



World Health
Organization

COUNTRY OFFICE FOR India

STANDARDS FOR TB CARE IN INDIA



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Development process

The first edition of the Standards for TB Care in India was conceived by a wider community of clinicians, public health specialists, community workers and patient advocates both within and outside of the Government of India as a necessary step in requiring and monitoring a widely accepted standard of TB care for the people of India. International guidelines and standards for TB care which existed such as International Standards for TB Care 2006 and 2009 editions, American Thoracic Society Standards, European Standards 2011, WHO Guideline for Treatment of TB 2010 and WHO Guidelines for PMDT 2011 were used as a foundation for developing India's standards. However with its unique challenges, approximately one third of the world's TB burden, and long history of dealing with a TB problem that appears to be resilient to the best efforts, it was felt that India should have its own standards that could be used as a benchmark by all providers managing TB patients within India. It is hoped that a set of standards recognized as appropriate for the specific challenges of India will spur observance to these standards by all care providers of India when managing a TB patient.

The standards developed and described here are the result of a long process that culminated in a three day national workshop organized by Central TB Division at New Delhi in December 2012 with technical assistance from WHO Country Office for India. The objective of the workshop was to develop the Standards for Tuberculosis Care in India that will be applicable to providers in public, private and other settings across India. About 120 experts from national and international level including various public health administrators, programme managers, representatives from various professional associations (Indian Medical Association, Association of Physicians of India, College of Physicians Association of India, Indian Association of Paediatricians, Federation of Obstetricians and gynecologists congress of India, Family Physician Association of India etc.), academicians and specialists from public and private sectors (pulmonologists, physicians, surgeons, paediatricians, gynaecologists, orthopaedic surgeons, microbiologists, public health specialist etc.), donors, technical and implementation partners, pharmaceutical companies, pharmacists

association, consultants, management experts, social science experts and civil society representatives participated at the workshop and actively worked to develop the evidence based Standards for Tuberculosis Care in India.

The methodology consisted of panel discussions and group work and the approach was to find appropriate answers to the following questions:

- What should be the standard tools and strategies for early and complete detection?
- What should be the standards of treatment in terms of drugs and regimens for best patient outcome?
- What should be the public health standards including regulations, strategies and systems for public health impact?
- What should be standards for patient support systems, both in public and private sectors and for community engagement for social inclusion?

As part of the development process, noted experts in the field of TB in India modified the international standards, following detailed review of India-specific and India-relevant evidence. As an output of the workshop, 26 standards developed and the India-relevant evidence debated, and listed for each of the standards in this document. This includes a new set of standards for social inclusion that goes beyond the areas covered in the International Standards for TB Care (ISTC) 2009. After the statement of each standard a brief summary of the international and national evidence are described along with the references to the literature. The standards thus evolved, are intended to be used to enhance quality and mutually acceptable engagement with the private and other sectors in India to enhance TB care. This is thus, an important tool for achieving the goal of universal access to quality TB care .

Introduction

India, the world's second most populous country, accounts for a quarter of the world's annual incidence of TB. Every year around two million people develop TB in India and 300,000 die of TB. Over 15 million patients have been treated and three million additional lives have been saved by the Revised National TB Control Programme (RNTCP) over the last decade. Cure rates have consistently been above 85% and the TB Millennium Development Goals are reachable. However, despite a comprehensive national TB control program guiding states for implementation of TB diagnosis and treatment there is still a long way to go. The decline in TB incidence has been slow, mortality remains unacceptably high and the emergence of drug-resistant TB has become a major public health concern.

There are many challenges for TB control in India. Prompt, accurate diagnosis and effective treatment of TB are not only essential for good patient care, but they are also the key elements in the public health response to tuberculosis and the cornerstone of any initiative for tuberculosis control. The private sector holds a factual predominance of health care service delivery in India. There is very little information about the TB patient from the private sector available to the programme and little is known about their quality of treatment, including treatment outcomes. Engaging the private sector effectively is the single most important intervention required for India to achieve the overall goal of universal access to quality TB care.

The vision of India's national TB control programme is that the people suffering from TB receive the highest standards of care and support from healthcare providers of their choice. It is spelt out in the National Strategic Plan (2012-17) to extend the umbrella of quality TB care and control to include those provided by the private sector (i). The need for quality and standards for TB care is made particularly acute where a largely unregulated and unmonitored private sector accounts for almost half of the TB care delivered in India with gross challenges as far as quality of diagnosis and treatment is concerned. Thus, it was felt essential to develop and disseminate the standards of TB care that is particularly relevant in Indian 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.

To paraphrase the ISTC, the standards in this document differ from existing guidelines in that the standards present what should be done whereas guidelines describe how the action is to be accomplished. There are comprehensive national guidelines from the Central TB Division, Gol [www.tbcindia.nic.in] that are regularly reviewed and updated. These standards represent the first what is expected from the Indian healthcare system. It is expected that the standards discussed in this document are clear and usable and will be accessible to all TB providers as an easy reference.

Reference:

1. National Strategic Plan (2012-17) for Tuberculosis – Directorate of Health Services, Central TB Division, Ministry of Health & Family Welfare (MoHFW), Government of India, New Delhi. www.tbcindia.nic.in

STCI summary

Standard 1: Testing and screening for Pulmonary TB

1.1 Testing:

- Any person with symptoms and signs suggestive of TB including cough >2 weeks, fever >2 weeks, significant weight loss, haemoptysis etc. and any abnormality in chest radiograph must be evaluated for TB.
- Children with persistent fever and/or cough >2 weeks, loss of weight / no weight gain, and/or contact with pulmonary TB cases must be evaluated for TB.

1.2 Screening:

- People living with HIV (PLHIV), malnourished, diabetics, cancer patients, patients on immunosuppressant or maintenance steroid therapy, should be regularly screened for signs and symptoms suggestive of TB.
- Enhanced case finding should be undertaken in high risk populations such as health care workers, prisoners, slum dwellers, and certain occupational groups such as miners.

Standard 2: Diagnostic technology

2.1 Microbiological confirmation on sputum:

- All patients (adults, adolescents, and children who are capable of producing sputum) with presumptive pulmonary TB should undergo quality-assured sputum test for rapid diagnosis of TB (with at least two samples, including one early morning sample for sputum smear for AFB) for microbiological confirmation.

2.2 Chest X-ray as screening tool:

- Where available, chest X-ray should be used as a screening tool to increase the sensitivity of the diagnostic algorithm.

2.3 Serological tests:

- Serological tests are banned and not recommended for diagnosing tuberculosis.

2.4 Tuberculin Skin Test (TST) & Interferon Gamma Release Assay (IGRA)

- TST and IGRA are not recommended for the diagnosis of active tuberculosis. Standardised TST may be used as a complimentary test in children.

2.5 CB-NAAT (cartridge-based nucleic-acid amplification test) is the preferred first diagnostic test in children and PLHIV.

2.6 Validation of newer diagnostic tests:

- Effective mechanism should be developed to validate newer diagnostic tests.

Standard 3: Testing for extra-pulmonary TB

- For all patients (adults, adolescents and children) with presumptive extra-pulmonary TB, appropriate specimens from the presumed sites of involvement must be obtained for microscopy/culture and drug sensitivity testing (DST)/CB-NAAT/molecular test/histo-pathological examination.

Standard 4: Diagnosis of HIV co-infection in TB patients and Drug Resistant TB (DR-TB)

4.1 Diagnosis of HIV in TB patients:

- All diagnosed TB patients should be offered HIV counselling and testing.

4.2 Diagnosis of multi-drug resistant TB (MDR-TB):

- Prompt and appropriate evaluation should be undertaken for patients with presumptive MDR-TB or Rifampicin (R) resistance in TB patients who have failed treatment with first line drugs, paediatric non-responders, TB patients who are contacts of MDR-TB (or R resistance), TB patients who are found positive on any follow-up sputum smear examination during treatment with first line drugs, diagnosed TB patients with prior history of anti-TB treatment, TB patients with HIV co-infection and all presumptive TB cases among PLHIV. All such patients must be tested for drug resistance with available technology, a rapid molecular DST (as the first choice) or liquid / solid culture-DST (at least for R and if possible for Isoniazid (H); Ofloxacin (O) and Kanamycin (K), if R-resistant/MDR).
- Wherever available DST should be offered to all diagnosed tuberculosis patients prior to start of treatment.

4.3 Diagnosis of Extensively Drug Resistant TB (XDR-TB):

- On detection of Rifampicin resistance alone or along with isoniazid resistance, patient must be offered sputum test for second line DST using RNTCP approved phenotypic or genotypic methods, wherever available.

Standard 5: Probable TB

- Presumptive TB patients without microbiological confirmation (smear microscopy, culture and molecular diagnosis), but with strong clinical and other evidence (e.g. X-ray, Fine Needle Aspiration Cytology (FNAC, histopathology) may be diagnosed as “Probable TB” and should be treated.
- For patients with presumptive TB found to be negative on rapid molecular test, an attempt should be made to obtain culture on an appropriate specimen.

Standard 6: Paediatric TB

6.1 Diagnosis of paediatric TB patients:

- In all children with presumptive intra-thoracic TB, microbiological confirmation should be sought through examination of respiratory specimens (e.g. sputum by expectoration, gastric aspirate, gastric lavage, induced sputum, broncho-alveolar lavage or other appropriate specimens) with quality assured diagnostic test, preferably CB-NAAT, smear microscopy or culture.

6.2 Diagnosis of probable paediatric TB patients:

- In the event of negative or unavailable microbiological results, a diagnosis of probable TB in children should be based on the presence of abnormalities consistent with TB on radiography, a history of exposure to pulmonary tuberculosis case, evidence of TB infection (positive TST) and clinical findings suggestive of TB.

6.3 Diagnosis of extra-pulmonary paediatric TB patients:

- For children with presumptive extra-pulmonary TB, appropriate specimens from the presumed sites of involvement should be obtained for rapid molecular test, microscopy, culture and DST, and histo-pathological examination.

Standard 7: Treatment with first-line regimen

7.1 Treatment of New TB patients:

- All new patients should receive an internationally accepted first-line treatment regimen for new patients. The initial phase should consist of two months of Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E). The continuation phase should consist of three drugs (Isoniazid, Rifampicin and Ethambutol) given for at least four months.

7.2 Extension of continuation phase:

- The duration of continuation phase may be extended by three to six months in special situations like bone & joint TB, spinal TB with neurological involvement and neuro-tuberculosis.

7.3 Drug dosages:

- The patients should be given dosages of the drugs depending upon body weight in weight bands

7.4 Bio-availability of drugs:

- The bioavailability of the drug should be ensured for every batch, especially if fixed dose combinations. (FDCs) are used, by procuring and prescribing from a quality-assured source.

7.5 Dosage frequency:

- All patients should be given daily regimen under direct observation. However, the country programme may consider daily or intermittent regimen for treatment of TB depending on the available resources and operational considerations as both are effective provided all doses are directly observed.
- All paediatric and HIV infected TB patients should be given daily regimen under direct observation.

7.6 Drug formulations:

- Fixed dose combinations (FDCs) of four drugs (Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol), and three drugs (Isoniazid, Rifampicin and Ethambutol) and two drugs (Isoniazid and Rifampicin) are recommended.

7.7 Previously treated TB patients:

- After MDR-TB (or R resistance) is ruled out by a quality assured test, TB patients returning after lost to follow up or relapse from their first treatment course or new TB patients failing with first treatment course may receive the retreatment regimen containing first-line drugs: 2HREZS/1HREZ/5HRE

Standard 8: Monitoring treatment response

8.1 Follow up sputum microscopy:

- Response to therapy in patients with pulmonary tuberculosis, new as well as retreatment cases, should be monitored by follow-up sputum microscopy (one specimen) at the time of completion of the intensive phase of treatment and at the end of treatment.

8.2 Extension of intensive phase:

- The extension of the intensive phase is not recommended.

8.3 Offer DST in follow up sputum positive cases:

- If the sputum smear is positive in follow-up at any time during treatment, a rapid molecular DST (as the first choice) or culture-DST (at least for R and if possible for Isoniazid (H); Ofloxacin (O) and Kanamycin (K), if R-resistant/MDR) should be performed as laboratory facilities become available.

8.4 Response to treatment in extra-pulmonary TB:

- In patients with extra-pulmonary tuberculosis, the treatment response is best assessed clinically. The help of radiological and other relevant investigations may also be taken.

8.5 Response to treatment in children:

- In children, who are unable to produce sputum the response to treatment may be assessed clinically. The help of radiological and other relevant investigations may also be taken.

8.6 Long-term follow up:

- After completion of treatment the patients should be followed up with clinical and/or sputum examination at the end of six months and 12 months.

Standard 9: Drug Resistant TB management

9.1 Treatment of M/XDR-TB (or R resistant TB):

- Patients with tuberculosis caused by drug-resistant organisms (especially M/XDR or only R resistance or with O or K resistance), microbiologically confirmed by quality assured test, should be treated with specialized regimens containing quality assured second-line anti-tuberculosis drugs.

9.2 Model of care for drug resistant TB:

- Patients with MDR-TB should be treated using mainly ambulatory care rather than models of care based principally on hospitalization. If required, a short period of initial hospitalisation is recommended.

- 9.3 Regimen for MDR / R-Resistant TB cases:
- The regimen chosen for MDR-TB may be standardized and/or based on microbiologically confirmed drug susceptibility patterns. At least four drugs (second line) to which the organisms are susceptible, or presumed susceptible, should be used. Most importantly the regimen should include at least a later-generation Fluoroquinolone (such as high dose Levofloxacin) and a parenteral agent (such as Kanamycin or Amikacin), and may include Pyrazinamide, Ethambutol, Ethionamide (or Prothionamide), and either Cycloserine or PAS (P-aminosalicylic acid) if Cycloserine cannot be used.
- 9.4 Regimen for MDR patients with Ofloxacin and/or Kanamycin resistance detected early:
- Treatment regimen may be suitably modified in case of Ofloxacin and/or Kanamycin resistance at the initiation of MDR-TB treatment or during early intensive phase, preferably not later than four to six weeks.
- 9.5 Surgery in MDR/XDR TB patients:
- All patients of MDR/XDR-TB should be evaluated for surgery at the initiation of treatment and/or during follow up.
- 9.6 Treatment Duration in MDR TB patients:
- Till newer effective drugs are available with proven efficacy with shorter duration of MDR-TB treatment; total treatment should be given for at least 24 months in patients newly diagnosed with MDR-TB (i.e. not previously treated for MDR-TB) with recommended intensive phase of treatment being six to nine months. The total duration may be modified according to the patient's response to therapy.
- 9.7 Specialist consultation in M/XDR TB patients:
- Consultation with a specialist experienced in treatment of patients with MDR/XDR tuberculosis should be obtained, whenever possible.
- 9.8 Ensuring adherence in M/XDR TB patients:
- Patient support systems, including direct observation of treatment, are required to ensure adherence. It should be ensured that the patient consumes all the doses of the drugs.
- 9.9 Single sample follow-up culture in M/XDR TB patients:
- The use of sputum culture (1 sample) is recommended for monitoring of patients with MDR-TB during treatment.

9.10 Second line DST during treatment of MDR TB:

- During the course of MDR TB treatment, if the sputum culture is found to be positive at 6 months or later, the most recent culture isolate should be subjected to DST for second-line drugs (at least O and K) to decide on further course of action. DST to other drugs namely Moxifloxacin, Amikacin and Capreomycin may also be done if laboratory facilities are available to guide treatment.

9.11 Regimen for MDR patients with Ofloxacin and/or Kanamycin resistance detected later:

- The patients with MDR-TB found to be resistant to at least Ofloxacin and/or Kanamycin during the later stage of MDR TB treatment must be treated with a suitable regimen for XDR TB using second line drugs including Group 5 drugs such as Amoxicillin Clavulanate, Clarithromycin, Clofazimine, Linezolid, Thioacetazone, Imipenem to which the organisms are known or presumed to be susceptible.

9.12 New drugs:

- New drugs need to be considered for inclusion in regimens whenever scientific evidence for their efficacy and safety becomes available as per the national policy for newer antimicrobials. Appropriate regulatory mechanisms for distribution control needs to be ensured.

Standard 10: Addressing TB with HIV infection and other comorbid conditions

10.1 Treatment of HIV infected TB patients:

- TB patients living with HIV should receive the same duration of TB treatment with daily regimen as HIV negative TB patients.

10.2 Anti-retroviral & Co-trimoxazole prophylactic therapy in HIV infected TB patients:

- Antiretroviral therapy must be offered to all patients with HIV and TB as well as drug-resistant TB requiring second-line anti-tuberculosis drugs, irrespective of CD4 cell-count, as early as possible (within the first eight weeks) following initiation of anti-tuberculosis treatment. Appropriate arrangements for access to antiretroviral drugs should be made for patients. However, initiation of treatment for tuberculosis should not be delayed. Patients with TB and HIV infection should also receive Co-trimoxazole as prophylaxis for other infections.

10.3 Isoniazid preventive therapy in HIV patients without active TB:

- People living with HIV should be screened for TB using four symptom complex (current cough or, fever or weight loss or night sweats) at HIV care settings and those with any of these symptoms should be evaluated for ruling out active TB. All asymptomatic patients in whom active TB is ruled out, Isoniazid Preventive Therapy (IPT) should be offered for six months or longer.

Standard 11: Treatment adherence

11.1 Patient centered approach for adherence:

- Both to assess and foster adherence, a patient-centered 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.

11.2 Measures for treatment adherence:

- Supervision and support should be individualized and should draw on the full range of recommended interventions and available support services, including patient counselling and education. A central element of the patient centred strategy is the use of measures to assess and promote adherence to the treatment regimen and to address poor adherence when it occurs. These measures should be tailored to the individual patient's circumstances based on details of the patient's clinical and social history and be mutually acceptable to the patient and the provider.

11.3 Trained treatment supporter for treatment adherence:

- Such measures may include identification and training of a treatment supporter (for tuberculosis and, if appropriate, for HIV, Diabetes Mellitus etc.) who is acceptable, accessible and accountable to the patient and to the health system.

11.4 Use of Information Communication Technology (ICT) to promote treatment literacy and adherence:

- Optimal use of ICT should be done to promote treatment literacy and adherence

Standard 12: Public health responsibility

- Any practitioner treating a patient for tuberculosis is assuming an important public health responsibility to prevent on-going transmission of the infection and the development of drug resistance.
- To fulfil this responsibility the practitioner must not only prescribe an appropriate regimen, but when necessary, also utilize local public health services / community health services, and other agencies including

NGOs to assess the adherence of the patient and to address poor adherence when it occurs.

Standard 13: Notification of TB cases

- All health establishments must report all TB cases and their treatment outcomes to public health authorities (District Nodal Officer for Notification).
- Proper feedback need to be ensured to all healthcare providers who refer cases to public health system on the outcome of the patients which they had referred.

Standard 14: Maintain records for all TB patients

- A written record of all medications given, bacteriologic response, adverse reactions and clinical outcome should be maintained for all patients.

Standard 15: Contact investigation

- All providers of care for patients with tuberculosis should ensure all household contacts and other persons who are in close contact with TB patients are screened for TB
- In case of pediatric TB patients, reverse contact tracing for search of any active TB case in the household of the child must be undertaken.

Standard 16: Isoniazid Prophylactic therapy

- Children <6 years of age who are close contacts of a TB patient, after excluding active TB, should be treated with isoniazid for a minimum period of 6 months and should be closely monitored for TB symptoms.

Standard 17: Airborne infection control

- Airborne infection control should be an integral part of all health care facility infection control strategy.

Standard 18: Quality assurance (QA) systems

18a QA for diagnostic tests:

- All health care providers should ensure that all diagnostic tests used for diagnosis of TB are quality assured.

18b QA for anti-TB drugs:

- Quality assurance system should ensure that all anti-TB drugs used in the country are subjected to stringent quality assurance mechanisms at all levels.

Standard 19: Panchayati Raj Institutions

- Panchayati Raj Institutions and elected representatives have an important role to share the public health responsibility for TB control with the healthcare providers, patients and the community.

Standard 20: Health education

- Every TB symptomatic should be properly counselled by the healthcare provider.
- TB patients and their family members should get proper counselling and health education at every contact with healthcare system

Standard 21: Death audit among TB patients

- Death among TB patients should be audited by a competent authority.

Standard 22: Information on TB prevention and care seeking

- All individuals especially women, children, elderly, differently abled, other vulnerable groups and those at increased risk should receive information related to TB prevention and care seeking.

Standard 23: Free and quality services

- All patients, especially those in vulnerable population groups, accessing a provider where TB services are available should be offered free or affordable quality assured diagnostic and treatment services which should be provided at locations and times so as to minimize workday or school disruptions and maximize access.

Standard 24: Respect, confidentiality and sensitivity

- All people seeking or receiving care for TB should be received with dignity and managed with promptness, confidentiality and gender sensitivity. Ensure that infection control procedures do not stigmatise TB patients.

Standard 25: Care and support through social welfare programmes

- Patient support system should endeavour to derive synergies between various social welfare support systems to mitigate out of pocket expenses such as transport and wage loss incurred by people affected by TB for the purpose of diagnosis and treatment.

Standard 26: Addressing counselling and other needs

- Persons affected by TB should be counselled at every opportunity, to address information gaps and to enable informed decision making. Counselling should address issues such as treatment adherence, adverse drug reactions, prognosis and physical, financial, psycho-social and nutritional needs.

Standard 1

Testing and screening for Pulmonary TB

1.1 Testing:

- Any person with symptoms and signs suggestive of TB including cough >2 weeks, fever >2 weeks, significant weight loss, haemoptysis etc. and any abnormality in chest radiograph must be evaluated for TB.
- Children with persistent fever and/or cough >2 weeks, loss of weight / no weight gain, and/ or h/o contact with pulmonary TB cases must be evaluated for TB.

1.2 Screening:

- People living with HIV (PLHIV), malnourished, diabetics, cancer patients, patients on immunosuppressant or maintenance steroid therapy, should be regularly screened for signs and symptoms suggestive of TB.
- Enhanced case finding should be undertaken in high risk populations such as healthcare workers, prisoners, slum dwellers, and certain occupational groups such as miners.

The most common symptom of pulmonary TB is prolonged cough that lasts longer than the cough with most other acute lung infections. However cough is a common symptom and most coughing patients do not have TB (1). Many countries have attempted to distinguish likely TB cases from other lung infections by specifying a chronic cough lasting two to three weeks (2,3). The evidence from India suggests that cough lasting > 2 weeks is a more sensitive indicator for TB than >3 weeks cough and is thus recommended here (4,5,7,8). A high level of clinical suspicion for TB is necessary as many TB patients will not have a cough, particularly if they are infected with HIV or are

otherwise immunosuppressed. Children can present a diagnostic challenge and a high level of suspicion for TB must accompany the approach to any child with prolonged illness not otherwise explained, especially if there is a history of contact with a pulmonary TB case (5).

Enhanced case finding means maintaining a high index of suspicion for TB in all encounters, with proactive exclusion of TB using the appropriate combination of clinical queries, radiographic or microbiologic testing. For PLHIV, the WHO has developed a four-symptom screen that has proven highly sensitive for active TB (3,6). Recent evidence from surveys in southern India has pointed to the significant comorbidities of TB and type 2 diabetes (10, 11) and consequently diabetics are included in the high risk categories for regular screening (12). Any other immunosuppressed patients are also at considerably heightened risk and should be enquired about symptoms of TB at every healthcare encounter. In addition, slum dwellers are a large and recognized portion of Indian urban society where the transmission of infection is high. A recent estimate of the ARTI in Delhi was 2.3-3% (9), indicating that screening for active TB may be cost-effective and sensible. Occupational groups such as miners have been reported to have high risk of tuberculosis and they could be specially targeted for active case finding. An additional group with high risk for TB is certain indigenous populations in the tribal areas of India.

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Standard 2

Diagnostic technology

2.1 Microbiological confirmation on sputum:

- All patients (adults, adolescents, and children who are capable of producing sputum) with presumptive pulmonary TB should undergo a quality-assured sputum test for rapid microbiological diagnosis of TB

2.2 Chest X-ray as screening tool:

- Where available, chest X-ray should be used as a screening tool to increase the sensitivity of the diagnostic algorithm

2.3 Serological tests:

- Serological tests are banned and not recommended for diagnosing tuberculosis.

2.4 Tuberculin Skin Test (TST) & Interferon Gamma Release Assay (IGRA):

- TST and IGRA are not recommended for the diagnosis of active tuberculosis. Standardized TST may be used as a complimentary test in children.

2.5 Cartridge-Based Nucleic-acid Amplification Test (CB NAAT) is the preferred first diagnostic test in children and PLHIV

2.6 Validation of newer diagnostic tests:

- Effective mechanism should be developed to validate newer diagnostic tests. One of the first responsibilities of the TB programme is to endeavour to make a bacteriological diagnosis of TB if at all possible. Currently, only sputum tests are sufficient and recommended under the programme for the microbiologic testing of

TB (1). The Government of India recently issued government orders banning the manufacture, importation, distribution and use of serological tests for diagnosing TB (2). In addition Tuberculin Skin Test (TST) and Interferon-Gamma Release Assays (IGRA) are not recommended for diagnosis of TB, although in certain cases TST may be useful as an additional test for the diagnosis of children(3). Chest radiograph is an unquestionably sensitive test for the detection of pulmonary disease in adults and children, and is recommended as a screening tool for TB. Due to the non-specific nature of radiographic testing for TB, any abnormal chest radiograph should prompt further bacteriologic and clinical assessment for TB (4).

As sputum tests are the key to TB diagnosis, attention to collection of a good sputum sample is paramount; a number of studies have looked at this, including studies in India. A consensus is that two samples are almost as good as three samples and a morning sample is better than a spot sample for detection of mycobacteria (5,6,7).

Acceptable methods for bacteriologic testing of sputum include sputum smear microscopy (both conventional and fluorescent), culture (on solid or liquid media), commercial line probe assay (LPA), or CB NAAT. The most commonly-used method for bacteriologic diagnosis of TB for the last 70 years, sputum smear microscopy, has had enormous value in TB diagnosis, but has limited sensitivity, particularly in children where microscopy is less than 50% sensitive. Sputum culture remains a highly sensitive, specific, and under-utilized method for TB diagnosis, but requires weeks to yield results and hence alone does not help clinicians for early diagnosis. Nucleic acid amplification testing (NAAT) offers enormous potential for accurate rapid diagnosis, but only commercial kits have been validated and are trustworthy for replicable results(8).

While both “in-house” manual NAAT is widely available, their lack of reproducibility and quality assurance concerns means that such in-house assays cannot be recommended(9). Commercial semi-automated NAAT have been developed in India, these are yet to be validated, hence are not recommended. With the advent of CB-NAAT the sensitivity and specificity of rapid TB diagnosis from sputum has increased to approximately levels seen in solid-media sputum culture, particularly valuable for the assessment of children.

A list of RNTCP approved diagnostics tests are given in the guidelines for TB notification accessible at www.tbcindia.nic.in.

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Standard 3

Testing for extra-pulmonary TB

3.1 Testing for extra-pulmonary TB

- For all patients (adults, adolescents and children) with presumptive extra-pulmonary TB, appropriate specimens from the presumed sites of involvement must be obtained for microscopy/culture/ CB-NAAT/molecular test/histopathology examination and drug sensitivity testing (DST).

Even as pulmonary TB presents significant diagnostic challenges, extra-pulmonary TB diagnosis can be more challenging. Signs and symptoms are not specific and yield of mycobacteria are generally low from most tissue and fluid sources (1,2,3). Extra-pulmonary TB is comparatively common in PLHIV (approximately 30% of cases) and in these hosts the non-specificity of symptoms and low yield of mycobacteria present an even greater challenge. The basic principle of seeking bacteriologic diagnosis at every opportunity where TB is suspected applies to extra pulmonary TB as well. The use of unvalidated non-commercial 'in-house' NAAT on tissue specimens is not recommended; histopathology examination, smear microscopy, culture and validated commercial NAAT are the only acceptable options. Recently the use of CB-NAAT for specimens other than sputum was explored in many studies; although the test is not as sensitive on most of these samples compared with its sensitivity on sputum nevertheless it performs well and in all cases better than smear microscopy (4,5).

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Standard 4

Diagnosis of HIV co-infection in TB patients and diagnosis of Drug Resistant TB (DR-TB)

4.1 Diagnosis of HIV in TB patients:

- All diagnosed TB patients should be offered HIV counselling and testing.

4.2 Diagnosis of Multi-Drug Resistant TB (MDR-TB):

- Prompt and appropriate evaluation should be undertaken for patients with presumptive MDR-TB or Rifampicin (R) resistance in TB patients who have failed treatment with first line drugs, paediatric non-responders, TB patients who are contacts of MDR-TB (or R resistance), TB patients who are found positive on any follow-up sputum smear examination during treatment with first line drugs, diagnosed TB patients with prior history of anti-TB treatment, TB patients with HIV co-infection and all presumptive TB cases among PLHIV. All such patients must be tested for drug resistance with available technology, a rapid molecular DST (as the first choice) or liquid / solid culture-DST (at least for R and H; and at least for Ofloxacin (O) and Kanamycin (K), if MDR).

Wherever available DST should be considered and offered to all diagnosed tuberculosis patients prior to start of treatment.

4.3 Diagnosis of Extensively Drug Resistant TB (XDR-TB):

- On detection of Rifampicin and isoniazid resistance, patient must be offered sputum test for second line DST using quality assured phenotypic or genotypic methods, wherever available.

TB is a very clear clinical sign of possible HIV infection, and all TB patients deserve to have HIV ruled out through voluntary counselling and testing. India is considered a low HIV endemic area with high rates of TB, and the country-wide average HIV prevalence in TB patients is around 5%. In any given case of TB, at any age, HIV infection is possible. Early detection of HIV offers the opportunity for potentially life-saving additional interventions. Thus it is recommended that all patients with active TB be tested for HIV (1). If HIV infection is detected then, TB treatment and anti-retroviral therapy is as described in Standard 10.

Drug resistant TB is a growing problem worldwide including in India. Current surveillance data estimates a prevalence of MDR-TB of 2-3% in new, untreated TB patients and more than 15% in previously treated TB cases (2). The Programmatic Management of Drug Resistant TB (PMDT) has recently been expanded in order to treat DR-TB in the RNTCP and extend standards and monitoring of DR-TB treatment to the private sector. The laboratory support for this programme is in development and a growing network of accredited, quality-assured drug sensitivity testing labs will support the goal of universal DST for all TB patients. In order to provide timely information to the clinical team treating the patient and reduce primary transmission of DR-TB, rapid testing for rifampicin resistance is recommended (3).

The emergence of extensively-drug resistant TB (XDR-TB) underlines the importance of developing a laboratory infrastructure to support DST for second-line drugs. The most important tests are for resistance to the Fluoroquinolones (Ofloxacin) and the injectable agent (Kanamycin), which forms the backbone of MDR-TB treatment and resistance to these drugs defines XDR-TB. (4). It is recommended that, as facilities allow, all MDR-TB isolates are further tested for Ofloxacin and Kanamycin resistance.

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Standard 5

Probable TB

5.1 Probable TB

- Patients with symptoms suggestive of TB without microbiological confirmation (sputum smear microscopy, culture and molecular diagnosis), but with strong clinical and other evidence (e.g. X-ray, Fine Needle Aspiration Cytology (FNAC), histopathology) may be diagnosed as “Probable TB”. (1)

Despite the advent of new tests for TB diagnosis with greater sensitivity than smear microscopy of appropriate sputum samples, about 20-30% of TB patients will not have microbiologic confirmation. This figure may be much higher in children and patients with extra-pulmonary TB or PLHIV. Although it is recommended that any sample from a suspected TB patient that is initially negative by a rapid diagnostic test be cultured for TB growth and confirmed diagnosis, there will be a group of patients that have TB but without microbiologic confirmation. These are included in the Government of India TB case notification as “patients diagnosed clinically as a case of TB, without microbiologic confirmation, and initiated on anti-TB drugs” (2).

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Standard 6

Paediatric TB

6.1 Diagnosis of paediatric TB patients:

- In all children with presumptive intra-thoracic TB, microbiological confirmation should be sought through examination of respiratory specimens (e.g. sputum by expectoration, gastric aspirate, gastric lavage, induced sputum, broncho-alveolar lavage or other appropriate specimens) with a quality assured diagnostic test, preferably CB-NAAT, smear microscopy or culture.

6.2 Diagnosis of probable paediatric TB patients:

- In the event of negative or unavailable microbiological results, a diagnosis of probable TB in children should be based on the presence of abnormalities consistent with TB on radiography, a history of exposure to pulmonary TB case, evidence of TB infection (positive TST) and clinical findings suggestive of TB.

6.3 Diagnosis of extra-pulmonary paediatric TB patients:

- For children with presumptive extra-pulmonary TB, appropriate specimens from the presumed sites of involvement should be obtained for rapid molecular test, microscopy, culture and DST, and histo-pathological examination.

Diagnosis of TB in children is particularly challenging as in small children it can be difficult to collect samples and the paucibacillary nature of TB in children reduces the sensitivity of testing. Regardless, there should be every effort to obtain bacteriologic diagnosis. Standardised TST may be used as a complimentary test in children, in combination with microbiological investigations, history of contact, radiology, and symptoms. The guidelines of

the Indian Academy of Paediatrics (IAP) and paediatric TB guidelines of the RNTCP recommend obtaining specimens for mycobacteriology, the use of standardised TST with a cut-off of 10mm induration in non-immunosuppressed children, and specialist consultation. Serodiagnostic tests and IGRA have no role in paediatric TB diagnosis.

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Standard 7

Treatment with first-line regimen

7.1 Treatment of New TB patients:

- All new patients should receive an internationally accepted first-line treatment regimen for new patients. The initial phase should consist of two months of Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E). The continuation phase should consist of three drugs (Isoniazid, Rifampicin and Ethambutol) given for at least four months.

7.2 Extension of continuation phase:

- The duration of continuation phase may be extended by three to six months in special situations like Bone & Joint TB, Spinal TB with neurological involvement and neuro-tuberculosis.

7.3 Drug dosages:

- The patients should be given dosages of the drugs depending upon body weight in weight bands.

7.4 Bio-availability of drugs:

- The bioavailability of the drug should be ensured for every batch, especially if fixed dose combinations (FDCs) are used, by procuring and prescribing from a quality-assured source.

7.5 Dosage frequency:

- All patients should be given daily regimen under direct observation. However, the country programme may consider daily or intermittent regimen for treatment of TB depending on the available resources and operational considerations as both are effective provided all doses are directly observed.

- All paediatric TB patients and HIV associated TB patients should be given daily regimen under direct observation.

7.6 Drug formulations:

- Fixed dose combinations (FDCs) of four drugs (Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol), three drugs (Isoniazid, Rifampicin and Ethambutol) and two drugs (Isoniazid and Rifampicin) are recommended.

7.7 Previously treated TB patients:

- After MDR-TB (or R resistance) is ruled out by a Quality Assured test, TB patients returning after lost to follow up, relapsing from their first treatment course or new TB patients failing with first treatment course may receive the retreatment regimen containing first-line drugs: 2HREZS/1HREZ/5HRE

Treatment of drug-susceptible pulmonary TB with RHZE for two months followed by four months of RH or RHE has been highly effective in clinical trials (1). More than 95% of patients are cured using this regimen (1, 2, 3). The results are so impressive and repeatable that the lower rates of cure in national TB programs highlight the operational challenges of delivering a daily regimen over an extended period of time (4,5). The concept of daily, directly observed therapy, incorporating a full six months of R has been adopted by the majority of countries worldwide as a major part of Stop TB Strategy (5). India implemented the Revised National TB Control Program (RNTCP) in 1996 as a national government run system that used a thrice weekly regimen administered by DOT (6). Cure rates in India have been comparable with countries using daily dosing, TB mortality has dropped significantly, and the prevalence of TB has declined slightly over the last two decades (6). Nevertheless, high relapse rate of 11-13% has been reported in patients treated by DOT in the RNTCP in India from several different locations over the last several years (21, 23, 24). In places where the background of H resistance is high and/or HIV co-infection is common and in patients with cavitary disease the daily regimen is preferred because the intermittent dosing schedules result in higher rates of treatment failure and relapse (7, 8, 9). In India, H resistance is 11% in untreated TB patients and 37% in previously treated cases and the prevalence of HIV co-infection is 5% (6). In countries where H resistance is prevalent a full six months course of

Rifampicin is recommended with a third drug, Ethambutol, added to the four months continuation phase (2, 3, 18, 19). Recent data indicates that this is also safe in paediatric patients (20). The extension of the continuation phase for extra-pulmonary TB to 9 or 12 months is based on expert opinion rather than evidence.

The recommendation for “category 2” treatment for previously treated cases with the addition of streptomycin to the intensive phase is currently under review and it is safe to say that a drug sensitivity test, if available, is a better guide to retreatment TB than a “category 2” regimen (13, 14, 15, 16, 17, 18, 19, 21, 22, 23). The addition of a single drug to a failing regimen violates one of the tenets of TB therapy so close follow up of patients on a retreatment regimen is especially important (14).

Fixed dose combinations (FDCs) are desirable as they simplify drug procurement and logistics, the delivery of DOT and may increase adherence (10). It is important that the provider prescribe only quality-assured pills of fixed drug combinations in RNTCP and WHO recommended dosing (2,3,10). Individual drug dosing should be reserved for patients with toxicities or contraindications to one or more components of the FDC (10). The RNTCP guidelines outline dosing based on weight bands. Suggested weight bands for adults are: 30-39kg, 40-54kg, 55-70kg and >70kg. Recommended weight bands for paediatric patients are: 6-8kg, 9-12kg, 13-16kg, 17-20Kg, 21-24kg and 25-30kg.

The expert group acknowledged that the intermittent regimen used under the programme over the past decade is equally effective under direct observation as compared to the daily regimen, and choosing daily regimen does not undermine the successes of the programme (11,12). However, based on the above evidences and in the interest of having uniformity of care across all healthcare sectors to achieve the future vision of the programme for universal access to quality TB care and prevention of further drug resistance to TB; the choice for daily regimen was required. It was recommended that the programme to undertake an operational research to assess the feasibility of implementing daily therapy using FDCs under direct observation under programmatic settings.

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Standard 8

Monitoring treatment response

8.1 Follow-up sputum microscopy:

- Response to therapy in patients with pulmonary tuberculosis, new as well as retreatment cases, should be monitored by follow-up sputum microscopy/culture (one specimen) at the time of completion of the intensive phase of treatment and at the end of treatment.

8.2 Extension of intensive phase:

- The extension of the intensive phase is not recommended.

8.3 Offer DST in follow up sputum positive cases:

- If the sputum smear is positive in follow-up at any time during treatment, a rapid molecular DST (as the first choice) or culture-DST (at least for R and if possible for Isoniazid (H); Ofloxacin (O) and Kanamycin (K), if R-resistant/MDR) should be performed as laboratory facilities become available.

8.4 Response to treatment in extra-pulmonary TB:

- In patients with extra-pulmonary tuberculosis, the treatment response is best assessed clinically. The help of radiological and other relevant investigations may also be taken.

8.5 Response to treatment in children:

- In children, who are unable to produce sputum, the response to treatment may be assessed clinically. The help of radiological and other relevant investigations may also be taken.

8.6 Long- term follow up:

- After completion of treatment the patients should be followed up with clinical and/or sputum examination at the end of six and 12 months.

International standards recommend that a sputum sample should be collected at the end of the intensive phase (two months) and at the end of treatment (six months) to monitor the success of therapy (1,2). Recent evidence from India shows that collecting more than one sample added little to the detection of failure of treatment and therefore only one sample at two months is recommended for initial treatment monitoring (3,4,6). If the sample is positive for TB then it is recommended that a DST be done to guide further selection of therapy, either by a molecular probe for drug resistant loci or phenotypic DST in liquid culture. Consensus summarised by the WHO found little benefit for extending the intensive phase to three months if the two months smear was positive (2). It is, however, necessary to re-address adherence issues and/or other comorbid conditions that may have affected proper completion of the two months intensive phase (1).

Follow up of extra-pulmonary and smear negative TB is challenging and best done by regular clinical review. Chest X-ray has shown limited accuracy (5).

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Standard 9

Drug Resistant TB management

9.1 Treatment of M/XDR-TB(or R resistant TB):

- Patients with TB caused by drug-resistant organisms (especially M/XDR or only R resistance or with O or K resistance), microbiologically confirmed by an accredited laboratory, should be treated with specialized regimens containing quality assured second-line anti-tuberculosis drugs.

9.2 Model of care for drug resistant TB:

- Patients with DR-TB should be treated using mainly ambulatory care rather than models of care based principally on hospitalization. If required, a short period of initial hospitalisation is recommended.

9.3 Regimen for MDR - TB (or R resistant cases):

- The regimen chosen for MDR-TB may be standardized and/or based on microbiologically confirmed drug susceptibility patterns. At least four drugs (second line) to which the organisms are known or presumed to be susceptible, should be used. Most importantly the regimen should include at least Pyrazinamide, Ethambutol, a later-generation Fluoroquinolone (such as high dose Levofloxacin) and a parenteral agent (such as Kanamycin or Amikacin), Ethionamide (or Prothionamide), and either Cycloserine or PAS (P-aminosalicylic acid), if Cycloserine cannot be used.

9.4 Regimen for MDR-TB patients with O and/or K resistance detected early:

- Treatment regimen may be suitably modified in case of Ofloxacin and/or Kanamycin resistance at the initiation of MDR-TB treatment or during early intensive phase, preferably not later than four to six weeks.

9.5 Surgery in M/XDR-TB patients:

- All patients of M/XDR-TB should be evaluated for surgery at the initiation of treatment and/or during follow up.

9.6 Treatment duration in MDR-TB patients:

- Till newer effective drugs are available with proven efficacy with shorter duration of MDR-TB treatment; total treatment should be given for at least 24 months in patients newly diagnosed with MDR-TB (i.e. not previously treated for MDR-TB) with recommended intensive phase of treatment being six to nine months. The total duration may be modified according to the patient's response to therapy.

9.7 Specialist consultation in M/XDR-TB patients:

- Consultation with a specialist experienced in treatment of patients with M/XDR-TB should be obtained, whenever possible.

9.8 Ensuring adherence in M/XDR-TB patients:

- Patient support systems, including direct observation of treatment, are required to ensure adherence. It should be ensured that the patient consumes all the doses of the drugs.

9.9 Single sample follow up culture in M/XDR-TB patients:

- The use of sputum culture (1 sample) is recommended for monitoring of patients with M/XDR-TB during treatment.

9.10 Second line DST during treatment of MDR-TB:

- During the course of MDR-TB treatment, if the sputum culture is found to be positive at 6 months or later, the most recent culture isolate should be subjected to DST with second-line drugs (at least Ofloxacin and Kanamycin) to decide on further course of action. DST to other additional drugs may also be done if laboratory facilities are available to guide treatment.

9.11 Regimen for MDR-TB patients with Ofloxacin and/or Kanamycin resistance detected later:

- The patients with MDR-TB found to be resistant to at least Ofloxacin and/or Kanamycin during the later stage of MDR-TB treatment must be treated with a suitable regimen for XDR-TB using second line drugs including Group 5 drugs such as Amoxicillin-Clavulanate, Clarithromycin, Clofazimine, Linezolid, Thioacetazone, Imipenem to which the organisms are known or presumed to be susceptible.

9.12 New drugs:

- The new drugs e.g. Bedaquiline, Delamanid may be considered whenever scientific evidence for their efficacy and safety becomes available as per the national policy for newer antimicrobials. Appropriate regulatory mechanisms for distribution control needs to be ensured.

The treatment of drug resistant TB is much more complex and challenging than the treatment of drug susceptible TB and requires drugs with greater toxicities for longer periods of time with relatively less encouraging outcomes. Unfortunately the evidence for drug regimen recommendations for drug-resistant TB are based on observational studies and expert opinion and no large scale randomized controlled clinical trial data has been generated across the globe. Newer agents and newer regimens are becoming available and it is hoped the level of evidence for treatment choices increases in the next few years.

The new drugs e.g. Bedaquiline, however, may be considered whenever scientific evidence for their efficacy and safety is available as per the national policy for newer antimicrobials. Appropriate regulatory mechanisms for distribution control need to be ensured. This is of utmost importance to safeguard the new drugs from the risk of unregulated irrational use and emergence of resistance to these precious drugs.

Laboratory based microbiological confirmation of drug resistance is an important pre-requisite for deciding on an appropriate treatment regimen under consultation with a specialist experienced in management of M/XDR TB, wherever possible. Patients with tuberculosis caused by drug-resistant organisms (especially M/XDR or only Rifampicin resistance or with Ofloxacin or Kanamycin resistance), microbiologically confirmed by an accredited laboratory, should be treated with specialized regimens containing quality

assured second-line anti-tuberculosis drugs. For all practical purposes, Rifampicin resistance should be considered as a surrogate of MDR-TB and treated with the same regimen for MDR-TB. While all efforts should be made for microbiological confirmation, in exceptional circumstances (e.g. paediatric and extra-pulmonary cases) the MDR treatment may be considered in absence of the microbiological confirmation. Clear guiding principles need to be laid down by the national programme to define the eligibility of patients under such exceptional circumstances for treatment with second line anti-TB drugs in absence of microbiological confirmation.

The basic principles of drug-resistant TB treatment include using at least four second line drugs that the organism has demonstrated susceptibility to through DST or that guided by the current epidemiology of drug-resistance in the relevant population. In the treatment of patients with MDR-TB, four second-line anti-TB drugs likely to be effective (including a parenteral agent), as well as Pyrazinamide and Ethambutol should be included in the intensive phase (1, 2), the duration of that should be at least for six to nine months. Consider extending treatment at least 18 months beyond the last evidence of mycobacteria in a culture from the patient. Thus, the total duration of treatment should be at least 24 months up to a maximum of 27 months in patients newly diagnosed with MDR-TB (i.e. not previously treated for MDR-TB). The total duration of treatment may be modified according to the patient's response to therapy.

In the treatment of patients with MDR-TB, regimens should thus include at least Pyrazinamide, a Fluoroquinolone, a parenteral agent, Ethionamide (or Prothionamide), and either Cycloserine or PAS (P-aminosalicylic acid) if Cycloserine cannot be used. (1, 2). Treatment regimen may be suitably modified in case of Ofloxacin and/or Kanamycin resistance detected early at the initiation of MDR-TB treatment or during early intensive phase, preferably not later than four to six weeks. However, for patients on MDR-TB regimen that are found to be resistant to at least Ofloxacin and/or Kanamycin during the later stage of MDR-TB treatment; they must be treated with a suitable regimen for XDR-TB using second line drugs including Group 5 drugs to which the organisms are known or presumed to be susceptible.

Ambulatory care is the preferred choice for management of DR-TB patients rather than models of care based principally on hospitalization as there are

convincing evidences that improving access to treatment for DR-TB through decentralization of care to centers near the patient's residence reduced the risk of default (2,3). However, if required, a short period of initial hospitalisation is recommended (2). Patient support systems, including direct observation of treatment, are required to ensure adherence. It should be ensured that the patient consumes all the doses of the drugs as missed doses for more than a week increases the odds of further augmentation of drug resistance and adversely affects treatment outcomes. Monitoring of treatment should be done by collecting a single monthly sample of sputum for culture from month three to month seven and then quarterly until the end of therapy. It has been observed in an operational research conducted under the RNTCP that there is no meaningful advantage in using two specimens and a single specimen policy could be safely implemented with negligible clinical effect on MDR-TB patients and favourable resource implications for RNTCP(4). Prompt identification of early failures of MDR-TB regimen and timely actions for initiating second line DST in culture isolates of such patients is alluded to in Standard 4. However, if the sputum culture is found to be positive at six months or later and the patient has no clinical or radiological deterioration, a repeat DST may be done to confirm sensitivity status.

Last but not the least, it must be emphasized that treatment of drug resistant TB can be complicated by drug toxicities, drug to drug interactions and emerging DST patterns and enlisting the help of an expert in DR-TB should be sought sooner rather than later through more than 100 established DR TB centers across the country.

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Standard 10

Addressing TB with HIV infection and other comorbid conditions

10.1 Treatment of HIV infected TB patients:

- TB patients living with HIV infection should receive the same duration of TB treatment with daily regimen as HIV-negative TB patients.

10.2 Anti-retroviral therapy and co-trimoxazole prophylactic therapy in HIV infected TB patients:

- Anti-retroviral therapy must be offered to all patients with HIV and TB as well as drug-resistant TB who require second-line anti-TB drugs, irrespective of CD4 cell-count, as early as possible (within the first eight 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. Patients with TB and HIV infection should also receive Co-trimoxazole as prophylaxis for other infections.

10.3 Isoniazid preventive therapy in HIV patients without active TB:

- People living with HIV (PLHIV) should be screened for TB using four symptom complexes (current cough or fever or weight loss or night sweats) at HIV care settings and those with any of these symptoms should be evaluated for ruling out active TB. All asymptomatic patients in whom active TB is ruled out, Isoniazid Preventive Therapy (IPT) should be offered to them for six months or longer.

PLHIV are more susceptible to TB infection, more likely to develop active TB disease after infection and more likely to suffer from severe TB and disseminated, extra-pulmonary TB. In general, the treatment for TB in PLHIV is the same as treatment for patients without HIV and treatment outcomes are successful although the mortality rate of PLHIV is higher, more so with DR-TB

comorbidity than the HIV uninfected (1). With growing evidences it is globally recommended, that HIV infected TB patients should be treated with daily regimen (2,3,4,5). Intermittent regimen has been proven to lead to higher risk for relapse and development of acquired Rifampicin resistance if intermittent dosing of Rifampicin was started during the intensive phase of treatment in HIV-infected patients treated with Rifampicin-based regimens. (2,3,4,5)

Anti-retroviral therapy must be offered to all patients with HIV and TB as well as drug-resistant TB who require second-line anti-TB drugs, irrespective of CD4 cell-count, as early as possible (within the first eight weeks) following initiation of anti-TB treatment(2,3,5). A number of recent studies have investigated the optimal timing of TB and HIV treatment to reduce mortality and it seems clear that as soon as possible after initiating treatment for active TB in a PLHIV they should be started on antiretroviral therapy (2, 5). ART reduces the risk of TB relapse and acquired drug resistance to rifampicin in HIV infected TB patients (2,3,5). Further, in settings with high Fluoroquinolone resistance and extensive prior second-line treatment, encouraging results are being achieved in an ambulatory MDR-TB programme in a slum setting in India. Rapid scale up of both Antiretroviral Therapy (ART) and second-line treatment for MDR-TB are needed to ensure survival of co-infected patients and mitigate this growing epidemic (6). Considerations such as the ability to tolerate a large pill burden, drug interactions and toxicities all have to be balanced with the life-saving treatment of both TB and HIV simultaneously.

Appropriate arrangements for access to anti-retroviral drugs should be made for patients. However, initiation of treatment for TB should not be delayed. Patients with TB and HIV infection should also receive co-trimoxazole as prophylaxis for other infections (3). In PLHIV that do not appear acutely ill and do not have one or more of the WHO recommended four symptom screens for active TB are very unlikely to be suffering from active TB and may safely be given Isoniazid Preventative Therapy (IPT) for at least six months as part of a comprehensive package of HIV care(7). IPT should be given to such individuals irrespective of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women (7). Recent studies have demonstrated the profound protective effect of IPT although those that derive the most benefit are TST positive. In addition, evidence from India, along with other countries, points to a prolonged course of IPT being more protective than the standard six month course.

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Standard 11

Treatment adherence

11.1 Patient-centered approach for adherence:

- To assess and foster adherence, a patient-centered 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.

11.2 Measures for treatment adherence:

- Supervision and support should be individualized and should draw on the full range of recommended interventions and available support services, including patient counselling and education. A central element of the patient centered strategy is the use of measures to assess and promote adherence to the treatment regimen and to address poor adherence when it occurs. These measures should be tailored to the individual patient's circumstances based on details of the patient's clinical and social history and be mutually acceptable to the patient and the provider.

11.3 Trained treatment supporter for treatment adherence:

- Such measures may include identification and training of a treatment supporter (for tuberculosis and, if appropriate, for HIV, Diabetes Mellitus etc.) who is acceptable, accessible and accountable to the patient and to the health system.

11.4 Use of ICT to promote treatment literacy and adherence:

- Optimal use of ICT should be done to promote treatment literacy and adherence

Treatment adherence is a critical determinant of treatment outcomes, prognosis and further emergence of DR-TB in patients experiencing irregular and incomplete treatment. The DOTS Strategy has been the backbone of most country's TB programmes for the last decade. In certain places, strict

healthcare worker DOTS has been cost-effective and sustainable and resulted in control of limited TB epidemics. However, accumulating evidence has pointed to the effectiveness of a wide variety of approaches including community and family-centered DOTS, which is more achievable for most developing healthcare systems and produce comparable outcomes to healthcare worker supervised DOTS(1).

However, treatment adherence goes beyond the realm of DOTS to a larger concept of treatment support system developed with mutual trust and respect between the patient, family, providers, treatment supporters and the health system at large to promptly identify and address all possible factors that could lead to treatment interruptions. This includes not only medical factors such as promptly addressing co-morbidities, adverse drug reactions and emergencies but also spans out to addressing various social, vocational, nutritional, economic, psychological stress experienced by the patient throughout the course of treatment. Periodic regular and effective supervision by the public health supervisors at various levels and close monitoring of the progress made by the patient on treatment by the treating provider are critical components to ensure high standards of care. Capacity building and engaging with local community based organizations, self-help groups and patient support groups could prove to be effective interventions to promote treatment adherence (2, 3).

India is enabled with highly functional ICT systems and a population that is technology-literate. Through the use of SMS reminders and call center linkages between patients, providers and pharmacists, it is hoped that adherence to treatment will reach the necessary levels to reduce the prevalence of TB throughout India.

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Standard 12

Public health responsibility

- 12.1 Any practitioner treating a patient for tuberculosis is assuming an important public health responsibility to prevent on-going transmission of the infection and the development of drug resistance.
- 12.2 To fulfil this responsibility, the practitioner must not only prescribe an appropriate regimen, but when necessary, also utilize local public health services / community health services, and other agencies including NGOs to assess the adherence of the patient and to address poor adherence when it occurs. (1)

India continues to have high TB incidence and the mortality due to TB is still unacceptably high. The challenges of TB control in India are magnified by the existence of parallel systems for TB diagnosis and treatment – the public and private. Each system takes care of approximately half the TB cases (2) and methods and standards vary greatly depending on whether public or private care is accessed and furthermore what type of private care is sought, from super-speciality tertiary institutions to non-qualified providers (3). In part publishing, these standards of care attempts to standardise care so that certain responsibilities of the provider, whether public or private, are clear. In addition Standard 13, the notification of TB cases from both public and private providers, is expected to improve surveillance and quality of the care delivered and a subsequent reduction in the burden of TB in India.

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Standard 13

Notification of TB cases

- 13.1 All health establishments must report all TB cases and their treatment outcomes to public health authorities (District Nodal Officer for Notification).
- 13.2 Proper feedback need to be ensured to all healthcare providers who refer cases to public health system on the outcome of the patients which they had referred.

TB is a notifiable disease in India as per the government order dated 7 May, 2012 and requires that all healthcare providers who have diagnosed a case of TB through microbiological testing or clinically diagnosed and/or started treatment for TB must report to the District Nodal Officer for Notification(1). Notification is a basic public health activity common to diseases of public health importance. With notification, public health authorities can identify TB patients and offer necessary public health care, supervise and support for the quality of treatment, and monitor disease trends. Ensuring notification of all TB cases is the most important step for a comprehensive TB surveillance system, which is required for effective TB control in the country. Cases are defined as anyone who has a microbiological (smear or culture) or approved molecular test proven disease or anyone who has a clinical syndrome consistent with active TB and is started on TB treatment. The requirement for reporting applies equally to government-run facilities and to private facilities. In both settings, it is the primary TB care provider or laboratory diagnostician's responsibility to ensure that the required notification is completed (2). RNTCP has an electronic TB notification system (NIKSHAY) wherein all providers can register and notify cases -<http://nikshay.gov.in>

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Standard 14

Maintain records for all TB patients

14.1 A written record of all medications given, bacteriologic response, adverse reactions and clinical outcome should be maintained for all patients.

Patient-level recording of details of diagnosis, treatment and outcome are the foundations of any effective public health surveillance system. Use of appropriate technology such as Nikshay should improve the quality and accessibility to a primary provider initiated record that is linked at every level from a primary clinic to the State Department of Health. In turn, it is the duty of the programme to monitor outcomes, both at primary level and aggregated into larger units, on a regular basis and reports the information that allow timely actions to improve services as needed.

The Government of India through a gazette notification has made all anti-TB drugs under schedule H1. These drugs should not be dispensed without a valid prescription from a qualified practitioner. A copy of the prescription should be maintained and details of the patient to be recorded by the chemist and should be made available for verification by the responsible public health authorities.

Standard 15

Contact investigation

- 15.1 All care providers to patients with TB should ensure all household contacts and other persons who are in close contact with TB patients are screened for TB as per defined Diagnostic Standards.
- 15.2 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.

The highest priority contacts for active screening are:

- o Persons with symptoms suggestive of tuberculosis
- o Children aged <six years
- o Contacts with known or suspected immune-compromised patient, particularly HIV infection
- o Contacts with Diabetes Mellitus
- o Contacts with other higher risks including pregnancy, smokers and alcoholics etc.
- o Contacts of patients with DR-TB. In case of contact with a DR-TB index case, close clinical monitoring should be provided, as there is no evidence that treatment of latent infection with available drugs is presently effective

A contact investigation should focus on those in close contact with the index case, most importantly family members and other members of the household who may have prolonged exposure. Among this group of contacts past studies have found 4.5% to have TB (1, 2). A recent study in India found 8.7% of household contacts were diagnosed with TB (3). Particular attention should be paid to contacts with the highest susceptibility to TB infection and subsequent active disease, namely small children and immunosuppressed people.

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Standard 16

Isoniazid Prophylactic therapy

16.1 Children <6 years of age who are close contacts of a TB patient, after excluding active TB, should be treated with isoniazid for a minimum period of six months and should be closely monitored for TB symptoms.

Because children are more susceptible to TB infection, more likely to develop active TB disease soon after infection, and more likely to develop severe forms of disseminated TB, it is widely recommended (The Union, WHO) that close contacts of index cases under the age of 6 who do not have active TB should receive IPT. Close contacts of index cases with proven or suspected DR-TB should be monitored closely for signs and symptoms of active TB as isoniazid may not be prophylactic in these cases.

Standard 17

Airborne infection control

- Airborne infection control should be an integral part of all health care facility infection control strategy.

Each healthcare facility caring for patients who have, or are suspected of having, TB should develop and implement an appropriate airborne infection control plan as per the national guidelines. Administrative, environmental and personal protective measures should be implemented in all health care facilities as per national airborne infection control guidelines. Protection of health care workers from airborne infection should be ensured through adequate preventive measures including training, personal protection measures in high risk situations and periodic screening at least once a year.

TB is an airborne bacillus spread through inhalation of droplets. Therefore, in addition to general infection control procedures recommended for all health care facilities such as regular hand-washing, attention must be paid to limiting risk from airborne transmission. Airborne infection control measures are generally grouped into three main categories; environmental, administrative and managerial. Environmental controls require safe infrastructure and involve designing buildings and systems that promote safe air exchange e.g. HVAC systems, air flow management and UV light sterilization of areas. These tend to be expensive and installation is disruptive. Managerial controls refer to management plans that promote and enable safe practices in every facility and as such every healthcare facility, whether public or private, should have clear plans for an airborne infection control strategy that are implemented and monitored for completeness. Administrative controls are the most cost-effective and should be within the reach of every facility. They include screening and timely diagnosis of TB in all clients of the facility, respectful and non-stigmatizing removal of people with active TB from the general circulation of clients for rapid assessment and care, and use of personal protective equipment by active TB patients and staff to protect both staff and other patients. Such guidelines for Indian facilities are available at www.tbcindia.nic.in

Standard 18

Quality assurance systems

18.1 Quality assurance for diagnostic tests:

- All healthcare providers should ensure that all diagnostic tests used for diagnosis of TB are quality assured.

18.2 Quality assurance for anti-TB drugs:

- Quality assurance system should ensure that all anti-TB drugs used in the country are subjected to stringent quality assurance mechanisms at all levels (from manufacturer to patients). Providers should ensure that all anti-TB drugs prescribed come from a Quality assured source.

India has banned the use of commercial serology tests for diagnosis of TB. However, any diagnostic test used for diagnosing TB should have a quality assurance system in place. India's national TB programme (RNTCP) have established a good external quality assurance system for TB diagnostics, and is available to both public and private laboratories.

The same principle applies to the use of drugs; the drugs should be from a quality assured source and should be under a standard Quality Assurance process.

Standard 19

Panchayati Raj Institutions

19.1 Panchayati Raj Institutions (PRIs) and elected representatives have an important role to share the public health responsibility for TB control with the healthcare providers, patients and the community.

Health being an important responsibility of the PRIs in India, there are many opportunities for greater involvement of the PRIs for TB control. Because the diagnosis and treatment of TB is complicated and takes long, and mistreatment of TB and emergence of drug-resistant TB affects everybody in the community, the Panchayat should be involved in all aspects of TB control. PRIs can facilitate good communication between facilities, public or private, that diagnose and treat TB and the communities, which they serve thus greatly helping in mobilizing community support for TB control. PRIs can help TB patient to link to other social welfare schemes, can help in nutritional and rehabilitation support etc.

Standard 20 Health education

- 20.1 Every TB symptomatic should be properly counselled by the healthcare providers
- 20.2 TB patients and their family members should get proper counselling and health education at every contact with healthcare system

Proper health education to the patient and family is very important for TB care. There should be systems for education and counselling as an integral part of TB treatment. Every visit of the patient to the healthcare provider and visit of the health worker to the patient's home should be utilised for health education.

Standard 21

Death audit among TB patients

21.1 Every death among TB patients should be audited by a competent authority.

Investigation into the cause of death is an important standard which needs to be followed to study the conditions that led to the death in order to initiate actions to prevent development of such conditions to other TB patients. Every TB death should be notified to the concerned authority. Competent authority at the district level should do the death audit of every TB death and provide a report to the programme to take necessary steps for preventing avoidable deaths.

Introduction to Standards for Social Inclusion for TB

The principles for introducing Standards for Social Inclusion in TB Care are:

- To ensure all individuals presenting to the healthcare facility are treated with dignity, irrespective of their health and socio-economic status.
- To ensure universal delivery of quality assured TB diagnostic and treatment services across public and private sector.
- To ensure visibility and accessibility of the TB service programme to all, irrespective of socio-economic status.
- To find and treat women, children and the elderly within hard to reach populations (Marginalized communities in rural and urban populations).
- To eliminate out of pocket expenditure including those incurred on covering travel costs and bridging the nutrition gap.
- To address loss of income when work day is lost due to TB.
- To ensure no one is left without a plan of action to address their presenting complaint if it is not because of TB.

The Patients Charter (accompanying the ISTC) is the key operational guideline in engaging with patients in all TB care settings.

Standard 22

Information on TB prevention and care seeking

22.1 All individuals especially women, children, elderly, differently abled, other vulnerable groups and those at increased risk should receive information related to TB prevention and care seeking.

Standard 23

Free and quality services

- 23.1 All patients, especially those in vulnerable population groups, should be offered free or affordable quality assured diagnostic and treatment services, which should be provided at locations and times so as to minimize workday or school disruptions and maximize access.

Standard 24

Respect, confidentiality and sensitivity

24.1 All people seeking or receiving care for TB should be received with dignity and managed with promptness, confidentiality and gender sensitivity. Public health responsibilities including notification, contact tracing, chemoprophylaxis, fast tracking, outcome monitoring etc. should be sensitive to respect and confidentiality of patients.

Standard 25

Care and support through social welfare programmes

25.1 Healthcare providers should endeavour to derive synergies between various social welfare support systems such as RSBY, nutritional support programmes, national rural employment guarantee scheme etc. to mitigate out of pocket expenses such as transport and wage loss incurred by people affected by TB.

Standard 26

Addressing counseling and other needs

26.1 Persons affected by TB and their family members should be counselled at every opportunity, to address information gaps and to enable informed decision-making. Counseling should also address issues such as healthcare, physical, financial, psycho-social and nutritional needs.



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