB on the course of HIV. Hence, initiation of treatment is very important soon after the diagnosis of TB. Among HIV-infected persons, treatment of TB is same as that in the HIV-negative TB patients.

Anti-TB Treatment of HIV infected TB patients:

- Based on the clinical history and investigation reports ART MO will categorize patients as Rifampicin sensitive/ rifampicin sensitivity status not known/ clinically diagnosed TB cases, prior history of taking Anti-TB drugs (Cat I /Cat II) accordingly and initiate daily anti TB treatment in Fixed Dosage Combination as per NTEP guidelines at ART Centre itself.
- All HIV-infected TB patients if not tested already should be tested for drug susceptibility before initiation of treatment. Staff nurse will refer the patient to the nearest drug resistant TB centre in coordination with to NTEP and record the same in the line list as DRTB /Rif resistant patient. PLHIV with drug resistant TB should be managed by DR-TB center in consultation with ART centre.
- The STS of TU where ART Centre / CBNAAT site is located (nodal TU) will link the patient to the concerned TU based on the residence of the patient for TB treatment provision and follow up as per NTEP guidelines. STS (nodal TU) will also be responsible to get the registration details from the concerned TU. Overall responsibility of this linkage and coordination lies with District HIV –TB and PMDT coordinator.

- TB patients living with HIV infection should receive the same duration of TB treatment with daily regimen as HIV-negative TB patients.
- If drug sensitive TB patient and on second line ART, Rifampicin should be replaced with Rifabutin 300 mg three times a week or 150 mg daily.
- TB Treatment card for these patients will be prepared by staff nurse in duplicate and will be duly signed by medical officer. One copy of the TB treatment card is to be handed over to the patient. Patient will be registered in Nikshay by data manager of ART Centre and patient ID will be created. Under this ID, treatment details of the patient will be entered by the data manager.
- Pharmacist will maintain the inventory of stocks of Anti-TB drugs at ART centre. District HIV- TB and PMDT coordinator should ensure availability of adequate stock of Anti-TB drug and logistics in coordination with ART centre, District TB Officer, District Drug store pharmacist
- NTEP will identify local treatment supporter for all HIV –TB co-infected patients. Anti TB treatment will be supervised by the local treatment supporter and any adverse drug reactions should be informed immediately to local medical officer at PHI and ART medical officer.
- Regular follow up of the patients, testing for sputum as per NTEP Guidelines and adherence to ATT & ART treatment is to be ensured by the treatment supporter, STS, STLS, ART MO. ART Counsellor should ensure proper counselling in all the HIV-TB co-infected patients regarding adherence and possible side effects to ART and ATT.
- A mechanism of ensuring and checking adherence has been instituted by sending a missed call by patient to pre-printed phone numbers hidden behind selected pills after taking dose. As the sequence of hidden numbers cannot be predicted by patients, but are known by the system for each month of medication prescribed, the system offers high confidence that patients who respond correctly have indeed taken their medication.
- PLHIV with drug resistant TB should be managed by DR-TB centre in consultation with ART centre. The treatment of HIV positive individual with MDR-TB is the same as for HIV negative patients. However, treatment is more difficult and adverse events more common. Due to the increased frequency of adverse drug events, rigorous monitoring in this particular group of patients is required in order to ensure adherence to treatment, early identification and treatment of adverse events and reduce lost to follow up.

Anti-retroviral therapy and co-trimoxazole prophylactic therapy in HIV infected TB patients:

In addition to TB treatment, all HIV-infected TB patients must be provided access to care and support for HIV disease, including co-trimoxazole preventive therapy and antiretroviral therapy. ART reduces TB case fatality rates and the risk of recurrent TB. Co-trimoxazole preventative therapy has been shown to reduce mortality among PLHIV by preventing opportunistic infections.

- Anti-retroviral therapy must be offered to all patients with HIV and TB as well as drug-resistant TB, irrespective of CD4 cell-count, as early as possible (after 2 weeks) following initiation of anti-TB treatment. Appropriate arrangements for access to anti-retroviral drugs should be made for patients. However, initiation of treatment for TB should not be delayed.

Initiation of first-line ART in relation to anti-TB therapy

Clinical staging	Cd4 cell count (cells/mm3)	Timing of ART in relation to initiation of TB treatment	ART Recommendations
Start ART irrespective of any clinical stage	Cd4 count of any value	• Start ATT first • Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months)	Start ART Regimen TLE for patients not on ART. For patients already on 1st line ART, ZLN, shift to ZLE & continue ZLE even after ATT is stopped.
Rationale for ART recommendation during TB treatment: In the absence of ART, TB therapy alone does not significantly increase the CD4 cell count. Nor does it significantly decrease the HIV viral load. Thus, CD4 counts measured during active TB are likely to reflect the actual level of immune suppression The use of HAART in patients with TB can lead to a sustained reduction in the HIV viral load. It can also facilitate immunological reconstitution, and decrease AIDS-defining illness and mortality. This benefit is seen across different ranges of CD4 counts			

- The use of the standard 600mg/day dose of EFV is recommended for patients receiving EFV and Rifampicin.
- *In women of child-bearing age, the use of contraceptives should be ascertained because of drug reaction, as and when NNRTIs and Rifampicin are being used
- *Special Attention to be paid for monitoring hepatotoxicity

Rifabutin Drug Interactions

Rifabutin is an anti-mycobacterial agent similar to Rifampicin however Rifabutin has significantly less effect on drugs metabolised by cytochrome P 450 3a enzymes; this may reduce the magnitude of drug- drug interactions. Drugs that induce or inhibit CYP3A metabolizing enzymes can influence Rifabutin concentrations leading to the need for Rifabutin dose adjustment, which adds to the complexity of co-treatment. If a patient whose Rifabutin dose was decreased to avoid drug interactions related to co-treatment with antiretroviral therapy, subsequently stops taking the interacting antiretroviral drug (e.g., ritonavir), the resulting Rifabutin concentrations can become sub-therapeutic, putting the patient at risk of tuberculosis treatment failure or emergence of "Rifamycin" resistance.

Management of HIV –TB co-infection Specific Situations

SCENARIO	ACTION
TB treatment in PLHIV on Protease Inhibitor (PI) Based ART	• Rifampicin suppresses bioavailability of bosted Pis (Atazanavir/ ritonavir, Lopinavir/ritonavir, Darunavir/ritonavir). However, Rifabutin, an effective anti-TB derivative of Rifamycin group, does not inhibit effectiveness of these drugs • Rifabutin is not available in FDC and hence should be provided as a loose drug. Substitute Rifampicin with Rifabutin (150 mg daily) for the entire duration of Anti-TB treatment in such cases • Anti-TB treatment initiation should be done as soon as TB is diagnosed even in patients on PI based ART. If substitution of Rifampicin with Rifabutin can not be done immediately, then try to replace Rifampicin with Rifabutin later, whenever Rifabutin is available. If Rifampicin is continued for longer duration, thiswill make the boosted PI based regimen ineffective and will fasten the emergence of drug resistance mutants and eventral treatment failure for ART
TB treatment in children living with HIV (CLHIV) on Protease Inhibitor (PI) based ART	• Super boosting of Lopinavir (LPV) with Ritonavir is recommended in children in proportion of 1:1 • If super boosting of LPV is contraindicated, triple NRTI is to be considered as next choice • Higher dose of Nevirapine (NVP) is to be considered as the last choice
Pregnant women	• Streptomycin is ototoxice to the foetus and should not be used during pregnancy • Injection Streptomycin should not be used in pregnant women
Use of Integrase Inhibitor (Raltegravir)	Drug interaction between Rifampicin and Raltegravir-dosage of RAL–800 mg twice daily

Immune reconstitution inflammatory syndrome (IRIS) may occur in up to one-third of patients who have been diagnosed with TB and who have started ART. It typically presents within three months of the initiation of ART but can occur as early as five days. Patients with TB-associated IRIS most commonly present with fever and worsening of pre-existing lymphadenopathy or respiratory disease. The symptoms are similar to the paradoxical reactions seen in immuno-competent patients on ATT, but occur more frequently. Most cases resolve without any intervention and ART can be safely continued. Serious reactions, such as tracheal compression caused by massive adenopathy or respiratory difficulty, may occur. Therapy may require the use of corticosteroids.

First Line ART for HIV-TB

TENOFOVIR 300mg + LAMIVUDINE 300 mg + EFAVIRENZ 600 mg (FDC)		
Regimen	Tenofovir + Lamivudine + Efavirenz	All new co-infected patients should be initiated on FDC of TLE single pill based regimen irrespective of HB level/ CD4 count. Those patients who are already on ART on ZLN regimen at the time of TB diagnosis need to be changed to regimen ZL+E at the initiation of ATT due to interaction of ATT & NVP. Such patients will not be changed from EVF to NVP after ATT is completed and will continue on ZLE regimen. There is no change of regimen for patients who are already on ZLE at the time of TB diagnosis & treatment

Second Line ART for HIV-TB:

The following regimens are available under the National Programme currently for second line ART:

Tenofovir + Lamivudine + PI (Atazanavir/ritonavir or Lopinavir/Ritonavir)
Zidovudine + Lamivudine+ PI (Atazanavir/ritonavir or Lopinavir/Ritonavir)
Stavudine+ Lamivudine + PI (Atazanavir/ritonavir or Lopinavir/Ritonavir)
Abacavir+ Lamivudine+ PI (Atazanavir/ritonavir or Lopinavir/Ritonavir)

Rifampicin alters the metabolism of Protease Inhibitors, including Atazanavir and Ritonavir and reduces their effectiveness in standard doses

Provision of Co-trimoxazole Prophylaxis Therapy (CPT) to HIV-Infected TB patients:

- Co-trimoxazole is a fixed dose combination of sulfamethoxazole and trimethoprim; it is a broad spectrum antibiotic that targets a range of gram-positive and gram-negative organisms, fungi, and protozoa. Co-trimoxazole is given routinely for the prevention of opportunistic infections in HIV-infected persons; this strategy is called Cotrimoxazole prophylaxis therapy. CPT reduces morbidity and mortality of HIV-infected patients in general and HIV-infected TB patients in particular. Additional points to remember include:
- Dose for prophylaxis for adults (> 14 years old) and > 30 kg body weight): 960 mg (800 mg sulfamethoxazole + 160 mg trimethoprim) daily.
- For children and very low-weight adults (<30 kg), CPT for these patients is managed by ART centres as per separate protocol.
- CPT is provided to patients in monthly pouches.
- CPT is self-administered by the patient on a daily basis, and not under direct observation.
- CPT can be taken alongside anti-tuberculosis treatment (ATT) and ART. Many patients who are eligible for ART would also have CPT continued at ART center.
- Pregnant patients are also eligible, regardless of foetus gestational age.
- Patients should have no history of a serious drug allergy to sulpha drugs or glucose-6 phosphate dehydrogenase (G6PD) deficiency.

Isoniazid Preventive Therapy (IPT) For PLHIVs

IPT is one of the 3 I's globally recommended for prevention of incident TB among HIV infected individuals. Isoniazid is the most effective bactericidal, anti-TB drug available at currently. While it protects against progression of latent TB infection to active disease i.e. reactivation, it also prevents TB reinfection post the exposure to an open case of TB. In 2011 the World Health Organization (WHO) issued specific recommendations regarding the use of IPT in its guidelines on "Intensified TB case finding and isoniazid preventive therapy for people living with HIV in resource constrained settings". The key recommendations included the following:

a) Adults and adolescents living with HIV should be screened for TB with a clinical algorithm and those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT. The guideline group strongly recommend use of Isoniazid 300 mg once daily for 6 months, in adult and adolescents,

b) Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB

c) Children living with HIV who have any one of above symptoms may have TB and should be evaluated for TB and other conditions. If evaluation shows no TB, such children should be offered

IPT regardless of their age.

d) Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening, and have no contact with a TB case should receive six months of IPT (10 mg/kg/ day) as part of a comprehensive package of HIV prevention and care services

e) All children living with HIV who have successfully completed treatment for TB disease should receive INH for an additional six month

f) Although IPT is more effective among Tuberculin Skin Test positive individuals (TST), it is not a requirement for initiating IPT intervention among the PLHIV considering difficulty in logistics and administration of the TST

g) Providing IPT to people living with HIV does not increase risk of developing isoniazid (INH) resistant TB later. Therefore, concerns regarding development of INH resistance should not be a barrier to providing IPT

Steps in Provision of Isoniazid Preventive Therapy (IPT): The IPT provision involves following steps:

a) TB symptom screening at ART centre /Link ART-Plus and Link ART centres
b) Investigations for diagnosis of TB, if found symptomatic
c) If found Asymptomatic, assessment for the eligibility of Isoniazid Preventive therapy
d) If found eligible, initiation of IPT and Registration in IPT register maintained at the Nodal ART centre
e) Monthly collection of Isoniazid
f) Systematic recording and reporting e.g., Use of IPT Card
g) Continued TB symptom screening on each follow-up visits and reconsideration of IPT if symptoms develop

Monthly collection of Isoniazid: All eligible patients are to be initiated on IPT. The regimen prescribed are as below:

a) Adult and Adolescent: Isoniazid 300mg +Pyridoxine 50mg (Vitamin B6) per day for 6 months
b) Children above 12 months: Isoniazid 10mg/kg +Pyridoxine25 mg (Vitamin B6) per day for 6 months

The strategy for monthly collection of Isoniazid + Pyridoxine is as follows:

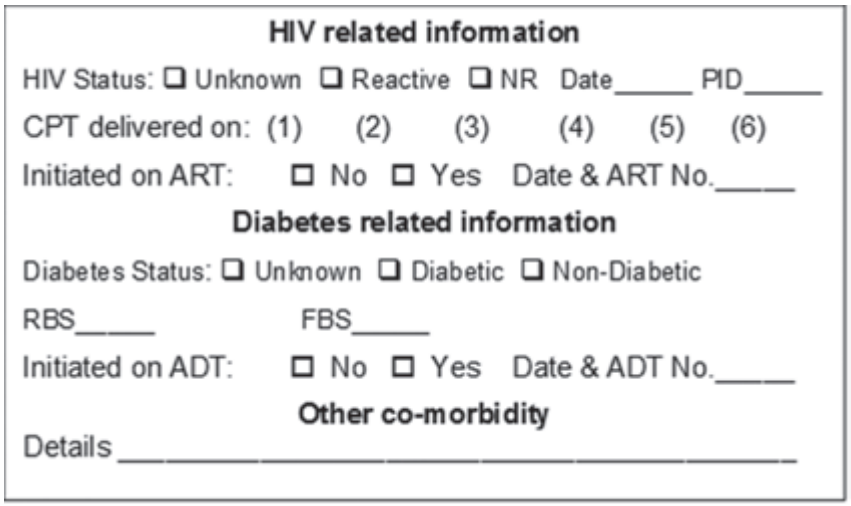
a) Patients on ART monthly collection from the ART centre, LAC-Plus or LAC along with monthly collection of the ART
b) Patients in pre-ART care visit the ART centre only once in six months. These patients may collect the monthly Isoniazid/Pyridoxine packet from the designated stand-alone ICTC.

Systematic recording and reporting:

All events in the cascade of IPT implementation including symptom screening at all contacts, IPT eligibility assessment, investigations, and the compliance with regimen are to be systematically recorded and reported.

Recording & reporting

1. Information on HIV status and treatment details are captured in treatment card and notification register



The following documents of NACP & NTEP are used for recording & reporting

- Line-List of Persons Referred from ICTC to NTEP
- ICTC TB-HIV monthly report
- HIV-TB Line List
- HIV/TB -Intensified TB Case Finding Report
- HIV TB Register

TB and Diabetes

As a consequence of urbanization as well as social and economic development, there has been a rapidly growing epidemic of Diabetes Mellitus (DM). India has second largest number of diabetic people in the world. As per recent estimates, there are around 66 million DM cases, with a further 77 million people having impaired glucose tolerance.

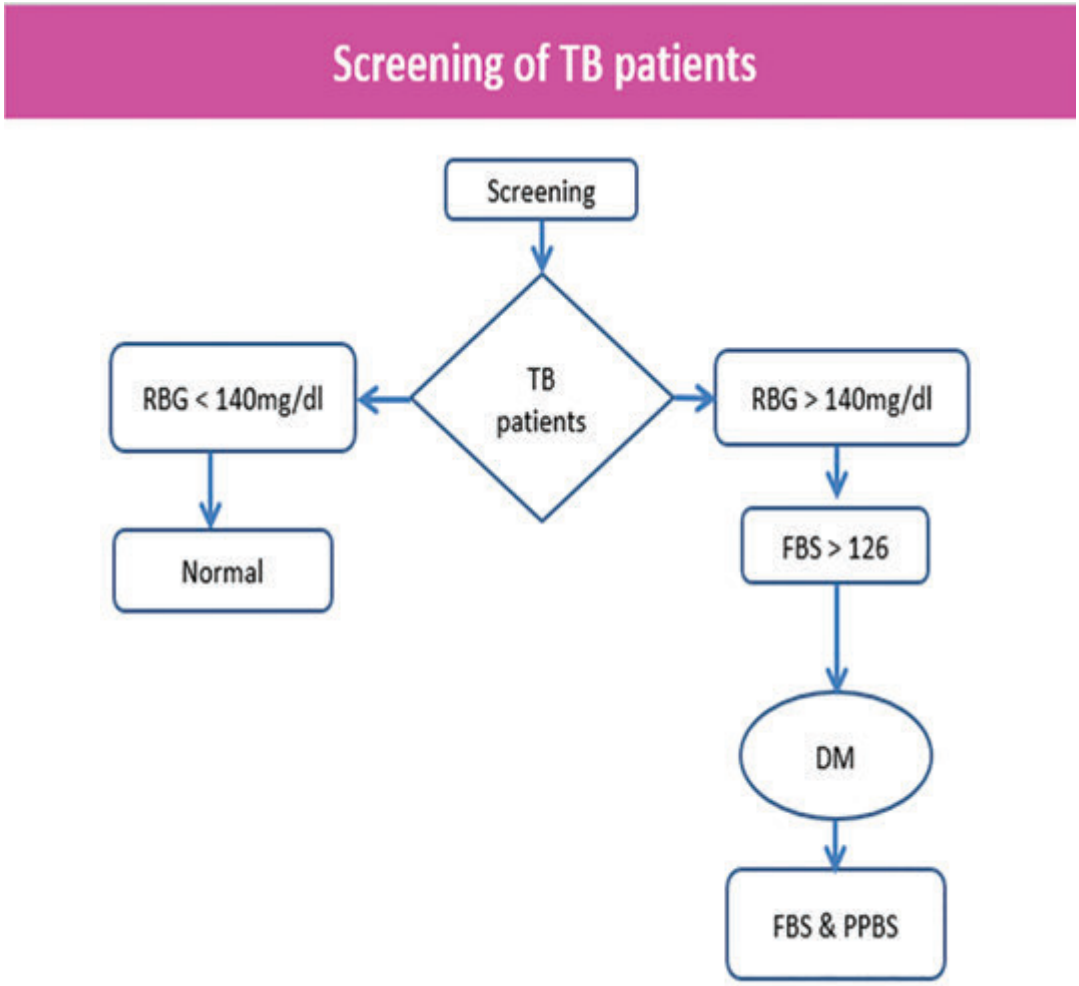
People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB. Hence, people with diabetes have a 2-3 times higher risk of TB compared to people without diabetes.

- About 10% of TB cases globally are associated with diabetes.
- A large proportion of people with diabetes as well as TB is not diagnosed, or is diagnosed too late. Early detection can help improve care and control of both diseases.
- DM can lengthen the time to sputum culture conversion and theoretically this could lead to the development of drug resistance if a 4-drug regimen in the intensive phase of therapy is changed after 2 months to a 2-drug regimen in the presence of culture-positive TB.
- People with diabetes who are diagnosed with TB have a higher risk of death during TB treatment and a higher risk of TB relapse after completing treatment.
- DM is complicated by the presence of infectious diseases, including TB.

- It has been argued that good glycaemic control in TB patients can improve treatment outcomes
- The precise biological mechanisms that result in this interaction between Diabetes and TB are still not clear. Epidemiological models have shown that DM accounts for 20% of smear-positive pulmonary TB and recent analyses have indicated that the increase in DM prevalence in India has been an important obstacle to reducing TB incidence in the country

Screening Intervention and Diagnosis of Diabetes among TB patients

- All TB patients who have been diagnosed and registered under NTEP will be referred for screening for Diabetes. Referral of TB patients for screening for DM and its recording & reporting is responsibility of the Peripheral Health Institutions (PHI) where TB treatment is initiated.
- The screening for DM will follow the guidelines stipulated by NPCDCS in India. Those guidelines stipulate that fasting blood glucose (FBG) be carried out using a finger prick and glucometer with cut-off thresholds in line with those recommended by the NPCDCS.



Screening TB patients for DM should be conducted as early as possible after diagnosis of TB; but can be done at any time during the course of TB treatment. Because of the difficulties in getting TB patients to first come to the clinic in a fasting state, TB patients will be initially screened with a random blood glucose (RBG) using a glucometer. If the RBG is less than 140 mg/dl, this is a normal result and no further tests need be carried out. If the RBG is at or greater than 140 mg/dl, this might indicate an abnormal glucose state and there is a possibility of DM. The patient will be asked to return in a fasting state, and a fasting blood glucose (FBG) will be carried out. FBG value at or greater than 126 mg/dl indicates DM.

WHO criteria for diagnosing Diabetes will be as follows.

Diagnosis	Fasting Glucose (mg/dl)	2-hour Post-Glucose Load (mg/dl)
Diabetes Mellitus	≥126	≥200
Impaired Glucose Tolerance	≥110 to <126	>140 to <200

- Criteria for suspected Diabetes case is reading of 140 mg/dl for Random Blood Glucose by glucostrip. The suspected case needs to undergo Fasting Blood Glucose test and Post Prandial tests to confirm diabetes
- The blood glucose testing will be done by a person designated and trained for the purpose at every peripheral health institution (PHI). Though, this would vary from site to site the following general principles would apply. Wherever, NPCDCS is being implemented, the ANM (Auxiliary Nurse Midwife) has been trained to use glucometer and screen people for DM. In case this mechanism is not available, the laboratory technician working in the PHI will be trained to do the test. If a PHI does not have a laboratory technician, then either the staff Nurse or any other staff designated by the MO-PHI will be trained to do the test.

Linkage of TB patients with DM for Diabetes care and management –

All Diabetic TB patients should be linked for diabetic care. In the districts where NPCDCS is being implemented, TB patients with DM or with a FBG at or higher than 126 mg/dl will be referred to diabetes care using a referral form for definite diagnosis and management. A referral and feedback mechanism will be developed to enable timely exchange of information. Good cooperation and collaboration will need to be developed between the two sets of staff working in the different service areas.

- At districts where NPCDCS is not implemented, TB patients should be referred to the nearest healthcare facility for further diagnosis and management of TB-DM comorbidity.
- TB patients diagnosed with Diabetes should receive the same duration of TB treatment with daily regimen as non- Diabetic TB patients.

Screening and referral of Diabetic patients for TB

- Four-symptom complex screening for active TB in Diabetes patients is to be done. Screening is expected to be carried out every time the patient visits the DM clinic. Patients will be asked whether they are on TB treatment, and if not, they would be screened for four-symptom complex, i.e. Cough of any duration, Fever, Weight loss, Night sweat.
- The Screening results for Diabetes are to be recorded in the patient NPCDCS register
- NCD clinic will implement basic infection measures as stipulated in NTEP guidelines

Linkage of Diabetic patients with TB for TB case management

On screening, patients with one or more symptoms will be referred to nearest diagnostic facility for diagnosis of TB. A referral and feedback mechanism will be developed to enable timely exchange of information. The patients diagnosed for TB would be initiated on TB treatment as per management guidelines stipulated in NTEP.

TB & NUTRITION

Undernutrition is considered as one of the risk factors in the development of TB, since undernutrition is known to adversely affect the immune system. Still, there remains a question as to whether malnutrition predisposes to tuberculosis, or whether it is a consequence of the disease. There is as yet little evidence showing that additional nutrition support improves TB-specific outcomes, but low body mass index as well as lack of adequate weight gain during TB treatment are associated with an increased risk of TB relapse and death.

The basic recommendations to address nutritional needs of TB patients are discussed below-

1. Conducting an initial nutrition assessment of TB patients with further monitoring;
2. Providing ongoing counselling for patients on their nutritional status; Diet for TB patients starting treatment should include: cereals (maize, rice, sorghum, millets, etc.); pulses (peas, beans, lentils, etc.); oil; sugar, salt; animal products (canned fish, beef and cheese, dried fish); and dried skimmed milk.
3. Management of severe acute malnutrition should be treated according to national guidelines and WHO recommendations;
4. Management of moderate under nutrition for TB patients who fail to regain normal Body Mass Index (BMI) after two months of TB treatment or appear to lose weight during TB treatment should be evaluated for a proper treatment adherence and other comorbidities. If indicated, these patients should be provided with locally available nutrient- rich or fortified supplementary foods. Special categories of TB patients such as
    - Children who are less than 5 years of age should be managed as any other children with moderate under nutrition.
    - Pregnant women with active TB, patients with MDR TB should be provided with locally available nutrient- rich or fortified supplementary foods.
5. Micronutrient supplementation for all pregnant women as well as lactating women with active TB. These women should be provided with iron and folic acid and other vitamin and minerals to complement their maternal micronutrient needs. In situations when calcium intake is low, calcium supplementation is recommended as part of antenatal care.

For this the guidelines for nutrition for the TB patients are available. A mobile application [N-TB] is available for decision making on nutritional support to TB patients.

Undernutrition and underlying food insecurity are among the most important determinants of TB. Improving nutritional status at population level is important for TB prevention. This should be part of broader actions on social determinants. All efforts should be made to link TB patients for the nutritional support. It can be through the existing public distribution system, local self-government or NGO or donor agencies or through corporate sector under Corporate Social Responsibility (CSR).

Management of severe acute malnutrition: Children below 5 years, School-age children and adolescents (5 to 19 years), and adults, including pregnant and lactating women, with active TB and severe acute malnutrition should be managed for severe acute malnutrition.

TB & Tobacco

India is the second largest consumer and the third largest producer of tobacco in the world (FAO, 2005). Nearly one million Indians die from tobacco use every year, which is much more than combined mortality resulting from HIV/AIDS, TB and Malaria. As per Global Adult Tobacco Survey, (GATS 2010, a household survey of persons 15 years of age and above) there are 275 million adult tobacco users in India. It is estimated that more than one- third (35%) of adults in India use tobacco in some form or the other. The prevalence of smokeless tobacco use (26%) is almost twice that of the prevalence of smoking tobacco (14%).

Tobacco smoke contains toxic chemicals which cause disturbances in the bronchial surface of the lung. It also weakens the immunity of the patient to fight with the TB bacteria.

The following evidence emerges from several studies conducted to look at the association of TB and tobacco in India:

- Almost 38% of TB deaths are associated with the use of tobacco.
- Prevalence of TB is 3 times as high among ever-smokers as compared to that of among never-smokers.
- Mortality from TB is 3 to 4 times as high among ever-smokers as compared to that among never-smokers.
- Smoking contributes to half the male deaths in 25-69 age groups from TB in India.

Exposure to tobacco smoke has also been found to affect TB in the following ways:

- Increase the risk of tuberculous infection and the risk of developing TB
- Affect clinical manifestations and increase risk of relapse among TB patients
- Affect microbiological conversion (sputum smear or culture) and outcome of treatment in TB patients
- Increase tuberculosis mortality and drug resistance to anti–tubercular drugs

Integrating Brief Advice for Tobacco Cessation

- When a patient gets registered as a tuberculosis case, the status of tobacco use is enquired.
- The information will be recorded in the TB treatment card in front portion using stamp
- If the TB patient is a smoker or tobacco user, he/she is offered 'Brief Advice' to quit tobacco used based on 5As and 5 Rs model
- The patient is assessed at every visit for follow up for TB and the status of tobacco use or quitting. At the end of treatment, his/her status of tobacco use is recorded in treatment card.
- If the patient has not quit tobacco use, he/she will be referred to the nearest Tobacco Cessation Clinic (TCC) or Quit line or m- cessation initiative.
- The information recorded in treatment card will be sent through the existing HMIS under NTEP

Brief advice for quitting tobacco use consists of 5 'A's

1. Ask the patient if he/she is a tobacco user, during the course of every visit.
2. Briefly Advise against continuing tobacco use and link the current condition/ailment to continued tobacco use, where possible. Eg, "Quitting smoking/tobacco use would improve your health and will aid in early recovery from illness."
3. Then Assess readiness to quit by asking the patient whether he or she is ready to quit tobacco use at this time. Eg, "How recently have you thought about quitting tobacco?" If the patient appears ready to change (quit), next steps are:

4. Assist the tobacco user in making a quit plan.
5. Arrange for follow-up by setting the next contact date.

If the tobacco user is not yet thinking about quitting tobacco use, the doctor/counsellor/ treatment supporter will promote greater awareness of the Relevance to the patient of the advice to quit, the Risks of tobacco use and the Rewards (benefits) of quitting. Many tobacco users are largely unaware of the potential harm that continued tobacco use can do to them. If the patient is not ready to quit, the doctor/ counsellor/treatment supporter must not push the patient. People usually need time to change the mindset. If the patient is at least thinking about quitting, the doctor/ counsellor/treatment supporter can find out the patients' Roadblocks to quitting and help the patient see ways to overcome these. This process will assist the patient to get ready for quitting the tobacco use, without being pushy.

The 5 R's are for non-willing tobacco users:

- Relevance of quitting
- Risks of continuing
- Rewards of quitting
- Roadblocks to quitting
- Repeat at each visit

Awareness and IEC

- All the DOTS centre /Clinics will be made tobacco free
- IEC material will be displayed at TUs, DMCs and Tobacco Cessation Clinics.
- DMCs and TUs will display IEC material about the hazards of tobacco use, along with the brief advice.
- Tobacco Cessation Clinics will display hygiene and TB awareness related materials.
- Awareness building efforts will be done at both units for patients and staff.
- Sensitisation of all stakeholders (partners, policy-makers and administrators) will be done on regularly basis.
- Every effort will be made by both the programme divisions to sensitise the community about the ill effects of TB and tobacco use

Recording & reporting- Information on tobacco usage and its status is captured in treatment card.

Addiction related information

Current Tobacco user ❑ Yes ❑ No
If yes, ❑ Smoking ❑ Smokeless Linked for cessation ❑ Yes ❑ No
If tobacco user, status of tobacco use at end of treatment ❑ Quit ❑ Not quit

H/o Alcohol intake❑ Yes ❑ No
If yes, linked for deaddiction ❑ Yes ❑ No

Involvement of NTCP in tuberculosis control

For enhancing active screening of TB patients through NTCP, the following process is indicated:

- Screening of four symptoms of active TB among tobacco users registered at the District TCC clinic and NCD Clinic at CHC- cough, fever, night sweat and weight loss
- Quit line established for tobacco cessation advice to conduct follow up of comorbid patients (TB patients with tobacco use) registered as TB cured, to identify TB relapse cases

- m-cessation initiatives to include TB-screening symptoms in cessation modules to identify active TB cases in people registered for tobacco cessation
- Ensure implementation of infection control guidelines in TCC Clinics
- Tobacco training modules prepared for teachers to include TB symptoms for increasing awareness among children and young adults

TB & SILICOSIS

Occupational high-risk group: Although reliable statistics are not available in India, it is known that thousands of workers and local residents are exposed to hazardous silica levels during stone crushing operations. Studies have shown increased morbidity and mortality rates among stone crushing mill workers from silicosis, lung cancer, and other lung diseases. Several other occupations also increase risk for tuberculosis including coal and other mining, tobacco (bidi rolling) and carpet weaving. Vulnerable and socially marginalised groups including tribal communities, children and migrant population are often used in these industries and do not have access to routine health services.

The NTEP is in process of engaging with the Ministry of Labour and Mining to identify high priority districts with stone crushing units / mining industry. The specific guidelines will be developed to support persons with an occupational risk for TB and provide access, diagnosis and treatment services from the programme.

Exercise 4

COMPLETION OF TUBERCULOSIS TREATMENT CARDS

Use a calendar for 2018-19 and exercise 3. Treatment begins in 2018. Neither diagnosis nor treatment (DOT) is initiated on Sundays. Use your own state, district and sub-district names on the Tuberculosis Treatment Card. Be sure to indicate outcome and date on back side of the Tuberculosis Treatment Card.

Remember that you must make up for missed doses. For this exercise, names and addresses of contact persons and treatment supporter are not given. In practice, the names and addresses of contact persons and treatment supporter must be filled up to aid in retrieving patients who have interrupted treatment. Use the NTEP request form for examination of biological specimens for TB that you completed in previous Exercise to record the results of investigations in front side of Tuberculosis Treatment Cards.

1. Arun Kumar (Patient A) is 24-year-old male, labourer from 7 Institutional slum Area, Lodhi Road, 110006, weighing 40 kg with pain in the chest and cough for two weeks. His sputum was sent for smear examination and was found to be positive for AFB. There was no history of ATT in the past. He was initiated on treatment on 10thSeptember 2018. He took all the doses of treatment regularly under direct observation. His follow-up sputum was done at end of IP and found to be negative. His end CP result was negative. What is the advice**?**

2. Pooja Gupta (Patient C) is 13-year-old female student from 1064, Paranthe Wali Gali, Chandni Chowk – 110008, weighing 36 kgs with non-tender swelling of the lymph nodes in the interior and posterior areas of the left side of the neck noticed for the last ten days. She was diagnosed as having TB by CBNAAT. She has never been treated for TB before. She was initiated on treatment on 13thSeptember 2018. She responded to treatment well. She had taken all doses of IP under direct observation except 10th and 11th dose which she had missed and continued the rest of treatment from 12th day. She had taken all doses of CP as prescribed.

3. Lakshmi Kumari (Patient D) is 46-year-old woman from 223 Gandhi Dham, Bapu Nagar - 110013 weighing 45 kg who has had cough for two months with fever, sweats at night, and occasional coughing up of blood. Her sputum examination was found to be positive. She was initiated on treatment on 13th September 2018. She took 20 doses under direct observation. After 20 doses she requested to continue her treatment at her place of residence near PHI 101. She was given 5 doses for unsupervised consumption during her transit. From 26th dose, she continued her treatment at PHI 101. Her End CP sputum follow up was found to be positive.

4. Narendra Kumar (Patient F) is 50-years known diabetic and alcoholic male from 223 Gandhi Dham, Bapu Nagar – 110013 weighing 40 kgs. He has had cough for a month. He gives no history of taking ATT in the past. His sputum was found to be positive and was diagnosed as Pulmonary TB. He was started on TB treatment on 10th September 2018. He took all the doses of IP regularly under direct observation. At the end of IP, his weight was 43 kg and smear was negative. In CP, he discontinued the treatment after taking 76th dose.

5. Girija Devi (Patient H) is 50-year old female from 225 Gandhi Dham, Bapu Nagar- 110013 weighing 45 kgs. She has cough for a month. When asked about previous history of taking TB treatment, she remembers receiving multiple tablets taken for a few months once which made her urine turn orange. She recalls that these medicines helped her feel much better. Her CBNAAT was now done and found to be M. TB positive and Rifampicin sensitive. She is a known HIV positive. Patient on ART and CPT. She was initiated on TB treatment at ART centre on 10thSeptember 2018. Her sputum was found to be positive at the end of IP. What next is expected of you for her further management? She was started on CP and completed treatment.

6. Kailash Nath (Patient J) is 35-year-old, from 2586 Gali No. 3, Gobind Puri, Near Gurudwara 110036, weighing 60 kg. He is coughing and spitting blood. When asked, he reports that he has been coughing for several years. He has not taken any treatment before. His sputum examination was found to be positive. He has two children aged 5 and 8 years at home who are asymptomatic. He was initiated on treatment on 11th September 2018. He experienced vomiting after 10th dose due to which drugs were withheld for one week and reintroduced afterwards. The rest of the doses were under direct supervision and end of IP and end CP sputum was negative.

Drug-Resistant TB

The management of DR-TB is very complex, and hence preventing it's development by the effective implementation of the DOTS strategy under NTEP is crucial. Selection of appropriate treatment regimen for patients by medical officer, after eliciting history of previous treatment, is very important. The diagnosed patients should be explained why it is essential to reveal previous TB treatment and to take drugs under direct observation. Similarly, treatment supporter should be educated and convinced about the importance of Directly Observed Treatment (DOT). DOTS has been documented to not only prevent the emergence of drug resistant TB, but also to decrease its prevalence in the community.

Prevention of spread of DR-TB infection:

While prevention of development of drug resistance is of paramount importance for ending TB, early detection and immediate enrolment as well as completion of an effective treatment regimen are keys to interrupt on-going transmission, to prevent death and reduce chances of sequelae post-treatment.

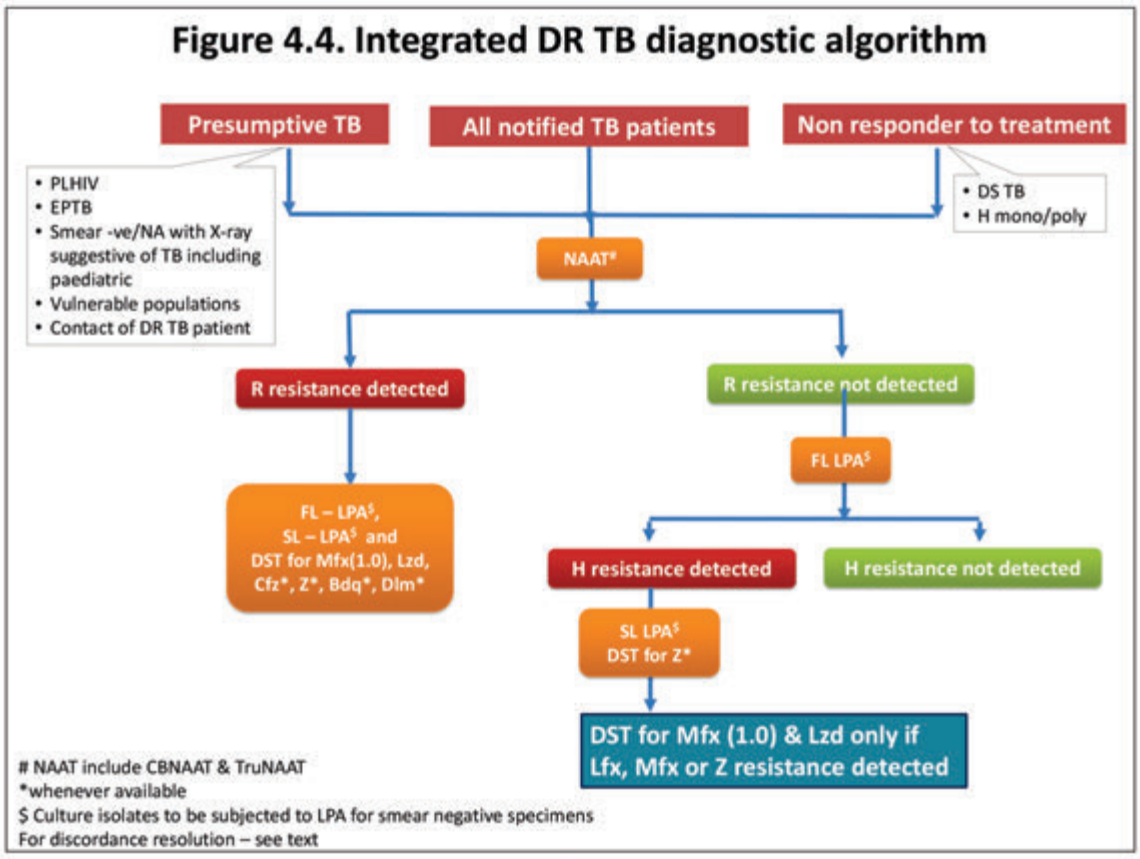
Besides, counselling patient and family members on infection control measures like cough etiquette and sputum disposal is important to cut the chain of transmission in community. Screening of contacts for early detection of DR-TB cases is also needed.

Integrated drug-resistant TB algorithm

The integrated DR TB algorithm clearly indicates the management strategies to be followed right from the day the result of NAAT test is available. The programme must strive to offer DST to all notified TB patients at diagnosis of TB or a maximum within 15 days of first line treatment initiation. The algorithm further offers FL LPA for the patients found R resistance not detected on NAAT. The states must ensure availability of LPA lab capacity in consultation with central TB division, for both SL and FL LPA as per the estimated requirement including patient notified from the private sector. Within the first 2 months, patients would receive the LC DST results, reach their final classification and treated with the appropriate regimen.

- any other reason as per treating physician's advice.

Integrated DR TB Diagnostic Algorithm



The left path of the algorithm starts with persons presumed to have TB. From this group those belonging to the PLHIV, EP group or with a smear negative chest X-ray suggestive of TB (including children), vulnerable group as defined by TOG – 2016 and contact of DR TB patient will be offered NAAT test. By virtue of using NAAT as the TB diagnostic test, the R status is also available simultaneously along with TB detection.

The middle and right path begins with offer of NAAT to all notified TB patients &non respondent at different time place. Based on the result obtained on the NAAT, the patient would be classified

as R resistant detected (RR TB) or R resistance not detected to guide decision of the appropriate treatment. As soon as the NAAT results are available, the reports must be immediately updated in Nikshay by the NAAT lab and communicated to the concerned district, DDR TBC, DTO, MO PHI and the patient.

For patients with NAAT result as M.tb detected (irrespective of R status), the second specimen will be reflexly transported in cool chain from the NAAT lab to the C-DST lab. In rare circumstances when the second specimen is used at NAAT lab itself to repeat the test, a fresh specimen is to be collected from the patient and transported in cool chain to the concerned C-DST lab.

However, this may not be always possible for EP specimen. Reconfirmation of RR among the new TB patients will be carried out at C-DST lab by FL LPA with the second specimen sent from NAAT site.

Management of DR-TB

Guidelines for Programmatic Management of Drug resistant TB was released under NTEP in the year 2019. This document gives detailed guidelines about structures of DR-TB centres, integrated diagnostic algorithm for DR-TB and treatment regimen for various types of DR-TB patients. In this section of the module, only brief overview of pre-treatment evaluation and treatment regimens are discussed. For detailed guidelines on DR-TB management, PMDT 2019 document may be referred to.

DR-TB management has to be preferably undertaken only at district DR-TB or
nodal DR-TB centres where expertise and facilities are available for pre- treatment evaluation, initiation and monitoring of treatment are available.

Pre-treatment evaluation for DR TB patients

Pretreatment evaluation for any TB patient including DR TB patients should include, a thorough clinical evaluation by a physician including

- history and physical examination,
- height/weight,
- random blood sugar (RBS),
- urine pregnancy test (in women of reproductive age group),
- chest X-ray and
- HIV testing

No additional investigations are required for H mono/poly DR TB patients unless clinically indicated.

In majority of DR TB patients, pretreatment evaluation can be done on an outpatient basis. The DTO can arrange pretreatment evaluation at N/DDR TBC or at sub-district level health facility, wherever possible. The patient should be fast-tracked for pretreatment evaluation and for infection control purposes and a separate space for specimen and blood collection should be identified.

Patients will be referred to the N/DDR TBC with pretreatment evaluation results for initiation of treatment. The physician may decide for admission to N/DDR TBC for initiation of treatment or get it done on an outpatient basis. A specialist consultation along with reports of pre-treatment evaluation tests can be arranged, if required. Since the drugs used for the treatment of DR TB have significant adverse effects, a pretreatment evaluation is essential to identify patients at increased risk of developing such adverse effects. In addition to the above pre-treatment evaluation, the evaluation of MDR/RR TB patients will also include:

Complete Blood Count (Hb, TLC, DLC, Platelet count) 2. B. Urea & S. Creatinine 3. Audiometry 4. Liver Function Tests 5. Thyroid Stimulating Hormone levels to assess the thyroid function (TSH levels alone are usually sufficient to assess the thyroid function of the patient) 6. Urine examination – Routine and Microscopic 7. Psychiatric evaluation if required 8. Serum electrolytes (Na, K, Mg, Ca) only for new drugs 9. S. protein (Albumin, Globulin and total proteins) (only if on Dlm) 10. ECG (if on Mfx, Bdq, Cfz or Dlm) 11. urine pregnancy test (in women of reproductive age group) 12. Ophthalmologist opinion – rule out chorioretinitis/uveitis (only if on Linezolid) 13. Surgical evaluation if required Each of the DR TBCs (N/DDR TBC) must ensure that capacity to carry out pre-treatment investigations and consultancy services of various specialists are available, either in-house supported under institutional/state government mechanism or through outsourced mechanisms including tie up under Free Diagnostic Initiative. Tie up with private facility under Partnership Guidelines should be undertaken for investigations that are not available.

The concerned DR TBC committee provides counselling, initiates activities related to active drug safety monitoring (aDSM) like, assessing the baseline history of known adverse/serious adverse events (AE/SAE), biochemical investigations, ECG, Audiometry etc., and initiates the patient on an appropriate treatment regimen. Care must be taken to correct any electrolyte imbalance before treatment initiation.

DRTB patients can be initiated on an appropriate standard treatment regimen at N/DDR TBC. If required, the DDR TBC may refer the patients to NDR TBC for management of patients with additional drug resistance, drug intolerance, contraindication, failing regimen, return after treatment interruption of >1 month, emergence of exclusion criteria for standard regimen, for expert opinion, management of any complications warranting regimen change.

Active drug safety management and monitoring (aDSM) treatment initiation form needs to be completed and uploaded on Nikshay for all DR TB patients at the time of initiation of each new episode of treatment.

Providing health education/ counselling to patient and family members

Providing counselling and health education to the DRTB patient and family members about the disease, the mechanism of transmission and necessity of taking regular and adequate treatment, is of utmost importance. Health education and counselling is provided to all patients and family members at different levels of health care, from the periphery to the DDR TBC facility. It is started at the initial point of contact and continued during all visits by the patient to a health facility. Confidentiality and informed decision-making process according to sound ethics standards is paramount when performing education and counselling to patients and their family members.

N/DDR TBC counsellors to provide counselling for all DR TB patients on the following:

- nature and duration of treatment;
- possible change in the regimen based on the additional investigations carried out;
- importance of adherence to treatment and need for complete and regular treatment;
- possible side effects of drugs;
- mechanism of transmission;
- Cough etiquette; and
- consequences of irregular treatment or premature cessation of treatment.

It is advisable to involve close family members during the counselling, since family support is an essential component in the management. Patients should be advised to report any side effects immediately. Female patients should receive special counselling on family planning. The treatment must be presented as an option and include information on any uncertainty about the adverse effects of drugs as detailed in the patient treatment booklet.

The counsellors would be trained exclusively with a counsellors training module on an e-learning platform by NTEP. This covers the various approaches, steps involved in counselling, tools, activities to be undertaken as well as the records and reports to be maintained by the counsellors. A counselling register must be maintained for all patients for recording information about patients' situation and counselling services provided from the time of diagnosis till post-treatment follow-up period.

Pretreatment counselling must serve as an informed decision-making process that enables patients to make a duly informed decision regarding the use of all anti-TB drugs including newer drugs like Bdq/Dlm. No separate written consent is needed for any treatment regimen under the programme.

Classes of anti -TB drugs recommended for treatment of DR TB patients (WHO)

The anti-TB drugs recommended for treatment of MDR/RR TB patients are grouped based on efficacy, experience of use and drug class and aligned with revised classification as per WHO consolidated guidelines for treatment of drug resistant TB (2019). WHO guideline development group assessed the individual contribution to patient outcomes of drugs used in longer MDR TB regimens using primarily the estimates of effect from the 2018 individual patient data – meta analysis (IPD-MA) and Trial 213 (Delamanid) and summarized of evidence for each drug as well as the evidence-to-decision framework. Following a thorough assessment of the relative benefits and harms, recommendations were made for each drug and they were classified into three groups. The same is explained in the table below.

Grouping of anti-TB drugs for longer MDR regimen (Table XXX)

GROUPS & STEPS	DRUG	
Group A	Levofloxacin OR Moxifloxacin Bedaquiline Linezolid	Lfx Mfx Bdq Lzd
Group B	Clofazimine Cycloserine OR Terizidone	Cfz Cs Trd
Group C	Ethambutol Delamanid Pyrazinamide Imipenem-cilastatin OR Meropenem	E Dlm Z Ipm-Cln Mpm
	Amikacin (OR Streptomycin) Ethionamide OR Prothionamide p-aminosalicylic acid	Am (S) Eto Pto PAS

Other drugs that are not included in Groups A–C are:

- Kanamycin and Capreomycin, which were associated with poorer outcomes when used and are therefore no longer recommended for use in MDR TB regimens;
- Gatifloxacin and high-dose Isoniazid were used in very few patients and thioacetazone was not used at all. Quality-assured preparations of Gatifloxacin are not currently available following its withdrawal from the market due to concerns about dysglycaemias. Thioacetazone is unlikely to have a role in contemporary longer regimens and is not currently available in a quality-assured formulation.
- Clavulanic acid should be included in MDR/RR TB regimens only as a companion agent to the carbapenems (Imp-Cln and Mpm). When used in this way, it should be given with every dose of carbapenem and should not be counted as an additional effective TB agent.

The risk–benefit considerations for the use of Bdq in patients aged 6–17 years and Dlm in patients aged 3-5 years are similar to those considered for adults. On the basis of findings in adults and on the pharmacological and safety data reviewed, extrapolations on efficacy and safety should be restricted to children aged 3–5 years but not to children younger than 3 years.

The prioritized order of the drugs in the groups has been derived from the evidences on efficacy (Table - 2) and safety of the second line anti-TB drugs (Table - 3).

Relative risk for (i) treatment failure or relapse and (ii) death (versus treatment success), 2018 IPD-MA for longer MDR TB regimens and delamanid Trial213 (intent-to-treat population) Table-2:

	Medicine	Treatment failure or relapse versus treatment success		Death versus treatment success	
		Number treated	Adjusted odds ratio (95% confidence limits)	Number treated	Adjusted odds ratio (95% confidence limits)
A	Levofloxacin *OR* moxifloxacin	3 143	0.3 (0.1–0.5)	3 551	0.2 (0.1–0.3)
	Bedaquiline	1 391	0.3 (0.2–0.4)	1 480	0.2 (0.2–0.3)
	Linezolid	1 216	0.3 (0.2–0.5)	1 286	0.3 (0.2–0.3)
B	Clofazimine	991	0.3 (0.2–0.5)	1 096	0.4 (0.3–0.6)
	Cycloserine *OR* terizidone	5 483	0.6 (0.4–0.9)	6 160	0.6 (0.5–0.8)
C	Ethambutol	1 163	0.4 (0.1–1.0)	1 245	0.5 (0.1–1.7)
	Delamanid	289	1.1 (0.4–2.8)*	290	1.2 (0.5–3.0)*
	Pyrazinamide	1 248	2.7 (0.7–10.9)	1 272	1.2 (0.1–15.7)
	Imipenem–cilastatin *OR* meropenem	206	0.4 (0.2–0.7)	204	0.2 (0.1–0.5)
	Amikacin	635	0.3 (0.1–0.8)	727	0.7 (0.4–1.2)
	Streptomycin	226	0.5 (0.1–2.1)	238	0.1 (0.0–0.4)
	Ethionamide *OR* prothionamide	2 582	1.6 (0.5–5.5)	2 750	2.0 (0.8–5.3)
	p-aminosalicylic acid	1 564	3.1 (1.1–8.9)	1 609	1.0 (0.6–1.6)
Other medicines	Kanamycin	2 946	1.9 (1.0–3.4)	3 269	1.1 (0.5–2.1)
	Capreomycin	777	2.0 (1.1–3.5)	826	1.4 (0.7–2.8)
	Amoxicillin–clavulanic acid	492	1.7 (1.0–3.0)	534	2.2 (1.3–3.6)

Note: * The values are the unadjusted risk ratios as defined by the study investigators of Trial 213 by month 24.

Table -3: Serious adverse events (SAEs) in patients on longer MDR TB regimens*

Medicine	Absolute risk of SAE	
	Median (%)	95% credible interval
Bedaquiline	2.4	[0.7, 7.6]
Moxifloxacin	2.9	[1.4, 5.6]
Amoxicillin–clavulanic acid	3.0	[1.5, 5.8]
Clofazimine	3.6	[1.3, 8.6]
Ethambutol	4.0	[2.4, 6.8]
Levofloxacin	4.1	[1.9, 8.8]
Streptomycin	4.5	[2.3, 8.8]
Cycloserine/terizidone	7.8	[5.8, 10.9]
Capreomycin	8.4	[5.7, 12.2]
Pyrazinamide	8.8	[5.6, 13.2]
Ethionamide/prothionamide	9.5	[6.5, 14.5]
Amikacin	10.3	[6.6, 17.0]
Kanamycin	10.8	[7.2, 16.1]
p-aminosalicylic acid	14.3	[10.1, 20.7]
Thioacetazone	14.6	[4.9, 37.6]
Linezolid	17.2	[10.1, 27.0]

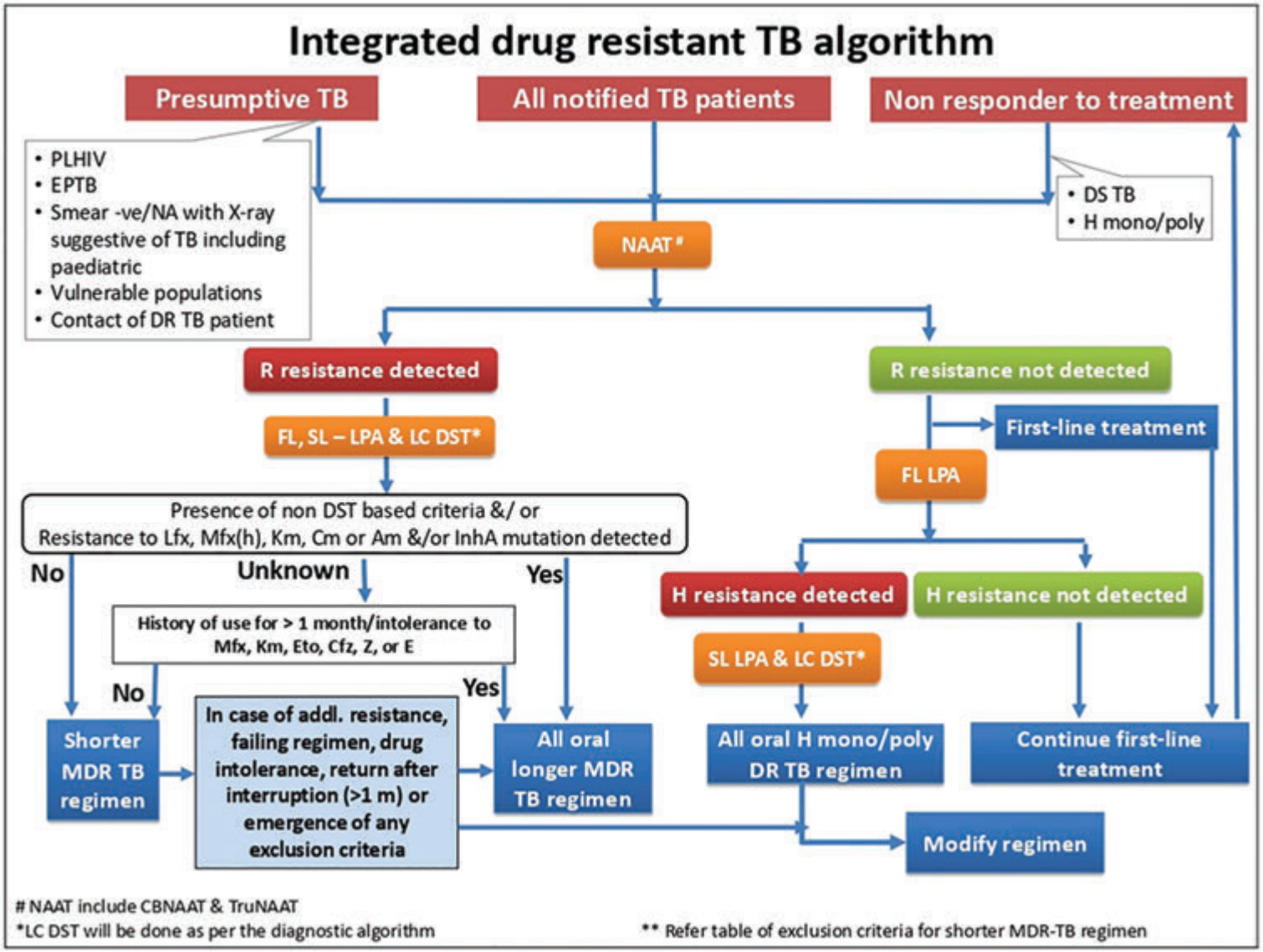
* From an "arm-based network" meta-analysis of a patient subset from the 2016 IPD for which AEs resulting in permanent discontinuation of a TB medicine (27 studies) or classified as Grade 3–5 (3 studies) were reported. There were insufficient records on delamanid, imipenem–cilastatin and meropenem to estimate risks. Agents that are not in Groups A, B or C are italicized.

Newer anti-TB drugs

After almost five decades of discovery of Rifampicin, the two new drugs named Bedaquiline and Delamanid with anti-TB effect were approved for treatment of multidrug resistant TB by The Central Drugs Standard Control Organization (CDSCO).

Bedaquiline is a new class of drug, diarylquinoline that specifically targets mycobacterial ATP synthase, an enzyme essential for the supply of energy to Mycobacterium TB. Strong bactericidal and sterilizing activities against M.tb have been shown in pre-clinical, laboratory and animal experiments. The drug has a high volume of distribution, with extensive tissue distribution, highly bound to plasma proteins and is hepatically metabolized. The drug has an extended half-life, which means that it is still present in the plasma up to 5.5 months post stopping BDQ. The dosing schedule has been established after extensive pharmacokinetic/ pharmacodynamic (PK/PD) studies in animals and humans and hence need to be administered as per the manufacturer's advice. BDQ has shown significant benefits in improving the time to culture conversion in MDR TB patients. Bedaquiline is now well incorporated within the programme as a part of standard all oral longer regimen for eligible patients.

Delamanid is the first approved drug in the class of nitro-dihydro-imidazo-oxazoles for the treatment of MDR TB. It is bactericidal drug with 36 hrs of Half-life and act with two different mechanism of action. It blocks the synthesis of mycolic acids (i.e., stopping the bacteria from creating building blocks important for their cell walls) as well as poison the bacilli with nitric oxide, which the drugs release when metabolized.


Integrated drug resistant TB algorithm
Presumptive TB
All notified TB patients
Non responder to treatment
• PLHIV
• EPTB
• Smear -ve/NA with X-ray suggestive of TB including paediatric
• Vulnerable populations
• Contact of DR TB patient
• DS TB
• H mono/poly
NAAT #
R resistance detected
R resistance not detected
FL, SL – LPA & LC DST*
First-line treatment
FL LPA
Presence of non DST based criteria &/ or
Resistance to Lfx, Mfx(h), Km, Cm or Am &/or InhA mutation detected
No
Unknown
Yes
H resistance detected
H resistance not detected
History of use for > 1 month/intolerance to Mfx, Km, Eto, Cfz, Z, or E
SL LPA & LC DST*
No
Yes
Shorter MDR TB regimen
In case of addl. resistance, failing regimen, drug intolerance, return after interruption (>1 m) or emergence of any exclusion criteria
All oral longer MDR TB regimen
All oral H mono/poly DR TB regimen
Continue first-line treatment
Modify regimen
NAAT include CBNAAT & TruNAAT
*LC DST will be done as per the diagnostic algorithm
** Refer table of exclusion criteria for shorter MDR-TB regimen

As per the algorithm, the patients with R resistance not detected TB will be initiated on first line treatment regimen while awaiting the results of FL LPA and continued on first line treatment if H resistance is not detected. These patients will be monitored closely and in patients with signs of non-response to treatment during follow up, another NAAT test will be offered. All follow up positive, failures and clinical non-responders of DS-TB treatment are also eligible for NAAT irrespective of NAAT being offered at the initiation of DS TB treatment.

If H is found to resistant, the patient will be initiated on all oral H mono-poly DR TB regimen at the PHI level while awaiting the results of SL LPA and the regimen would be appropriately modified at the N/DDR TBC if Lfx/Mfx(h) resistance is detected on SL LPA. The patients with RR TB will be considered for shorter MDR TB regimen at N/DDR TBC after ruling out the exclusion criteria for shorter MDR TB regimen. Decision to start shorter MDR TB regimen will be based on non-DST and DST based exclusion criteria mentioned in the table below. The patients excluded from shorter MDR TB regimen would be initiated on all oral longer MDR TB regimen at N/DDR TBC. In case of additional resistance on LC DST, the all oral longer MDR TB regimen would be appropriately modified.

Criteria for patients to receive standard DR TB regimen

Standard DR TB regimen	Inclusion criteria	Exclusion criteria
All oral H mono/poly regimen	Isoniazid-resistant TB with confirmed result for Rifampicin-resistance not detected (RS)	No specific criteria except drug interaction/intolerability with any other drug used concomitantly
Shorter MDR TB regimen	Patient with Rifampicin-resistant pulmonary or extra pulmonary TB	**Non-DST based criteria:** • Pregnancy • Any extrapulmonary disease in PLHIV • Disseminated, meningeal or central nervous system TB • Intolerance to any drug in the shorter MDR TB regimen or risk of toxicity from a drug in the shorter regimen (e.g. drug–drug interactions) • If result for DST (FQ, SLI, Inh A mutation, Cfz* & Z*) is not available, history of use for > 1 month to Mfx(h), Km, Eto or Cfz **DST based criteria:** • If DST/DRT result for FQ or SLI is resistant or • presence of InhA mutation (for Eto) or • Resistance to Z (whenever available)
All oral longer regimen for MDR/ RR TB (with or without additional resistance)	Patients in whom shorter MDR TB regimen cannot be considered due to any reason	None

In presence of any non-DST based exclusion criteria for shorter MDR TB regimen like pregnancy, any extrapulmonary disease in PLHIV and disseminated, meningeal or central nervous system TB, the patient will be initiated on all oral longer MDR TB regimen. If SL LPA result or DST for Lfx, Mfx, Km, Am, Cm is not available at the time of treatment initiation, the patient will be initiated on shorter MDR TB regimen only if there is no history of use of any drug like Mfx, Km, Eto, Cfz, Z, or E for > 1 monthor intolerance to any drugs in the shorter MDR TB regimen. Rest of the patients will be initiated on the all oral longer MDR TB regimen.

In case of additional resistance, failing regimen, drug intolerance, return after interruption (>1m) or emergence of any exclusion criteria, the patients already on any MDR/RR TB regimen would be switched to all oral longer MDR TB regimen at the N/DDR TBC and evaluated further for presence of additional resistance. MDR/RR Patient with additional resistance to any second line drugs would also be considered for all oral longer regimen with modification in standard regimen as described later in this chapter.

Inclusion criteria for newer drugs (Bdq/Dlm)

- Patient aged > 6 years having MDR/RR TB. (Bdq/Dlm can be provided to the patient ≥ 18 yrs, for children & adolescents between 6 to 17 years, Dlm can be provided. Use of Bdq for 6 to 17 yrs and Dlm for 3 to 6 yrs may be considered only after approval of DCGI.
- non-pregnant females or females not on hormonal birth control methods are eligible. They should be willing to continue practicing birth control methods throughout the treatment period or have been post-menopausal for past 2 years; and
- patients with controlled stable arrhythmia can be considered after obtaining cardiac consultation.

Exclusion criteria for newer drugs (Bdq/Dlm)

- Pregnancy & lactating mother
- currently having uncontrolled cardiac arrhythmia that requires medication;
- having any of the following QTcF interval (Annexure 8) characteristics at screening:
- QTcF ≥ 500 at baseline & normal electrolytes, ECG to be repeated after 6 hours and If both ECGs show QTcF>500 then the patient should not be challenged with cardiotoxic drugs.
- history of additional risk factors for Torsade de Pointes, e.g. heart failure, hypokalaemia, family history of long QT syndrome;

If results of the serum chemistry panel, haematology or urinalysis are outside the normal reference range (including above listed parametres), the patient may still be considered if the physician judges that the abnormalities or deviations from normal to be not clinically significant or to be appropriate and reasonable. Hypokalaemia, hypomagnesaemia and hypocalcaemia should be corrected prior to a patient receiving any QTc prolonging drugs.

Caution must be exercised that Bdq/Dlm is not added to a failing regimen in any MDR RR TB patient already on DR TB treatment.

Caution to be exercised in choosing other group A and B drugs:

- Lzd may cause anaemia, thrombocytopenia, peripheral neuritis and optic neuritis. Adequate precaution may be taken accordingly.
- Cs should be used carefully in pre-existing seizure disorders not adequately control with medication. Neurologist consultation should be taken prior to initiation of Cs in such

patients, also psychiatrist opinion should be taken in severe depression as Cs can cause depression and suicidal tendency.

- Cfz causes dark brown discoloration of the skin. Accordingly, the patient should be counselled prior to initiation of treatment with Cfz

Regimen for DR TB treatment

Principles of designing a WHO recommended all oral longer MDR TB regimen

In MDR/RR TB patients on longer regimens, all three Group A agents (Lfx/Mfx, Bdq&Lzd) and one Group B agent (Cfz&Cs) should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of the treatment after Bdq is stopped. If only one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it.

As the likelihood of stopping Lzd due to toxicity is greater, the all oral longer MDR TB regimen for India would include the fifth drug Cs upfront to prevent the need for replacing Lzd, if dropped.

Under NTEP, the following are the standard DR TB regimens:

1. All oral H mono/poly DR TB regimen
2. Shorter MDR TB regimen
3. All oral longer MDR TB regimen

Standard regimen for initiating treatment of MDR/RR TB or H mono-poly DR TB

Regimen class	Intensive phase	Continuation phase
H mono/poly DR TB (R resistance not detected and H resistance)		
All oral H mono-poly DR TB regimen@	(6) Lfx R E Z	
MDR / RR TB		
Shorter MDR TB regimen@	(4-6) Mfx^{h} Km/Am* EtoCfz Z H^{h} E	(5) Mfx^{h}Cfz Z E
All oral longer MDR TB regimen@	(18-20) Bdq(6) LfxLzd#Cfz Cs	

*If the intensive phase is prolonged, the injectable agent is only given three times a week in the extended intensive phase.
Reduce Lzd to 300 mg/day after 6 to 8 months.
@ Pyridoxin to be given to all DR TB patients as per weight band.

- All oral H mono/poly DR TB regimen is of 6 months with no separate IP/CP.
- Shorter MDR TB regimen is of 9-11 months with 4-6 months of IP containing injectables and 5 months of CP.
  - If the IP is prolonged, the injectable is only given three times a week in the extended intensive phase.
- All oral longer MDR TB regimen is of 18-20 months with no separate IP/CP.
- Newer drugs like Bdq and Dlm would be given for 6 months duration while the dose of Lzd will be tapered to 300 mg after the initial 6-8 months of treatment.
  - This regimen will also be used for treatment of XDR TB patients with 20 months duration.

Treatment initiation

At Peripheral Health Institutions:

If LPA reveals H mono-poly DR TB, the patient will be initiated on the all oral H mono/poly regimen even at the PHI level. In case of any additional resistance, the patient may be sent to the N/DDR TB Center for modification in the regimen.

At N/DDR TB Centres

If the DRTs reveal MDR/RR TB, the patient must be counselled by the PHI staff to visit the N/DDR TBC with a family member for management without further delay. The first-line treatment will be stopped and the appropriate standard DR TB regimen (shorter or longer) will be initiated at the N/DDR TBC.

In patients put on shorter MDR TB regimen, if any exclusion criteria like detection of additional resistance, intolerability of shorter MDR TB regimen emerges, the patient is counselled by the PHI staff and referred to the N/DDR TBC immediately. The pretreatment evaluations and baseline a DSM assessment done at the N/DDR TBC would be considered valid, only if additional resistance is reported on the basis of direct SL LPA. However, the pretreatment evaluation would be need not to be repeated within one month, unless clinically indicated the additional resistance is reported on the basis of LC-DST, the standard shorter MDR TB regimen shall be stopped and the N/DDR TBC committee would consider initiating all oral longer MDR TB regimen with or without modifications as appropriate. As the patient would still be in early IP, the patient would be re-classified and re-registered for a new episode of treatment and updated on Nikshay on the same ID. For monitoring the treatment outcome, the patient would be accounted for the most recent episode of treatment. However, patients who need regimen change in CP will be declared with outcome as "Treatment failed" and re-registered for the next episode of an appropriate treatment.

The N/DDR TBC Committee can decide on a case-to-case basis, the need for admission of DR TB patients for initiation of treatment. The patient is initiated on standard regimen (shorter or longer) at N/DDR TBC on indoor or outpatient basis.

All oral longer MDR TB regimen can be initiated on outpatient basis if the patient is satisfying all following risk assessment criteria:

- QTcF< 450 ms in males and <470 ms in females at baseline.
- Normal serum K, Mg, Ca at baseline.
- No history of structural cardiac abnormalities (LVH or RVH secondary to hypertension can also cause ECG changes, however mere presence of LVH need not be an exclusion criteria) or ECG abnormalities.

Patients with QTcF between >450 to 500 ms in male and > 470 to 500 ms in female upto 500ms require daily monitoring of ECG for 3 days along with evaluation and correction of any electrolyte abnormalities. A cardiologist opinion may need to be taken.

The first dose is given under supervision at the treatment initiating facility for ambulatory patients. In patients who are admitted, the duration of indoor management would be decided by N/DDR TBC committee as clinically indicated. On discharge, the patient will be provided with a maximum seven days of drug supply for the transit.

Once initiated on treatment, MO-PHI to identify and prepare the treatment supporter and provide drugs and records to the treatment supporter DTO to coordinate for advance information to concerned PHI. The results of FL/SL LPA are expected to be available within a week of specimen submission. The results of LC DST are expected to be available after 6-8 weeks of specimen submission. Based on results, if no additional resistance is detected, the patient will be continued on the same regimen. The nodal officer of the N/DDR TB center must make all efforts to get the reports of SL LPA and SL LC DST from the C-DST lab at the earliest.

Patients need to be offered counselling with details of the nature and duration of treatment including information on the second line drugs; need for regular treatment; possible side-effects of these drugs; other drugs to be avoided and the consequences of irregular treatment or premature termination of treatment. Female patients will receive special counselling on family planning. Whenever standardized, WHO endorsed DST methods for Z, Cfz, Bdq, Dlm etc., are available and included as programme policy, patients found to be resistant to any of the above drugs would be managed with the all oral longer regimen with the modification in standard oral longer MDR TB regimen if required.

Replacement drugs in sequence of preference

Drugs of the component regimens will require to be replaced in case of an adverse drug reaction, poor tolerance, contraindication or non-availability of the component drugs of the combination regimen or resistance detected on baseline LC DST.

In case of the need for replacement of any of the component(s) in the all oral longer MDR TB regimen, the following broad principles apply:

1. The drugs are replaced according to their efficacy, no demonstrable resistance, prior use, side-effects profile and background resistance to the replacement drug in the country as per the NDRS report.
2. The regimen should preferably be fully oral. However, in certain circumstances, an Injectable may have to be used for the need of efficacy and side-effect profile.
3. Five drugs are to be used in IP and at least 4 drugs in CP. However, in case of individual need for replacement of one of either Lzd, Cs or Cfz without replacement of Bdq or FQ, there is no need to add another drug as there will still be minimum 4 effective drugs in IP and 3 drugs in CP as per the WHO principles. For replacement of Bdq or FQ, the scenarios have been given in the table below.
4. Dlm and Am will not be used in CP.
5. Though Imp-Cln is 4th in the sequence of drugs of group C, it will only be used as the last resort for designing the regimens, operational issues of a Peripherally Inserted Central Catheter (PICC) placement for the entire duration of its use, need for admission to a NDR TBC.

The following sections deal with the replacement of drugs in the various DR TB regimens:

Sequence of using replacement drugs to modify the regimen

<table>
<tr><th>Regimen</th><th>Sequence of using replacement drug to modify the regimen</th></tr>
<tr><td>All oral H mono/poly</td><td>• If SL LPA shows Lfx resistance - Replace Lfx with Mfx^{h} if SL LPA pattern suggests. Do LC DST for detection of resistance to Mfx^{h} and Z.
• If Mfx^{h} or Z can't be used – Replace with Lzd. If Lzd also cannot be given, replace with Cfz + Cs.
• If both Mfx^{h} and Z can't be used – Add 2 drugs of the 3 - Lzd, Cfz, Cs (in the order of preference).

Treat for 9 months in any of the above 3 situations. If R resistance – Switch to appropriate regimen.
If R resistance – Switch to appropriate regimen.</td></tr>
<tr><td>Shorter MDR TB regimen</td><td>• If there is a need for stopping/replacing any drug, stop the regimen and evaluate the patient to switch to all oral longer regimen.</td></tr>
<tr><td>All oral longer regimen (Lfx, Bdq, Lzd, Cfz, Cs)</td><td>
<table>
<tr><th>Replacement situations</th><th>Proposed composition of regimen after replacement</th></tr>
<tr><td colspan="2">Initial 6 months of treatment</td></tr>
<tr><td>I. if Lfx cannot be used, replace with Mfx(h) if SL LPA pattern suggests Mfx(h) can be used;</td><td>Mfx(h)*, Bdq, Lzd, Cfz, Cs</td></tr>
<tr><td>II. If Mfx(h) cannot be used, replace with 1 drug from replacement sequence</td><td>Bdq, Lzd, Cfz, Cs + 1 drugs from replacement sequence</td></tr>
<tr><td>I. If Bdq cannot be used, replace with Dlm;</td><td>Lfx, Dlm*, Lzd, Cfz, Cs</td></tr>
<tr><td>II. if Dlm cannot be used, replace with 1 drug from replacement sequence</td><td>Lfx, Lzd, Cfz, Cs + 1 drugs from replacement sequence</td></tr>
<tr><td colspan="2">• If one of Lzd, Cfz or Cs cannot be used, no replacement (if Bdq and Lfx/Mfx(h) can be given)
• If 2 or more drugs cannot be used, replace with 2 or more drugs respectively from replacement sequence to make 5 drugs IP
Replacement sequence: Z*, Am*, Eto*, PAS, E, Imp/Cln or Mpm +Amx/Clv in given order</td></tr>
<tr><td colspan="2">After 6 months of treatment</td></tr>
<tr><td colspan="2">If one drug (Lfx, Lzd, Cfz, Cs) cannot be used, no replacement
If two drugs cannot be used, replace with 2 drugs from Z*, Eto*, PAS, E in given order to complete the 4 drugs regimen</td></tr>
</table>
</td></tr>
<tr><td colspan="2">* Use Dlm – if available, no history of prior use and no exclusion criteria for its use, Z – if resistance not detected, Eto – If InhA mutation not present, Am – if SL LPA pattern suggests. DST for Lzd, Cfz and Z will be considered whenever it is available under programme.</td></tr>
</table>

Drug dosage and administration

The dosage of drugs would vary as per weight of the patients. Adult patients (≥ 18 years) would be classified in weight bands of <16 kg, 16-29 kg, 30-45 kg, 46-70 kg and >70kg. All drugs in the regimen are to be given on a daily basis under observation. Injectable will be administered for six days/week (excluding Sundays). All morning doses are to be supervised by the treatment supporter. After taking the morning doses on Saturday, next day's oral drugs would be given to the patient to be taken at home on Sunday. Empty blisters of drugs taken unsupervised in the evening and on Sundays are to be collected by treatment supporter. In cases of drug intolerance – Eto, Cs and Na-PAS can be given in divided doses (twice a day).

The dosage for drugs used in various DR TB regimens by weight bands for adults are enumerated in Table 6.7. These are in accordance to the WHO recommended doses of anti-TB drugs for adults and paediatric patients.

Bedaquiline: All patients eligible for Bdq will receive Tab. Bdq400 mg once daily for the first 2 weeks and 200 mg 3 times a week (with at least 48 hours between doses) for the following 22 weeks, in combination with the regimen. The regimen will be continued beyond 24 weeks of Bdq administration for the NTEP recommended duration of treatment.
Week 0–2: Bdq 400 mg (4 tablets of 100 mg) daily (7 days per week) + other drugs; Week 3–24: Bdq 200 mg (2 tablets of 100 mg) 3 times per week (with at least 48 hours between doses) for a total dose of 600 mg per week + other drugs; and

Week 25 (start of month 7) to end of treatment: Continue other second-line anti-TB drugs only as per NTEP recommendations.

If taking a light meal with Bdq and other anti-TB drugs, patients should not consume milk-containing products at the same time, as the calcium in these can decrease the absorption of FQs. Also, large fatty meals should be avoided, as these can impair absorption of some of the other anti-TB drugs (Cs, H, etc.,).

The following medications are disallowed during the 24-week administration of Bdq and up to one month after the last dose of Bdq because of potential drug–drug interactions:

- systemic use of moderate and strong CYP3A4 inhibitors, e.g. azole antifungals: ketoconazole, voriconazole, itraconazole, fluconazole; ketolides such as telithromycin and macrolide antibiotics other than azithromycin for more than 2 consecutive weeks;
- systemic use of strong CYP3A4 inducers, e.g. phenytoin, carbamazepine, phenobarbital, St. John's wort and rifamycins (rifampin, rifabutin, rifapentine); and
- cholesterol lowering medications of the "statin" class. (Add Annexure on Drugs to avoid with BDQ and Dlm)

Group	Safe to use	Drugs to be avoided
Antiemetics	Metoclopramide	Domperidone, Ondansetron
Analgesics	NSAIDs, Paracetamol	Tramadol
Antacids	Ranitidine, Milk of Magnesia	Pantoprazole, Omeprazole
Antihistaminics	Pheniramine, Fexofenadine	Diphenhydramine, Loratadine
Antimalarials	Artesunate	Chloroquine
Antibiotics	Penicillins, Cephalosporins, Tinidazole	Ciprofloxacin, Norfloxacin, Cotrimoxazole, Metronidazole
Antifungals	Terbinafine	Fluconazole, Ketoconazole, Itraconazole
Antiepileptics	Sodium Valproate	Phenytoin, Carbamazepine, Phenobarbital
Antidiabetics	Mostly safe	
Antihypertensives	Safe (except Diuretics)	Diuretics
Lipid Lowering Agents		Statins Best to avoid
Antiarrhythmics	Diltiazem, Lignocaine	Amiodarone, Procainamide, Digoxin
Other Cardiac Drugs	Nitroglycerine, Sorbitrate	Sotalol
Antiretrovirals	Tenofovir, Zidovudine, Nevirapine	Efavirenz
Anxiolytics	Benzodiazepines (Alprazolam)	Avoid other sedatives
Antipsychotics	Risperidone	Haloperidol, Clozapine, Quetiapine, Olanzapine
Antidepressants	Best to be avoided, give only if essential with ECG monitoring	Citalopram, Fluoxetine, Sertraline

Dosage of DR TB drugs for adults

Sl.No	Drugs	16-29 kg	30-45 kg	46-70 kg	>70 kg
1	Rifampicin(R)[1]	300mg	450mg	600mg	750mg
2	High dose H (H^h)	300 mg	600 mg	900 mg	900 mg
3	Ethambutol(E)	400 mg	800 mg	1200 mg	1600 mg
4	Pyrazinamide(Z)	750 mg	1250 mg	1750 mg	2000 mg
5	Levofloxacin(Lfx)	250 mg	750 mg	1000 mg	1000 mg
6	Moxifloxacin (Mfx)	200 mg	400 mg	400 mg	400 mg
7	High dose Mfx (Mfx^h)	400mg	600mg	800mg	800mg
8	Bedaquiline (Bdq)	Week 0–2: Bdq 400 mg daily Week 3–24: Bdq 200 mg 3 times per week			
9	Linezolid (Lzd)	300 mg	600 mg	600 mg	600 mg
10	Clofazimine (Cfz)	50 mg	100 mg	100 mg	200 mg
11	Cycloserine (Cs)[4]	250 mg	500 mg	750 mg	1000 mg
12	Delamanid (Dlm)	50 mg twice daily (100 mg) for 24 weeks in 6-11 years of age 100 mg twice daily (200 mg) for 24 weeks for >11 years of age			
13	Imipenem/cilastatin (Ipm / Cls)[4]	1000 mg imipenem/1000 mg cilastatin twice daily			
14	Meropenem(Mpm)[4]	1000 mg three times daily (alternative dosing is 2000 mg twice daily)			
15	Amikacin (Am)[2]	500 mg	750 mg	750 mg	1000 mg
16	Capreomycin (Am)[2]				
17	Kanamycin(Km)[2]	500 mg	750 mg	750 mg	1000 mg
18	Ethionamide (Eto)[4]	375 mg	500 mg	750 mg	1000 mg
19	Na-PAS (60% weight/vol)[3,4]	10 gm	14 gm	16 gm	22 gm
20	Amoxyclav (Amx/Clv) (In child: WHO 80mg/Kg in 2 divided doses)	875/125 mg BD	875/125 mg BD	875/125 mg (2 morning +1 evening)	875/125 (2 morning +1 evening)
21	Pyridoxine(Pdx)	50 mg	100 mg	100 mg	100 mg

[1]For H mono/poly resistant TB;

[2]For adult more than 60 yrs of age, dose of SLI should be reduced to 10mg/kg (max up to 750 mg)

[3]In patient of PAS with 80% weight/volume the dose will be changed to 7.5gm (16-29Kg); 10 gm (30-45 Kg); 12 gm (46-70 Kg) and 16 gm (>70 Kg)

[4]Drugs can be given in divided doses in a day in the event of intolerance

Bdq should be used with caution in PLHIV infection treated with ARVs that exhibit drug-drug interactions with Bdq (efavirenz) or prolong the QT interval (lopinavir/ritonavir) as well as in patients with comorbidities (such as diabetes) or persons with drug or alcohol use, due to limited or no information. Bdq has been used in large cohorts of patients. While experience is growing and drug monitoring is still required, concern is less, due to cohort data reviewed from South Africa. However, frequent clinical and cardiac evaluation is required in these patients.

Bdq will be provided through NTEP. The dosage of BDQ would apply to all weight bands while the dosage of other drugs in the regimen would be as per weight bands in accordance to guidelines.

Delamanid: All patients >12 yrs of age will receive Tab. Delamanid 100 mg (two tablets of 50 mg) orally twice a day for 24 weeks in combination with other drugs in the regimen while patients belonging to 6 to 11 yrs of age group will receive Tab. Delamanid 50 mg (one tablets of

50 mg) twice a day for 24 weeks. Remaining drugs in regimen will be continued beyond the 24 weeks of Dlm administration for the NTEP recommended duration of treatment. It is important that Dlm be taken daily preferably after a standard meal to improve bioavailability.

Patients should not consume milk-containing products at the same time, as calcium can decrease the absorption of FQs. Also, large fatty meals should be avoided as these can impair absorption of some of the other anti-TB drugs (Cs, H, etc).

Counselling for DR TB patients

Counselling offers an opportunity to explore and heal past and present difficulties faced by patients in a confidential and supportive environment, especially while dealing with life issues. The role of counselling in the management of DR TB is significant. A competent counsellor can sensitize patients in several key aspects of TB with particular emphasis on DR TB care and control. It is important to understand the mode of disease transmission and its prevention.

A counsellor can help the patient to better understand importance of regular treatment as well as consequences of deviation from the treatment. His/her role is to empower patients with disease related information and enable him to take informed decision related to treatment adherence. Treatment duration of any DR TB regimen is long enough for the patient which needs multiple sessions of counselling, preferably more frequently in the initial phase of treatment.

Documentation is an essential part of counselling. It helps the counsellor in being aware about the progress of the sessions and targets achieved in the process. It informs about the efforts made by the patients to make desired changes. It also gives space for the counsellor to record his/her observations. In case of any legal issue cropping up, the documentation stands as proof of the work done with the client. The DR TB counselling register that is available with the counsellor serves the purpose of documentation. NTEP provides a counsellor at every NDR TB centre for this purpose.

Extension of treatment in various DR TB regimens

All oral H mono-poly DR TB regimen

Total duration of H mono-poly DR TB regimen is 6 months can be extended to 9 months in certain conditions. In patients with extensive disease; uncontrolled comorbidity; extra-pulmonary TB; if smear at the end of 4th month is found positive and three conditions mentioned in table 6.6 sequence of replacement drugs where in regimen is modified, the treatment may be extended to 9 months. In CNS, skeletal and milliary TB, treatment may be given up to a year. In patients who remain sputum smear positive at the end of 5-month or later of treatment, the outcome will be declared as treatment failure.

Shorter MDR TB regimen

Total duration of shorter MDR TB regimen is for 9-11 months, depending on IP duration. IP should be given for at least four months. After fourth month of treatment, if the result of sputum microscopy is negative then CP should be initiated. If sputum smear microscopy does not become negative by the fourth month of treatment, subject the patient to FL LPA and SL LPA and culture DST. If no additional resistance is detected, the IP should be prolonged until sputum smear converts. If the intensive phase is prolonged, the injectable agent is only given three times a week. IP should be extended to 5th or 6th month based on smear results at the end of 4th and 5th month of treatment. This will be done for a maximum of 2 months (i.e., total duration of IP is not more than 6 months). Duration of CP is fixed for 5 months. If the patient remains smear

positive at the end of 6th month of treatment, the patient will be declared as "Treatment Failure", re-evaluated as per integrated DR TB algorithm and initiated on an appropriate modified regimen based on the extended DST.

All oral longer MDR TB regimen

Total duration of all oral longer MDR TB regimen is 18-20 months. At the end of 6th month of treatment, the patient must be reviewed based on the 5th month culture result. If 5th month culture result is not available at the end of 6th month, decision to tapper the dose of Lzd to half (300/150 mg) will be based on 4th month culture result. If the 5th or 4th month culture result (whichever applicable) remains positive, the dose of Lzd (600/300 mg) and the regimen is extended by 1 more month. However, the duration of new drugs (Bdq or Dlm) is limited to 24 weeks only. Decision for continuation of extended IP with Lzd (600/300 mg) beyond 7th month, is decided based on the culture results of 6th/5th month and the clinical/radiographic response. Extension of IP beyond 8th month is not permitted and patient should be switched to CP. (i.e., total duration of treatment is not more than 20 months).

If the patient continues to remain culture positive or reverts back to culture positive after 8 months of treatment, the patient is declared as "Treatment failed", re-evaluated as per integrated DR TB algorithm and initiated on an appropriate modified regimen based on the extended DST. For XDR TB patients the duration of all oral longer MDR TB regimen would be for 20 months.

Patient flow for DR TB patients

- N/DDR TBC and the PHI concerned should be involved actively in management of all DR TB patients;
- DDR TBC will be the reporting unit for the respective district and will register all MDR/RR TB and H mono/poly DR TB patients initiated on any regimen at N/DDR TBC. The patient will be registered in the PMDT notification register with issue of unique PMDT number. Patient details will also be entered and regularly updated on Nikshay;
- Similarly, NDR TBC will be the reporting unit for catering districts. All DR TB patients initiated on treatment from respective districts will be registered in PMDT notification register. Patient details would be entered and regularly updated on Nikshay. Overall accountability of all such patients will be shared by the concerned DDR TBC and DTO;
- PMDT treatment card of DR TB patients managed at the concerned DR TBC for pretreatment evaluation will be opened by responsible staff (SA at NDR TBC/ DR TB & TB HIV coordinator at DDR TBC) of N/DDR TBC;
- After pretreatment evaluation and initiation of treatment, the patient should be referred back to the PHI with up to a maximum of one week's supply of drugs, arrangements for injections in transit and a copy of the PMDT treatment book and referral form under intimation of the DTO. The respective DTO/ MO-PHI should be informed by the concerned DR TBC on referral of patients for ambulatory care in advance, by means of the NTEP PMDT referral for treatment form via Nikshay, email or mobile phone;
- Drugs provided to the patients to cover for transit period may be counted as unsupervised doses. However, as much as possible, efforts should be made by the district staff to restrict these transit doses;
- DTO arranges for availability of the monthly drug box to the treatment supporter (via the TU staff like STS/TBHV) and the patient records at the identified treatment support centre with timely information to the respective MO-PHI;

- MO-PHI is responsible for supplying patient records and drugs to the designated treatment supporter. The MO-PHI will need to make suitable arrangements during intensive phase of the treatment for daily injections, including free sterile needles and syringes; and
- Patient's information as per PMDT treatment book and aDSM treatment review form as detailed later must be regularly updated on Nikshay (at least weekly) by the concerned field staff responsible.

Overall responsibility of monitoring the patient's progress on treatment, including follow-up is with the MO-PHI where patient is being treated with support of the respective TU team.

Treatment Interruptions & DRTB

Management of DR TB patients with treatment interruptions and lost to follow-up

All efforts must be made to ensure that DR TB patients do not interrupt treatment or are lost to follow-up. Action should be taken to promptly retrieve patients who fail to come for their daily dose by the treatment supporter as discussed later. The following strategies are applicable for patients who interrupt treatment:

Patients who miss doses: In shorter MDR TB regimen, all missed doses during IP must be completed prior to switching the patient to CP. Similarly, all missed doses during CP must be administered prior to ending treatment. In longer MDR TB regimen, all missed doses during treatment must be administered prior to ending treatment.

Patients who interrupt treatment for less than one month: When the patient returns to resume treatment, the treatment will be continued. However, the duration of treatment will be extended to complete the regimen. The follow-up cultures will be done as per the schedule.

Patients who are "lost to follow-up" (interrupt treatment continuously for one month or more) and return back for treatment: Such patients will be given an outcome of "lost to follow-up". The patient would be subjected to repeat NAAT & FL /SL LPA and LC DST as per the diagnostic algorithm to restart with appropriate treatment. If there are signs of impending treatment failure for any MDR RR TB patient with or without additional resistant to second line drugs, the patient should be switched to an all oral longer DR TB regimen and evaluated further to modify appropriately based on DST results if required. If a patient has received the shorter MDR TB regimen for more than one month and returns for treatment after an interruption of one month or more, the patient is not restarted on a shorter MDR TB regimen.

MDR/RR TB patients on Bdq/Dlm containing regimen who interrupt treatment or are "lost to follow-up" or recurrent DR TB

Patients who interrupt Bedaquiline treatment during the first two weeks of Bdq course and returns to resume the treatment:

- if interruption is up to 7 days, Bdq containing regimen will be continued to complete the doses and the duration of treatment will be extended to complete IP. Follow-up cultures will be done as per the revised schedule; and
- if interruption is more than 7 consecutive days, Bdq course will be reloaded (started afresh) and a fresh specimen collected for culture. The culture isolate must be stored for Bdq DST in future.

Patients who interrupt Bedaquiline treatment during 3-24 weeks of Bdq course and return to resume treatment:

- if interruption is up to one month, Bdq containing regimen will be continued to complete the doses and duration of treatment will be extended to complete full course of Bdq . Follow-up cultures will be done as per revised schedule; and
- if interruption is more than one month, Bdq will be permanently discontinued. Such patients will be given an outcome of "Lost to follow-up" (LTFU), registered afresh and initiate all oral longer MDR TB regimen with appropriate modification. A sputum specimen will be collected for culture. The culture isolate must be stored for Bdq DST in future.

Delamanid:If the patient misses one or more doses of Dlm during treatment up to a maximum of one month, one should continue the treatment and complete the Dlm for rest of the period which may prolong the Dlm containing phase beyond 24 weeks from initiation of treatment to make the adjustment of missed dosage.

Patients who initiated on Bdq/Dlm containing regimen and return after treatment interruption of one month or more will be declared as "loss to follow up". Such patients would not be considered eligible for administration of same drug (Bdq/Dlm) anymore.

Where further treatment is concerned, if the patient has any indication of a treatment failure or recurrence, the NDR TBC Committee will be contacted to discuss whether s/he should be retreated. The decision will be made on a case-to-case basis, using all available bacteriological and clinical data.

Follow-up evaluations during treatment

The follow-up evaluation schedule during treatment for DR TB patients managed with various regimen classes are summarized in the table below:

Follow up evaluation schedule of DR TB patient during treatment by regimen

Regimen Class	All oral regimen for H Mono /Poly DR TB	Shorter MDR TB Regimen	All oral longer regimen for MDR/RR
Duration	6/ 9 months (no separate IP/CP)	9 – 11 months (4-6m IP, 5m CP)	18-20 months (no separate IP/CP)
Clinical + Wt.	Monthly	Monthly in IP, Quarterly in CP	Monthly in first 6 months, Quarterly beyond 6 months
Smear Microscopy	Monthly from 3rd month onwards	Monthly from 3rd month onwards till end of IP, Monthly in extended IP only if previous month S+ve.	With culture at C-DST lab
Culture	At end of 3rd, 6th and 9th month (if applicable)	At 3rd, 6th and end of Rx	Monthly from 3rd month onward to end of 6 months. Quarterly beyond 6 months, 2 consecutive monthly culture if any culture +ve from 6m onwards
DST	NAAT, SL LPA and LC DST as per algorithm if smear/ culture +ve at 3rd,6th and/or 9th month	FL & SL LPA and LC DST (Mfx 1.0, Lzd*, Cfz* & Z*) if any culture +ve (3rd, 6th and end of Rx) or smear +ve at end of IP, end of extended IP and end of Rx	FL & SL LPA and LC DST (Mfx 1.0, Lzd*, Cfz*, Bdq* & Dlm*) if any time culture +ve at end of 6 months or beyond 6 months.
S. Creatinine		Monthly till SLI course is completed	If Injectable is used, monthly till SLI course is completed
Audiometry		Every 2 months till SLI course is completed and then as and when clinically indicated	If Injectable is used, every 2 months till SLI course is completed and as and when clinically indicated
UPT	As and when clinically indicated	As and when clinically indicated	As and when clinically indicated
CBC/platelets ^	As and when clinically indicated	As and when clinically indicated	15th day, monthly in first 6 months, then as and when clinically indicated
TSH & LFT#	As and when clinically indicated	At end of IP, then as and when clinically indicated	LFT quarterly, as and when clinically indicated
CXR	As and when clinically indicated and at end of Rx	At end of IP, end of treatment, then as and when clinically indicated	At end of 6 months, end of treatment, as and when clinically indicated
ECG$	As and when clinically indicated	At 2 wks, monthly in IP, then as and when clinically indicated	At 2 wks, monthly in first 6 months, then as and when clinically indicated
S. Electrolytes (Na, K, Mg, Ca)	As and when clinically indicated	As and when indicated and in case of any QTcF prolongation	As and when indicated and in case of any QTcF prolongation
Specialist consultation	As and when clinically indicated	As and when clinically indicated	As and when clinically indicated
Colour vision test	Once in two months (in children)	Once in two months (in children)	Ophthalmic exam once in 3 months

The most important evidence of response to DR TB treatment is conversion of sputum smear and culture to negative. Good quality sputum specimen is therefore essential to get reliable results that form the basis of monitoring bacteriological response to treatment.

Smear examination would be used on a monthly basis from 3rd month onwards to guide the decision on moving from IP to CP in shorter MDR TB regimen and extension of treatment to 9 months for all oral H mono/poly regimen.

For H mono/poly regimen, follow up culture would be done at 3rd, 6th and 9th month (if applicable)

For shorter MDR TB regimen, smear microscopy would be continued on monthly basis from 3rd month onwards if IP needs to be extended if the previous month smear is positive up to a maximum of six months while follow-up culture will be done at the end of IP, end of extended IP and end of treatment. If smear/culture remains positive at the end of IP and/or extended IP, a fresh specimen/culture isolate of that time will be subjected to FL/SL-LPA to check for amplification of resistance to FQ/ SLI or InhA mutation. If the patient is found to be susceptible to both FQ and SLI at fourth month of treatment, the intensive phase will be extended on monthly basis up to a maximum of six months. At end of extended IP or later, if any resistance is detected by SL-LPA OR InhA mutation detected on FL-LPA OR if found to be culture positive, the patient will be declared as treatment failure. The patient is then re-evaluated for all oral longer MDR TB regimen with appropriate modification if required.

DST to Mfx (1.0), Lzd, Z*, Cfz*, Bdq* and Dlm* (*whenever available) will be set up on liquid culture on the LPA deposits only for all MDR/RR TB patients if patient remains smear/culture positive at beyond end of IP in shorter MDR TB regimen and beyond 6th month treatment for any longer MDR RR TB regimen. Long term follow-up will be done with six monthly cultures among symptomatic patients till two years after completion of any DR TB regimen.

Smear conversion is less reliable than culture conversion, which reflects viability of tubercle bacilli even in very low bacilli per ml of sputum and is a more accurate reflection of response to treatment. Hence, for all patients put on all oral longer regimen, culture will be done as per table 7.1 to decide on extension of treatment regimen. Patients will be considered smear converted after having two consecutive negative smears taken at least one month apart. Patients will be considered culture converted after having two consecutive negative cultures taken at least one month apart.

Time-to-culture conversion is calculated as the interval between the date of DR TB treatment initiation and date of the first of these two negative consecutive cultures (date of sputum specimens collected for culture should be used).

Follow-up sputum culture should be done on liquid culture. In case of extension of treatment, the follow-up culture months will shift by every month of extension of treatment till maximum limit specified for all regimen classes. However, it must be noted that the final treatment outcome of all DR TB patients will be declared on the basis of follow-up culture results only.

Treatment outcomes

The progress of the patient on treatment would be monitored using interim as well as final treatment outcomes for various DR TB regimens.

Interim outcomes

Culture conversion: Patient is considered to have culture converted when two consecutive

cultures, taken at least 1 month apart, are found to be negative. In such a case, the specimen collection date of the first negative culture is used as the date of conversion.

Culture reversion: Patient is considered to have culture reverted when, after an initial culture conversion, two consecutive cultures, taken at least 1 month apart, are found to be positive. For the purpose of defining Treatment failed, reversion is considered only when it occurs in the continuation phase.

The term microbiological conversion/reversion can also be used either for smear or culture based follow ups.

Final outcomes

The final treatment outcome definitions would vary with type of regimen & the duration of treatment.

Outcomes for all oral H mono/ poly DR TB patients

The definitions to use when assigning outcomes are the same ones as for drug-susceptible TB. No new outcome definitions (or registration categories) are warranted.

Cured: Microbiologically confirmed H mono/poly DR TB patients at the beginning of treatment who was culture negative at the end of the complete treatment (To be discussed)

Treatment completed: A H mono/poly DR TB patient who completed treatment without evidence of failure or clinical deterioration BUT with no record to show that the smear or culture results of biological specimen in the last month of treatment was negative, either because test was not done or because result is unavailable.

Failure: A H mono/poly DR TB patient whose biological specimen is positive by smear or culture at 5 months or later (check if the definition of failure given under "Outcome for all oral longer regimen" will apply here also).

Lost to follow up: A H mono/poly DR TB patient who interrupted treatment for consecutive 1 month or more

Not Evaluated: A H mono/poly DR TB Patient for whom no treatment outcome is assigned. This includes former "transfer-out" & "still on treatment"

Regimen Changed: A need for permanent discontinuation of existing regimen and initiation of new regimen with change of at least one or more anti-TB drugs prior to being declared as failed. (To be discussed- same as above)

Died: A patient who has died during the course of anti-TB treatment

Outcomes for shorter MDR TB regimen

Cure: Microbiologically confirmed MDR/RR TB patient at the time of beginning of the treatment, completed the treatment and culture was negative at end of treatment and on at least one previous occasion.

Treatment completed: A patient who has completed treatment according to guidelines but does not meet the definition for cure or treatment failure due to lack of microbiological results.

Failure: Treatment terminated or need for permanent regimen change in CP because of lack of microbiological conversion by end of extended intensive phase or microbiological reversion in the continuation phase after conversion to negative or evidence of additional acquired resistance to drugs in the regimen or adverse drug reactions (ADR).

Died: A patient who dies for any reason during the course of treatment.

Lost to follow-up: A patient whose treatment was interrupted for one month or more for any reasons prior to being declared as failed.

Not evaluated: A DR TB patient for whom no treatment outcome is assigned, this includes former "transfer-out".

Regimen changed: A need for permanent discontinuation of existing regimen and initiation of new regimen with change of at least one or more anti-TB drugs prior to being declared as failed.

Outcomes for all oral longer regimen for MDR/RR TB (except shorter MDR TB regimen) and/or XDR TB patients

Cure: Microbiologically confirmed MDR/RR TB patient at the time of beginning of the treatment completed the treatment and three or more consecutive cultures taken at least 1 month apart from 6-8 months onwards are negative including culture at the end of treatment.

Treatment completed: Treatment completed as recommended by the national policy without evidence of failure but no record to declare it as cured.

Treatment failed: Treatment terminated or need for permanent regimen change of at least two or more anti-TB drugs from 8th months onwards because of

- lack of microbiological conversion by the end of the 8th month of treatment or
- microbiological reversion in the 8th month or later after conversion to negative or
- evidence of additional acquired resistance for drugs in regimen or
- adverse drug reactions (ADR).

Died: A patient who dies for any reason during the course of treatment.

Lost to follow-up: A patient whose treatment was interrupted for one month or more for any reasons prior to being declared as failed.

Not evaluated: A patient for whom no treatment outcome is assigned, this includes former 'transfer- out'.

Regimen changed: A need for permanent discontinuation of existing regimen and initiation of new regimen with change of at least one or more anti-TB drugs prior to being declared as failed. (To be discussed – will this also apply to regimen changes because of baseline resistance report that comes 1 month later / Will this apply to drug change due to toxicity / Will this apply to regimen change due subsequent development of resistance)

Treatment outcome is defined by reviewing patient PMDT treatment card. The treatment outcome and date the patient stopped treatment is written in the appropriate column in the TB treatment card. Transferred out patient should be tracked vigorously before declaring them as not evaluated or lost to follow up. The date on which the patient stopped treatment is the date of the last dose of drugs taken. Details of treatment outcome should be updated in Nikshay. The MO of the PHI should record the treatment outcome in the treatment card and sign it. The treatment card of the patients whose outcome has been declared should be handed over to the STS during his routine monthly visits. Every patient started on treatment must be given one and only one treatment outcome for each episode of treatment regimen.

Non-Tuberculous Mycobacteria (NTM)

A large number of Mycobacteria other than Mycobacterium tuberculosis are being increasingly recognized as a cause of human disease. Commonly referred to as non-TB Mycobacteria (NTM), they are also known as atypical mycobacteria, anonymous mycobacteria or mycobacteria other than tubercle bacilli (MOTT). NTM are ubiquitously distributed in the environment and hence also known as environmental mycobacteria. They are distinct from M.tb in their characteristics that they can survive outside the human or animal host. They are generally nonpathogenic or opportunistic pathogens and most commonly causes disease when there is immunosuppression or injury, except for few species which infect immune-competent humans.

Often these bacteria inhabit the respiratory passages in the form of commensal organisms. Pulmonary infection from NTM though rare, can cause disease similar to TB. They more commonly infect the skin, soft tissue, lymph nodes, implant devices, wounds, bones and joints. Disseminated NTM disease is mostly seen in patients who are immunosuppressed or who have Acquired Immunodeficiency Syndrome (AIDS).

Though NTM are widely distributed in the environment, the clinical infection is rare. They may be falsely recovered from clinical specimens due to laboratory contamination or contamination of medical instruments. Chronic pulmonary infection due to M. avium complex and M. Kansasii generally occurs in elderly persons especially males who are smokers or who have preexisting lung lesions. Cervical lymphadenopathy occurs in children due to M. Scrofulaceum, while skin and soft tissue infections may develop from M. Fortuitum, M. Chelonei, M. Xenopi and M. Ulcerans. Exposure of humans to NTM may occur while bathing, swimming and drinking and the organism can also gain entry through cuts and abrasions. However, the risk of infection is generally less. Disseminated lesions are found in immunocompromised patients due to infection from M. Avium complex. Sometimes, M. Chelonei may cause very indolent pulmonary infection.

Diagnosis of NTM

Because of their omnipresence in our environment, isolation of NTM from non-sterile body sites does not imply true infection or disease, per se. Repetitive isolation, signs of clinical disease, radiological abnormalities, the exact species isolated and predisposing conditions of the patient involved, are all helpful in determining whether the isolated mycobacteria are to be considered causative agents of the patient's disease. In normally sterile sites, isolation of NTM, preferably backed up by histological evidence of granulomatous inflammation, suffices for the diagnosis of NTM disease.

Table : Most frequently isolated Non-TB Mycobacteria and their sites of infection

Species	Main site of infection	Growth rate
M. Avium complex (M. Aviaum, M. Intracellulare, minor species)	Pulmonary, lymph nodes, disseminated disease	Slow
M. Kansasii	Pulmonary, disseminated disease	Slow
M. Xenopi	Pulmonary	Slow
M. Malmoense (NW Europe)	Pulmonary	Slow
M. Ulcerans	Skin	Slow
M. Marinum	Skin	Intermediate
M. Abscessus	Pulmonary, skin	Rapid
M. Chelonae	Skin, soft tissues, disseminated disease	Rapid
M. Fortuitum	Skin, soft tissues, pulmonary	Rapid
M. Scrofulaceum	Lymph nodes	
M. Haemophilum	Disseminated disease	

The minimum evaluation of a patient presenting with features suggestive of non-TB Mycobacterial (NTM) lung disease should include the following:

- chest radiograph or chest high-resolution computed tomography (HRCT) scan. HRCT may be done in settings where access to this technology is available. However, it is not mandatory for evaluation and decision to treat the patient;
- three or more sputum specimens for acid-fast bacilli (AFB) analysis;
- exclusion of other disorders, such as TB;
- expert consultation should be obtained when NTM are recovered that are either infrequently encountered or that usually represent environmental contamination. Patients suspected of having NTM lung disease but who do not meet the diagnostic criteria should be followed until the diagnosis is firmly established or excluded; and
- making the diagnosis of NTM lung disease does not, per se, necessitate the institution of therapy, which is a decision based on potential risks and benefits of therapy for individual patients.

Clinical, radiological and microbiological criteria are equally important and all must be met to make a diagnosis of NTM lung disease. The following criteria apply to symptomatic patients with radiographic opacities, nodular or cavitary or an HRCT scan that shows multifocal bronchiectasis with multiple small nodules. These criteria best fit with Mycobacterium avium complex (MAC), M. Kansasii and M. Abscessus.

Clinical

- pullusion of any other etiologies.

Radiological

- radiological findings pertain to nodular or cavitary opacities on chest radiograph; and/or
- HRCT scan that shows multifocal bronchiectasis with multiple small nodules.

Microbiological

Table: Microbiologic criteria for diagnosis of NTM lung disease

The diagnostic processes for NTM to be followed at C-DST laboratories are detailed in Annexure 7. The laboratory staff would be separately trained in these standard operating procedures for laboratory confirmation of NTM. For more information on NTM including extra-pulmonary NTM, microbiologists are encouraged to refer to the latest American Thoracic Society (ATS) guideline.

Treatment of NTM:

NTM are uncommonly encountered clinical pathogens; some species, in fact, are much more likely to be isolated as a result of specimen contamination than as a result of disease. It can also be isolated from patients with lower respiratory infections especially from patients who live in areas of higher density of environmental NTM presence. This is a transient carriage and usually does not meet the criteria for NTM disease. However, even these species can, under some circumstances, cause clinical disease. The clinician, therefore, must always know the context in which an NTM isolate was obtained to assess accurately the clinical significance of that isolate. Given these complexities, the treatment of NTM will be the prerogative of the NDR-TBCs. When questions about the clinical significance of an NTM isolate arise, expert consultation is strongly encouraged. In this context, important points to note would be:

- treatment recommendations for infrequently encountered NTM are made on the basis of only a few reported patients. With that limitation in mind, unless otherwise stated, the duration of therapy for most pulmonary NTM pathogens is based on treatment recommendations for more frequently encountered species such as MAC and M. kansasii (e.g., continue therapy for at least 12 months after the last negative sputum culture). For disseminated disease, treatment duration for most NTM pathogens is the same as for disseminated MAC infection;
- treatment of NTM disease is generally not directly analogous to the treatment of TB. In vitro susceptibilities for many NTM do not correlate well with clinical response to antimycobacterial drugs. Recommendations for routine in vitro susceptibility testing of NTM isolates are limited. The clinician should use in vitro susceptibility data with an appreciation for its limitations;
- empiric therapy for suspected NTM lung disease is not recommended; and
- there are not widely accepted criteria for choosing patients with NTM lung disease for resectional surgery. In general, the more difficult an NTM pathogen is to treat medically, the more likely surgery should be considered from a risk/ benefit perspective. Expert consultation is strongly encouraged at NDR-TBC.

Suggested treatment regimen covering maximum NTMs mainly MAC

- Rifampicin 450-600 mg OD;
- Ethambutol 800 – 1200 mg OD;
- Clarithromycin 1gm OD (split into two doses); and.
- Add injection Amikacin 750mg-1gm thrice weekly for the first 2-3 months.

Intensive phase is for 3 months and can be extended to a maximum of 6 months with all four drugs. Continuation phase of treatment will be with the same drugs except injectable. This should be continued for 12 months after sputum culture conversion. Drugs will be given as per the standard weight bands. If the patient does not culture covert by end of 3 months, then species identification and DST is required for further management by the NDR-TBC committee based on expert consultations.

Note:- As the proportion of the patients estimated is very low, drugs will not be available through NTEP but will have to be made available through the general health system.

Points to note for treatment of NTM

- recommended initial regimen for most patients with nodular/bronchiectatic MAC lung disease is a thrice-weekly regimen including Clarithromycin 1000 mg or Azithromycin 500 mg, E 25 mg/kg, and R 600 mg administered three times per week;
- recommended initial regimen for fibro-cavitary or severe nodular/bronchiectatic MAC lung disease includes clarithromycin 500–1000 mg/day or azithromycin 250 mg/ day, E15 mg/kg/day, and R 10 mg/kg/day (maximum, 600 mg). An initial 2 months of E at 25 mg/kg/day is no longer recommended;
- intermittent drug therapy is not recommended for patients who have cavitary disease, or patients who have been previously treated or patients who have moderate or severe disease;
- primary microbiologic goal of therapy is 12 months of negative sputum cultures while on therapy; therefore, sputum must be collected from patients for AFB examination throughout treatment on monthly basis in IP and quarterly basis in CP after culture conversion is achieved;

- macrolides should not be used as monotherapy for MAC because of the risk for developing macrolide-resistant MAC isolates;
- macrolide with a single companion drug, E, may be adequate for nodular/ bronchiectatic MAC disease but should not be used in patients with fibro-cavitary disease because of the risk of emergence of macrolide resistance;
- patients respond best to MAC treatment regimens the first time they are administered; therefore, it is very important that patients receive recommended multidrug therapy the first time they are treated for MAC lung disease; and
- expert consultation should be sought for patients who have difficulty tolerating MAC treatment regimens or who do not respond to therapy.

For further details on management of individual NTMs including EP NTMs, the physicians of NDR-TBC are encouraged to refer to the latest ATS guidelines.

IMPROVING INTERPERSONAL COMMUNICATION SKILLS IN NTEP TRAINING:

KEY CONCEPTS AND SAMPLE ROLE PLAYS

The principles of the NTEP are:

a. Political and administrative commitment
b. Good quality diagnosis, primarily by sputum microscopy (using microscopy to examine sputum smears among patients in health facilities)
c. Uninterrupted supply of Good quality drugs (short-course chemotherapy, patient-wise boxes)
d. Direct Observation of treatment (The right treatment, given the right way)
e. Systematic monitoring and accountability (outcome of each and every case initiated on treatment).

Successful application of each of these principles depends, in part, upon developing and maintaining positive relationships among the individuals who work in the Programme, as well as with the community and patients who are served by the Programme. While technical and clinical aspects of the Programme must be adequately addressed, social and communication dimensions are equally necessary to make this information acceptable, and to encourage Programme participation. Interpersonal communication (IPC) skills are invaluable at all levels of the NTEP, and are powerful tools to help cure patients, and thereby, to control TB.

For example, quite often patients discontinue treatment as soon as they start feeling better. They may not understand about drug-resistant TB and that it can be very difficult to cure. This sort of information needs to be conveyed to patients and their families without causing undue alarm. Service providers should be able to communicate with the patients in a way that makes patients feel comfortable and ensures that patients develop confidence in the service providers and ultimately in the services received. The best way to make a patient comfortable is to communicate in a language that is easily understood by the patient. Sympathy and concern about the patient and his/her disease should invariably emerge during the conversation. Good IPC encourages patients to complete treatment and also consult the service provider in case of any questions or concerns (such as adverse effects of the medications). Willingness to contact the service provider to clarify any apprehensions is an important indicator of good IPC between patients and providers.

In addition to improving interactions with patients, good IPC skills will help NTEP staff obtain

participation from officials, laboratory personnel, public sector physicians, and treatment observers.

PRINCIPLES OF PATIENT-PROVIDER INTERACTION

How we learn to change behaviour

People adopt habits and behaviour for a variety of reasons. Changing behaviour is often a gradual and complex process.

I**nformation:** We often become aware of the need to change behaviours by receiving information. But information alone is rarely enough to bring about the change. We often have information but are still not motivated to change our behaviour. Some reasons for this are:

- We don't believe the information
- We don't believe that we are capable of changing
- We believe that the behaviour is not under our control
- We believe that the change is not warranted.

Motivation: We often actually get started on a change as a result of a personal experience or crisis that provides us with the motivation to try a difficult change.

Support: To succeed, most of us receive some form of support. Support comes from something we find within ourselves and/or from peers, family, health workers and others who are important to us.

To help people change their behaviour, good IPC, or "counselling" skills will work toward providing information, motivating, helping people to overcome obstacles, and providing support to try to change.

Counselling is a process of enabling/helping someone to overcome a problem; meet a need, make a decision, or accept their situation. Counselling differs from education. Education involves providing information. Counselling is a process of helping others use information and relate it to their own lives. Counselling is not giving advice alone. The aim of counselling is not to solve other people's problems but to enable people to solve their own problems. Good counselling is client-cantered, which means counselling must centre on the client's feelings, thoughts, concerns and needs. Thus, counselling is a process of empowering clients to make their own decisions through defining feelings and providing objective information.

Characteristics of effective counselling:

- Confidential
- Non-judgmental
- Non-directive
- Empathetic
- Encouraging
- Reinforcing

Types of Communication

There are two types of communication—verbal and non-verbal. Verbal communication is for correctly providing facts. This is important, but is only one component of communication. The other component is non-verbal communication.

Non-verbal communication creates the atmosphere of the interaction. It can create either a welcoming, caring environment that makes the facts acceptable and easy to understand, or a formal, confusing, or even hostile environment that makes it difficult for the facts to be understood or accepted.

Effective communication skills include active listening, praise and encouragement, paraphrasing (repeating in slightly different words), questioning, reflecting, and non-verbal communication. Communication is a process by which information, ideas and/or feelings are exchanged between individuals. The ability to communicate effectively can be learnt.

The development of good verbal and non-verbal communication by improving IPC skills is the focus of this module. It will help trainers and trainees to develop insights into and improve their own behaviour. Role plays are a good way to practice interacting with others and to improve IPC skills.

The skills involved in good interpersonal communication include:

- Listening and Understanding
- Demonstrating caring, concern and commitment
- Problem solving and Motivating

Listening and understanding involve more than simply being present while someone is speaking. Active listening means genuinely hearing the other person's words. Often, we think we are listening, but we actually do not pay close attention or do not really hear what the other person is trying to say. Some key points for improving listening and understanding skills include:

DO:

Offer a seat before interacting with the patient

- Allow sufficient time for the interaction
- If time must be limited, give your full attention during the time you have and the same should be apparent to the patient
- Be prompt so the other person does not have to wait a long time for your attention
- Sit with the other person so you are at their level
- Maintain eye contact
- Move your head to indicate you are paying attention
- Apologize for any unforeseen interruptions
- Ask open-ended questions (questions that cannot be answered with "yes" or "no") such as questions that begin with "What", "Why" or "How". These questions require more than just a few words in the answer
- Periodically summarize what the other person has said to ensure that you have understood; use their own words to repeat the ideas back to them.

DON'T:

- Interrupt while the other person is speaking
- Yell at the other person
- Ask questions that can be answered with just one word (for example, questions that begin with "Do")
- Perform other activities during the meeting
- Ask difficult/embarrassing questions

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You can demonstrate that you care by expressing your understanding of the feelings and concerns of the other person and by letting them know that you want to help them. You can reflect the other person's emotions back to them with facial expressions that show you are concerned. You can also provide verbal feedback to them to show acknowledgement and recognition of their fears and concerns. Some key points are:

DO:

- Greet the patient
- Say, "Hello, please be seated."
- Address the person by name or appropriate title but always with respect
- Acknowledge and respond to each of their concerns
- Emphasize that your job is to help them
- Ask about family members
- Treat the person with respect
- Smile.

DON'T:

- Minimize or dismiss their concerns
- Put down the other person
- Act superior
- Assume the person knows their way to another person/room/office; give them proper guidance to their next destination
- Argue with the patient.

****

After listening, understanding and showing that you care, you can then use your knowledge of the NTEP to discuss ways you can work together to solve any problem the other person has with participating in the Programme. Some key points for this include:

DO:

- Listen carefully to their point of view
- Paraphrase and summarize frequently to make sure that you understand the problem Use non-technical words
- Help them to comply
- Demonstrate that you are concerned about the patient
- Convey that you understand their fears and apprehensions
- Make them comfortable
- Identify obstacles to their participation

DON'T:

- Assume you know all the answers
- Use technical words
- Treat them as your student
- Tell them to comply
- Assume you know their condition
- Expect compliance without explanation.

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Finally, you can use all of the knowledge, understanding and trust you've gained during your interaction to continue to motivate each person to maintain involvement in the Programme. Here are some of the main points to keep in mind for motivating:

DO:

- Repeat important information in different ways each time you meet
- Emphasize that your job is to help them
- Emphasize that they will be cured
- Use examples from your own experience
- Tell them that this is what you would recommend to your family members
- Compliment the other person on what they have done well
- Recognize their progress
- Emphasize that their welfare is your concern/job

DON'T:

- Use technical words
- Ignore the efforts the other person has made so far
- Overlook their fear and anxiety
- Ignore or minimize practical barriers
- Criticize their omissions/commissions.

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How To Use This Section

This section contains role play examples for NTEP trainers. Groups should perform the role plays in the section that pertains to their defined role in NTEP. This section must be used throughout the training to ensure that participants receive consistent information. Role plays should be performed at appropriate time in the course of training.

The section begins with a role play that should be performed by the trainer(s) to exhibit as many poor IPC skills as possible. The trainer(s) should tell the group to watch this role play looking for poor IPC behaviours. The trainer(s) will perform the scene using many of the "DON'Ts" listed earlier and performing as many incorrect IPC skills as possible. Stress these poor behaviours to the point of comedy. It must be made clear that poor IPC behaviours are NOT acceptable for good IPC.

After the performance, have the group make a list and discuss the exhibited poor IPC skills. Then, address each of these behaviours in turn, and discuss ways that good IPC skills could be substituted for the poorer ones. Finally, the trainers should perform the same role play again, using only good IPC skills. After this performance, discuss with the participants the differences between the two scenes. Also have the participants discuss how they think each person in the scene felt and the differences in their feelings between the first and second scene.

Once this discussion is finished, you will have the participants form smaller groups of no more than six people per group. Then, ask the group members to perform relevant scenes listed in this book using as many effective IPC skills as possible. Participants who play the role of patient or person being supervised should be told that they should freely add/invent details which are realistic. Groups do not need to perform ALL of the scenes listed, but continue to have them

perform scenes until you feel the important points have been covered sufficiently and everyone in the group appears to be able to exhibit good IPC skills. Trainers and participants should invent more role play scenes that depict their own experiences and use these in addition to or instead of the role play scenes in this book.

Motivate the participants. If they are reluctant to do role plays because they feel they are not "actors", tell them that they do indeed act every day. Everyone does. Each time they interact with another person, they are acting. Whenever they try to convince someone to do something, they are acting. If they are tired but must appear energetic toward their boss, they are acting. When they first met their wife or husband and wanted to impress them, they put on their best behaviour. This is normal, natural behaviour and is acting.

Give them these and other examples from your own experience to help them realize they already have the skills to do the role plays.
During the role plays, observe each group but avoid interrupting them; interrupt only if the participants are having extreme difficulty or are going totally out of context.

It will be your job to answer questions, talk with the participants about the role plays, lead group discussions and generally give participants any help they need to successfully develop better IPC skills. To do this, you will need to be very familiar with the material being taught.

Ensure that each participant understands what they are expected to do in the role play exercises. By participating in the role play scenes, they will be able to:

- observe and practice the desired practical responses to patients and others
- discuss and share ideas with each other about the situations
- use what they have practised when they encounter these situations during the course of their own work.

Role plays should be used to sharpen IPC skills so that these skills will come naturally during NTEP work.

Demonstrate good interpersonal skills yourself

Answer questions from the participants

Encourage the participants to ask questions and make comments. This means that you need to be available when participants are working on the role play. Respond positively to questions (for example, say, "Yes, I see what you mean." or "That's a good question."). Avoid facial expressions and comments that convey that the question is trivial. Always spend enough time with each participant to answer their questions fully so that both you and the participant are satisfied. If you cannot answer a question, say so. Get help from others in the group or from a colleague.

Clarify any issues that the participant finds confusing

Role plays allow you to see what participants do and do not understand. Do not always wait for a participant to ask for help. Instead, as you watch the participants, offer help during pauses or breaks, without interrupting. Help the participants understand how to solve practical problems in actual situations. Identify gaps in a participant's understanding and skills and provide help to correct them. If a participant has difficulty with the language used, make sure they receive the help needed to understand the concepts. Use language which is familiar to the participants.

Lead group discussions at the end of each role play

Ask questions to spark discussion. Use open-ended questions to get participants to share

information and experience. Open-ended questions are questions that require more than a yes or no answer. When you ask a question, pause long enough to give participants a chance to think about their answer and to respond. Allow silences so participants can have time to think before responding.

Check to see if participants are having problems, even if they do not ask for help

If you show interest and give each participant undivided attention, they will be more motivated. Also, if the participant knows that someone is interested in what they are doing, they are more likely to ask for help when they need it. Be available to the participants at all times; remain in the room and look approachable.

Answer participants' questions willingly and encourage them to ask questions when they arise rather than waiting until a later time. Call the participants by name when you talk with them. Maintain eye contact with the participants. Present information in the form of a conversation rather than by just reading it. Move around the room and use natural hand gestures. Speak clearly. Vary the pace and pitch of your voice. Paraphrase and summarize frequently to keep participants focused and clear on a particular idea and to keep discussions on track. Demonstrate enthusiasm for the work that the participants are doing.

Complement each participant for improvements in understanding, approach or progress. Get everyone in the group to share experiences so they can learn from each other. Encourage participants to explore how the role plays apply to their activities and how the IPC skills will help them in improving cure and case detection.

Manage

Make sure participants have access to supplies and materials when they need them (for example, chalk and board to write) and that there are no major obstacles to learning (such as too much noise, not enough light or not enough work space). Make the course interesting by giving examples from real work situations. Think about the skills taught in the role plays and how they can be applied to the participants' jobs. Add these to the points to be made when introducing or summarizing the role play. Discuss the application of new concepts to real problems. Ask participants whether they can use the skills that were taught, and discuss any potential difficulties in implementation of these skills. Do not summarily reject alternative methods suggested by the participants; discuss alternative methods thoughtfully and positively.

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ROLE PLAYS FOR DOCTORS

Example Role Play

INTRODUCTION

You are a doctor talking to a newly diagnosed TB patient. The Patient does not believe he has TB. He agrees for an X-ray, but not for sputum examination.

Sample Key Messages

Role Play Scenarios

1. Doctor is meeting with a patient diagnosed as having TB by a private doctor on the basis of an X-ray report. The patient wants free drugs without delay and without further examination.
2. Doctor is meeting with a newly diagnosed TB patient, a daily wage-earner and who is reluctant for direct observation because he does not want to miss work
3. Doctor is meeting with a chest symptomatic patient who is reluctant to give two sputum samples and is ready to bribe the doctor
4. Doctor is meeting with a newly diagnosed schoolboy who does not want to disclose his illness
5. Doctor is meeting with a newly diagnosed patient who is a truck driver and who says he will have difficulty coming to the local facility for DOTS when he is working
6. Doctor is meeting with a chest symptomatic patient from a tribal area who insists on hospitalization
7. Doctor is meeting with a newly diagnosed married woman who does not want her husband or family to know about her illness
8. Doctor is meeting with the father of a woman who is to be married and he does not want the community to know that his daughter has TB
9. Doctor is meeting with a newly diagnosed TB patient who wants to leave the area
10. Doctor is meeting with a newly diagnosed sputum-positive TB patient who is reluctant to bring in her family members for examination because she feels guilty about possibly having infected them

INTERPERSONAL COMMUNICATION

INTRODUCTION

For developing good interpersonal communication (IPC) skills, you, the trainer, will need to be aware of the duties that the doctors have to perform. These include explaining to the patient about TB and the importance of continuing treatment. They also include developing a strong bond with the patient to help motivate them to continue participation in the treatment. Doctors also need to be able to gain the trust of the patient's family and community. In addition, doctors must provide an example to their staff about how to interact with patients.

In this section, you will help the doctor participants become better at these duties through role plays. Through the role plays, poor IPC skills and good IPC skills will be demonstrated. Demonstrating poor IPC skills develops insight into common behaviours that occur in real situations. Identification of these will help in working towards developing good IPC skills. Therefore, for the role plays to be effective, two sessions will have to be done for each scene; one highlighting poor IPC skills and the other showing good IPC skills. In order to help the participants, understand the importance and potential pitfalls of non-verbal communication, perform the following exercise: Tell the participants to just observe you without making any comments. Then, sit down in a chair with your arms and legs crossed, your body turned slightly away from the participants, and an annoyed expression on your face. Swing your legs and gaze around the room. After about 30 seconds, ask the participants to describe what they were feeling when you were sitting in front of them. List their responses on the board or flip chart.

Then discuss:

- Do we communicate without words?
- Describe ways that we communicate without words.

Discuss with them that we need to be aware of what we are communicating non- verbally, for example, boredom, dislike, superiority, impatience We also need to be aware of what our patients and others communicate non-verbally, such as fear, embarrassment, discomfort and shame.

After this discussion, you will tell the participants that you are going to enact a role play scene for them. Tell them to watch for behaviours that depict poor IPC skills.

Next, choose another trainer (if available) or a participant (if no other trainer is available) to play the part of the patient in the following role play. A trainer should play the part of the Doctor. You will then enact the following role play scene using as many poor IPC skills as possible (for example, you will yell at the patient, you will have them stand while you sit, you will tell them facts using big words that they don't understand, and so forth).

After you have completed enacting the scene, ask the participants to list the poor IPC skills. Write these on the chalk board or flip chart. Then, go through each item listed and discuss the ways in which the poor behaviours could be improved. Spend as much time as needed to thoroughly discuss the poor behaviours. Be sure to discuss non-verbal communication elements such as eye contact, posture, nodding, encouraging or discouraging sounds, etc. Also discuss the messages about the NTEP that were conveyed during the scenario. Discuss the accuracy of the messages and, for inaccurate messages, discuss how they could be more accurately conveyed.

Once the discussion is finished, perform the scene again using only good IPC behaviours. Afterward, ask the participants to discuss the differences in the two role play scenes. Encourage them to discuss how the two different scenarios made them feel and how they think the patient and Doctor felt in each scene.

After this discussion, inform the participants that everyone in the group is now going to practice IPC skills by doing role plays themselves, with the other participants. Tell them that you will be handing out their roles and that they will perform the scene twice; once using poor IPC skills, followed by a group discussion on how the behaviours can be improved, and then again using good IPC skills.

Split the group of participants into smaller groups of no more than six people per group. Make sure each small group contains an even number of participants. Then, choose scenarios from the list of "Role Play Scenarios for Doctors" which can be found at the end of this chapter and write the roles on separate pieces of paper to give to the participants in each small group. You can also use your own experiences to come up with other role play scenarios and roles. Make sure that everyone receives a role.

After you have handed out the roles, give the participants a few minutes to think about how they will act out their role. Then, have the participants play each scenario in front of their small group using good IPC skills.

During the play by the trainees, circulate to each group to ensure that participants are exhibiting the appropriate IPC skills, such as smiling, sitting with the patient or other person, looking at the other person when speaking, pausing after asking questions, asking open- ended questions, etc. Also, use the following list of "Key Messages" to guide you as you watch the role play. After each role play by the participants, stop and have the group discuss the good ideas and IPC skills that were exhibited in the role play scene, and also discuss things that could improve IPC skills and improve the accuracy of NTEP messages.

Sample key messages

Listening and understanding

"Please sit-down."

"How are you feeling**?**"

"How many children do you have**?**"

"Where do you stay? How long have you been residing in this area**?**"

"What are their ages**?**"

"How is your wife/husband**?**" "Are they doing well**?**"

"What do you do for a living**?**"

"Tell me when you first fell sick. Since becoming ill what you have done to feel better**?**" "Have you ever been ill like this before**?**"

"Have you ever had to take injections for over two weeks**?**" "Have you ever had to take pills for many months**?**"

"Do you have a cough**?**"

"For how long have you been having a cough**?**"

"Is the cough dry or associated with expectoration**?**" "Do you have any fever**?**"

"What colour is the expectoration? Is it ever blood-stained**?**"

"Do you get a pain in the chest when you cough**?**"

"How is your appetite?"
"Have you noticed any weight loss, lethargy or weakness?" "What other symptoms do you have?"
"What medicines are you taking?"
"What medicines have you taken in the past?"
"Have you ever taken a medicine that turned your urine orange-red?"
"Has anyone in your family had an illness like this before?"
"Does anyone in your family also have cough?"
"Have you heard of TB?"
"What do you understand TB to be?" "What do you think causes TB?"
"Have you ever seen an X-ray?"
"What do you think X-ray shows?"
"Have you heard of the microscope sputum test to diagnose TB?"
"Have you ever had a blood or sputum test?"
"Do you know that we need to test your sputum two times to confirm whether you have TB?"
"Do you know that TB can be cured?"
"Do you know that TB can spread from one person to another if it is not properly cured?"
"Do you know that other people in your house can contract TB from you?"
"Do you know that till complete investigations are done we cannot assess the degree of damage that has been caused?"
"The tests to detect TB are simple and will have to be done at regular intervals to monitor improvement in your condition."
"You will have to take your medicines as prescribed so that your illness does not get worse."
"If you do not take medicines as prescribed, you can develop a more dangerous form of TB and you will spread the same to your family."
"Covering your mouth when you cough can prevent the spread of TB to others."

Demonstrating caring

"TB is not a disease which should cause worry as it is curable if drugs are taken regularly." "We want to make sure that you are completely cured."

"By following the treatment schedule, you will also make sure that you do not spread the disease to your near and dear ones."

"All treatment is free here, so please don't even think about money."

"Anti-TB medicines are strong drugs that must be taken under direct observation. This will ensure that you not only take the medicines regularly but also in the right dosage. This way I can know that you are responding well to treatment and if you have any problems."

"Anti-TB drugs can have side-effects in some people. If you take them under our supervision, we will make sure you do not have any uncomfortable side-effects and if you do we will be able to tackle them at the earliest and prevent any problems."

"At times people develop resistance to certain drugs and show no improvement when taken irregularly. If you take the medicines under our supervision, we will be able to observe that the drugs are having the required effect and you will continue to constantly getting better."

"If you have any doubts regarding the duration of treatment, the dosages of the drugs or any side-effects, please feel free to clarify your doubts with me."

"To make sure that I have explained things well, please show me on this calendar [show the patient a calendar] how long you must take medicines."

"I want to make sure that I give you the best medicines. That is why a sputum test is so important—so we can be sure that you are getting the right medicines."

"We don't want to unnecessarily give you a strong medicine, which is why all the tests are important. The tests will tell us how severe your condition is and we can give you the best medicines."

"If you have any doubts about the disease or the medicines, do not hesitate to ask me." "It is my responsibility to cure you."

"I am not only worried about you, but if you have TB and are not treated then your family may get sick, and obviously I do not want that to happen and I am sure you also don't want that to happen."

Motivating and Problem solving

"An ordinary cough does not last that long. You have been coughing for a month and we must find out why. Only when we know the cause can we cure it completely."

"A sputum test is very important in diagnosing the type of TB. Only then can we be sure that you are getting the right medicines for the right duration of time."

"TB is a disease and should not be a cause for worry as it is fully curable now but it should be diagnosed early so that it doesn't spread to other parts of the body or to others. Therefore, it is necessary to have your sputum tested."

"A chest X-ray will only tell us that you MAY HAVE TB. X-rays are just shadows and, like any shadow, can be caused by many different things. X-ray is not a 'pucca' test for TB."

"Sputum examinations do not cause any harm or discomfort. You just have to have two sputum examinations done as all treatment will be based on their results."

"If you have any doubts regarding sputum examination or want to know how to bring out sputum, you can either ask me or the laboratory technician. We will be happy to clarify your doubts and help you."

"If the sputum test confirms your disease you will get regular attention and treatment."

"A sputum test is very important for us to know what medicines should be given to you. We will start treatment as soon as we get the results of sputum examination."

"If I or my wife/husband had your symptoms, I would certainly have two sputum examinations done."

"The reason for conducting two sputum examinations is because one test may not be enough to detect the TB germs."

"It is important to understand that the better the diagnosis, the better will be the treatment and faster the cure. And for a good diagnosis you must go through all the tests as prescribed. The test

results will help us prescribe the best drugs for you."

"Yes, as soon as your sputum test results are available, we will also tell you whether you need to bring your family members for examination."

"Yes, your symptoms suggest that you MAY HAVE TB, but we cannot be sure till we test your sputum."

"Sputum tests are done free here, and of excellent quality. The test here is better than what you can get even in a private laboratory."

"The sputum test is much more accurate than an X-ray. We can actually see whether you have TB germs when we look at your sputum with a microscope."

"It is not just you but everyone like you who has a cough for two weeks or more has to go through all the tests, so that we can know exactly what the problem is and treat you accordingly."

"If it is convenient for you to come for your sputum tests on your off days, we could make adjustments for you accordingly. However, you must come for your tests on the appointed day without fail."

"To check your progress towards cure we shall again examine your sputum after two months."

"Tuberculosis is fully curable if complete treatment is given under DOTS."

"It is very important that the disease does not spread to anyone else, especially to your family members."

"After only a few days on the medication, you will stop infecting others, but you will have to continue on your medication for the full duration of 6 to 7 months."

"We will arrange for medicines to be provided near your home."

"I can understand that it is difficult for you to come every day. We will find a treatment observer near your place of work." Or "We will arrange for the treatment observer to give you medicines before you go for work."

"If I had TB, I would certainly come every day for treatment for six months and hence you will also be required to come."

"I understand that you do not want others to know that you have TB. We will be careful about that. But it is equally important that others do not get TB from you. If you do not take your medicines as advised, you will spread TB to others at home and work."

"Although TB is curable, cure can only take place through constant monitoring. This helps us to assess your response to the drugs. We have to make sure that there is continuous improvement and no untoward effects of medicines and that is why you are required to come on every day for six months."

"TB can be cured completely only if treatment is uninterrupted. And the only way to ensure regular treatment is to monitor it."

"Every dose is crucial and the treatment is designed for your complete cure."

"It is not in your interest to take medicines home. Medicines can be lost. It is also easy to forget to take medicines every day."

"If you forget to take even a few doses of medicine, you may fall ill again, in which case the dosage and duration of treatment may increase and would be very expensive and your chances of getting fully cured will be reduced."

"If you come in everyday, we can make sure you are getting better and we can observe if you are having any problems with the medicines."

"Once you are cured you will be able to work much better and earn more. So, it is in your interest to complete the entire course and come for regular check-ups as prescribed. These are all aimed at curing you completely."

"You don't want your wife and children to get tuberculosis from you. So, for their sake you should get well and for that you must take the prescribed treatment regularly and completely."

"If any of them have symptoms of the disease, they also need to be examined and treated."

"If your children are infected, they will be physically weak and may not be able to help out with the household chores or in the fields. More money will be spent on medications. So, it is better that you get yourself fully treated so that the question of their getting infected does not arise and they enjoy good health."

ROLE PLAY SCENARIOS

(These are only some examples. Use your own experiences to come up with other scenarios and roles.)

Scenario 1: Doctor is meeting with a patient diagnosed as having TB by a private doctor on the basis of an X-ray report. The patient wants free drugs without delay and without further examination

Write the following instructions on two separate pieces of paper and hand them out to two participants.

Doctor: You are a doctor who is seeing a patient diagnosed as having TB by a private doctor on the basis of an X-ray report.

Patient: You are a newly diagnosed TB patient who wants free drugs without further examination.

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Scenario 2: Doctor is meeting with a newly diagnosed TB patient, a daily wage-earner who is reluctant for direct observation because he does not want to miss work

Doctor: You are a doctor who is seeing a newly diagnosed TB patient in your office.

Patient: You are a TB patient who is a daily wage-earner and you do not want to come for direct observation because you do not want to miss work.

****

Scenario 3: Doctor is meeting with a chest symptomatic patient who is reluctant to give two sputum samples and is ready to bribe the doctor

Doctor: You are a doctor who is seeing a new patient in your office.

Patient: You are a person who has had a cough for several weeks with blood in your sputum and you have come to see the doctor. You do not want to give two samples of sputum and you are ready to bribe the doctor to just give you medicines without the sputum samples.

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Scenario 4: Doctor is meeting with a newly diagnosed schoolboy who does not want to disclose his illness

Doctor: You are a doctor seeing a schoolboy who has been newly diagnosed with TB.

Patient: You are a schoolboy who has been told you have TB and you do not want to disclose your illness to your family or your friends.

Scenario 5: Doctor is meeting with a newly diagnosed patient who is a truck driver and who says he will have difficulty coming to the local facility for DOTS when he is working

Doctor: You are meeting with a newly diagnosed patient in your office.

Patient: You are a truck driver and it is difficult for you to come to the local DOTS facility when you are working.

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Scenario 6: Doctor is meeting with a chest symptomatic patient from a tribal area who insists on hospitalization

Doctor: You are meeting with a new patient in your office.

Patient: You are a woman who has had symptoms of TB for several weeks and you want to be hospitalized until you feel better.

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Scenario 7: Doctor is meeting with a newly diagnosed married woman who does not want her husband or family to know about her illness

Doctor: You are a doctor meeting in your office with a woman who is a newly diagnosed TB patient.

Patient: You are a married woman who has been newly diagnosed with TB and you do not want your husband or family to know about your illness.

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Scenario 8: Doctor is meeting with the father of a woman who is to be married and he does not want the community to know that his daughter has TB

Doctor: You are a doctor meeting with a man who is not one of your patients but wants to talk with you.

Father of TB Patient: You are the father of a woman who is being treated for TB and you do not want the community to know that your daughter has TB.

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Scenario 9: Doctor is meeting with a newly diagnosed TB patient who wants to leave the area

Doctor: You are a doctor meeting in your office with a TB patient.

Patient: You are a newly diagnosed TB patient who wants to leave the area.

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Scenario 10: Doctor is meeting with a newly diagnosed sputum-positive TB patient who is reluctant to bring in her family members for examination because she feels guilty about possibly having infected them

Doctor: You are a doctor meeting in your office with a newly diagnosed sputum-positive TB patient and you would like her to bring in her family members for examination.

Patient: You are a newly diagnosed sputum-positive TB patient who is reluctant to bring in your family members for examination because you feel guilty about possibly having infected them.

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MODULE 4

PROGRAM MANAGEMENT IN PERIPHERAL HEALTH INSTITUTIONS FOR TB ELIMINATION

Learning objectives:

in this section the participants will learn about the following:

- Peripheral Health Institutions
- Role of PHIs in TB Elimination
- Patient care in PHI
- Infection control
- Program management in PHI
- TB Notification
- Ensuring notification of all TB patients
- Incentives
- Public Health Action by MO-PHI

Introduction

Prevention of infection, early diagnosis, universal DST, appropriate & prompt treatment and long-term follow-up for early detection of recurrence, are the key steps for elimination of tuberculosis. Management of LTBI & Co-morbidities are important components of NTEP. Patients suffering from tuberculosis are residing in the community with their close contacts. Hence all the above activities have to happen as close as possible to the patients' residences for the highest impact. Like all other communicable diseases, tuberculosis also has to be managed by the primary health care network of the country, which is designed for the delivery of public health services including basic clinical care.

Since the beginning of NTEP, TB units were considered as the basic reporting units. To facilitate recording and reporting, a Tuberculosis register was placed in all TUs. All patients initiated on NTEP treatment in any health facility in the jurisdiction of a TU had to be registered in the TB

register of concerned TU (Notification of TB cases on treatment in public sector). The responsibility of registering cases within a month of initiating treatment was vested with the Senior Treatment Supervisor of the TU.

However, this practice had one serious drawback. We were missing information on patients who were diagnosed but not initiated on treatment (initial loss to follow up) and patients treated with non-NTEP regimen. This prevented the high quality NTEP services to be extended to these patients. It also prevented loss of highly relevant programmatic information essential for planning and implementing TB elimination activities in the country. To overcome this, all cases of TB need to be tracked from the time of diagnosis irrespective of health care sector and notified from that time point.

Government of India has made TB a notifiable disease by an executive order of 7th May 2012 followed by a gazette notification on 19th March 2018. Based on the gazette, whenever a case of TB is diagnosed in the country by any healthcare provider, they must mandatorily notify this to the relevant public health authority. Failing to notify will attract prosecution under sections 269 and 270 of the Indian Penal Code (IPC), as the case may be (269 – Negligent act likely to spread infection of disease dangerous to life / 270 – Malignant act likely to spread infection of disease dangerous to life).

Notification can be directly done on Nikshay (Public and Private) by a registered healthcare provider/ Facility. Nikshay also allows further case management in terms of referral for advanced testing and transfer to any public/ private health facility across the country.

In this section, we will learn about the functions of a peripheral health institution in diagnosis, management and notification of TB cases.

Peripheral Health Institution

Peripheral Health Institution (PHI) is any health facility managed by at least one medical officer where diagnosis and management of TB happens. The range of services provided by various types of PHIs may vary. For example, a primary health centre (PHC) is a PHI managed by only one medical officer (a few in some cases) and supportive staff. All community based public health services like immunization, family planning, surveillance of communicable diseases and basic clinical services like diagnosis and management of uncomplicated diseases happen in PHCs. Referral centres like Sub-district/Taluka hospitals are PHIs with more medical officers including specialists and more supportive staff for specialized clinical care and minimal public health services. District Hospitals, General Hospitals and Medical College Hospitals are examples of PHIs with highly specialized tertiary care and limited public health activities. In all these PHIs, TB is diagnosed, treated and notified.

Is District TB Centre (DTC) a PHI? A DTC is the central program management unit of the district where the program manager is the District TB Officer (DTO). The post of DTO is a sanctioned and regular designated post and DTC is a program management unit at District level. DTC is supported by a Medical Officer, District Pharmacist, District Programme Coordinator (DPC), Public-Private Mix (PPM) Coordinator, DRTB/HIVTB supervisor, Accountant and Nikshay operator in program management. However, there is a PHI in DTC managed by Medical Officer of DTC (sometimes DTO acts as MO-DTC also), pharmacist, staff nurse, nursing assistant, laboratory technicians (LTs), clerical staff etc. It is called a DTC PHI and is always a DMC and most of the times a CBNAAT site also. Hence DTC not a PHI. Similar is the case of TB Unit, where the program manager is the MOTC (Block Medical Officer) supported by the Health Supervisors, STS and

STLS, and TU-PHI is managed by medical officers, staff nurses, pharmacists, LTs and nursing assistants.

NTEP has provided additional contractual staff to support general health system staff in program management at various levels. For example, a DPC, DRTB/HIVTB supervisor, and PPM coordinator is posted at DTC level, STS and STLS at TU level and a TBHV at PHI level in urban settings and medical colleges. Designated Microscopy Centre (DMC) and CBNAAT site are situated at PHIs level.

This description provides an overview of organization of NTEP activities at central and peripheral levels.

Role of PHIs in Program Management for TB Elimination

All PHIs diagnose and manage cases of TB. PHIs with predominant public health components do community interventions too. PHIs with predominantly clinical components do diagnosis and clinical management of TB. Thus, a primary health centre will do ACSM activities, active case finding, diagnosis and treatment of TB, treatment adherence support, contact investigation, domestic airborne infection control support, referral for universal DST, diagnosis of co-morbidities like HIV and diabetes, tobacco cessation, and support for direct benefit transfer, additional nutrition and Comprehensive Real time TB Information Management System–NIKSHAY. A medical college or district hospital in addition to diagnose and treat TB, will provide indoor facility for management of those TB patients who are seriously ill, have drug resistant TB, adverse drug reactions and co-morbid conditions. Medical College also support DTC in capacity building of health system through trainings and supportive supervision.

Let us now understand the role of a PHI in TB elimination in detail. As we have discussed, a PHC has the complete responsibility of public health activities including prevention, early detection, treatment and follow-up of all communicable diseases including TB among the population it caters to. Thus, the most important responsibility of a PHC/CHC in TB Elimination are as follows.

1. Case Finding Activities

1.1. Intensified case finding among the outdoor and indoor patients in the health facility.

1.1.1. Patients with TB symptoms may often report them to MO and staff (self-reporting/passive case finding). However, in many occasions, patients may fail to identify their symptoms. Hence it is always better to ask patients in the OPD and IPD about symptoms for TB. This activity is termed as intensified case finding from the health facility. Patients may be encouraged through appropriate audio/visual messages to report symptoms.

1.1.2. Referral for appropriate laboratory investigations

1.1.3. Current national policy is to have designated microscopy centre in as many or all PHIs according to requirement and wherever there is availability of a LT and a binocular microscope to improve access to diagnosis. Medical Officer should refer all identified presumptive pulmonary TB cases for sputum smear microscopy & Chest X-ray and presumptive EPTB cases for appropriate investigations.

1.1.4. MO of PHI not having a microscopy centre may maintain a 'presumptive TB register' for recording the details of presumptive TB cases identified in the OPD and referred for diagnosis, to track patients who do not report for testing. If the PHI is enrolling all presumptive TB cases in Nikshay, the register may be extracted from Nikshay

1.1.5. Presumptive TB cases with a negative sputum test result should not be ignored. Chest X-ray followed by CBNAAT is important to complete the diagnostic algorithm to ensure no TB case is missed.

1.2. Active case finding

1.2.1. Active case finding (ACF) is identifying population with high risk for TB and screening them for early detection of disease.

1.2.2. District TB centre, under the guidance of District Chief Medical Officer, will identify the population for active case finding. Each Block Chief Medical Officer (BCMO), in his block, will prepare the block wise micro plan with support from MO PHIs

1.2.3. MO PHI and team should organize field activities with good microplanning.

1.2.4. Logistics support will be provided by the DTO.

1.2.5. Under supervision of MO of PHIs, Government Health workers (MPW/ANM and equivalents), with the help of community volunteers, ASHA, Anganwadi workers, etc., should conduct field visits to identify presumptive TB cases and refer them to the MO using a referral slip.

2. Notification of all diagnosed TB cases

2.1. TB cases may be diagnosed amongst the presumptive cases referred for tests by the MO PHI or diagnosed elsewhere and transferred to the PHI for treatment. All these cases have to be entered in the 'PHI TB notification register'. If they are not notified in Nikshay earlier (process of notification in Nikshay is described below), MO and the PHI staff should notify them in Nikshay. All diagnosed cases, irrespective of their treatment status have to be notified.

2.2. After notification at diagnosis, cases that are expected to be initiated on treatment at other PHIs should be transferred to the respective PHI. This will help the MO and staff of the receiving PHI to enter the patients details in their notification register as a 'transferred in' case and arrange for treatment at a place and time convenient to the patient.

3. Universal DST

3.1. All diagnosed TB patients should be subjected for CBNAAT test for early diagnosis of resistance to Rifampicin.

3.2. All Rif sensitive TB patients will be subjected to first-line LPA. If H resistance is detected then it will be subjected to second line LPA and DST for Z. If there is rifampicin resistance, then it is subjected to First- and second-line LPA (for details refer to Integrated algorithm). Where the smear is negative, culture isolate is expected to be subjected for LPA.

4. Initiation of diagnosed patients on treatment

4.1. All patients residing in the area of the PHI, whether diagnosed in the PHI or transferred in, have to be initiated on treatment. Process of initiation of treatment has been discussed in detail in Module 3.

4.2. Patients with known susceptibility to Rifampicin and INH have to be initiated on first line regimen [2HREZ / 4HRE].

4.3. Patients with resistance to Rifampicin have to be started on shorter MDRTB regimen. After the diagnosis, patient should be counselled for pre-treatment evaluation and reporting to DTC.

4.4. Patients with H mono resistance have to be treated with H-mono/poly resistant regimen

4.5. All other patients (status of Rifampicin and INH unknown) have to be initiated on first-line regimen. Treatment regimen may be modified with availability new DST results.

4.6. Initiation of treatment should not be delayed waiting for DST results. Thus, for practical reasons, appropriate specimen for DST may be collected from all patients and first-line regimen may be started and later modified according to DST result. It is important to tell patients in advance that treatment regimen may change as more DST results become available.

5. Filling up of original and duplicate treatment cards

5.1.MO should fill the original (it is 'original' since it is the document written by the MO) treatment card with details of regimen according to weight-band and DST pattern.

5.2. Pharmacist / Nursing Staff / MPW / ANM should make a copy (duplicate) of the original card and send it to the treatment supporter with the drugs.

5.3. Pharmacist / Nursing Staff / MPW / ANM should also fill an identity card for the patient.

6. Providing support for treatment adherence

6.1. MO and staff should identify appropriate treatment supporter for the patient, educate patient, family members and treatment supporter on direct observation of treatment, ICT based adherence monitoring, ADR and follow up schedule.

7. Collection and entry of bank account details

7.1. MO and staff should ensure that the bank account details of the patient are collected and enteredin Nikshay for Direct Benefit Transfer of Nikshay Poshan Yojana.

8. Initial home visit

8.1. MPW / ANM should visit the house of the patient within a week of starting treatment

8.2. They will Counsel the patients and their families

8.3. They will screen contacts for symptoms

8.4. They will provide IPT to children under 6 years of age, after ruling out TB

8.5. They will Link the patient with other social support schemes

9. Monitoring adherence to treatment

9.1 Treatment supporter will observe each and every dose that the patient takes and makes entries in the treatment card.

9.2.Health supervisor / MPW / ANM will visit treatment supporter and patients regularly during every visit to the village

9.3. Health supervisor / MPW / ANM to check daily the ICT based treatment monitoring and also updates original treatment card at the PHI.

9.4. MO-PHI to review treatment cards and ICT based monitoring once in a week.

9.5. Retrieval of patients interrupting treatment within 24 hours of discontinuation be the Treatment supporter or ANM/ MPW

10. Monitoring of response to treatment, ADR and co-morbidities

10.1. MO-PHI to clinically review patients at least once in a month and as and when required

10.2. Follow up sputum examination at the end of IP and at the end of treatment

10.3. Other laboratory investigations to ensure control of co-morbidities, e.g. blood sugar

10.4. Referral to ICTC / F-ICTC for HIV testing

10.5. Referral to higher centres if necessary, to manage ADR and co-morbidities

11. Training and supervision of staff

11.1. MO-PHI and Health supervisors have to train their staff on NTEP, Nikshay and active case finding with the support of TU and DTC

11.2. They should also supervise the staff in their activities for TB elimination

11.3. They should ensure that all PHI level records of NTEP are maintained by the respective staff

11.3.1. Presumptive TB register (if any), referral slips

11.3.2. Stock registers of drugs, consumables and other logistics

11.3.3. TB Laboratory register

11.3.4. TB Notification Register

11.3.5. Supervisory register

11.3.6. Original treatment cards

11.3.7. Copies of monthly PHI report

12. Reporting

MO-PHI should submit a monthly report on program management and logistics (monthly PHI report to MOTC).

12.1 Add time line/ freezing policy

12.2 Add Monthly PHI report

13. ACSM Activities

13.1. Generation of awareness about TB in the community is important for prevention of infection and promoting seeking care for TB symptoms at the earliest. Medical officer and staff should plan for awareness activities through community meetings, door to door campaigns, school-based activities and similar communication strategies. Appropriate communication materials will be provided by the DTO.

13.2. Advocacy with local self-government officials, administrators and private sector managers for TB elimination will help MO and staff to gather local resources for TB elimination

13.3. Social mobilization activities by engaging local self-help groups, activists and TB survivors will generate demand commitment for TB elimination.

13.4. TB Forum-For a community-led response to TB, an institutional mechanism has been set up to support TB patients through their treatment and recovery

Infection control at PHI

Administrative control strategies for health-care facilities Administrative control measures (policies and work practices) have the greatest impact on preventing TB transmission. They serve as the first line of defense for preventing the spread of TB in health care settings.

Table 2: Summary of key recommendations on administrative controls

Outpatient Settings • Screen for respiratory symptoms as early as possible upon patient's arrival at the tealth care facility • Provide patient education on cough hygiene and sputum disposal • Segregate patients with respiratory symptoms • Fast-track patients with respiratory symptoms
Inpatient Settings • Minimize hospitalization of TB patients • Establish separate rooms, wards, or areas within wards for patients with infectionus respiratory diseases • Educate inpatients on cough hygiene and provide abeqate sputum disposal • Establish safe radiology procedures for patients with infectious respiratory disease, including smear-positive TB cases or TB suspects

Administrative controls for outpatient areas

The aim of administrative interventions in the outpatient area of any healthcare facility that manages patients with suspected tuberculosis is two-fold: (a) reduce the total time period that such a patient stays in the healthcare facility, and (b) reduce airborne transmission to other patients and healthcare workers in this limited time period. Given the heavy patient load at most health care institutions, it is but natural that patients of tuberculosis, like any other patient, have to sometimes wait long periods before they are actually examined by the physician. During this period, these patients are a constant source for airborne spread of disease to others. Reducing the overall stay of such patients in the healthcare facility is likely to prove the single-most effective measure of reducing airborne disease transmission in these areas. This can be achieved by fast tracking these patients, which itself can be accomplished by several measures that are not mutually exclusive. Fast-tracking will also depend upon the type of healthcare facility. At a chest centre/hospital, most patients are chest symptomatics where fast-tracking has no real application. But the process will be more useful for general hospitals and OPDs. The implementation of the key administrative interventions (screening, education, segregation, and fast tracking) would vary from facility to facility.

Screening: Screening for respiratory symptoms should occur as early as possible upon patient's arrival at the health care facility. Patients can be effectively screened at the registration counter itself by asking simple questions related to chronic respiratory symptoms, and those suspected to have tuberculosis can be given special cards or priority slips. The services of existing staff at the registration counter can be used for this purpose, or a special screening counter can be established prior to the registration process. This screening can be performed by physicians, nurses, paramedical staff and/or volunteers specially deputed for this purpose. If a separate screening counter is used, patients can be encouraged to first visit this counter if they have suggestive symptoms, by appropriate advertisements, posters or announcements in the registration area. Even if screening at registration is not possible, screening can occur when patients register at specific clinics or when in waiting areas.

Education on cough etiquette and respiratory hygiene: Another physical method that can prove useful for reducing airborne transmission is the provision patient education on cough hygiene and sputum disposal. This education can easily be imparted to patients through posters and other means in the waiting area, as well as by actual discussion by a paramedical staff or volunteers while the patient is waiting for his turn. Where possible, disposable medical masks can be provided to patients by health care workers or volunteers. These workers should also explain to patients how and when to use masks. Cough etiquette should be reinforced by all staff members when poor cough etiquette is observed. Disposal of sputum at health care settings need to be considered. Outpatient settings should make available tissue papers, and make bins with disinfectants accessible to patients for disposal of sputum. Wall posters with instructions on cough etiquette and sputum disposal should be provided; these handouts should be available at the NTEP IEC resource centre.

Patient segregation: Segregation of patients with respiratory symptoms can be achieved by having a separate waiting area for chest symptomatics, within the overall outpatient area. This is particularly important in larger institutions with heavy OPD loads. If feasible, a separate doctor can be deputed to assess these patients in the segregated waiting areas, so that these patients do not mix with other patients waiting in the outpatient area. Another alternative is to implement a patient flow control mechanism at the entry point of the waiting area, so that chest symptomatics (who have been screened earlier and are carrying priority slips or other similar identification) are diverted to this special area rather than the common waiting area. The outpatient area, more so this segregated area, should be well ventilated to reduce overall risk of airborne transmission.

Fast tracking of patients with respiratory symptoms: Those identified as patients with respiratory symptoms can be further fast-tracked in both their clinical and laboratory evaluation. One option could be to directly send these patients for sputum smear examination before they see a doctor. The other options are to allow these patients to jump the routine queue and be seen earlier than other patients, or to have totally segregated physician areas for these patients. The other important area where these patients can be given priority is while performing chest radiography. It is acknowledged that limited evidence is available to support the feasibility and effectiveness of these administrative interventions. In a setting of high patient load, it may prove difficult to screen and fast-track some patients at the expense of others, although with proper counselling and explanation, this may still be feasible. Patient misgivings, for instance in visiting the laboratory before the doctor, also need to be factored in. The site(s) of screening and the personnel involved need to be identified and/or created, and this may mean more administrative approvals. With all the ethnic, linguistic, social, economic and educational diversity existing in Indian patients, it is unlikely that a single measure will work well for all groups of patients. This field is an important area of operational research, and pilot projects need to be undertaken to identify what sets of administrative measures are likely to yield good results in a particular setting.

Administrative interventions in the inpatient areas

Minimize hospitalization of TB patients: One of the most effective means to reduce the risk of transmission of airborne pathogens such as M. tuberculosis in hospital settings is to manage such patients in the outpatient setting whenever possible. Many patients can be managed entirely as outpatients, thereby avoiding hospitalization and the risk of exposing other patients and staff. If hospitalized, patients should be re-evaluated frequently for possible discharge with continuation of therapy as outpatients.

Establish separate rooms, wards, or areas within wards for patients with infectious respiratory diseases: When hospitalization is required, patients with infectious respiratory diseases should be physically separated from other patients so that others are not exposed to the infectious droplet nuclei that they generate. Policies on patient separation inevitably generate concern about stigma, but with appropriate measures – such as training and public posting of separation rules – stigma can be minimized. Administrative procedures should ensure that separation happens promptly and automatically, similar to the automatic separation of men and women during inpatient admission. If sputum-smear microscopy or other relevant diagnostic tests are performed for patients with respiratory symptoms at the time of admission, then those who are most infectious can be quickly identified for separation from other patients.

Suggested priorities for separation of patients are as follows:

1. Separation of patients with confirmed or suspected diseases of public health concern, such as epidemic influenza, from all other patients.
2. Separation of sputum-smear positive TB patients from immune-compromised patients.
3. Separation of patients with known or suspected drug-resistant TB from immunecompromised patients.
4. Separation of patients with known or suspected TB from all other patients.

The best choice for infectious or potentially-infectious patients is to house and manage them in airborne precaution rooms. Where such airborne precaution rooms are not feasible, other options for physical separation include:

- Having a few small 'airborne precautions rooms' for patients with infectious respiratory disease patients.
- Having a separate ward designated for patients with infectious respiratory disease.
- Keep a designated area with better ventilation available for the placement of potentially-infectious patients.
- Where it is not possible to have a designated airborne precaution room, ward, or area of a ward, there can at least be an area designated as a "No Immune-Compromised Patient Area", where TB inpatients would be preferentially placed. This approach avoids specifically labelling patients as immune-compromised, HIV+, or having infectious TB. If properly implemented, this approach would keep vulnerable immune-compromised patients safely away from areas where infectious TB patients (if any) might be housed.

Educate inpatients on cough hygiene and provide adequate sputum disposal: Wards housing infectious patients should display sign boards in the ward demonstrating cough hygiene. All patients admitted in the ward/area should be issued surgical masks and counseled on their proper use. Adequate measures for safe collection and disposal of sputum

Establish safe radiology procedures for patients with infectious respiratory disease, including smear-positive TB cases or TB suspects: When caring for an infectious TB case / suspect, the radiology departments should attempt to:

- Schedule inpatient chest radiographs on infectious and suspect TB patients for non-busy times, such as the end of the afternoon.
- Provide coughing patients with a surgical mask to wear, or tissues or cloth to cover their mouths.
- Provide priority service to potentially infectious TB patients to minimize the length of time spent in the department.
- Restrict access to the radiology suite to patients and essential personnel only.
- Use the room with the best ventilation for taking images of potentially infectious TB patients.

Environmental controls

Environmental control measures are the second line of defense for preventing the spread of TB in health care settings. Environmental controls include ventilation (natural and mechanical), ultraviolet germicidal irradiation, filtration and other methods of air cleaning. It is important to recognize that if administrative controls (policies and work practices) are inadequate, environmental controls may not eliminate all the risk. Some environmental control measures are simple and inexpensive while many others are technically complex and expensive Environmental controls work on the same basic principle – dilution of infectious particles through real or 'effective' air exchange. In the case of ventilation, that dilution occurs through the introduction of fresh, uninfected air and the removal of infected air. In the case of UVGI or filtration, dilution is 'effective' through the creation and re-circulation of 'cleaned' air, in which infectious particles have been removed by irradiation or physical extraction. Certain circumstances may require directional control of airflow, so that air containing infectious particles is not introduced into clean air where staff or other patients are located.

Table 3: Summary of key recommendations on environmental controls

- Health-care facilities should seek to achieve minimum standards for air exchange. High-risk settings should be prioritized for immediate assessment and implementation of improved ventilation.
- In most settings, natural ventilation is the preferred method for ensuring adequate air exchange. Specific guidance on design and implementation of natural ventilation in health care facilities is available from WHO.[2]
- In existing health-care facilities relying on natural ventilation, ensure effective ventilation at all times and in all climatic conditions through proper operation and maintenance, and by regular checks to ensure fixed, unrestricted openings. If mechanical ventilation is used, the system should be well designed, maintained and operated, to achieve adequate airflow rates and air exchange.
- In high-risk settings where it is not possible to achieve adequate air exchange using natural ventilation, a complementary option is to use upper room or shielded ultraviolet germicidal irradiation (UVGI) devices.
- Optimal arrangement of patients and staff should be implemented in all outpatient departments, DOT centers, microscopy centers, and radiology
- Directional control of air flow is recommended in specific high-risk settings where infectious patients with drug-resistant TB or other acute respiratory diseases of potential concern are likely to be managed – i.e. airborne precaution rooms, MDR-TB wards and clinics, and bronchoscopy suites

2 World Health Organization. Natural Ventilation for Infection Control in Health Care Settings. Available at http://www.who.int/water_sanitation_health/publications/natural_ventilation/en/index.html

Ventilation

Ventilation can reduce the risk of infection through dilution and removal. When clean or fresh air enters a room, by either natural or mechanical ventilation, it dilutes the concentration of airborne particles, such as droplet nuclei, in room air. This is similar to opening of windows and doors to remove foul odours. Dilution reduces the likelihood that a person in the room will breathe air that may contain infectious droplet nuclei. As room air exchange doubles, the concentration of airborne particles in the room falls by half. Improved ventilation in health-care facilities is essential in preventing transmission of airborne infections and is strongly recommended. Better ventilation lowers the risk of transmission of TB and other airborne infections.

Table 4: Summary of advantages and disadvantages of different types of ventilation systems for health care settings

	Mechanical Ventilation	Natural Ventilation	Hybrid (mixed-mode) ventilation
Advantages	Suitable for all climates and weather	Suitable for warm and temperate climates	Suitable for most climates and weather
	More controlled and comfortable environment	Lower capital, operational, maintenance costs for simple implementations	Energy saving, relative to mechanical ventilation
	Occupants have limited control to affect ventilation	Capable of achieving very high ventilation rates	More flexible
Disadvantages	Expensive to install and maintain	Easily affected by outdoor climate and occupants behavior	May be more costly or difficult to design
	Can fail to deliver required ventilation rates, through faulty design, maintenance, or operation	May be difficult to plan, design, and predict performance	
	Noise from equipment	Reduced comfort level of occupants in extreme weather	
		Cannot achieve directional control of airflow, if required	

Natural ventilation is "controlled" when openings are fixed and unrestricted to maintain air flow at all times. Unrestricted openings (i.e. those that cannot be closed) on opposite sides of a room provide the most effective natural ventilation (Figure 1. In existing health-care facilities that have natural ventilation, when possible, effective ventilation should be achieved by proper operation and maintenance of openings, and by regular checks to see that openings remain free of obstruction at all times.

Figure 1: Schematic of a room with natural ventilation. Fixed unrestricted openings on both sides allow for adequate air exchange.

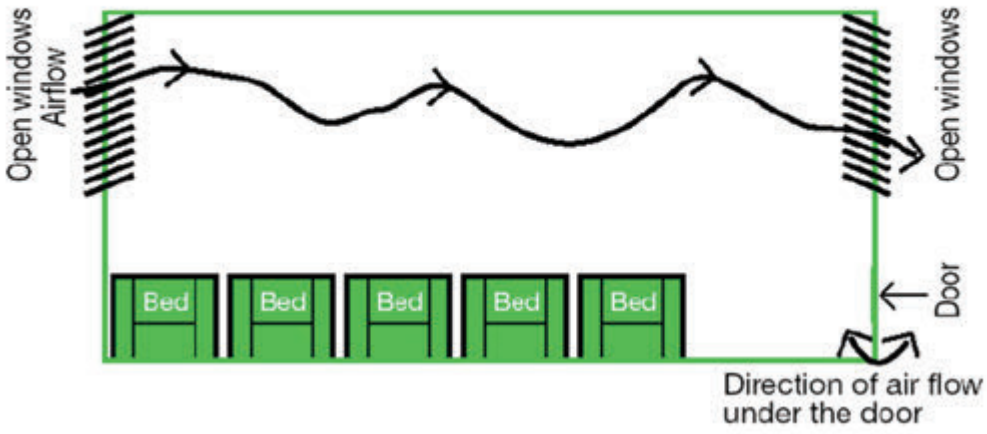


Table 4: Minimum air-changes per hour required for various health care settings

Type of Health-Care Setting	Minimum Air-Changes per Hour (ACH)	Minimum hourly averaged ventilation rates (liters/second/patient)
Registration areas	>6 ACH[3]	>40 l/s/patient
Outpatient departments and their waiting areas	>6 ACH	>40 l/s/patient
Inpatients departments	>6 ACH	>40 l/s/patient
High-risk settings and their waiting areas ART centres	>12 ACH[4]	80–160 l/s/patient

[3] Equivalent to >40 liters/second (l/s) for a 4×2×3m (24 m^3) room.
[4] Equivalent to >80 l/s for a 4×2×3m (24 m^3) room.

Where ACH is not able to be measured, as is usually the case in rooms with natural ventilation, the following standards for ventilation should be followed to ensure that air exchange is safely >12 ACH under all climactic conditions.

- Natural ventilation should be "controlled", with fixed, unrestricted openings that are insensitive to climactic conditions
- Openings should constitute >20% of floor area
- Openings should be on 2 sides, preferably opposite sides. For example, a 100 ft2 room should have >10 ft2 fixed, unrestricted openings on two sites, for a total of 20 ft2

Considerations for hot climates

Climactic extremes may require some adjustments to ensure that minimum ventilation standards are achieved. In the case of hot climactic conditions, the following design considerations should be made.

- Air conditioners are to be avoided, or very cautiously used in patient care areas. If air conditioners are used, it must be acknowledged that the need to maintain adequate ventilation for airborne infection control may to some degree necessarily compromise the comfort of room occupants and the efficiency of the air conditioner.
- Minimize solar heat gain through proper use of sunshades or external shading.
- Use outdoor shaded waiting areas to the greatest extent possible.
- Where augmentation of ventilation is required, use air supply fans may help improve thermal comfort, compared to exhaust fans.
- The use of evaporative coolers ("desert coolers") may be an effective solution to achieve both comfort and adequate ventilation, as these tend to have powerful fans. Proper maintenance, however, is essential.

An online tool for estimating the total fan rating for a given room can be found at http://www.csgnetwork.com/airexchangecalc.html. This reference is provided for convenience, and is not an endorsement of the site.

- The installation of "whirlybirds" (also known as whirligigs or wind turbines) that do not use electricity and provide a roof exhaust system can greatly increase both ventilation and comfort.

Considerations for cold climates In cold climates, high ventilations rates may adversely affect thermal comfort, and are difficult to achieve as windows may be closed to keep the building warm. Even if normal heating is introduced, high ventilation rates usually mean energy efficiency will be low. Therefore, ventilation and heating strategies must be planned carefully.

- Building design should seek to capture the solar heat and minimize conduction loss through the wall. Proper insulation of walls and the use of double glazing on windows are desirable.
- Where augmentation of ventilation is required, use air exhaust fans may help maintain adequate ventilation, even where windows or doors are closed.
- Targeted radiant or direct near-body heating methods are more effective than common convective radiators. This includes modern electric coil heaters and heated blankets/mattresses.

Optimal arrangement of patient and staff should be implemented in all settings. Health care staff should be mindful of the direction of airflow to ensure they are closest to the clean air source, and that patients are closest to the exhaust. This involves arranging patients and staff so that contaminated air is not likely to cross directly into staff/patient spaces. The natural direction of air flow should be between patients and staff, and not across patients and staff (Figure 4). This is especially important for settings such as DOT centres, OPD exam rooms, and smear microscopy laboratories.

Directional control of air flow is recommended in specific high-risk settings where infectious patients with drug-resistant TB or other acute respiratory diseases of potential concern are likely to be managed – i.e. airborne precaution rooms, MDR-TB wards and clinics, and bronchoscopy suites. This simply means having in place a system to minimize the chance that airflow goes from. In a room relying on natural ventilation that is situated away from other patient care areas, no additional changes would be required as there would be no area of concern for contaminated air to flow. It is important to keep the doors to corridor or other rooms closed, to prevent escape of infectious aerosols to other parts of the facility. The direction of air movement can be easily assessed using smoke tubes, strips of ribbon, or simply by observing the directionality of dense smoke from "Dhoop" or incense. Directional control of airflow can be achieved in mixed mode ventilation by proper attention to adequate exhaust and supply ventilation (as in Figure 3 above).

Figure 5: Schematic showing seating arrangement for patient and health care worker (red cross). In (A), natural ventilation would allow potentially infected air to cross health care worker. In (B), with this seating arrangement the chance of such exposure is lessened somewhat.

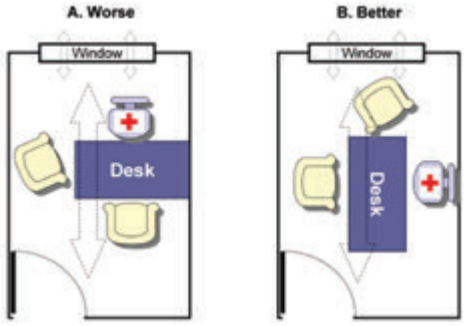
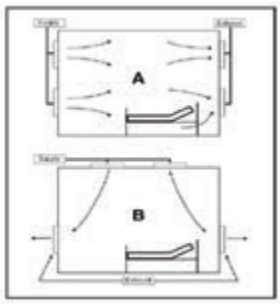


Figure 6: Schematic diagrams of mechanical ventilation, with optimal directional control or airflow in the room. In (A), supply is on one side, exhaust from the other, so aerosols are not dispersed to other patients or staff. In (B), supply is from the top, and again exhaust near the patient's head, for optimal directional control.



UVGI

Priority should be given to achieving adequate air exchange using ventilation (natural or mechanical). However, in some settings it is not possible to achieve adequate ventilation; for example, because of climatic changes (e.g. in winter or during the night), or building structure. In addition, in settings such as MDR-TB wards and ART centres, transmission of TB poses a high risk of morbidity and mortality. In high-risk settings where adequate ventilation is not possible, a complementary option is to use upper room or shielded ultraviolet germicidal irradiation devices.

Notification at Diagnosis

Let us try to understand more about the concept of notification at diagnosis.

A TB patient may be diagnosed in two ways, by any TB care provider. One way is to diagnose with microbiological evidence (microbiologically confirmed TB case) and the other way is to diagnose TB clinically in absence of microbiological evidence (clinically diagnosed TB). Health care providers who diagnose TB in either methods have to notify TB cases in Nikshay as early as possible, preferably on the same day (real-time entry). This process is termed as notification at diagnosis.

Basics of process of notification

As we know, the diagnostic process starts with identification of a presumptive TB case. Nikshay has a provision to enter the details of the presumptive TB case (Enrolment) and request for a diagnostic test online. This is a direct or prospective enrolment. However, in majority of the cases, the enrolment may start after diagnosis. In this situation, data entry should begin from the presumptive TB status. This is a lateral enrolment or retrospective enrolment.

To understand this concept better, let us think about a presumptive TB case identified by the Medical Officer of the PHI. The MO or the supportive staff in PHI can refer the patient for laboratory diagnosis to any NTEP diagnostic facility (e.g. DMC, CBNAAT site) by requesting a test. This can be done by filling up a Test request form on paper (NTEP Request Form for examination of biological specimen for TB) and/or in Nikshay. We have discussed the information to be collected and filled in during this step in Module 2.

Once all the relevant information pertaining to the presumptive TB case are entered in Nikshay and saved, a numeric ID is generated in Nikshay. This ID is termed 'Patient ID' and will uniquely identify the person. The patient can go to any NTEP diagnostic facility with this Patient ID for obtaining a test. After performing the test, to report the test result, a laboratory technician can log on to Nikshay, search for the patient details with the patient ID and simply enter the test result. Once the test result is updated in Nikshay, if it is microbiologically positive (AFB positive/MTB detected), the system identifies the patient as a diagnosed TB patient. This is real time notification.

Scenarios of Notification process

Scenario 1: Consider patient who was referred for laboratory investigation through a paper-based form. Here, the laboratory technician does not have an opportunity to search the patient in Nikshay by patient ID. Hence the LT has to enter all information from the request form in Nikshay (patient demographics and test request information). When the LT does that a patient ID will be generated. When the result is available, the LT enters the test result in Nikshay. If it is microbiologically confirmed (AFB positive / MTB detected), the system identifies the patient as a diagnosed TB patient. This process is also real time notification.

Instead of entering the details of all presumptive TB patients in Nikshay, the LT may enter the details of only the diagnosed TB cases starting with their presumptive status. Once the positive test results are entered, Nikshay recognises this patient as TB case. This process also is real time notification.

Scenario 2: Now let us consider a patient who is referred by a MO PHI through paper-based request form. The LT also reports a positive test result on the paper form. Since entry has not been done in Nikshay, it has not recognised this patient as a TB patient, and notification has not happened. Later the patient returns to the referring PHI, the MO or the supporting staff of the PHI, has to enter the details of the patient starting with presumptive TB status and the test result in Nikshay. And when the test result entered is positive, Nikshay recognises this patient as a TB patient. This process also is real time notification.

Scenario 3: Let us consider another example where a patient is clinically diagnosed as TB. In this case all his microbiological tests are negative. He is diagnosed by a clinician. Nikshay will recognise this case as a TB patient only if the status is updated in Nikshay as clinically diagnosed TB.

Scenario 4: Consider a TB patient seeking care in a private health facility. He may either be referred for diagnosis to a NTEP facility or a non-NTEP one. He is diagnosed to have TB. When referred to a NTEP facility, there is a high probability of the patient to be notified real time. If not, the information on diagnosis may reach NTEP late. It leads to a notification, but it will be a delayed notification done by the health system as proxy for the health practitioner.

Among all scenarios explained above, the most prompt and fastest notification happens through a prospective enrolment and real time notification. The worst situation would be a retrospective enrolment with a delayed notification where NTEP misses the opportunity to provide important public health actions to the TB patient. Hence NTEP encourages prospective enrolment where all presumptive TB patients are referred for diagnosis through Nikshay.

When all presumptive TB cases are referred for diagnosis through Nikshay, a few may not reach the laboratory and complete the test (Test pending). After testing, a few may be diagnosed to have TB microbiologically or clinically (Notified). Among majority of the presumptive TB, the disease will be ruled out by microbiological and clinical examination (TB not confirmed).

Example: 100 presumptive TB cases are referred for diagnosis from a PHC by enrolling in Nikshay. 10 were AFB positive in DMC, 4 had M.Tb detected in CBNAAT site. One was clinically diagnosed to have TB by expert clinician after negative reports from sputum smear microscopy and CBNAAT. All results including clinical diagnosis are updated in Nikshay. 10 presumptive TB cases did not reach any diagnostic laboratory. In this example, the number enrolled is 100, test pending is 10, notified TB is 15 and TB not confirmed is 75.

Nikshay dash board on desk-top, tablet PC or mobile application will show these numbers on logging-in.

Thus, enrolling all presumptive cases in Nikshay provides an opportunity to trace and test all the patients with a status of 'test pending' and re-evaluate the patients with a status of 'TB not confirmed' in future if necessary. This is crucial to accelerate the efforts to end TB in India by early and complete diagnosis of all TB cases.

If it is not feasible to refer all presumptive TB cases through Nikshay, the next best option is to enrol the patient retrospectively but immediately after diagnosis by completely updating the test

results including the clinical diagnosis. In this scenario, the 'test pending' and TB not confirmed will be always zero in Nikshay.

To achieve prompt enrolment and notification, medical officers, practitioners and their supportive staff of the public and private health facilities are to be sensitised/trained on enrolment and notification processes. Sensitization or training of these personnel one of the most important responsibilities of NTEP program managers (STO/ DTO/ MOTC) and key staff (STS/ STLS/ TBHV/ DEO).

Supportive systems for real time notification

We have understood the concept of real time notification. It is ideal to have all presumptive TB patients to be referred for appropriate tests by directly enrolling in Nikshay. However, availability of computer systems and internet connectivity is not uniformly adequate with every public PHI and private health care provider of the country. Even then immediate priority is to get all diagnosed TB patients enrolled and notified in Nikshay. Tablet computers have been made available to all NTEP key staff with this objective. However, states are encouraged to use the computer systems and internet connectivity in the PHIs and health facilities and the mobile phone applications for faster and effective notification.

While locally the most appropriate situation is enrolment and notification after diagnosis (retrospective enrolment and real time notification), the information of all patients diagnosed in the PHI must be available at one place. Though the treatment card of the TB patients is a good source of this information, it would be available for only patients initiated on NTEP treatment. Information on patients initiated on treatment using private ATT and patients in the private sector would be missed. Hence it is decided that all health facilities (public/private/individual TB practitioners) need to maintain a paper-based TB notification register which will contain all important information required for notifying a diagnosed TB patient in Nikshay.

Concept of an episode of TB

A person/ citizen may get affected with TB more than once in his lifetime. There is a chance that he may get re-infected with TB or there may be a change in the type of TB Disease (New to relapse or DRTB). So, one person may become a case of TB more than once and each event of that person getting diagnosed TB is a fresh episode of TB. For example; Mr. Ramu got diagnosed as a case of TB in January 2015 as a new case and later got cured; later in December 2015 he got diagnosed with TB again as a case of recurrent TB. The recurrent TB is the second TB episode of Ramu.

All episodes are required to be notified and each episode will be considered

as a fresh notification. For example, there might be 2456 notifications from your district; however, there might only be 2000 persons affected with TB.

In Nikshay each person is provided with a Patient ID and each episode is uniquely identified with an 'Episode ID'.

NTEP TB Notification register

TB notification register is different from erstwhile TB register. TB register was based at the TB unit and contained information on patients initiated on treatment somewhere in the jurisdiction of the TU. TB notification register is based at the PHI/health facility and contains information on all patients diagnosed in the PHI. Some of the patients in the notification register may be initiated on treatment in a different health facility, area, district or even in a different state. Additionally,

there may also be cases transferred in from other PHIs after being notified from there; these cases also are entered into the TB Notification Register of the PHI.

(If the patient is to be initiated on treatment in a different PHI, the patient has to be transferred to that facility through Nikshay or a paper-based transfer form as discussed in the previous module. Transfer for may have also to be used when a patient has to be transferred from one PHI to another during treatment. The State/District/TU/PHI from where the patient is currently on treatment is termed as Current State/ District/ TU/ PHI).

Check annexure for TB Notification register

The TB notification register has two portions. The left-hand side is to record information till initiation of treatment. The right-hand side is for follow up during and after treatment till 24 months after successful completion of treatment. We will now have a detailed understanding about each information recorded in the TB notification register.

Information on the left-hand side of TB notification register

TB Notification number (Episode ID): This is a seven-digit ID generated in Nikshay after his/her status has changed to Notified. This ID can be entered in notification register only after enrolling and updating a TB diagnosis result in Nikshay. The patients in a PHI notification register will not have serial IDs specific to that PHI. If the first patient of a PHI has a patient ID 1018192, the immediate next patient may have a patient ID 1976543 since other PHIs in the country might have enrolled many patients by the time in Nikshay.

Though enrolling a patient in Nikshay will generate the patient ID, notification process will not be complete. Notification will be complete only when a positive microbiological test result or clinical TB status of the patient is updated in Nikshay. Otherwise this patient will be shown as 'Test pending' in Nikshay.

Name in Full:
Age:
Sex:
Complete Address:

PIN code: PIN code of the post office of patient's address

Mobile/Landline number: If more than one number are available, record all

Aadhaar number: Aadhaar number is the Unique Identification Digit of an Indian Citizen. It will ensure that the correct person is provided TB care services. In addition, it will also ensure that the benefits like Nikshay Poshan Yojana are not denied to the to the right individual. However, Aadhaar number is not mandatory for TB services. Patient may be encouraged to voluntarily share the same.

Key population: Some patients are at increased risk for tuberculosis due to the presence of certain factors. Individuals with these vulnerabilities are included in the key population. These are contacts of TB patients, Diabetics, Tobacco Users, Prison Inmates, Miners, Migrants, refugees, Urban Slum Dwellers and Health Care Workers. Apart from the patients belong to key population, PLHIV, Children and EPTB will be directly tested with CBNAAT.

Type of patient: New, Recurrent, Treatment after Failure, Treatment After Loss to Follow Up, Transfer-in and Others

Site (P/EP): Pulmonary/Extrapulmonary
Case Definition:

Microbiological confirmation test result

Date:
Lab name:
Lab No.:

Test: Type of the microbiological test used to confirm diagnosis. If the patient is clinically diagnosed, mention the microbiological test, if done, and its result (Negative/M. Tb not detected) in the next column

Result of Test: Result of the test as described above.

Result of other tests: Result of other tests used to clinically diagnose TB (X-ray, FNAC, Histopathology, Clinical diagnosis etc.)

HIV status: Reactive, Non-reactive or Unknown. 'Unknown' will be marked only when the outcome of treatment is provided and the patient still has not undergone HIV testing

Diabetes status: Diabetic, Non-Diabetic, Unknown. Unknown will be marked only when the outcome of treatment is provided and the patient still has not undergone test for Diabetes

Date of sample sent for DST: After diagnosis, all new patients are expected to undergo universal DST with CBNAAT for Rifampicin and all previously treated TB patients with LPA for Rifampicin and INH. Specimen may not be available for some clinically diagnosed patients. Collecting second sample may be difficult in a few cases like EPTB, Children etc. Therefore, they are subjected for an upfront CBNAAT. If the patient is tested with CBNAAT upfront, the date of sample sent for DST is mentioned as the same date when the sample for CBNAAT is collected.

Result of DST: Rif sensitive, Rif Resistant, H Sensitive, H Resistant

Status of treatment: All patients are expected to be initiated on treatment as soon as possible after diagnosis. Patients with known resistance to Rif and/or INH will be initiated on respective regimens. All others will be initiated on a standard first-line regimen for 6 months. However, some of the patients might be transferred for treatment after notification to a health facility other than the diagnosing PHI, some may not be initiated on treatment, and some may be on private treatment. Another few may be wrongly diagnosed (especially clinical TB) when the diagnosing clinician revokes his decision. All these statuses are to be mentioned in this column.

Health facility for treatment: Health facility where the patient is initiated on treatment

Date of initiation of treatment: date on which the patient is initiated on treatment.

Information on the right-hand side of the TB notification register

Type of Regimen: The regimen on which the patient is initiated on treatment is recorded here. First Line regimen, if the patient is on a standard 6-month fist-line regime for new and previously treated patients (2HREZ + 4HRE). Shorter MDR-TB regimen, Conventional MDR-TB regimen, H-Mono/poly regimen, Regimen for MDR-TB with additional resistance to quinolones, Regimen for MDR-TB with additional resistance to SLID, XDR-TB regimen, new dug containing regimen and DST guided regimen are the currently available treatment regimen for DR-TB patients in NTEP.

Weight at the beginning of treatment: Weight has to be accurately measured and recorded in Kg for starting the patient on appropriate dosage in the correct weight band, to monitor

response to treatment and to manage malnutrition if present.

Dosage Frequency: Currently only daily regimen is administered under NTEP.

Follow-up Smear Examination

End of IP

Date: Date on which the sputum smear result is collected for follow up.

DMC Name: Name of the DMC where the follow up examination was performed.

Smear result: Grading in red ink if the result is positive and Neg in blue if smear is negative.

Date of sample collected for DST: All patients found to be smear positive on follow up are identified as presumptive DRTB cases. Fresh paired samples of sputum have to be collected from them and sent for CBNAAT. The date on which the sample was collected for CBNAAT has to be mentioned here.

Result of DST: Result of CBNAAT is to be mentioned here.

End of Treatment

Date: Date on which the sputum smear result is collected for follow up.

DMC Name: Name of the DMC where the follow up examination was performed.

Smear result: Grading in red ink if the result is positive and Neg in blue if smear is negative.

Date of sample collected for DST: All patients found to be smear positive at the end of treatment are "Failure" and identified as presumptive DRTB cases. Fresh paired samples of sputum have to be collected from them and sent for CBNAAT. The date on which the sample was collected for CBNAAT has to be mentioned here.

Result of DST: Result of CBNAAT is to be mentioned here.

Treatment Outcome

Outcome with date: Cured, Treatment Completed, Died, Lost to follow up, Failure, Not evaluated or Treatment change

If HIV reactive

All PLHIV have to be started on Co-trimoxazole Preventive Therapy (CPT) and Antiretroviral Therapy (ART). These treatments are started from the ART Centre. The information is to be sought and updated in the notification register with the dates of starting ART and CPT.

Post Treatment follow-up

TB patients are followed up periodically after successful completion of treatment for 24 months.

They are to be told at the time of declaration of outcome that in case they develop TB symptoms later, they should report for testing for TB. Even if they do not report in between, MO-PHI and supportive staff have to screen all patients for presence of symptoms of TB at the end of 6th, 12th, 18th and 24th month after completion of treatment and do a sputum culture in presence of symptoms to diagnose recurrent TB.

Notification of patients seeking care in private sector

A significant proportion of the TB cases seek care in the private sector. Preference of health care sector is the choice of the patient. NTEP is committed to provide TB care services to all TB patients irrespective of the sector of choice. A private care provider is doing an important TB elimination service by diagnosing TB patients and providing correct and complete treatment.

All health care providers including private providers have to notify TB cases at diagnosis. To enable this process, District TB Officers have to ensure that all such providers (Hospitals, clinics, laboratories, individual practitioners, chemists) are registered in Nikshay. Healthcare providers can register themselves on Nikshay (and obtain user credentials) or DTO register them in Nikshay (and convey user credentials to each private provider). This will enable them to log on to Nikshay and notify TB cases while ensuring the confidentiality of their patient data. The patient data is available only to the public health authorities. This information will help public health authorities to provide public health action to all TB patients.

For seamless notification, there needs to be facilitatory mechanisms in the premises of private providers and between the private provider and NTEP authorities. Let us understand this through a few examples.

Example 1. Let us consider a major private hospital, with a number of specialty departments, units and indoor and outdoor patients. This health facility has a Nikshay User ID and password. However, unless the information of all patients diagnosed in the hospital reach the personnel handling the user ID and password, all the cases will not be notified. Hence all major hospitals should have a single window system established, which will collect the information of newly diagnosed TB cases from all departments on a daily basis and notify them in Nikshay. Alternatively, staff from various units can visit the single window, document the details in the notification register and the nodal person for notification [PRO, nursing assistant, receptionist, pharmacist etc.] can notify the same in Nikshay on the next day. It is also to be mentioned here that, an incentive of Rs.500/- is provided to enable these processes. DTO and key staff are expected to support the private health facility to establish the single window system and train the nodal person from the concerned private facility in Nikshay. A PPM coordinator is provided to assist DTO and support NTEP key staff in coordinating with private providers.

Additionally, the single window will also help the hospitals to track patients by phone calls [and also by house visits where capacity for outreach activities is there] and to remind them on follow up schedules and treatment. This will serve as support mechanism for adherence.

Filling up of TB Notification register

Exercise -4

Using workbook E3, complete the TB Notification register using six treatment cards which you have completed in exercise E2.

Arun Kumar (Patient A)
Pooja Gupta (Patient C)
Lakshmi Kumari (Patient D)
Narendra Kumar (Patient F)
Girija Devi (Patient H)
Kailash Nath (Patient J)

Exercise-5

Complete the transfer form for the appropriate patient mentioned in module three.

Exercise -6

1. What information is recorded in the TB notification Register at the time of notification?
2. Who is responsible for notification of TB patients and when should be the patient notified?
3. What is public health action and who is supposed to do it? list the actions to be taken.

Notes

ANNEXURES

- NTEP Request Form for examination of biological specimen for TB
- TB Laboratory Register
- Referal slip
- TB identity card
- NTEP PMDT Treatment Card
- NTEP PMDT Treatment Book
- Referral /Transfer form for treatment
- NTEP PMDT Referral for treatment form
- TB Notification Register
- NTEP PMDT Treatment Register
- NTEP Laboratory Register for CBNAAT and CDST
- Annexure EQA formats

Annexure 15A

NTEP Request Form for examination of biological specimen for TB

(Required for Diagnosis of TB, Drug susceptibility Testing and follow up)

Patient Information			
Patient name		**Age (in yrs):**____	**Gender:** ☐M ☐F ☐TG
Patient mobile no. or other contact no.		**Specimen collection date** (DD/MM/YY) _____	☐ **Sputum** ☐ **Other (specify)**_____
Aadhaar no.(If available)			
Patient address with landmark		**HIV Status:** ☐Reactive ☐Non-Reactive ☐Unknown	
		Key populations: ☐Contact of known TB Patient ☐Diabetes ☐Tobacco ☐Prison ☐Miner ☐Migrant ☐Refugee ☐ Urban slum ☐Health-care worker ☐Other(specify) _____	

Name and Type of referring facility
(PHI/DMC/TU/ DTC/ICTC/ART/Medical College/DR-TB Centre/Private Others, specify):
_____
Health Establishment ID (NIKSHAY): _ _ _ _

Episode ID: _____

Test request ID: _____

State: _____ **District:**_____ **Tuberculosis Unit (TU):** _____

Reason for Testing

Diagnosis and follow up of TB		
Diagnosis of TB		Follow up (Smear and culture)
H/O anti TB Rx for >1 month: ☐ Yes ☐ No		Reason: ☐ End IP ☐ End CP Post treatment: ☐ 6m ☐ 12m ☐ 18m ☐ 24m
☐ Presumptive TB ☐ Repeat Exam ☐ Private referral ☐ Presumptive NTM	Predominant symptom _____ Duration _____ days	

Diagnosis and follow up Drug-resistant TB		
Diagnosis of DR TB (DRT/ DST)		Follow up (Smear & culture)
Presumptive MDR TB	☐ New ☐ Previously treated ☐ At TB diagnosis ☐ Contact of MDR/RR-TB ☐ Follow up Sm+ve ☐ Private referral ☐ Discordance resolution	Type of case: ☐ H mono/poly TB ☐ MDR/RR TB ☐ XDR TB Regimen Type: ☐ All oral H mono/poly TB ☐ Shorter MDR TB regimen ☐ All oral longer regimen
☐ Presumptive H mono/poly		
Presumptive XDR TB	☐ MDR/RR TB at Diagnosis ☐ Follow up culture positive _____Months ☐ Failure or recurrent of MDR/RR-TB regimen ☐ Discordance resolution	Regimen composition for all oral longer regimen: ☐ Lfx ☐ Mfx^{h} ☐ Bdq ☐ Lzd ☐ Cfz ☐ Cs ☐ Z ☐ E ☐ Eto ☐ Dlm ☐ Am ☐ Km ☐ Cm ☐ _____ Treatment follow up month: _____

Test requested:

☐Microscopy ☐TST ☐IGRA ☐Chest X-ray ☐Cytopathology ☐Histopathology ☐ CBNAAT ☐ TrueNat ☐ Culture ☐DST ☐FL -LPA ☐SL -LPA ☐Gene Sequencing ☐Other (Please Specify) _____

Requested by (Name, Designation and Signature): _____
Contact Number:_____ Email ID:_____

Results: **NIKSHAY ID** Generated: _____

Microscopy (☐ ZN ☐ Florescent)							
	Lab Sr. No	Visual appearance	Result				
			Negative	Scanty	1+	2+	3+
Sample A		S M B					
Sample B		S M B					

Date tested: _____ **Date Reported:**_____ **Reported by:**_____
Laboratory Name: _____ **(Name and Signature)**

Nucleic Acid Amplification Test (NAAT)	Lab serial _____			
Type of test	☐ CBNAAT	☐ TrueNat		
Sample	☐ A	☐ B		
M. Tuberculosis	☐ Detected	☐ Not Detected	☐ N/A	
Rif Resistance	☐ Detected	☐ Not Detected	☐ Indeterminate	☐ N/A
Test	☐ No Result	☐ Invalid	☐ Error – Error Code_____	(Please arrange for fresh sample)

Date tested: _____ **Date Reported:**_____ **Reported by:**_____
Laboratory Name: _____ **(Name and Signature)**

Culture (☐ LJ ☐ LC)

Lab Sr. No	Negative	Positive	NTM (write species)	Contamination

Date Result: _____ **Date Reported:**_____ **Reported by:**_____
Laboratory Name: _____ **(Name and Signature)**

First line LPA

Lab serial _____ ☐ Direct ☐ Indirect

Drug	Resistant detected	Final interpretation	Remark
Rifampicin (R)	☐ Yes ☐ Inferred ☐ No	If yes or inferred, R should not be given	
Isoniazid (Kat G)	☐ Yes ☐ Inferred ☐ No	If yes or inferred, H(h) should not be given	
Isoniazid (Inh A)	☐ Yes ☐ Inferred ☐ No	If yes or inferred, H (h) can be considered & Eto should not be given	

Date Result: _____ **Date Reported:** _____ **Reported by:** _____
Laboratory Name: _____ **(Name and Signature)**

Second line LPA

Lab serial _____ ☐ Direct ☐ Indirect

Drug	Resistant detected	Final interpretation	Remark
Levofloxacin	☐ Yes ☐ Inferred ☐ No	If yes or inferred, Lfx should not be given. Mfx (h) can be considered.	
Moxifloxacin	☐ Yes ☐ Inferred ☐ No	If yes or inferred, Lfx & Mfx (h) should not be given	
Amikacin	☐ Yes ☐ Inferred ☐ No	If yes or inferred, Am should not be given	
Kanamycin	☐ Yes ☐ Inferred ☐ No	If yes or inferred, Km should not be given	
Capreomycin	☐ Yes ☐ Inferred ☐ No	If yes or inferred, Cm should not be given	

Date Result: _____ **Date Reported:** _____ **Reported by:** _____
Laboratory Name: _____ **(Name and Signature)**

Drug Susceptibility Test (DST) results

Lab Sr.No	1st line drugs					SLI				FQ				Other										
	R	H (inhA)	H (katG)	Z	E	S	Km	Cm	Am	Lfx	Mfx (0.5)	Mfx (1)	Mfx (2)	PAS	Lzd	Cfz	Clr	Azi	Bdq	Dlm	Eto	Cs		

Date Result: _____ **Date Reported:**_____ **Reported by:**_____
Laboratory Name: _____ **(Name and Signature)**
R: Resistant; S: Susceptible; C: Contaminated; -- Not done

Other tests for TB diagnosis

Test (Please Specify): _____
Result:_____
_____
Date reported:_____ **Reported by:**_____
Laboratory Name: _____ **(Name and Signature)**

Annexure 15 K

TB Laboratory Register

Lab. Serial No.	Date of collection of first specimen	Name (in full)	Age	Sex M/ F/TG	Complete address (for diagnosis patients) & Phone No.	Key Population[1]	Name and type of referring health facility[2]	Reasons for Examination						
								Presumptive TB / RE / Presumptive NTM	Predominant symptom[3] & its duration[4]	History of >1 month ATT (Yes/No)	Follow-up			
											Patient ID	Regimen New / H mono/ Shorter	Month	Post Treatment follow up month

[1] Key population – 1. Contact of TB/DRTB case, 2. Tobacco, 3. Prison inmates, 4. Miner, 5. Migrant, 6. Refugee, 7. Urban slum, 8. Health-care worker, 9. Other vulnerable population (specify)

[2] Name of referring health facility-PHI/DMC/TB/DTC/ICTC/ART/Medical College/DR-TB centre / Private/ Others, specify

[3] Predominant symptoms: Cough-C, Fever-F, Haemoptysis-H, Weight loss-W, Night Sweat - N Others-O, No symptoms - NS

[4] Duration of predominant symptoms should be recorded in days

Type of specimen	Visual appearance[5]		Results		Date of Result	HIV status (Reactive/ Non Reactive/ Unknown)	Diabetic status (Diabetic/ Non Diabetic/ Unknown)	Sample for DST sent (Y/N) with date	DST result[7] (write the drugs to which resistance is demonstrated)	Episode ID (notification no.)	Treatment initiation details (TB No. & TU details) / Referral for treatment	Signature	Remarks[8]
	a[6]	b[6]	a[6]	b[6]									

[5]Visual appearance- mention M, B, or S., Mucopurulent, Blood stained or Saliva

[6]a- stands for supervised spot sample, b- stands for early morning sample

[7] Sensitive= if sensitive to tested drugs, Name of drug if resistant to any – R= Rifampicin, H=Isoniazide, E=Ethambutol, Z=Pyrazinamide, SM=Streptomycin Lx=Levofloxacin, Mx (0.5) or (1) =Moxifloxacin, Km=Kanamycin, Cm=Capreomycin, Am=Amikacin, Eto=Ethionamide, Lzd=Linezolid, Cfz=Clofazimine

[8] Remarks column can include date of starting treatment, treatment regimen, TB no., referral details with date, remarks on un blinded rechecking, etc.

SR No. _____

REFERRAL SLIP

(Referring health facility copy)

Date: .....Lab referred to:.....
Name of referring HF: .....
Name of Patient: .....
Age: ..... years Sex: M / F / TG
Address of patient (with landmarks)

.....

.....

.....
Patient's / Contact person's Mobile number :

_____

Kindly tick

- ☐ Cough.....days
- ☐ Fever.....days
- ☐ Loss of weight .....days
- ☐ Night sweat .....days
- ☐ Blood in sputum/ cough .....days

☐ Contact of TB / MDR TB

Patient ID. _____ _____

Stamp of HF Referred by (Name & Sign)

SR No. _____

REFERRAL SLIP

(Patient copy)

Date: .....Lab referred to:.....
Name of referring HF: .....
Name of Patient: .....
Age: ..... years Sex: M / F / TG
Address of patient (with landmarks)

.....

.....

.....
Patient's / Contact person's Mobile number :

_____

Kindly tick

- ☐ Cough.....days
- ☐ Fever.....days
- ☐ Loss of weight .....days
- ☐ Night sweat .....days
- ☐ Blood in sputum/ cough .....days

☐ Contact of TB / MDR TB

Patient ID. _____ _____

Stamp of HF Referred by (Name & Sign)

SR No. _____

REFERRAL SLIP

(Lab Copy)

Date: .....Lab referred to:.....
Name of referring HF: .....
Name of Patient: .....
Age: ..... years Sex: M / F / TG
Address of patient (with landmarks)

.....

.....

.....
Patient's / Contact person's Mobile number :

_____

Kindly tick

- ☐ Cough.....days
- ☐ Fever.....days
- ☐ Loss of weight .....days
- ☐ Night sweat .....days
- ☐ Blood in sputum/ cough .....days

☐ Contact of TB / MDR TB

Patient ID. _____ _____

Stamp of HF Referred by (Name & Sign)

TB identity card

Name: _____

Sex ☐ M ☐ F ☐ TG Age: _____

Address: _____

_____

_____

Contact No: _____

Aadhar ID. _____

PHI _____ TU _____ District _____

Episode ID: _____

Name and designation of treatment supporter:

_____

Contact number and address of treatment supporter:

_____

☐ CPT ☐ ART ☐ Diabetic ☐ Smoker

Date of starting treatment: _____ (DD/MM/YYYY)

Weight Band:

Adult: ☐ 25-34 Kg ☐ 35-49 Kg ☐ 50-64 Kg ☐ 65-75 Kg ☐ ≥75 Kg

Pediatric: ☐ 4-7 Kg ☐ 8-11 Kg ☐ 12-15 Kg ☐ 16-24 Kg ☐ 25-29 Kg ☐ 30-39 Kg

Site of Disease

☐ Pulmonary ☐ Extra pulmonary

Type of Patient

☐ New
☐ Recurrent
☐ Treatment after Lost to Follow up
☐ Treatment after Failure
☐ Other, Previously treated
☐ Transferred in

Case Definition

☐ Microbiologically confirmed
☐ Clinically diagnosed TB

Dosage:

☐ FDC or ☐ loose medicines

Sputum results

	Smear Date	Smear Result	Culture Date	Culture Result
Diagnosis				
End IP				
End RX				
6 months				
12 months				
18 months				
24 months				

Treatment outcome: _____

Date: _____

Appointment dates

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

In case of side effects or queries please contact

Name and contact number:

_____

_____

Annexure 15 C

National Tuberculosis Elimination Programme

Treatment Card

Episode ID _____

State:_____ City / District: _____ TB Unit:_____ PHI: _____ Area: Tribal / Rural / Urban / Urban slum

Name: _____Sex: ☐ M ☐ F ☐ TG Age: ____ Marital status: _____ Occupation: _____ Socioeconomic status: APL/ BPL

Complete Address: House No. _____ Road: _____ Important landmark: _____ Ward/Village: _____ Town/City: _____

Taluka/Mandal:_____Pin code: _____ Mobile:_____ Aadhaar No.: _____ Key population: Contacts / Miners / Refugees / Migrants / Prison inmates

Name and Address of contact person _____ Mobile No. _____

Name of Treatment Supporter _____Designation _____Mobile No.: _____

Initial home visit by _____ Date_____ Type of Treatment Adherence – DOT / Family DOT / ICT supported, specify _____ / Other _____

Predominant symptom _____ Duration _____day Number of health care providers visited before diagnosis for current episode: _____

Site of disease

☐ Pulmonary
☐ Extra Pulmonary
Site _____

Type of Patient

☐ New ☐ Recurrent
☐ Transferred in ☐ Treatment After Failure
☐ Treatment after lost to follow up ☐ Others, previously treated (Specify)_____

Case Definition

☐ Microbiologically confirmed
☐ Clinically diagnosed TB

Investigations (ZN / FM / NAAT / Liquid C / Solid C)	Date	Lab	Lab. No.	Test result	Sample sent to CDST (date)	DST result
Pre-treatment						
End of Intensive Phase						
End of treatment						

H/O of Previous ATT: ___ months of treatment ___ months since end of last episode

Source of treatment: ❑ Public ❑ Private Previous regimen: _____

Other investigations (if any) with date and result

HIV related information

HIV Status: ❑ Unknown ❑ Reactive ❑ NR Date_____ PID_____

CPT delivered on: (1) (2) (3) (4) (5) (6)

Initiated on ART: ☐ No ☐ Yes Date & ART No._____

Diabetes related information

Diabetes Status: ❑ Unknown ❑ Diabetic ❑ Non-Diabetic

RBS: At diagnosis _____ FBS_____ End IP____ End of Rx____

Initiated on ADT: ☐ No ☐ Yes Date & ADT No._____

Other co-morbidity

Details _____

Signature of MO with date _____

	<6yrs	>6yrs
No. of household contacts		
No. screened		
No. with symptoms		
No. evaluated		
No. diagnosed		
No. put on treatment		

No of children less than 6 years given chemoprophylaxis = _____

Name	Wt (Kg)	Dose (mg)	1	2	3	4	5	6

Addiction related information

Current Tobacco user ❑ Yes ❑ No
If yes, ❑ Smoking ❑ Smokeless Linked for cessation ❑ Yes ❑ No
If tobacco user, status of tobacco use at end of treatment ❑ Quit ❑ Not quit
H/o Alcohol intake❑ Yes ❑ No
If yes, linked for deaddiction ❑ Yes ❑ No

Date of initiation of intensive phase _____ **Date of initiation of continuation phase** _____

Weight _____ (kg) Height_____ (cm) Drug packaging ❑ PWB ❑ Strips Dosages: FDC _____ pill per day/ Loose drug

Weight Band: Adult: ☐ 25-34 Kg ☐ 35-49 Kg ☐ 50-64 Kg ☐ 65-75 Kg ☐ ≥75 Kg

Pediatric: ☐4-7Kg ☐8-11 Kg ☐12-15 Kg ☐16-24 Kg ☐25-29 Kg ☐30-39 Kg

Loose drugs		H	R	Z	E
	Dose				
	Pills				

Mark ✓ when doses are taken under direct observation, ✓ when the dose was not observed, O when missed the dose

Record CP from fresh line

Month/ year	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	Wt

Retrieval Actions for Missed Dose

Date	By Whom	Whom contacted	Reason for missed doses	Outcome of retrieval action

Details of Adverse events

Date of adverse event	Details of symptoms	Action taken	Duration of management for adverse event	Outcome of adverse event

Post treatment follow up clinical & sputum (Results with date)

Follow up	Clinical	CXR	Smear	Culture	Impression
6 mths of Rx					
12 mths of Rx					
18 mths of Rx					
24 mths of Rx					

Remarks_____

Nikshay Poshan Yojan: Cash/ Kind

Benefit paid till ☐1st ☐2nd ☐3rd ☐4th ☐5th ☐6th months

Treatment outcome: _____ **Date:**_____

Signature of MO with date: _____

NTEP PMDT Treatment Card

Episode ID	PMDT No.	PMDT No.

Patient's name: _____

Age: _____yrs Gender: ☐ M ☐ F ☐ TG

Address: _____

_____

Marital status: _____

Occupation: _____

Contact No: _____

Aadhar ID _____

Name, designation of treatment supporter: _____

_____Contact no:_____

State:_____ District: _____TB Unit: _____

PHI:_____

Initial home visit: Date _____ By:_____

DR TB Centre:_____ District _____State _____

Reason for Testing	
☐ New ☐ Previously Treated	
☐ Presumptive TB ☐ Private Referral ☐ Presumptive NTM	
Presumptive MDR TB	☐ At diagnosis ☐ Contact of MDR/RR TB ☐ Follow up Sm+ve at end IP ☐ Private referral
☐ Presumptive H mono/poly	
Presumptive XDR TB	☐ MDR/RR TB at Diagnosis ☐ Follow up culture positive _____Months ☐ Failure or recurrent of MDR/RR-TB regimen

Drug Susceptibility Test (DST) results at Diagnosis													Spec. coll. Date:								
R	H (inhA)	H (katG)	S	E	Z	Km	Cm	Am	Lfx	Mfx (0.5)	Mfx (2)	FQ class	SLI class	SLI (eis)	Eto	PAS	Lzd	Cfz	Clr	Azi	Bdq	Dlm
Name of the lab														Result report date								

*R: Resistant; S: Resistance not detected; C: **Contaminated**; **--** Not done/available*

Contact tracing	<6yrs	>6yrs
No of household contacts		
No of members screened		
No of presumptive TB cases identified		
No of presumptive TB cases evaluated		
No diagnosed with TB		
No of DR-TB diagnosed		
No. put on treatment		

HIV Testing:

Date: _____

□ Reactive □ Non-reactive □ UN

PID number: _____

CPT start date: _____

ART start date: _____

Pre-treatment investigation					
Test	**Date**	**Result (units)**	**Test**	**Date**	**Result (units)**
ALT (SGPT)			Chest X-Ray findings Cavities (Y/N)		
AST (SGOT)					
Bilirubin- Direct -Indirect					
S. Albumin					
WBC (TC/DC)			ECG (QTc & other findings)		
Haemoglobin			Creatinine		
ESR			Creatinine Clearance		
Platelet count			Blood Urea		
Lactic acid			Visual acuity		
RBS			Audiogram		
CD4 Count			Psychiatric evaluation		Yes/ No
Hepatitis markers			Surgical evaluation		Yes/ No
TSH			Ophthalmic evaluation		Yes/ No
Urine (R/M)					
UPT					
Potassium					
Magnesium					
Calcium					

TB Site: ☐ Pulmonary ☐ Extra Pulmonary If extra pulmonary, please specify _____

Type of Case

☐ H mono/poly TB

☐ MDR/RR TB

☐ XDR TB

Treatment regimen type

☐ All oral H mono/poly TB

☐ Shorter MDR TB regimen

☐ All oral longer regimen

Drugs and Dosages																				
Drugs	H	R	E	Z	Km	Am	Cm	Lfx	Mfx	Cs	Eto	PAS	Lzd	Cfz	Amx clv	Clr	Bdq	Dlm		
IP Dose (mg)																				
CP Dose (mg)																				

If patient is eligible for new drug, mention patient decision

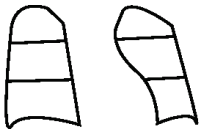
_____

Name & Signature of Treating Physician:_____

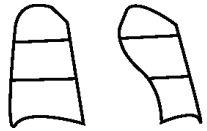
DR-TB Centre Committee – dates and decisions on regimen composition, extension of IP/ first phase; change of IP to CP or first phase to second phase; completion of treatment; severe adverse reactions; change of treatment, declaring treatment outcome stop/reintroduction/dosage adjustment of drugs at the time of ADR, change in regimen composition, patient transfer, etc

Date	Decision

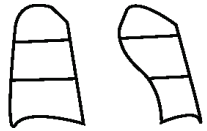
Month of Treatment	Smear/Culture Results				Other Investigations						
	Date	Lab No	Smear	Culture	S. Cr	LFT	ECG*-QTcF	CBC/ Platelets	Electrolyte (K, Mg, Ca)	RBS	TSH, T3,T4
2 Weeks											
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											
16											
17											
18											
19											
20											
21											
* If baseline ECG is normal, repeat to be done after two weeks, then monthly in IP, and when clinically indicated											



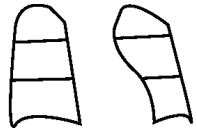
Date :_____
Finding: _____



Date :_____
Finding: _____



Date :_____
Finding: _____



Date :_____
Finding:

Patient name :_____

Initial Weight: _____kgs Height:_____cms

Weight band: ☐ <16 Kg ☐ 16-29 Kg ☐ 30-45 Kg ☐ 46-70 Kg ☐ >70 Kg

Date of starting intensive phase: _____

Date of starting continuation phase:_____

Details of change in regimen composition during treatment		
Date	Changed regimen drugs	Reason for change

DST result during course of treatment (LJ/LC/LPA/CBNAAT)				
Specimen collection date				
Drug	Month___	Month___	Month___	Month___
Type of test				
R				
H (inhA)				
H (katG)				
E				
Z				
Km				
Cm				
Am				
S				
Lfx				
Mfx (0.5)				
Mfx(1.0)				
FQ class				
SLID class				
SLI (eis)				
Eto*				
PAS*				
Lzd				
Cfz*				
Bdq*				
Dlm*				

*Whenever available

ADMINISTRATION OF DRUGS (one line per month) **Patient's Name:**_____

Month/Yr)	Day																														Weight in kg
	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	

Mark in the boxes: ✓= directly observed; ✓ supervised; ◯ drugs not taken; X = initiation of new box; Recording of CP should start from fresh line.

Month/Yr	Day																														Weight in kg
	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	

Mark in the boxes: ✓= directly observed; (✓)=unsupervised; ◯= drugs not taken; X = initiation of new box; Recording of CP should start from fresh line.

Date of retrieval action	By whom	Who contacted	Reason for missed doses	Outcome of retrieval action

Date of clinical follow up visits		
1st visit:_____	6th visit:_____	11th visit:_____
2nd visit: _____	7th visit: _____	12th visit: _____
3rd visit:_____	8th visit:_____	13th visit:_____
4th visit:_____	9th visit:_____	14th visit:_____
5th visit: _____	10th visit: _____	15th visit: _____

Treatment outcome (Cured, Treatment completed, Died, Failure, Lost to follow up, Regimen Change, Not evaluated)	**Date**	**Remarks (**provide cause of death, reason for lost to follow up/Failure (culture non conversion, reversion, ADR, Additional drug resistance), latest TB no. in case of failure and put on treatment further)

Date of adverse drug reaction	Details of symptoms	Action taken

Comments: _____

_____

_____

_____

Name & Signature of Treating Physician:

_____

Post treatment follow up clinical & sputum (Result with date)					
Follow up	**Clinical**	**Smear**	**Culture**	**CXR**	**Impression**
6 months					
12 months					
18 months					
24 months					

Patient's name:

_____

Address:

_____

_____

Contact No: _____

Episode ID:_____

Type of Case: _____
(H mono/poly TB, MDR/RR TB, XDR TB)

Treatment initiation date_____

NTEP PMDT Treatment Book

Annexure 15M

DR TB Centre:_____

District _____

State _____

Patient's name: _____

Age: _____yrs Gender: ☐ Male ☐ Female ☐ Transgender

Address: _____

_____

Marital status: _____ Occupation: _____

Contact No: _____

Aadhar ID _____

Name, designation of treatment supporter:_____

_____

_____ Contact no:_____

State:_____ District: _____

TB Unit: _____ PHI:_____

Initial home visit: Date _____ By:_____

DR TB Centre:_____ District _____ State _____

Reason for Testing	
☐ New ☐ Previously Treated	
☐ Presumptive TB ☐ Private Referral ☐ Presumptive NTM	
Presumptive MDR TB	☐ At diagnosis ☐ Contact of MDR/RR TB ☐ Follow up Sm+ve ☐ Private referral
☐ Presumptive H mono/poly	
Presumptive XDR TB	☐ MDR/RR TB at diagnosis ☐ follow up culture positive ☐ Failure or recurrent case of MDR/RR-TB regimen

Drug Susceptibility Test (DST) results																						
Date of sample collection	R	H (inhA)	H (katG)	Z	E	S	Km	Cm	Am	Lfx	Mfx (0.5)	Mfx (1)	FQ class	SLID class	SLID (eis)	Eto*	PAS*	Lzd	Cfz*	Clr*	Azi*	Bdq*	Dlm*
Name of the lab														Date of report									
*R: Resistant; S: Susceptible; C: Contaminated; -- Not done *whenever available*																							

Contact Investigation	**<6 yrs**	**>6yrs**
No of members screened		
No of presumptive TB cases identified		
No of presumptive TB cases evaluated		
No diagnosed with TB		
No of DR-TB diagnosed		

HIV Testing:
Date:_____
Result:_____
PID number:_____
CPT start date:_____
ART start date:_____
Blood Sugar Testing:
Date:_____
RBS:_____
FBS:_____
ADT*
(*write date of starting)

TB Site: ☐ Pulmonary ☐ Extra Pulmonary If extra pulmonary, please specify _____

Type of Case

☐ H mono/poly TB
☐ MDR/RR TB
☐ XDR TB

Treatment regimen

☐ Regimen for INH mono/poly resistant TB
☐ Shorter MDR-TB Regimen
☐ All Oral Longer Regimen for MDR/RR TB

Initiation Date: _____ **Registration Date:** _____

DR-TB Centre Committee meetings – dates and decisions		
Date	Decision	Duration of indoor stay

Pre-treatment investigation					
Test	**Date**	**Result (units)**	**Test**	**Date**	**Result (units)**
ALT (SGPT)			Chest X-Ray findings Cavities (Y/N)		
AST (SGOT)					
Bilirubin- Direct -Indirect					
Albumin					
WBC (TC/DC)			ECG (QTc & other findings)		
Haemoglobin			Creatinine		
ESR			Creatinine Clearance		
Platelet count			Blood Urea		
Lactic acid			Visual acuity		
RBS			Audiogram		
CD4 Count			Psychiatric evaluation		Yes/ No
Hepatitis markers			Surgical evaluation		Yes/ No
TSH			Ophthalmic evaluation		Yes/ No
Urine (R/M)					
UPT					
Potassium					
Magnesium					
Calcium					

Initial Weight: _____kgs Height:_____cms

Weight band:

☐ <16 Kg ☐ 16-29 Kg ☐ 30-45 Kg ☐ 46-70 Kg ☐ >70 Kg

Drug and Dosages		
Drugs	**Dose during IP (mg)**	**Dose during CP (mg)**
H		
R		
E		
Z		
Km		
Am		
Cm		
Lfx		
Mfx		
Cs		
Eto		
PAS		
Lzd		
Cfz		
Amx Clv		
Clr		
BDQ		
Dlm		
Final status of decision-making procedure for patient eligible for New Drug* _____		
Name & Signature of Treating Physician: _____		

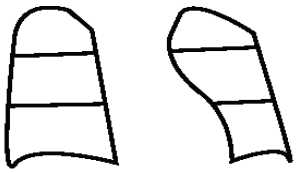
Month of Treatment	Smear/Culture Results				Other Investigations						
	Date	Lab No	Smear	Culture	S. Cr	LFT	ECG*-QTcF	CBC/ Platelets	Electrolyte (K, Mg, Ca)	RBS	TSH, T3,T4
2 Weeks											
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											
16											
17											
18											
19											
20											
21											

* If baseline ECG is normal, repeat to be done after two weeks, then monthly in IP, and when clinically indicated

DST result during course of treatment (LJ/LC/LPA/CBNAAT)				
Specimen collection date				
Drug	Month___	Month___	Month___	Month___
Type of test				
R				
H (inhA)				
H (katG)				
E				
Z				
Km				
Cm				
Am				
S				
Lfx				
Mfx (0.5)				
Mfx(1.0)				
FQ class				
SLID class				
SLI (eis)				
Eto*				
PAS*				
Lzd				
Cfz*				
Bdq*				
Dlm*				

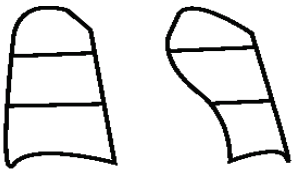
*Whenever available

Patient's Name:_____



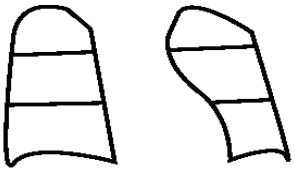
Date :_____

Finding: _____



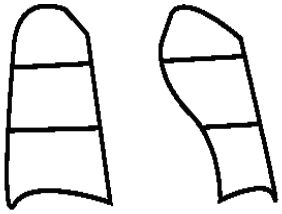
Date :_____

Finding: _____



Date :_____

Finding: _____



Date :_____

Finding: _____

Date of starting intensive phase: _____

Date of starting continuation phase:_____

Details of change in regimen composition during treatment		
Date	Changed regimen drugs	Reason for change

ADMINISTRATION OF DRUGS (one line per month)

Month & Yr	Day																													Wt in Kg
	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	

Month & Yr	Day																													Wt in Kg
	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	

Month & Yr	Day																													Wt in Kg
	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	

Mark in the boxes: ✓= directly observed; ✓ Unsupervised; ✓ = drugs not taken; X = initiation of new box; Recording of CP should start from fresh line.

Date of retrieval action	By whom	Who contacted	Reason for missed doses	Outcome of retrieval action

Date of adverse drug reaction	Details of symptoms	Action taken

Clinical Notes	
Date of visit: Chief Complaints: Clinical examination (major findings) : Counselling notes: Weight	Investigations Treatment

Clinical Notes	
Date of visit: Chief Complaints: Clinical examination (major findings) : Counselling notes: Weight	Investigations Treatment

Clinical Notes	
Date of visit: Chief Complaints: Clinical examination (major findings) : Counselling notes: Weight	Investigations Treatment

Clinical Notes	
Date of visit: Chief Complaints: Clinical examination (major findings) : Counselling notes: Weight	Investigations Treatment

Clinical Notes	
Date of visit: Chief Complaints: Clinical examination (major findings) : Counselling notes: Weight	Investigations Treatment

Date of clinical follow up visits		
1st visit: _____	**6th visit:** _____	**11th visit:**_____
2nd visit: _____	**7th visit:** _____	**12th visit:** _____
3rd visit: _____	**8th visit:** _____	**13th visit:**_____
4th visit: _____	**9th visit:** _____	**14th visit:**_____
5th visit: _____	**10th visit:** _____	**15th visit:** _____

Treatment outcome (Cured, Treatment completed, Died, Failure, Lost to follow up, Regimen Change, Not evaluated)	**Date**	**Remarks (**provide cause of death, reason for lost to follow up/Failure (culture non conversion, reversion, ADR, Additional drug resistance), latest TB no. in case of failure and put on treatment further)

Post treatment follow up clinical & sputum (Result with date)					
Follow up	**Clinical**	**Smear**	**Culture**	**CXR**	**Impression**
6 months of Rx					
12 months of Rx					
18 months of Rx					
24 months of RX					

Do's and Don'ts for patient

Infection Control

Do's

- Cover your mouth with a tissue, handkerchief or upper sleeves of your clothing while coughing.
- Wash your hands with soap and water or an alcohol based handwash.
- The room where the patient stays for a considerable time should be well ventilated and with proper sunlight.
- Any family member who develops cough should also follow similar cough etiquette.

Don'ts

- Do not cough and spit in the open.
- Do not close or obstruct your windows to ensure proper ventilation.

Nutrition

Do's

- Take complete meals inclusive of rice/roti, dal, vegetables, eggs, fish, meat (if available).
- At the start of the treatment, there may be some nausea and stomach upset. Kindly consult your doctor for the same.

Don'ts

- Do not stop or skip any meal.

Side effects

Do's

- If you have any side effects or discomfort on taking treatment, report to your doctor or treatment provider immediately.
- For any other illness developed during treatment, report to your doctor or treatment provider immediately.

Don'ts

- be complacent about side effects or discomfort.
- Do not try to take medications for side effects on your own.

Carry your treatment booklet whenever you visit any doctor.
Take your medicines regularly and complete the full course of treatment as prescribed by your doctor.

Annexure 15 G

NATIONAL TUBERCULOSIS ELIMINATION PROGRAMME

Referral / Transfer form for treatment Serial Number

To be filled in triplicate. One copy to be sent to the DTO receiving the patient, one copy to the health facility where the patient is referred to, and one copy to the patient

Name and address of referring health facility _____

Contact Number and e-mail address of referring health facility: _____

Name and address of health facility to which patient is referred _____

_____

Name of patient_____ **Age**_____ **Sex M** ☐ **F**☐ **TG**☐

Complete Address_____

_____**Contact no.**_____

Patient detail	
Site of disease ☐ Pulmonary ☐ Extra Pulmonary, Site _____ **Type of Patient** ☐ New ☐ Recurrent ☐ Transferred in ☐ Treatment After Failure ☐ Treatment After Lost to Follow-up ☐ Others, previously treated (Specify)_____ **Case Definition** ☐ Microbiologically confirmed ☐ Clinically diagnosed **H/O of ATT:** ___ months of treatment ___ months since end of last episode	**Diagnosis details** Date of diagnosis: __/__/___ Name of laboratory: Type of test: ZN / FM / CBNAAT / Culture Result : TB notification number: HIV Status: ☐ R ☐ NR ☐ Unknown DST Status: ☐ Rif Sensitive ☐ Rif Resistant ☐ Unknown, if unknown **Sample sent for DST to** _____ Date: __/__/__ **Treatment regimen:** ☐ New **Date of treatment initiation: : __/__/__** **Number of doses:**_____

Referred for:

☐ Initiation of treatment

☐ Adverse drug reaction (give details) _____

☐ Transfer out (give details)_____

☐ Any other (give details)_____

Name and designation of the referring doctor_____

Date referred

----------✂----------✂----------

Serial Number_____

For use by the health facility where the patient has been referred

Name of receiving health facility_____ Name of TB Unit and District_____

Name of patient _____ TB No (if available) _____

Age_____ Sex M ☐ F☐ TG☐ Date of receipt of patient_____

Date of initiation of treatment _____ Treatment regimen _____

Result of End IP specimen examination _____ Date of end IP specimen examination _____

Treatment outcome _____ Date of treatment outcome _____

Signature_____ Designation_____

Date_____

This portion of the form has to be sent back to the referring unit as soon as the patient has been initiated on RNTCP treatment

NTEP PMDT Referral for treatment form — Annexure 15H

(Fill in duplicate. Send one copy to the concerned facility receiving the patient, and file the duplicate)

Name and address of referring unit (District TB Centre/DR TB Centre):_____
E-mail address of referring unit: _____
Name of the facility where patient is referred: _____
Name of patient: _____ Age: _____ Gender: _____
Complete address: _____

Patient detail

Type: ☐ New ☐ Recurrent ☐ Treatment after Lost to follow-up ☐ Treatment after Failure
☐ Others, previously treated

Reason for testing
☐ New ☐ Previously Treated
☐ **Presumptive TB**
☐ **Private referral**
☐ **Presumptive NTM**
☐ **Presumptive MDR-TB**
☐ At diagnosis
☐ Contact of MDR/RR TB
☐ Follow up Sm +ve
☐ Private referral
☐ **Presumptive H mono/poly**
☐ **Presumptive XDR-TB**
☐ MDR/RR TB at Diagnosis
☐ Follow up culture positive _____Months
☐ Failure or recurrent of MDR/RR-TB regimen

Disease site:
☐ Pulmonary
☐ Extra pulmonary (site_____)

Type of case:

☐ H mono/poly TB
☐ MDR/RR TB
☐ XDR

Latest regimen:
☐ All oral H mono/poly resistant TB
☐ Shorter MDR TB regimen
☐ All Oral Longer Regimen for MDR/RR TB

Sputum, culture and DST details

Date of culture result: __/__/___
Date of DST/LPA/CBNAAT result: __/__/___
DST/LPA/CBNAAT result* :
☐R ☐H(inhA) ☐H(katG) ☐E ☐Z
☐FQ Class ☐Lfx ☐Mfx (0.5) ☐Mfx (2.0)
☐SLI Class ☐SLI (eis) ☐Km ☐Cm ☐Am ☐S
☐Eto ☐PAS ☐Lzd ☐Cfz ☐Bdq ☐Dlm ☐ __
(*Tick the drugs to which resistance is demonstrated)

DR TB treatment details

Episode ID _____

DR TB Centre: _____

Date of DR TB regimen initiation: : __/__/__

Number of doses:_____

Date of regimen change and details of change: _____
Past exposure to second-line anti TB drugs: Drugs (duration)_____
HIV Status: ☐ Pos ☐ Neg ☐ Not known Date of CPT initiation: _____ Date of ART initiation: ____
Date of referral to DR-TB Centre / DTC: Day _____ Month _____ Year _____

Referred for:
☐ Initiation of treatment
☐ Adverse drug reaction (give details) _____
☐ Transfer out (give details)_____
☐ Ambulatory treatment (if the patient is referred to DTC)
☐ Any other (give details)_____

Name and designation of the referring doctor_____

Reminder for the health facility where the patient has been referred

Please send an e-mail to the referring unit, informing the referring doctor of the date that the above named patient reported at the receiving health facility.

National Tuberculosis Elimination Programme - TB Notification Register

Year _____ PHI_____ Health Facility ID _____

Episode ID & Patient ID	Name (in full)	Age	Sex (M/F/TG)	Complete Address *(including district / state)*	Pin code	Mobile / Landline Number	Aadhaar No.	Key population*	Type of patient**	Site (P/EP)	Case Definition£	Microbiological confirmation test results					Results of Other tests (X-Ray/Histo patho/ FNAC/ Clinical/ /Other, specify)	HIV Status±	Diabetes Status^	Date of sample sent for DST *(NO if not sent, NA if not applicable)*	Result of DST@	Status of treatment ***	Health facility for treatment (Details)	Date of initiation of treatment
												Date	Lab Name	Lab no.	Test ¥	Results of Test#								
	.....			.....																				
	.....			.....																				
	.....			.....																				
	.....			.....																				
	.....			.....																				
	.....			.....																				
	.....			.....																				

***Key population**
1. Contact of TB/DRTB case, 2. Tobacco, 3. Prison inmates, 4. Miner, 5. Migrant, 6. Refugee, 7. Urban slum, 8. Health-care worker, 9. Other vulnerable population (specify)

** **Type of patient (use complete words)** →New, Recurrent, Treatment after Failure, Treatment after Lost to Follow up, Other Previously Treated, Transferred in, All oral H mono/poly

£ Case Definition →Microbiologically Confirmed, Clinically Diagnosed

¥ Test →ZN, FM, Culture, CBNAAT, FL LPA

 # Result of test
For Smear result – Grades for smear positive (Scanty with no. of bacilli, +1, +2, +3), NEG for smear negative
For GX result – MTB detected Rif Resistance, MTB detected Rif sensitive, MTB detected Rif Indeterminate, MTB not detected, Error, Invalid, No result
For Culture result – Grades for culture positive, NEG for culture negative

± HIV Status
HIV status as reported before or during TB treatment R – Reactive, NR – Non-Reactive, U – Unknown.

^Diabetes Status → D=Diabetes, **N**=NonDiabetes, **U** = Unknown

@ Sensitive= if sensitive to tested drugs, Name of drug if resistant to any – R= Rifampicin, H=Isoniazide, E=Ethambutol, Z=Pyrazinamide, Sm=Streptomycin Lx=Levofloxacin, Mx=Moxifloxacin, Km=Kanamycin, Cm=Capreomycin

*****Status of treatment-**
1. Initiated on First line treatment in the same Health Facility
2. Initiated on treatment outside Health Facility
3. Initiated on second line treatment
4. Treatment initiated outside RNTCP
5. Incomplete/ incorrect address
6. Died
7. Migrated & untraceable
8. Refuse for treatment
9. Repeat diagnosis
10. Patient already on treatment/ Follow up patient
11. Wrong diagnosis
12. Referred for treatment with pending feedback
13. Other

National Tuberculosis Elimination Programme - TB Notification Register

Year _____ **PHI**_____ **Health Facility ID** _____

Type of regimen (N / H mono / Outside RNTCP)	Weight at beginning of treatment	Dosage Frequency (Daily / Intermittent)	Follow-up smear examinations										Treatment Outcome#		If HIV-Reactive		Post treatment follow up														Treatment supporter details		Remarks
			End of IP					End of Treatment Exam									At 6 months Date_____				At 12 months Date_____				At 18 months Date_____				At 24 months Date_____						
			Date	DMC Name	Smear result	Date of sample collected for DST	Result of DST@	Date	DMC Name	Smear results	Date of sample collected for DST	Result of DST@	Outcome	Date	CPT (y/n) date	ART (y/n) date	Symptoms*	CXR	Smear	Culture	Symptoms	CXR	Smear	Culture	Symptoms	CXR	Smear	Culture	Symptoms	CXR	Smear	Culture	Name	Designation	

256

Treatment Outcome –
Cured, Treatment Completed, Died, Lost to follow up, Failure, Not evaluated or Treatment change

± **Additional treatments if patient HIV-Reactive**
Required only for patients known to be HIV Reactive. If provided by any source during TB treatment, enter "Y" and approximate date. If not provided / unknown, enter "N".
***Symptoms-** Mention predominant system- Cough-C, Fever-F, Haemoptysis-H, Weight loss-W, Night Sweat - N Others-O, No symptoms - NS

NTEPPMDT Treatment Register

Annexure 15J

Month _____ **Quarter** _____ **Year** _____ **District:** _____ **NAAT site:** _____ **C-DST Lab:** _____ **DDR-TB Centre:**_____ **NDR-TB Centre:**_____

Episode ID/ PMDT TB No	Patient ID	Patient's name in full	Gender (M/F/TG)	Age in yrs	Complete address & mobile number	Name of health facility, TU, District	@ Reason for Testing	Site of Disease (P/EP)	Type of patient (Public/ private)	Type (New, Recurrent, TALFU, Failure, Others)	DST/ DRT Details Type of DST/DRT (LJ/LC/ FL-LPA/SL-LPA/NAAT) Date and result of DRT/DST (R-Resistance detected, S- resistance not detected)																					
											R	H (inhA)	H (katG)	Z	E	S	Km	Cm	Am	Lfx	Mfx (0.5)	Mfx (1.0)	FQ class	SLID class	SLID (eis)	Eto	PAS	Lzd	Cfz	Bdq	Dlm	Cs
											DD/MM/YY																					
											DD/MM/YY																					
											DD/MM/YY																					
											DD/MM/YY																					
											DD/MM/YY																					

@ Presumptive TB – 1; Private referral – 2; Presumptive NTM – 3;

@ Presumptive MDR TB, At diagnosis–4; Contact of MDR/RR TB – 5; Follow up Sm +ve– 6; private referral – 7; Presumptive H mono/poly – 8;; Follow up culture positive–9; Failure or recurrent of MDR/RR-TB regimen –10;

Type of DR TB Patient H mono/poly/ MDR/RRTB/ XDR TB	DRTB Regimen #	Date of Treatment initiation	Microscopy, culture & DST Results during DR TB Treatment (Follow up months)															TB/HIV Collaborative activities					Final Treatment Outcome	Post treatment follow up				Remarks
			1	2	3	4	5	6	7	8	9/10/11	12/13/14	15/16/17	18/19/20				Date of Test	PID No	HIV Status	Date of CPT initiation	Date of ART initiation		6 m	12 m	18 m	24 m	
			SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C											
			DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM											
			SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C											
			DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM											
			SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C											
			DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM											
			SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C											
			DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM											
			SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C	SM / C											
			DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM	DD/MM											

Cases put on: All oral H mono/poly resistant TB – 1; Shorter MDR-TB regimen – 2; All Oral Longer regimen for MDR/RR TB – 3;

NTEP Laboratory Register for culture, CBNAAT and drug susceptibility testing

Annexure 15L

S No	Episode ID	Patient's full name (Address/contact details)	Age	Gender (M/F/TG)	Key Population[1]	Name and type (PHI / DMC / TU/ DTC / ICTC / ART / Medical College / DR-TB Centre / Private Others, specify) of referring health facility	Reason for testing					Date			Type (Sputum/other-specify)	Specimen condition # (M/B/S/C)	C&DST Lab Microscopy Result
							Diagnosis/DST			Follow up							
							New/ PT	@	Predominant symptom[2] and duration[3]	PMDT TB No	Month of FU	Specimen collection	Specimen sent to lab	Specimen receipt at laboratory			

@ Presumptive TB – 1; Private referral – 2; Presumptive NTM – 3;

@ Presumptive MDR TB, At diagnosis–4; Contact of MDR/RR TB – 5; Follow up Sm +ve- 6; private referral – 7;Presumptive H mono/poly – 8;Follow up culture positive–9; Failure or recurrent of MDR/RR-TB regimen –10;

M–Mucopurulent; B– Blood stained; S– Saliva; C– Contaminated

[1] Key population – 1. Contact of TB/DRTB case, 2. Tobacco, 3. Prison inmates, 4. Miner, 5. Migrant, 6. Refugee, 7. Urban slum, 8. Health-care worker, 9. PLHIV, 10. Other vulnerable (specify)

[2] Predominant symptoms: Cough-C, Fever-F, Haemoptysis-H, Weight loss-W, Night Sweat - N Others-O, No symptoms - NS

[3] Duration of predominant symptoms should be recorded in days

NTEP Laboratory Register for Culture, CBNAAT and Drug Susceptibility Testing

Rapid DST Results									Culture Results				Standard DST Results (R/S)																											Reporting of results		
Test performed (FL-LPA/SL-LPA/CBNAAT)	Date of receipt & CDL Episode ID	Valid* (Y/N)	TB † (Y/N)	RIF ‡ (R / S / I / N A)	INH (inhA) (R/S/NA) ‡	INH (KatG) (R/S/NA) ‡	FQ class resistance (R/S/NA)‡	SLI class resi (R/S/NA)‡	Type (LJ/LC)	Results §		Date of receipt & CDL Episode ID	Rifampicin	Isoniazid (0.1)	Isoniazid (0.4)	Streptomycin	Ethambutol	Pyrazinamide	Kanamycin	Capreomycin	Amikacin	Levofloxacin	Moxifloxacin (0.5)0.25	Moxifloxacin 1.0					PAS	Linezolid	Clofazimine			Delamanid	Bedaquiline		Date of reporting culture result	Date of reporting DST result	Remarks

* **Valid = Y** if both Amplification Control (AC) band & Conjugate Control (CC) band present; if either are missing, record **N**, and record no additional LPA results for this specimen.

† TB = Y if M. tuberculosis (TUB) band on LPA strip confirming identity as M. Tb or MTB Detected in CBNAAT, **N** if no TUB band on LPA strip or MTB Not Detected in CBNAAT

‡ R = Resistant Detected, **S** = Resistant not detected, **I** = Indeterminate, **NA** = no result, judged by no locus control band on LPA strip for *rpo-B* (RIF), or for *inh-A* or *kat-G* (INH) or for *gyr-A* or *gyr-B* for FLQ eis for low levelkm, or rrs for SLI. In case of CBNAAT, specify for NA, i.e. Error, Invalid, No Result

§ Negative = no growth, **Conta** = contaminated, **NTM** = Non-Tuberculosis Mycobacteria/fast grower, **3+** = confluent growth, **2+** = >100 colonies, **1+** = 10–100 colonies; **Sc#** Scanty <10 . Positive culture results should only be reported after identity for *M. tuberculosis* is confirmed with PNB, Niacin, Catalase, Rapid Immunoassay, or other methods.

- PNB and catalase are negative tests; the reagents used for Niacin are highly carcinogenic and hence the test is not being performed. Therefore the confirmatory test could indicate – Imuunochromatic test (ICT)/ Rapid immune assay, Nitrate Reductase Test (NRT) or other molecular methods.

On-Site Evaluation Checklist for STLS

I General Information

DMC:	
District:	
Number of Technicians:	
Qualifications of current staff: (Separate sheet to be attached to indicating information for each of Lab staff, if they are different from the previous visit)	
Supervisor/MO of DMC:	
Date of Visit:	
Name of visiting STLS:	

II Data on Slide volume for the last month:

This information is necessary to (i) select slides for Blinded Rechecking for the current month and as cumulative number for (ii) next annual SPR, (iii) next annual negative slides and (iv) annual total slides.

Sl. No.	Type of slide (Includes diagnosis and follow up slides)	Number
1	Positive slides	
2	Negative slides	
3	Total	

III Action required as per the previous visit:

IV Current visit particulars

Sl. No	Item	Adequate/ Acceptable	Problems Identified
1	Standard Operating Procedure (charts, manuals and modules)	Y / N	
2	Separate area for TB Lab work	Y / N	
3	Separate platform / tables for specimen receipt / smear preparation / microscopy	Y / N	
4	Power supply	Y / N	
5	Running water supply	Y / N	
6	Waste containers with lid	Y / N	
7	Waste disposal by Autoclave/burning/buried	Y / N	
8	**Adequate Stock and Supply of**: Specimen cups	Y / N	
9	Slides	Y / N	
10	Lens Tissue	Y / N	
11	Spirit lamp or Bunsen burner	Y / N	
12	Filter paper	Y / N	
13	Smearing / Staining Equipment (staining racks, sticks etc)	Y / N	
14	Slide boxes	Y / N	
15	Staining reagents:	Y / N	
15 (a)	1% Carbol fuchsin	Y / N	**Within expiry date Y / N**
15 (b)	25% Sulphuric acid	Y / N	**Within expiry date Y / N**
15 (c)	0.1% Methylene Blue	Y / N	**Within expiry date Y / N**
16	Immersion oil		
17	Label on sputum container	Y / N	
18	New slides used for AFB microscopy	Y / N	
19	Slides labeled with Lab Sl. No.	Y / N	
20	Number of specimens collected for diagnosis and for re-examination for diagnosis	Y / N	
21	Number of specimens collected for follow up examination	Y / N	
22	Smears air-dried prior to fixing	Y / N	
23	Staining procedure	Y / N	
24	Follow grading chart	Y / N	
25	Are positive results entered in Red ink	Y / N	
26	Control smears are used for each new batch of stains received at DMC	Y / N	
27	Binocular Microscopes	Y / N	
28	Maintenance of microscope	Y / N	
29	Laboratory Register	Y / N	

Sl. No	Item	Adequate/ Acceptable	Problems Identified
30	Write TB number of 'Follow up' patients in all cases	Y / N	
31	Write TB number and category of smear positive patients in the remarks column when this becomes available	Y / N	
32	Laboratory forms	Y / N	
33	Any change in lab staff since last supervisory visit.	Y / N	
34	Personnel	Y / N	
35	Training status	Y / N	
36	Has each staff member participated in refresher training within past two years	Y / N	
37	Safety Practices	Y / N	
38	General order / cleanliness	Y / N	
39	Timely reporting of results to clinicians	Y / N	
40	Does the TB Register contain all smear positive patients recorded in the TB Lab Register	Y / N	
41	Are the smear results for follow up patients in the TB Lab Register the same as the results recorded in the TB Register	Y / N	

42	Are all slides kept as required by the RNTCP EQA Programme?	Yes	No
43	Are slides collected for EQA, do the number in the slide box correlate with the number in the Lab Register	Yes	No

V Review of five positive and five negative slides from RNTCP TB Lab Register:

(Systematic sampling, separately for positive and negative slides)

a) Of the 5 Pos slides, number re-read as positive by STLS _____

b) Of the 5 Neg slides, number re-read as negative by STLS _____

Tick appropriate column or write letter as indicated below table

Sl. No.	Slide No.	AFB result / Grade by		Specimen Quality		Staining		Size		Thickness		Evenness	
		STLS	LT of DMC	≥ 10 WBC/ field	< 10 WBC/ field	Good	Poor (U/O)	Good	Poor (B/S)	Good	Poor (K/N)	Good	Poor
		1		2		3		4		5		6	
1													
2													
3													
4													
5													
6													
7													
8													
9													
10													

1: Write smear and grade
2: Tick appropriate column
3: Tick if good; write 'U' if under-decolourized, 'O' if over-decolourized
4: Tick if good; write 'B' if too big, 'S' if too small
5: Tick if good; write 'K' if too thick, 'N' if too thin
6: Tick appropriate column

*** Please carefully review all discordant slides with the LT**

Overall summary (please tick appropriate alternative):

Specimen quality: Needs improvement ‰Yes ‰ No
Smear size: Needs improvement ‰Yes ‰ No
Smear thickness: Needs improvement ‰Yes ‰ No
Smear evenness: Needs improvement ‰Yes ‰ No
Staining: No

Name of STLS: _____ Signature of STLS: _____

Name of LT: _____ Signature of LT: _____

Name of MO-in-charge: _____ Signature of MO-in-charge: _____

Date_____

On-site evaluation summary of EQA of Smear Microscopy of DMC by DTO

(a copy of this summary to be submitted by DTO to MO of DMC for corrective actions)

DMC:	
Date of visit: (dd/mm/yyyy)	
Visiting STLS:	
Action required as per the previous visit:	

Summary

a) Operational problems (both pending and new)

b) Technical problems (both pending and new)

c) Overall remarks

d) Action Required

Name of STLS: _____ Signature of STLS: _____

Date_____

Remarks by DTO

Signature of DTO

Copy to CMO of the District

ANNEXURE B

NTEP

Smear Results Sheet for Blinded Rechecking

Microscopy Centre: _____ District: _____

Name of TU_____ Month/Year: _____

Sl. No.	Lab No.	Result of LT of DMC, including grade for positive smears
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.		

Name of Lab. Technician: _____

Signature: _____ Date _____

ANNEXURE C

NTEP EQA of Sputum Microscopy

Worksheet: Blinded Rechecking of DMC Slides

Microscopy Centre Code: _____ **TU**_____

District: _____ **Month and Year:** _____

Tick appropriate column or write letter as indicated below table

Sl. No.	Slide No.	AFB result / Grade by			Specimen Quality		Staining		Size		Thickness		Evenness	
		STLS	MC	Umpire	≥ 10 WBC/ field	< 10 WBC/ field	Good	Poor (U/O)	Good	Poor (B/S)	Good	Poor (K/N)	Good	Poor
		1			2		3		4		5		6	
1														
2														
3														
4														
5														
6														
7														
8														
9														
10														
11														
12														
13														
14														
15														
16														
17														
18														
19														
20														
Total														

1: MC result to be entered under supervision of DTO ***only after*** form completed by STLS
2: Tick appropriate column
3: Tick if good; write 'U' if under-decolourized, 'O' if over-decolourized
4: Tick if good; write 'B' if too big, 'S' if too small
5: Tick if good; write 'K' if too thick, 'N' if too thin
6: Tick appropriate column

Overall remarks:

Specimen quality: Needs improvement ‰Yes ‰No
Smear size: Needs improvement ‰Yes ‰No
Smear thickness: Needs improvement ‰Yes ‰No
Smear evenness: Needs improvement ‰Yes ‰No
Staining: Needs improvement ‰Yes ‰No

Remarks:

Date of examination: _____ Signature of first controller: _____

ANNEXURE D

NTEP

Quality Assurance Report on Sputum Microscopy

Microscopy centre: _____ TU and District:_____

Month/Year :_____

Result of MC-LT	Result of controller *				
	Negative	1-9 AFB/ 100 fields	1+	2+	3+
Negative	Correct	LFN	**HFN**	**HFN**	**HFN**
1-9 AFB/ 100 fields	LFP	Correct	Correct	QE	QE
1+	**HFP**	Correct	Correct	Correct	QE
2+	**HFP**	QE	Correct	Correct	Correct
3+	**HFP**	QE	QE	Correct	Correct

* Enter the number of slides on each box

No. of False result		Slide No. / Error
False (-)ve		
False(+)ve		

Name and signature of STLS of concerned DMC:_ _____ _____

Reporting Date:_____ **Signature of DTO_____**

On-site evaluation Quarterly report of EQA from DTOs to IRL

District:	
Quarterly Report	Quarter _____ Year _____

Details of corrective actions recommended and taken			
Sl. No.	**DMC**	**Recommended corrective actions and corrective actions taken**	**Remarks**

D) Any other remarks.

Signature of the DTO

Annexure E

District monthly report to IRL on random blinded rechecking

Sl. No.	DMC name	Annual slide volume*	Annual positive slides*	Slide positivity rate (SPR)*	Nos. of slides rechecked during the month@	HFP	HFN	LFP	LFN	QE	Total number of errors	Remarks
Total for the district												

* For the previous year.

@ Monthly sample size calculated from Annual sample size for 80% Sensitivity, 100% Specificity and ‘d’=0 and Confidence limit = 95%.

Annexure F

On-site evaluation Quarterly report of EQA from DTOs to IRL

District:	
Quarterly Report	Quarter _____ Year _____

Details of corrective actions recommended and taken			
Sl. No.	**DMC**	**Recommended corrective actions and corrective actions taken**	**Remarks**

D) Any other remarks.

Signature of the DTO

Proposed changes to annexure F

Onsite evaluation & RBRC quarterly report of EQA from DTOs to IRL

District: **First controllers:**
Qarter: **Second controller:**
Year: **DTO:**

Sl.No.	Name of DMC	Number of smears examined in the quarter in DMC*			Number of smears rechecked in the quarter at DTC#			Number of errors made from DMC-LT					Major OSE corrective recommendations and implementation status
		Pos	1-9 AFB	Neg	Pos	1-9 AFB	Neg	HFP	HFN	LFP	LFN	QE	
Total													

First controller$ evaluation compared to Umpire**

Name of First controller	No. of Positive smears by first controller	No. of Scanty smears by first controller	No of negative slide by first controller	Number of errors made by 1st controller					Remarks: corrective actions, in case of errors by 1st controller
				HFP	HFN	LFP	LFN	QE	

* Based on the data from the lab register captured in monthly OSE forms; # **B**ased on annexure B and C; **$** STLS; **Based on the annexure C data

Annexure G

IRL annual report to CTD and NRL on random blinded rechecking

Sl. No	Name of the district	Total number of DMCs	INFORMATION ON SLIDES									INFORMATION ON DMCs			% of DMCs with HF errors	% of DMCs with HFP errors
			Annual slide Volume*	Annual positive slides*	No. of slides rechecked during year@	Number and Type of errors in slides Rechecked, cumulative in the district during the Year						Number of DMCs in the district with HF errors**				
						HFP	HFN	LFP	LFN	QE		HFP	HFN	BOTH HFP & HFN		
Total																

* For the previous year

**Each HFP or HFN error committing DMC is counted only once in the reporting year

@LQAS Annual sample size for 80% sensitivity,100%Specificity and d=0 confidence limit=95%

Annexure H

EQA Guidelines

1) Standards for Reagents
    a. Specifications:
        i. Basic fuchsin
            1. The chemical name: Pararosaniline hydrochloride
            2. The chemical structure: $C_{19}H_{18}N_3Cl$
            3. Molecular Wt: 323.8
            4. Colour: Metallic green
            5. Dye content: Should be available on the container. Approximately 85% - 88% (to calculate the required amount of Basic fuchsin, divide the actual amount by dye content. For example: Dye content = 85%, actual amount = 10 gms, required amount = 10/0.85 = 11.76 gms.)
        ii. Carbolic acid:
            1. The chemical name: Phenol
            2. The chemical structure: C_6H_5OH
            3. Molecular Wt: 94.11
            4. Melting point: $40^oC \pm 2$
            5. Purity: 99.5%
            6. Please note: The critical concentration of Phenol in Carbol fuchsin is 5%.
            7. Phenol is highly corrosive, handle with extreme care.
        iii. Methylated spirit
            1. Chemical name: Ethanol denatured + 5% Isopropyl alcohol + 5% Methanol
            2. Molecular structure: C_2H_5OH
            3. Molecular wt: 46.07
            4. Purity: 90%
        iv. Sulphuric acid:
            1. Chemical structure: H_2SO_4
            2. Molecular wt: 98.08
            3. Purity: 95-97%
            4. Colour: Clear
        v. Methylene blue:
            1. The chemical name: Methylthionine chloride
            2. The chemical structure: $C_{16}H_{18}ClN_3S$.
            3. Molecular Wt: 319.9
            4. Dye content: Should be available on the container. Approximately 82% (to calculate the required amount of Methyl blue, divide the actual amount by dye content. For example: Dye content = 82%, actual amount = 1 gms, required amount = 1/0.82 = 1.22 gms.)
    b. Immersion oil:
        i. Immersion oil supplied by the manufacturer of microscope with refractive index closer to that of Glass or 1.515
        ii. Liquid paraffin (heavy), refractive index of 1.48, a colourless, odourless, transparent, free from fluorescence in day light with relative density of 0.827 to 0.890, viscosity of 110 to 230 mPa s., specific gravity of 0.76-0.78 at 15.5^oC.

2) Shelf life of prepared reagents: Carbol fuchsin, sulphuric acid, methylene blue reagents may be kept for a maximum period of 4 months.

3) Identification: All reagents should have a label with name of the reagent, name of the TU, name of MC, the date of preparation and the expiry date. The containers of Carbol fuchsin, Sulphuric acid, Methylene blue reagents should in addition have the name of the person preparing the reagent. Freshly prepared reagents should not be mixed with old stock.

4) Equipment:
    a. Slides:
        i. Size: 76 mm x 26 mm,
        ii. Thickness: 1.3 mm
        iii. Edges: Polished
        iv. Sealed in a moisture absorbing dessicant pack
    b. Balance:
        i. Type: Electronic or Analytical balance
            1. Electronic balance:
                a. General purpose table top laboratory balance, 220-230 V, stainless steel platform, keypad auto calibration function, auto off, prolonged battery life, overload and under load, low battery LCD indicator.
                b. Range: Wide range, 0.01 – 120 gms, (two digit decimal)
                c. Resolution: 0.01 gm
            2. Analytical balance:
                a. Enclosed in a glass box with shutters, dimensions of the box in cms: 46 x 34 x 20
                b. Oscillator type of balance, with levelling screws, two aluminium pans, plumb line for adjusting horizontal level
                c. Weighing capacity: 1 mg to 200 gms, with fractional weight and regular weight in boxes including rider and forceps to handle weights.
    c. Binocular microscopes:
        i. Specifications: As per Expert Committee recommendations.

Annexure J

TECHNICAL SPECIFICATIONS OF BINOCULAR BRIGHT FIELD MICROSCOPES
(National Tuberculosis Elimination Programme)

A. PREAMBLE

Binocular Microscopes are required for detecting acid fast bacilli in sputum smear and other materials for use in Tuberculosis Control Programme laboratories, including those at Peripheral Health Centres.

The usage requires long hours of viewing through the microscopes.

B. SPECIFICATIONS

1.	Body	Binocular, sturdy, stable base body with focus adjustment controls in a position comfortable for prolonged use. The body should be powder coated.
2.	Eye piece	Paired, high quality, (image of the object as seen through the binocular eyepiece should be well defined centrally in least 2/3 field of view), achromatic, widefield, 10x without in built pointer. The eyepiece should be aplanatic and have a minimum field number of 18. Diopter adjustment must be present on one/both eye pieces or on the eye piece tube.
3.	Objectives	Three objectives: 10x, 40x, 100x, 10x and 40x objectives should have numerical apertures of 0.25 and 0.65 respectively and should be of spring loaded type or otherwise. 100x should have numerical aperture of 1.25 and should be of oil immersion and spring loaded type. Suitable prominent marking should be provided on 100x for easy identification. Unbreakable containers to be provided for storing the objectives. All objectives should be widefield, achromatic and parfocal. Marking for the Objectives Each objective should be engraved with the following information:- a) Name/insignia of the manufacturer. b) Magnification and numerical aperture, for example, 10x/0.25. c) 100x objective should be engraved with the word 'Oil' In changing from one objective to another or reintroducing the same objective by rotation of the nosepiece, the object at the center of the field should not appear displaced by more than 0.02mm in the object plane in any direction.
4.	Nose piece	Revolving nose piece to accommodate a minimum of three objectives with click stops. It should be provided with ribbed grip for easy rotation mounted on a precision ball bearing mechanism for smooth and accurate alignment. Extra ports if any should be fitted with dust proof metallic/ebonite caps.
5.	Stage	Uniformly horizontal, mechanical stage having dimensions of length 140mm (+ 20mm) & breadth 140mm (+ 20mm) with fine vernier graduations (minimum reading accuracy of 0.1mm). The stage should be provided with spring loaded slide holder for exact positioning of

		specimen/slide. It should be designed with convenient sub-stage vertical coaxial adjustment for slide manipulation. The stage should have ball bearing arrangement to allow smooth travel in transverse directions i.e. 80mm (+ 5mm) and front to back direction, 50mm (+ 5mm).
6.	Sub-stage condenser	Abbe-type condenser, numerical aperature (N.A) 1.25, focusable with rack and pinion arrangement incorporating an aspherical lens and an iris-diaphram. The condenser should have a filter holder and removable/swing in/out blue filter (suitable for bright field Microscopy)
7.	Sub-stage illuminator	1. The system should have a built-in variable light source (Illuminator). This light source should have a 20W, 6V Halogen lamp. The circuitry for the light source should include a constant voltage supply. The system should be provided with a step down transformer and an on/off switch and intensity control. The lamp should be provided with a lamp socket which has the facility for easy replacement of the bulb. The housing of the light source should be such that it will prevent dispersion of light and heating up of the body of the microscope. 2. Power supply - voltage:220V, 50 Hz AC - should have one on-off power switch, 3 core power cord with a 3 point male plug. 3. The system should have an inbuilt protective/safety device to withstand fluctuations of voltage from 140V to 280V. 4. A plano-concave mirror in fork mounting should be supplied which would be attachable to the base of field use. (where power is not available.) 5. The fuse for the halogen lamp should be easily accessible to the operator. 6. The Illuminator should have a built-in field diaphragm for Kohler illumination.
8.	Eye piece tubes	Binocular eye piece tubes, inclined at 45 degrees, rotatable through an angle of 360 degrees, having inter-pupillary distance range of 54-74 mm or wider, covering the above mentioned range.
9.	Focusing knob	Co-axial coarse and fine focusing knobs capable of smooth fine focusing movement over the full range of coarse travel. The fine focusing movement should have sensitivity of two microns or less (finer) over the entire coarse focusing range. The focusing knob should be on both sides. A focusing stop safety arrangement should be provided.
10.	General	i) All optical parts including objectives, eye pieces and prisms should have anti-reflective coating which also gives anti-fungal property. ii) All metallic parts should be corrosion-proof, acid-proof and stain-proof. iii) All parts of the microscope (including removable parts) should have insignia of the manufacturer engraved on it. iv) The supplier will supply the complete assembled microscope in a wooden box along with dust free cover. The box carrying the microscope should be made of well-seasoned wood or teak ply or board. The box should be suitably padded from inside of eliminate the risk of shock during transportation. It should be complete with lock and key arrangement, a suitable locking screw for securing the

		microscope and a cross-piece to retain it in position during transit. The box should be of an appropriate design with a carrying handle at the top and appropriate internal receptacles for holding the objectives, eyepieces and accessories. It should contain a bag of activated silica gel to keep the interior moisture-free. v) Each assembled microscope should be accompanied by an authorized list of accessories and spare parts. vi) Technical brochure (catalogue) and working manual should be provided with each microscope. vii) A bottle of at least 25ml immersion oil, a roll of lens tissue paper and lens cleaning solution (100ml) should be provided with each microscope. viii) One piece of anti static cleaning brush should be provided with each microscope for cleaning purpose. ix) Each microscope should be supplied with Blue filter. The blue filter should be packed in the box and not fixed on the microscopes.
11.	Spare parts	Each microscope should be supplied with spare parts as under: (as mentioned in Schedule of Requirement) i) 100x oil immersion objective (as per the specifications given under B3)-One ii) Halogen bulb, (6 volts, 20w)-6 Nos. iii) Fuses-6 Nos.
12.	Warranty	Performance warranty of three years from the date of supply. For any malfunction, the supplier shall replace the parts or repair the same at the user site free of cost within 15 days of the receipt of the complaints. During warranty period all services/replacement ensuring smooth functioning of the Microscopes must be done free of cost by the supplier.
13.	Requirement of service centre for after sales services	The supplier should have adequate after sale service facilities covering all region of the country. They should have the infrastructure and trained manpower to attend to any complaints within 15 days of receipt of the complaint.
14.	Testing & calibration	i) The successful vendor should supply a type test-certificate of the relevant optical & mechanical tests from a recognized competent authority at the time of supply. ii) The manufacturer/supplier shall provide duly calibrated (by accredited authority) measure instruments and demonstrate specifications for the purpose of inspection.

Annexure K

Investigation of Errors

Sl. No.	Pattern of errors	Possible causes	Suggested Investigation Steps
1	HFP and HFN	Unusable microscope	Examine a 3+ using that microscope
		Staining problems, poor stains, insufficient staining time or heating	Check stains and staining procedure
		Technician cannot recognize AFB	Test with clear-cut positive & negative slides and good microscope
		Gross neglect, overworked, lack motivation	Exclude other causes
2	HFP with or without LFP	Administrative error	Compare lab-register and verify correct slide number and result? Exclude causes of more frequent HFP, such as low concentration of sulphuric acid, unusable microscope, untrained or inexperienced LTs.
		Poor registration routine	Check accuracy of lab-register and other record keeping
		Staining problems/Fading	Check stains and staining procedure, consider re-staining for rechecking. Assess concentration of Phenol, Basic Fuchsin and Methylene blue.
		Technician unclear on AFB appearance	Look for inconsistent results of suspects (regularly single pos / low positive) in lab register
3	Many LFP, with or without occasional HFP	Problem with controllers Technician unclear on AFB appearance Contaminated stain/ reagents	Evaluate controllers Recheck sample of LFP from laboratory register Test stain with known negative smears, check the distilled water used for stain preparation
4	HFN with or without LFN	Administrative error	Compare lab-register with QC-listing: correct slide number & result?
		Very thick smears and/or poor light	Evaluate quality of smear preparation, check microscope
		Gross neglect	Exclude other causes
		Staining problems	Check stains and staining procedure, consider re-staining for rechecking. Assess concentration of Phenol, Basic Fuchsin and Methylene blue.
		Poor smearing-technique	Test stain with known negative smears
		Problems with microscope	Check microscope with positive slide
		Careless microscopy	Exclude other causes
5	Very high proportion LFN.	Reading error	As above
		Concentrated Methylene blue	
9	Many QE (too low grading)	Poor staining	
		Problems with microscope	

* Refer RNTCP LT Module, Manual and STLS Module for causes of False Positive and False Negative results.

Sl. No	Finding	Possible reasons	Suggested corrective actions
1	Low ANSV (<500)	Inadequate referral of suspects,	Educate Medical Officers and Health Workers on chest symptoms
		Non-involvement of private sector	Involve private sector, without increasing the number of DMCs in the area
		Many DMCs in the area	Reassess the criteria for selection of DMCs. Generally health facilities with <60 daily new adult OPD attendance should not be involved as DMCs
2	Low SPR (<5%)	Improper or over selection of TB suspects	Educate Medical Officers and Health Workers on chest symptoms
		More of false negative smear results	Action as required for frequent HFN and LFN Re-stain and test with known positive slides
3	Low ANSV and SPR	As above	Evaluate as above and if required consider closing the concerned DMC
4	High ANSV (>5000)	High OPD attendance workload	Train more than one LT for AFB smear microscopy
5	High SPR (>15%)	Selective referral / delayed identification of TB suspects	Educate Medical Officers and Health Workers on chest symptoms
		More of false positive smear results	Action as required for frequent HFP and LFP / test with known negative slides

Annexure M

Tuberculosis Laboratory Monthly Abstract
(Record Numbers)

Month Year 200.	TB suspects examined for diagnosis	TB suspects found positive	TB suspects undergoing repeat sputum examination	TB suspects found positive on repeat examination	Follow-up patients examined	Patients positive in follow up	Total slides examined	Total positive slides	Total negative slides	Signature of LT and STLS
Jan										
Feb										
Mar										
Apr										
May										
Jun										
Jul										
Aug										
Sep										
Oct										
Nov										
Dec										
TOTAL										

Signature of the M.O