

**Kingdom of Swaziland**

**MINISTRY OF HEALTH**

**NATIONAL TUBERCULOSIS PROGRAMME**

**MANUAL**



CONTENTS

[PREFACE 8](#_Toc318970902)

[FOREWORD 9](#_Toc318970903)

[ACKNOWLEDGEMENT 10](#_Toc318970904)

[EXECUTIVE SUMMARY 12](#_Toc318970905)

[1.1 Purpose of the guidelines 12](#_Toc318970906)

[1.2 Target audience 12](#_Toc318970907)

[1.3 Scope 12](#_Toc318970908)

[1.4 Justification for guideline update 12](#_Toc318970909)

[1.5 Highlights of the new revision 13](#_Toc318970910)

[CHAPTER 1 INTRODUCTION 16](#_Toc318970911)

[1.1 The country 16](#_Toc318970912)

[1.2 The health system 16](#_Toc318970913)

[CHAPTER 2 THE NATIONAL TUBERCULOSIS CONTROL PROGRAMME 18](#_Toc318970914)

[2.1 Global Epidemiology of TB 18](#_Toc318970915)

[2.2 The Tuberculosis situation in Swaziland 18](#_Toc318970916)

[2.3 The National TB Programme 18](#_Toc318970917)

[2.4 The TB Control Strategy and framework for Swaziland 19](#_Toc318970918)

[2.4.1 Central Unit 19](#_Toc318970919)

[2.4.2 Regional Level 19](#_Toc318970920)

[2.4.3 Basic TB management units 19](#_Toc318970921)

[2.4.4 The National TB Hospital 20](#_Toc318970922)

[2.4.5 Community Level 20](#_Toc318970923)

[2.4.6 TB Laboratory services 20](#_Toc318970924)

[2.4.7 Intra-ministerial collaboration 20](#_Toc318970925)

[2.4.8 NTP Partners 21](#_Toc318970926)

[2.4.9 NTP funding 21](#_Toc318970927)

[2.5 Goals, Objectives and targets of the National TB Programme 21](#_Toc318970928)

[2.5.1 The Objectives: 21](#_Toc318970929)

[2.5.2 The targets: 21](#_Toc318970930)

[2.5.3 Programme Goal 22](#_Toc318970931)

[2.5.4 Objectives 22](#_Toc318970932)

[2.5.5 Swaziland Stop TB Partnership targets 22](#_Toc318970933)

[CHAPTER 3 TB CASE FINDING AND REGISTRATION 23](#_Toc318970934)

[3.1 Importance of TB case finding and registration 23](#_Toc318970935)

[3.2 Identification of persons suspected of having pulmonary TB: 23](#_Toc318970936)

[3.2.1 Sputum Collection, Labeling, Storage and Transport 23](#_Toc318970937)

[3.2.1.1 Sputum collection procedure 23](#_Toc318970938)

[3.2.1.2 Sputum labeling (Barcode reader?) 24](#_Toc318970939)

[3.2.1.3 Sputum storage 24](#_Toc318970940)

[3.2.1.4 Transportation of sputum specimens 24](#_Toc318970941)

[3.3 Identification of persons suspected of having Extra-Pulmonary TB: 25](#_Toc318970942)

[3.3.1 Common types of Extra-pulmonary TB 25](#_Toc318970943)

[3.4 Identification of Children with presumptive TB: 26](#_Toc318970944)

[3.5 Defining a case of tuberculosis 26](#_Toc318970945)

[3.5.1 The importance of defining a case 26](#_Toc318970946)

[3.5.2 The TB case definitions 26](#_Toc318970947)

[3.6 TB patients registration groups 27](#_Toc318970948)

[3.6.1 Site of TB disease 27](#_Toc318970949)

[3.6.2 Bacteriology (result of sputum smear) in pulmonary TB 27](#_Toc318970950)

[3.6.3 History of previous treatment 28](#_Toc318970951)

[New patients: 28](#_Toc318970952)

[CHAPTER 4 DIAGNOSIS OF TB 29](#_Toc318970953)

[4.1 Approach to TB diagnosis 29](#_Toc318970954)

[4.2 Bacteriological confirmation of pulmonary TB diagnosis 29](#_Toc318970955)

[4.2.1 Microscopy 29](#_Toc318970956)

[4.2.2 Xpert MTB/Rif (Gene Xpert) 31](#_Toc318970957)

[4.2.2.1 Practical considerations for use of Xpert MTB/Rif 31](#_Toc318970958)

[4.2.2.2 Use of Xpert MTB/Rif results 31](#_Toc318970959)

[4.2.2.3 Repeating Gene Xpert tests 32](#_Toc318970960)

[4.2.3 Use of interferon gamma tests: 32](#_Toc318970961)

[4.2.4 Use of Commercial sero-diagnostics 33](#_Toc318970962)

[4.3 Diagnosis of drug resistant tuberculosis 33](#_Toc318970963)

[4.3.1 Line Probe Assay (LPA) method 33](#_Toc318970964)

[4.3.2 Mycobacterial culture and drugs susceptibility testing (DST) 33](#_Toc318970965)

[4.3.2.1 Thin Layer Agar (TLA) culture method 34](#_Toc318970966)

[4.4 Sputum transportation 34](#_Toc318970967)

[4.5 Role of Other Investigations in TB Control 34](#_Toc318970968)

[4.5.1 Role of Chest x-rays 34](#_Toc318970969)

[4.6 Revised diagnostic Algorithms according to existing TB diagnostic equipment in Swaziland 35](#_Toc318970970)

[4.7 Confirming diagnosis of Extra-Pulmonary TB 38](#_Toc318970971)

[4.7.1 TB Meningitis 38](#_Toc318970972)

[4.7.2 Tuberculous Lymphadenopathy 40](#_Toc318970973)

[4.7.3 Miliary TB 40](#_Toc318970974)

[4.7.4 Tuberculous pleural effusions 40](#_Toc318970975)

[4.7.5 Tuberculosis of the spine 40](#_Toc318970976)

[CHAPTER 5 QUALITY ASSURANCE OF LABORATORY SERVICES 41](#_Toc318970977)

[5.1 Importance of Laboratory Services in TB Control 41](#_Toc318970978)

[5.2 TB laboratory Network in Swaziland 41](#_Toc318970979)

[5.2.1 The National Reference laboratory 41](#_Toc318970980)

[5.2.2 The Regional laboratories 42](#_Toc318970981)

[5.3 Assuring Quality of Smear Microscopy 42](#_Toc318970982)

[5.3.1 External Quality Assessment (EQA) 43](#_Toc318970983)

[5.3.2 On-site evaluation of Microscopy Centers: 43](#_Toc318970984)

[5.3.3 Panel Testing 44](#_Toc318970985)

[5.3.4 Random Blinded Rechecking of Routine Slides 44](#_Toc318970986)

[5.4 Conducting visits to microscopy centres 44](#_Toc318970987)

[5.4.1 Preparing for visits: 45](#_Toc318970988)

[5.4.2 Conducting the visit 45](#_Toc318970989)

[5.4.3 Follow up Quality improvement 45](#_Toc318970990)

[5.5 Monitoring documentation related to microscopy examinations and other diagnostic methods 45](#_Toc318970991)

[5.5.1 Laboratory Request form 46](#_Toc318970992)

[5.5.2 Tuberculosis laboratory register 46](#_Toc318970993)

[5.6 The Ziehl–Neelsen staining procedure 48](#_Toc318970994)

[5.6.1 Maintain an adequate supply of reagents and other materials 48](#_Toc318970995)

[5.6.2 Disposal of laboratory materials. 49](#_Toc318970996)

[CHAPTER 6 TREATMENT OF TUBERCULOSIS 51](#_Toc318970997)

[6.1 The aims of TB treatment 51](#_Toc318970998)

[6.2 Essential anti-TB drugs 51](#_Toc318970999)

[6.2.1 Fixed-Dose Combinations 51](#_Toc318971000)

[6.2.2 Advantages of FDCs compared to single formulation drugs 51](#_Toc318971001)

[6.3 Standard TB Treatment Regimens for Adults and adolescents 52](#_Toc318971002)

[6.3.1 Treatment of New tuberculosis cases – Adults and adolescents 53](#_Toc318971003)

[6.3.2 Treatment of previously treated cases 53](#_Toc318971004)

[6.3.3 Treatment of extra-pulmonary tuberculosis 54](#_Toc318971005)

[6.3.4 Important drug to drug interactions 54](#_Toc318971006)

[6.3.5 TB Treatment regimens in special circumstances 55](#_Toc318971007)

[6.3.5.1 Treatment for pregnant women 55](#_Toc318971008)

[6.3.5.2 Treatment for breastfeeding women 55](#_Toc318971009)

[6.3.5.3 Treatment for women taking the oral contraceptive pill 55](#_Toc318971010)

[6.3.5.4 Treatment for patients with liver disorders 55](#_Toc318971011)

[6.3.5.5 Treatment of patients with renal failure 56](#_Toc318971012)

[6.4 The Role of Adjuvant Steroid Treatment 56](#_Toc318971013)

[CHAPTER 7 PATIENT SUPPORT AND DOT PROVISION 58](#_Toc318971014)

[7.1 Importance of patient support 58](#_Toc318971015)

[7.2 Community Based DOTS (CB DOTS) 58](#_Toc318971016)

[7.2.1 Identification of treatment supporter 58](#_Toc318971017)

[7.2.2 Orient the supporter 58](#_Toc318971018)

[7.2.3 Provide enough drugs to last until the next visit. 59](#_Toc318971019)

[7.2.4 Keep regular contact with the patient and supporter 59](#_Toc318971020)

[7.3 Prevention of treatment interruption 59](#_Toc318971021)

[7.3.1 Role of Adherence Officers 59](#_Toc318971022)

[7.4 Nutritional support to TB patients 60](#_Toc318971023)

[7.4.1 Food by prescription 60](#_Toc318971024)

[7.4.2 Food Prescription Initiation procedure 60](#_Toc318971025)

[CHAPTER 8 MONITORING TUBERCULOSIS TREATMENT 63](#_Toc318971026)

[8.1 Basis for monitoring TB treatment 63](#_Toc318971027)

[8.1.1 Clinical monitoring: 63](#_Toc318971028)

[8.1.1.1 Monitoring Extra-pulmonary TB treatment 63](#_Toc318971029)

[8.1.2 Bacteriological monitoring: 63](#_Toc318971030)

[8.1.2.1 New sputum smear-positive pulmonary TB patients 64](#_Toc318971031)

[8.1.2.2 Previously treated pulmonary sputum smear-positive patients 64](#_Toc318971032)

[8.1.2.3 New sputum smear-negative pulmonary TB patients 64](#_Toc318971033)

[8.2 Management of treatment interruption 66](#_Toc318971034)

[8.2.1 Monitoring of TB Patients for Adverse Effects of Anti-TB Drugs 67](#_Toc318971035)

[8.2.1.1 Prevention of adverse effects of drugs 67](#_Toc318971036)

[8.2.1.2 Adverse effects of anti-tuberculosis drugs 67](#_Toc318971037)

[8.2.1.3 Symptom-based approach to management of drug side-effects 67](#_Toc318971038)

[8.2.1.4 Management of skin itching and rash 68](#_Toc318971039)

[8.2.1.5 Reintroduction of anti-TB drugs following drug reaction 69](#_Toc318971040)

[8.3 Determining TB Treatment Outcomes 69](#_Toc318971041)

[CHAPTER 9 MANAGEMENT OF CHILDHOOD TUBERCULOSIS 71](#_Toc318971042)

[9.1 Importance of childhood TB 71](#_Toc318971043)

[9.2 Approach to diagnosis of TB in children 71](#_Toc318971044)

[9.2.1 Evaluation for paediatric TB disease 72](#_Toc318971045)

[9.2.2 Clinical examination (including growth assessment) 73](#_Toc318971046)

[9.3 Special Investigations for paediatric TB 73](#_Toc318971047)

[9.3.1 Chest X-ray 73](#_Toc318971048)

[9.3.2 Role of a Tuberculin Skin Test 74](#_Toc318971049)

[9.3.3 Bacteriological confirmation of childhood TB 75](#_Toc318971050)

[9.3.3.1 Techniques for obtaining specimens from children 75](#_Toc318971051)

[9.4 Paediatric Extrapulmonary TB 76](#_Toc318971052)

[9.4.1 TB meningitis 76](#_Toc318971053)

[9.4.2 Lymph node TB 76](#_Toc318971054)

[9.4.3 Abdominal TB 77](#_Toc318971055)

[9.4.4 Bone and joint disease 77](#_Toc318971056)

[9.4.5 BCG disease 77](#_Toc318971057)

[9.5 Paediatric DR-TB 78](#_Toc318971058)

[9.6 PadediatricTB treatment 78](#_Toc318971059)

[9.6.1 Treatment of susceptible paediatric TB 78](#_Toc318971060)

[9.6.2 Use of Steroids in Pediatric TB forms 79](#_Toc318971061)

[9.6.3 Paediatric anti-TB drugs dosage 79](#_Toc318971062)

[9.7 Paediatric MDRTB treatment 80](#_Toc318971063)

[9.8 Follow up of children on TB treatment 81](#_Toc318971064)

[9.9 TB-HIV COINFECTION 81](#_Toc318971065)

[9.9.1 Anti-Retroviral Therapy 81](#_Toc318971066)

[9.9.1.1 Recommended regimens for HIV+ pediatric patients on TB treatment: 81](#_Toc318971067)

[9.9.1.2 Alternative ART regimen options for special situations requiring TB/HIV co-treatment: 82](#_Toc318971068)

[9.9.2 Cotrimoxazole Prophylaxis 82](#_Toc318971069)

[9.9.3 Administering treatment and ensuring adherence 82](#_Toc318971070)

[9.10 Prevention of Paediatric TB 83](#_Toc318971071)

[9.10.1 Paediatric Isoniazid Preventive Therapy 83](#_Toc318971072)

[CHAPTER 10 COLLABORATIVE TB AND HIV ACTIVITIES 84](#_Toc318971073)

[10.1 TB/HIV interaction 84](#_Toc318971074)

[10.2 HIV Testing and Counseling (HTC) 84](#_Toc318971075)

[10.3 HIV prevention in TB patients 84](#_Toc318971076)

[10.4 TB treatment in people living with HIV 84](#_Toc318971077)

[10.5 Co-trimoxazole preventive therapy 85](#_Toc318971078)

[10.6 Antiretroviral therapy 85](#_Toc318971079)

[10.6.1 Interactions with ART Regimens 85](#_Toc318971080)

[10.6.2 When to start ART? 86](#_Toc318971081)

[10.7 Drug susceptibility testing 86](#_Toc318971082)

[10.8 Dealing with TB diagnosed in patients already on ART 86](#_Toc318971083)

[10.9 HIV-related prevention, treatment, care and support 87](#_Toc318971084)

[10.9.1.1 Managing side effects in concurrent TB/HIV treatment 87](#_Toc318971085)

[10.9.1.2 Directly Observed Therapy for concomitant TB/HIV treatment 87](#_Toc318971086)

[10.9.1.3 Monitoring patients on concurrent ART and DOTS 87](#_Toc318971087)

[10.9.1.4 Immune Reconstitution Inflammatory Syndromeamong patients with HIV-related TB 88](#_Toc318971088)

[CHAPTER 11 INFECTION CONTROL 90](#_Toc318971089)

[11.1 Rationale 90](#_Toc318971090)

[11.2 Administrative Controls 90](#_Toc318971091)

[11.3 Environmental control measures 90](#_Toc318971092)

[11.4 Personal respiratory protection 91](#_Toc318971093)

[CHAPTER 12 MANAGEMENT OF MULTI-DRUG AND EXTENSIVELY RESISTANT TUBERCULOSIS 92](#_Toc318971094)

[12.1 Definitions 92](#_Toc318971095)

[12.2 Causes of MDR-TB 92](#_Toc318971096)

[12.3 When to Suspect MDR TB 93](#_Toc318971097)

[12.4 Laboratory Confirmation of MDR 93](#_Toc318971098)

[12.5 Management of MDR TB 94](#_Toc318971099)

[12.5.1 DR-TB treatment 95](#_Toc318971100)

[12.5.2 Completion of MDR therapy 95](#_Toc318971101)

[12.5.3 Follow-up after completion of MDR therapy 96](#_Toc318971102)

[12.5.4 Interruption and re-initiation of treatment 96](#_Toc318971103)

[12.5.5 MDR TB Treatment in Special Situations. 96](#_Toc318971104)

[12.5.5.1 MDR-TB treatment in Children: 96](#_Toc318971105)

[12.5.5.2 MDR TB treatment and pregnancy 97](#_Toc318971106)

[12.5.5.3 MDR TB treatment and diabetes 97](#_Toc318971107)

[12.5.5.4 MDR TB and renal insufficiency 98](#_Toc318971108)

[12.5.6 Extensively Drug Resistant Tuberculosis (XDR-TB) 98](#_Toc318971109)

[CHAPTER 13 SUPERVISION, MONITORING AND EVALUATION 99](#_Toc318971110)

[13.1 Importance of SME 99](#_Toc318971111)

[13.2 Programme supervision 99](#_Toc318971112)

[13.2.1 Monitoring tools 100](#_Toc318971113)

[13.3 Programme monitoring 100](#_Toc318971114)

[13.3.1 Programme indicators: 100](#_Toc318971115)

[13.3.1.1 Cohort Analysis 101](#_Toc318971116)

[13.3.1.2 Reports 101](#_Toc318971117)

[13.3.1.3 Quarterly Report on Case Finding 101](#_Toc318971118)

[13.3.1.4 Quarterly Report on Treatment Outcome 101](#_Toc318971119)

[13.3.1.5 Information Flow 102](#_Toc318971120)

[13.4 Programme evaluation 102](#_Toc318971121)

[13.5 Reporting and Recording system 102](#_Toc318971122)

[CHAPTER 14 ADVOCACY, COMMUNICATION, SOCIAL MOBILISATION 104](#_Toc318971123)

[14.1 Introduction 104](#_Toc318971124)

[14.2 Communication as an overarching theme 104](#_Toc318971125)

[14.3 Advocacy to change political agendas 104](#_Toc318971126)

[14.4 Social mobilization to build partnerships 104](#_Toc318971127)

[14.5 Selection of Advocacy Strategies and Tactics 105](#_Toc318971128)

[14.5.1 Media strategy 105](#_Toc318971129)

[14.5.2 NTP Publications strategy 105](#_Toc318971130)

[14.5.3 Coalitions and working with NGOs 105](#_Toc318971131)

[14.5.4 Insider strategy 106](#_Toc318971132)

[14.6 Message Development and Presentation 106](#_Toc318971133)

[14.7 Role of NGOs , Private Sector and communities in TB control and involvement in social mobilisation 106](#_Toc318971134)

[ANNEXES 109](#_Toc318971135)

[ANNEX 1: TB Programme Organogram 109](#_Toc318971136)

[ANNEX 2: Stop TB Partnership Organogram 110](#_Toc318971137)

[ANNEX 3: SPUTUM COLLECTION 111](#_Toc318971138)

[ANNEX 4: Prerequisites for implementation of XPERT MTB/Rif 112](#_Toc318971139)

[ANNEX 5: Key recommended actions at country level for Xpert MTB/Rif implementation 113](#_Toc318971140)

[ANNEX 6: BASIC GUIDE TO CXR READING 115](#_Toc318971141)

[ANNEX 7: TUBERCULIN SKIN TEST (TST) 116](#_Toc318971142)

[ANNEX 8: FINE NEEDLE ASPIRATION (FNA) 117](#_Toc318971143)

[ANNEX 9: GASTRIC ASPIRATE PROCEDURE FOR CULTURE OFM. *tuberculosis* 119](#_Toc318971144)

[14.8 Assure sample is well labeled and all forms correctly filled before sending the material to the laboratory.ANNEX 10: INDUCED SPUTUM IN CHILDREN 120](#_Toc318971145)

[ANNEX 11: PERFORMINGTHORACENTESIS 124](#_Toc318971146)

[ANNEX 12: PERFORMING LUMBAR PUNCTURE IN ADULTS 126](#_Toc318971147)

[ANNEX 13:PERFORMING LUMBAR PUNCTURE IN CHILDREN 128](#_Toc318971148)

[ANNEX 14: INFECTION CONTROL RISK ASSESSMENT TOOL 130](#_Toc318971149)

[ANNEX 15: HIV TESTING MODELS 131](#_Toc318971150)

[Annex 15 HUMAN RESOURCE DEVELOPMENT 133](#_Toc318971151)

[1 Planning Issues 133](#_Toc318971152)

[2How to Organize Training 133](#_Toc318971153)

[3 Monitoring and evaluation of training activities 134](#_Toc318971154)

[ANNEX 15:SUPPLIES AND LOGISTICS MANAGEMENT 135](#_Toc318971155)

[Rationale 135](#_Toc318971156)

[1. Estimating Drug Needs and Preparing Procurement Plan 135](#_Toc318971157)

[Estimate the expected number of cases in each treatment category and the drugs needed next quarter 135](#_Toc318971158)

[2 Logistics for laboratory materials 135](#_Toc318971159)

[Estimating Laboratory Materials Requirements 135](#_Toc318971160)

[3 Calculating number of Xpert catridges? 136](#_Toc318971161)

[REFERENCES 140](#_Toc318971162)

**List of tables:**

[Table 1: the usual clinical features and diagnostic tests of other forms of extrapulmonary TB 26](#_Toc318799532)

[Table 2: Guide for grading results of smear microscopy 31](#_Toc318799533)

[Table 3: Table showing symptom-based approach to the diagnosis of Extra-pulmonary TB 39](#_Toc318799534)

[Table 4: Essential anti-TB drugs 52](#_Toc318799535)

[Table 5: Recommended treatment regimen and anti-TB drug dosages for New TB cases 54](#_Toc318799536)

[Table 6: Recommended treatment regimen and dosages for relapse and return after interruption cases 55](#_Toc318799537)

[Table 7: Prednisolone indication and recommended doses in TB management 57](#_Toc318799538)

[Table 8: Recommended Schedule for follow up sputum examinations for PTB patients 64](#_Toc318799539)

[Table 9: Sputum follow-up algorithm for patients on anti-TB treatment 66](file:///C:\Users\samsonk\Desktop\Swaziland%20TB%20Manual-%2020%20Feb%202012msf_REVISED-SH_rev_WritingTeam-revisionsMarch12012.docx#_Toc318799540)

[Table 10: Management of TB treatment interruption 67](#_Toc318799541)

[Table 11: Guide to Management of side effects of first-line anti-TB drugs 68](#_Toc318799542)

[Table 12: Guide to performing anti-TB drug challenge and re-introduction 70](#_Toc318799543)

[Table 13: Definitions of TB treatment outcomes 70](#_Toc318799544)

[Table 15:Recommended Regimens for Pediatric Patients Naive to Treatment 83](#_Toc318799545)

[Table 16: Alternative Paediatric Regimens for Special Situations 83](#_Toc318799546)

[Table 17: Dosing for Cotrimoxazole Given Once Daily (TMP/SMX.CTX,Bactrim,Cotrim,Cozole) 83](#_Toc318799547)

[Table 18: Dosage of INH for prophylaxis in Children 84](#_Toc318799548)

[Table 19: TB Medicine/ARV Drug Regimen Recommendations 86](#_Toc318799549)

[Table 20: Overlapping Side effect adverse reactions to First-line anti-TB and ART drugs 90](#_Toc318799550)

[Table 21: Causes of DRTB 94](#_Toc318799551)

[Table 0.22: Classification (groups) of second line anti-tuberculosis drugs 96](#_Toc318799552)

[Table 23: Recording and reporting formats used in the National TB Programme 103](#_Toc318799553)

[Table 24: Analysis of training needs at various levels of the NTP 134](#_Toc318799554)

# PREFACE

Since the World Health Organization declared tuberculosis (TB) a global emergency in 1993, worldwide efforts to fight the disease have intensified considerably. In Swaziland, TB is associated with HIV and AIDS co-infection, social problems, difficulties in patient adherence and the threat of resistance against anti-tuberculous drugs. This is of great concern to the country, hence the need for the National Tuberculosis Control Programme (NTP) of Swaziland to be adequately positioned to face the challenges of controlling the disease.

The commitment of the Government of Swaziland to eliminate TB as a public health problem has resulted in strengthening the NTP at both national and Regional levels and increased allocation of funds to ensure universal access to quality TB services in line with the Abuja declaration. It should be mentioned here, that the efforts of the SG has been enhanced through 2 grants from the Global Fund to Fight AIDS, TB and Malaria (GFATM), which enabled rapid expansion of access to TB diagnostic and treatment services. Furthermore, a formidable in-country partnership has been built for TB which will ensure sustained action in a synergistic manner.

I note with great sense of fulfillment that Swaziland is among the countries of the world that have reached and even exceeded the 70% target for detection of infectious TB cases. However, the treatment success rate of 73% falls below the set target of 85%, which requires urgent implementation of the African TB emergency declaration to improve treatment outcomes.

The NTP produced the first edition of the Tuberculosis Control manual in 2006, am I am convinced that the document has been instrumental to the achievements of the programme so far.

This 2nd Edition which takes into consideration the most recent developments in TB control especially with respect to TB diagnosis and management under the influence of HIV/AIDS, MDR/XDR-TB management, management of TB in Children and issues of laboratory quality-assurance will no doubt add value to the quality of TB care in the country. I therefore congratulate the NTCP and partners for realizing the publication of this second edition, which is sure a product of considerable hard work.

I would like to reiterate that the Ministry of Health considers TB control a priority and is strongly committed to the fight against TB, and will continue to play facilitatory role towards achieving the MDG targets for TB by 2015.

**Minister of Health**

# FOREWORD

This manual describes the policy direction as well as guidelines for the diagnosis and management of tuberculosis patients in the Kingdom of Swaziland. It is also meant to serve as a guide for clinicians and other health workers involved in the management of tuberculosis patients with view to optimizing the quality of care for our people.

The clinical knowledge, policy guidelines and programme organization reflected in this document are derived from the strategic orientation of the World Health Organization (WHO), the Stop TB partnership, and other key stakeholders in the global tuberculosis control as reflected in the Stop TB Strategy.

This manual does not intend to provide the kind of comprehensive clinical knowledge on tuberculosis as obtainable from clinical textbooks. The manual, however, does intend to address the major elements relevant to addressing TB as a major public health problem in line with global and regional orientations; and in a user-friendly manner.

While the manual in its entirety is appropriate for TB control programme players at various levels, general practitioners and non-TB specialists may find the manual equally useful for quick reference on specific TB, TB/HIV and MDR-TB management topics.

Likewise, some of its chapters are relevant and useful for policy-makers and for our valuable partners who also support TB control as a public health initiative.

Specifically, the manual is composed of 14 chapters which, taken as a whole, provide an overview of TB control. Together, the chapters cover a broad spectrum of topics ranging from epidemiology, diagnosis, treatment, TB/HIV co-infection and MDR/XDR-TB management to topics such as TB control programme strategy and organization, Advocacy, communication and TB laboratory networks. Individual chapters may be easily consulted as reference on various topics and subtopics, such as case definitions, extra-pulmonary TB, BCG vaccination, managing TB risk groups and adverse anti-TB drug reactions.

In order to keep the manual to a practical length, repetition of the content has been kept to a minimum, and readers should refer to the index for further reference. Furthermore details of the management of other related conditions e.g. HIV and AIDS, MDR-TB, Infection Control etc should be sought in their respective guidelines.

It is our hope that all stakeholders in the fight against tuberculosis will find this manual useful in the planning and implementation of their activities within the framework of the national policy.

Finally, the ministry of health wishes to convey special appreciation to all our partners and stakeholders for the technical and financial contributions towards the successful revision of this National Tuberculosis Control manual.

**Director of Health Services**

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Programme Manager,

National Tuberculosis control Programme **GLOSSARY AND ABBREVIATIONS**

**AIDS** Acquired Immune Deficiency Syndrome

**AFB** Acid Fast Bacilli

**BCG** Bacillus de Calmette et Guérin

**CSF** Cerebrospinal fluid

**DOT** Directly Observed Treatment

**DOTS** Directly Observed Treatment Short-course

DTBC Regional TB Coordinator

DTBO Regional TB Officer

**DTD** Demonstration and Training Regional

**E** Ethambutol

**EPTB** Extra-pulmonary tuberculosis

**FDC** Fixed Dose Combination

**HIV** Human Immunodeficiency Virus

**IEC** Information, Education and Communication

**INH** Isoniazid

**IUATLD** International Union Against Tuberculosis and Lung Disease

**MDR-TB** Multi-drug resistant tuberculosis

**MTB** Mycobacterium Tuberculosis

**NDSO** National Drug Services Organization

**NGO** Non-Governmental Organization

**NNRTI** Non-nucleoside Reverse Transcriptase Inhibitor

**NRTI** Nucleoside Reverse Transcriptase Inhibitor

**NTCP** National TB Control Programme

**PHC** Primary Heath Care

MOH Ministry of Health

**PI** Protease Inhibitor

**PPD** Purified Protein Derivative

**PTB** Pulmonary Tuberculosis

**PZA** Pyrazinamide

**RR**  Recording & Reporting

**R** Rifampicin

**S** Streptomycin

**SCC**  Short Course Chemotherapy

**SCR** Smear Conversion Rate

**TAT**  Turn Around Time

**VCT** Voluntary Counseling Test

**UNAIDS** United Nations Joint Programme on HIV/AIDS

**UNICEF** United Nations Children Fund

URC University Research Corporation

MSF Medicins Sans Frontieres

**WHO**  World Health Organization

**Z** Pyrazinamide

**ZN Stain** Ziehl – Neelsen Stain

EXECUTIVE SUMMARY

Tuberculosis remains a major public health problem in Swaziland. Currently the country has the highest TB incidence of 1287 per 100,000 population, and also have one of the highest HIV prevalence among incident TB cases (83%). With an HIV prevalence rate of 26% among the general population, the TB epidemic is undoubtedly being fuelled by the prevailing HIV epidemic. The National TB programme established in the 1980’s published the first edition of the National TB management guidelines in 2006.

The first edition facilitated the implementation of the DOTS strategy across the country specifically in standardization of laboratory diagnostic and treatment protocols for effective TB management. The increased drive by the HIV epidemic on the TB situation coupled with the emergence of MDR-TB changed the dynamics of TB control in the country, and hence the need for a revision of diagnostic and treatment policies. The second edition of the National TB Control Programme Manual seeks to address the common issues in the diagnosis and management of tuberculosis in the context of high HIV prevalence and taking cognizance of recent development in the area of new TB diagnostic tools as well as recent WHO recommended changes in treatment policies.

## Purpose of the guidelines

The principal purpose of these guidelines is to assist the various clinicians and other health care providers in both public and private sectors to optimize tuberculosis patient cure: curing patients will prevent death, relapse, acquired drug resistance, and the spread of TB in the commu­nity in a context-specific manner and in line with current WHO recommendations. Their further purpose is to guide the national TB programme staff in ensuring adequate coordination of TB control activities in the country.

## Target audience

The primary target audience for the guidelines is the staff of NTCP, Health care professionals and other TB service providers working in public and private health care facilities at the peripheral or referral levels. It is also recommended to students undertaking pre-service training in health care training institutions.

## Scope

These guidelines address the treatment of active TB disease in adults. It includes key topics such as TB diagnosis, laboratory services, treatment of TB, monitoring treatment and patient support, paediatric TB, introduction to MDR-TB, drug procurement and supply management and in­fection control.

## Justification for guideline update

The Stop TB Strategy’s emphasis on universal access for all persons with TB to high-quality, patient-centred treatment. However, highly in­fectious, smear-positive patients remain the primary focus for other aspects of TB control, including contact tracing and infection control. The Patients’ Charter for TB Care specifies that all TB patients have “the right to free and equitable access to TB care, from diagnosis through treatment completion”.

Secondly, WHO published the fourth edition of the guidelines for National TB programme that contained major recommendations for changes in treatment categories, and emphasis on early detection of MDR-TB. For example, the Categories I–IV, which were used to prioritize patients for treatment has been abandoned in the current WHO. Guideline, and instead, to adopt standard regi­mens recommended for each group according to the likelihood of their having drug resistance.

The current guidance also recommends integration of detection and treatment of both HIV infection and MDR-TB, and thus should contribute towards achievement of the Stop TB Strategy’s universal access to high-quality MDR-TB and HIV care.

With regard to HIV detection, this edition incorporates recent WHO recommenda­tions for provider-initiated HIV testing of all persons with diagnosed or suspected TB.

## Highlights of the new revision

The guideline revision covered both clinical and some key programmatic areas of the National TB Control Programme operations. The current guideline has 17 chapters, the first two of which dealt with background information regarding the national context including a brief description of the health system (Chapter 1); as well as a brief description of the tuberculosis situation and the National programme organization, objectives and targets (Chapter 2).

Chapter 3 to 12 dealt with TB clinical management issues ranging from case detection, diagnosis, treatment, TB/HIV co-management to MDR-TB management and Infection Control. On the other hand, chapters 13 to 17 dealt with key programmatic issues including Supervision, monitoring and evaluation; logistics and supplies; human resource development for TB control as well as Advocacy, communication and Social mobilization (ACSM) and engagement of private care providers.

The key changes by chapter adopted based on the current WHO recommendations are as follows:

**Chapter 3. Case finding and registration:**

In this chapter, the issue of early TB case detection through rapid DST particularly the Xpert MTB/Rif (Gene Xpert) for all persons suspected of TB regardless of HIV status.

A revision of the TB registration is included with a decision not to use severity of disease as criteria for case definition. Furthermore, the use of the “Diagnostic categories I–IV” in the first edition of the NTCP guideline has been discontinued. Instead, this second edition uses the same patient regis­tration groups used for recording and reporting, which differentiate new patients from those with prior treatment and specify reasons for retreatment.

The recent WHO case definition for sputum smear-positive pulmonary TB has been applied to a definite case of TB, so that now a patient with one positive AFB smear is considered a definite case on the grounds of an existing functional external quality assurance (EQA) system for TB bacteriology in the country. In addition, bacteriology now includes culture and new methods for identification of M. tuber­culosis.

Similarly, in the definition for smear-negative TB, this guideline incorporates WHO policy reducing the number of specimens from three to two for screening patients sus­pected to have TB.

The patient registration group “Other” no longer includes “chronic”. Instead, patients whose sputum is smear-positive at the end of (or returning from) a sec­ond or subsequent course of treatment are classified by the outcome of their most recent retreatment course: relapsed, defaulted or failed.

New WHO data elements for recording and reporting, such as HIV status and MDR-TB, are also incorporated.

**Chapter 4. Diagnosis of TB:**

This chapter introduces the adoption of Xpert MTB/Rif as first initial diagnostic test for TB. It also elaborates on the optimization of the DST for rifampicin and Isoniazid using the LPA and the conventional DST using the MGIT. This edition also lays emphasis on using the results of rapid DST to inform treatment decisions.

The chapter also includes the introduction of two diagnostic algorithms based on availability of Xpert MTB/Rif in the local laboratory, while the other diagnostic pathway starting with microscopy and LPA for positive smear cases.

The trial of broad-spectrum antibiotics is no longer recommended to be used as a diagnostic aid for smear-negative pulmonary TB in persons living with HIV.

A section on the non-recommendation of the use of Inteferon Gamma Release Assay (IGRA) tests and commercial sero-diagnostic tests in Swaziland is also included in this chapter.

**Chapter 5. Laboratory services and QA**

This includes a description of the TB laboratory network and the recommended quality-assurance activities including external quality assessments (EQA), panel testing and blinded rechecking. The functions of the National TB Reference laboratory (NRL) in relation to the regional and peripheral levels have been elaborated as well as collaboration with the Supra-national reference laboratory (SNRL).

Consistent with Standard 3 of the International Standards for TB Care, culture and histopathological examination are recommended for specimens from suspected extra-pulmonary sites of TB. Examination of sputum and a chest radiograph are also suggested, in case patients have concomitant pulmonary involvement.

**Chapter 6. Treatment of tuberculosis:**

This chapter outlined the revised TB treatment regimens based on the new patient registration groups. In the treatment of new TB cases, 6 months rifampicin-containing regimen has been maintained. TB cases, and treatment initiation to be based on results of new rapid molecular-based tests i.e Gene Xpert and LPA.

For the purpose of treatment, previously treated patients are now to be defined by their likelihood of MDR-TB, and rec­ommendations for treatment regimen depend on reason for retreatment (failure, versus relapse and default). The chapter also provides for the possibility that, previously treated patients may have levels of MDR-TB that are high enough to warrant an MDR regimen while awaiting results of DST. Or they should be started on MDR-TB standardized treatment based on results of rapid DST (Gene Xpert or LPA).

In this chapter, the guideline also adopted the recommendations suggesting longer treatment for TB meningitis and for bone or joint TB. And for TB in special situation e.g patients with pre-existing liver disease, this edition includes regi­mens with one, two and no hepatotoxic drugs. A 9-month regimen of rifampicin and ethambutol is no longer included as an option.

Similarly, for TB patients with renal failure, this edition recommends the 6-month regimen with isoniazid, rifampicin, ethambutol and pyrazinamide, whereas the prior edi­tion omitted pyrazinamide. This edition recommends administering ethambutol (15 mg/kg) and pyrazinamide (25 mg/kg) three times per week. This edition now discourages the use of streptomycin in patients with renal failure; however, if it must be used, 15 mg/kg should be administered two to three times per week, with monitoring of drug levels.

**Chapter 7. Patient support and DOT provision**

The seventh chapter dealt with issues of treatment support provision for enhancing patient’s treatment adherence. This covers identification and training of treatment supporters as well as provison of enablers to TB patients. Nutritional support to TB control through the Food by prescription initiative as one of the main enablers has been elaborated in this chapter. The chapter concludes with measures to prevent and effectively manage treatment interruption.

**Chapter 8. Monitoring during treatment:**

In this chapter the performance of sputum smear microscopy at the completion of the inten­sive phase of treatment is reaffirmed with a recommendation to request for culture and DST if the smear result is positive. In this regard, the extension of the intensive phase for patients who have a positive sputum smear at the end of the second month has been abolished.

Similarly, in previously treated patients, if the specimen obtained at the end of the intensive phase (month 3) is smear-positive, this edition recommends that sputum culture and DST be performed then, rather than waiting until the 5th month. Also recommended that patients found to harbour an MDR-TB strain at any point during treatment are now to be classified as “treatment failure”. They are re-registered and begin an MDR regimen.

With respect to determination of treatment outcomes, mycobacterial Culture results has now included in the definition of cure.

This chapter also includes a revised version of the symptom-based approach to side-effects of anti-TB drugs including a guide to anti-TB drug challenge and re-introduction after an adverse reaction.

Updated information on management of treatment interruption taking into cognizance the use of new diagnostic tests has also been incorporated

**Chapter 9: Management of Childhood TB:**

Update on paediatric TB treatment and HIV-TB co-management including contact investigation. The chapter provides various options to optimize bacteriological confirmation of TB in children through various specimen collection techniques like fine needle aspiration (FNA), gastric and nasopharyngeal aspirate. In addition, additional information provided with regard to management of extra-pulmonary TB based on the current WHO recommendations.

The chapter also includes a section on ensuring adequate follow up of TB treatment in Children and a guide on Cortimoxazole prophylaxis.

**Chapter 10. Co-management of HIV and active TB disease:**

This chapter addresses the current recommended approaches to TB/HIV co-management particularly with respect to early initiation of HIV positive TB patients on ART. The current WHO recommendations for antiretroviral therapy and timing of initia­tion are incorporated, while the Provider-initiated HIV testing for all patients with known or suspected TB has been reinforced. It also includes current WHO recommendations to start co-trimoxazole as soon as possible when a person living with HIV is diagnosed with TB.

**Chapter 11. Infection control:**

The national TB Programme has a detailed National TB Infection Control guidelines. This chapter therefore provided a synopsis of the infection control measures described in the national guidelines. For a detailed information on the infection control measures, reference should be made to the National TB Infection Control guidelines.

**Chapter 12. Management of drug-resistant TB:**

This chapter has been extensively revised to reflect recent WHO recommendations for the programmatic management of drug-resistant TB. The 2011 update on the programmatic management of DR-TB was used. It addresses MDR-TB management guidelines including the role of Xpert MTB/Rif, and dealing with MDR-TB in children. It covers regimen design for standardized MDR-TB regimen and dosages for both adults and Children. Also includes monitoring MDR-TB treatment as well as evaluation of treatment outcomes.

**Chapter 13. Supervision, monitoring and evaluation:**

This chapter defines supervision and distinguishes it from monitoring and evaluation. At the same time it highlights their interrelatedness. It includes recommendations on how to plan and execute an effective supervision of TB control activities.

**Chapter 14. Advocacy, Communication and Social Mobilization (ACSM):**

The Chapter elaborates on how to effectively optimize ACSM for TB with the view to empower patients and communities using a target-specific approach. Also gives guidance on how to use ACSM to influencing the political agenda in favour of TB control, as well as developing and utilizing an effective approach to mass media advocacy.

Finally, the guideline also includes a list of annexes outlining key procedures, standard operating procedures on Human Resource development and Supplies and logistics management and protocols as well as essential recording and reporting forms of the National TB Control Programme.

1. INTRODUCTION

## The country

Swaziland is a small landlocked country situated between South Africa and Mozambique covering an area of 17,364km2. The country has a predominantly (77%) rural population of about 1.1 million (2006 Census) people.

Swaziland enjoys a tropical to a near-temperate climate along the western highlands, which rises to an altitude of over 1,800 metres above the sea level, while the low-veld areas are generally hot. The country lies in a summer rainfall region. The majority of the population consists of ethnic Swazis.

With a GNI per capita income of USD 2,280, Swaziland is classified by the World Bank as a low-middle income country and therefore placed in the IBRD lending category. However, the real GDP growth rate has fallen in recent years to 2.8% in 2007. However, despite this relative high per capita income, income distribution is markedly uneven (GINI index 51% according to PRSAP 2006). Life expectancy currently stands at 32 years, being 56 years in 1986, and 69% of the population living below the upper poverty line of USD 7.2 /capita/month. About 66% of the population lives below the poverty line (Swaziland Human Development Report, 2000) with high rural-urban disparities in access to basic services. For example, whilst 91% of the urban population has access to safe water, it is only 37% for the rural population. The per capita expenditure on health for the urban population is 3 times that for the rural population.

## The health system

The health care delivery system consists of both formal and informal sectors. The formal sector consists of both public and private service providers including NGOs, mission, industry health services and private practitioners, while the informal sector consists mainly of traditional and other complementary or alternative health care providers. An estimated 45% of health facilities are operated by the public sector, 23% by the private-for-profit sector, while the remaining 32% are operated by private not-for-profit sector including Faith based organizations (FBOs), Non-governmental organizations (NGOs) etc (see tables below).

The service delivery system itself is loosely organized into a three-tier system including (i) three national (referral) and five regional hospitals (total some 1800 beds); (ii) Primary Health Care services, being composed of Health Centres (HCs)[[1]](#footnote-1), Rural Clinics[[2]](#footnote-2) and a network of outreach sites and (iii) Community Based Care, where Rural Health Motivators (RHM), Traditional Birth Attendants (TBAs), Home Based Care (HBC) volunteers and traditional practitioners provide care, support and treatment.

Majority of the Swazi population (85%) live within a range of 8 km for a health facility. However, this does not translate to equitable access in view of internal variability in the distances to facilities, transportation accessibility and the range and quality of care provided by facilities. Furthermore, this still falls short of the 5 km benchmark recommended by the WHO and about 20% of the population have limited or no access to health service.

**Table . Distribution of hospitals, Health Centres and Clinics by region**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **REGIONS** | **POPULATION** | **GENERAL HOSPITAL** | **HEALTH CENTRES** | **CLINICS**  **Type A/B** | **TOTAL NO OF HF** | **HF/**  **100.000** |
| HHOHHO | 282.734 | 2 | 2 | 62 | 64 | 22.6 |
| LUBOMBO | 207.731 | 1 | 2 | 43 | 45 | 21.7 |
| MANZINI | 319.530 | 2 | 0 | 80 | 80 | 25.0 |
| SHISELWENI | 208.454 | 1 | 1 | 33 | 34 | 16.3 |
| **TOTAL** | **1.018.449** | **6** | **5** | **218** | **223** | **21.9** |

HF = Health Facility, being HCs + Clinics

Note: Public Health Units (7) exist in most HCs and in all Hospitals

**Table . Ownership of health facilities by region**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **REGIONS** | **Public Sector**  **(Clinic + HC)** | **Industry** | **Facilities** | **NGO** | **Private**  **(Doctor)** | **Private**  **(Nurse)** | **TOTALS** |
| HHOHHO | 24+2 | 4 | 11 | 4 | 19 | 0 | 64 |
| LUBOMBO | **21+2** | 8 | 7 | 0 | 4 | 3 | 45 |
| MANZINI | 28+0 | 15 | 12 | 4 | 18 | 3 | 80 |
| SHISELWENI | **22+1** | 1 | 3 | 4 | 3 | 0 | 34 |
| **TOTAL** | **95+5** | **28** | **33** | **12** | **44** | **6** | **223** |
| Percentages % | 45% | 12% | 15% | 5% | 20% | 3% | 100% |

HF = Health Facility, being HCs + Clinics

Note: Public Health Units (7) exist in most HCs and in all Hospitals

From a functional perspective, 172 HF provide ANC (77%); 137 provide PMTCT (61%); 70 HF provide ART (31%) and 170 provide AIDS testing and counselling (70%). SAM identified 204 doctors (40% Swazi; 20/100,000) and 1778 Nurses (90/100,000).

The health service indicators are summarized in table below:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Indicator** | **Hhohho** | **Lubombo** | **Manzini** | **Shiselweni** | **Total** |
| Population | 331,734 | 249,153 | 360,228 | 241,365 | 1,182,480 |
| # Health facilities | 40 | 35 | 52 | 27 | 154 |
| Health facilities per 100,000 pop | 12 | 14 | 14 | 11 | 13 |
| Facilities with in-patient beds | 9 | 9 | 14 | 4 | 36 |
| # in-patient beds | 363 | 302 | 813 | 257 | 1755 |
| In-patient beds per 100,000 pop | 115 | 121 | 226 | 106 | 148 |
| Doctors per 100,000 pop | 17 | 6 | 10 | 5 | 10 |
| Nurses per 100,000 pop | 70 | 52 | 57 | 41 | 56 |
| Midwives per 100,000 pop | 72 | 47 | 80 | 46 | 64 |
| Estimated population growth rate |  |  |  |  |  |

*Source: MOH Service Availability Mapping 2007*

At the community level, a network of community health workers exists, which consists of Rural Health Motivators to promote community participation in health activities at that level. Health committees are also in place to assist in the general management of health care facilities.

It is estimated that 85% of the population in the country currently lives within an 8km radius of a health facility, while nationally about 20% of the population have limited or no access to a health facility with the rural poor worst affected.

Despite a comparatively reasonable physical access to health services in comparison, quality of health care remains a challenge owing to the high disease burden, chronic shortage of human resources for health, deteriorating infrastructure, inadequate budgetary allocation and weak support supervision systems.

1. THE NATIONAL TUBERCULOSIS CONTROL PROGRAMME

## Global Epidemiology of TB

According to the WHO TB report of 2011, it is estimated that the global burden of disease caused by TB in 2010 are as follows: 8.8 million incident cases, 12 million prevalent cases, 1.1 million deaths among HIV-negative people and 0.35 million deaths among HIV-positive people. Most cases were in Asia (59%) and Africa (26%). An estimated 12–14% of incident cases were HIV-positive; the African Region accounted for approximately 82% of these cases.

Globally, there were 5.7 million notified cases of TB in 2010, equivalent to a case detection rate (CDR, defined as the proportion of incident cases that were notified) of 65% (range, 63–68%). India and China accounted for 40% of the world’s notified cases. At global level, the treatment success rate among new cases of smear positive pulmonary TB was 87% in 2009.

There were an estimated 650 000 prevalent cases of multi-drug resistant TB (MDR-TB) in 2010. Globally, less than 2% of new cases and 6% of retreatment cases were tested for MDR-TB. The four countries that had the largest number of notified cases of MDR-TB in 2010 were China (63 000), India (64 000), the Russian Federation (31 000), and South Africa (9 100). By July 2010, 58 countries and territories had reported at least one case of extensively drug-resistant TB (XDR-TB).

## The Tuberculosis situation in Swaziland

Tuberculosis poses a big public health challenge to the government and the people of the kingdom of Swaziland and constitutes an estimated 20% of institutional deaths. With an estimated TB incidence of 1,287 per every 100,000 of its population, Swaziland is one of the countries of world with the highest incidence of TB. Compared to a 1990 level of 267 new cases (all forms) per 100,000 population per year, TB incidence had increased six-fold, by 2010. and The incidence of the infectious cases (sputum smear positive pulmonary TB cases) tripled in the same period. In terms of prevalence of disease, there were 840 TB cases (all forms) per 100,000 in the country in 2010, which translates to about 9,600 prevalent TB cases at any point in time. Similarly, mortality from TB increased from 76 per 100,000 in 1990 to 304 per 100,000 in 2008. This mortality figure translates to about 2,780 deaths annually due to TB alone; and an estimated 17,000 TB-related deaths by 2015 if drastic actions are not taken. Most deaths were associated to HIV co-infection. In 2010, the International Classification of Diseases-10 (ICD-10) re-defined mortality to TB by excluding all cases of death due to HIV. This revision subsequently re-adjusted mortality rate due to TB to 32 per every 100,000 cases among HIV negative cases. The prevalence of HIV among newly diagnosed tuberculosis patients was 82% in 2010 according to the national tuberculosis control routine surveillance and has been rising over the last decade. In the general public, however, the HIV prevalence among the 15-49 years age group is estimated to be 26%. Moreover, a country-wide research on drug resistance among TB patients conducted in 2009 showed 7.7% of MDR among new cases of TB, as well as 33.9% among previously treatment cases of TB, which are incomparably high relative to other countries. Cumulatively 503 MDR-TB cases have been reported from 2006 to 2009.

The NTCP overall notified 852 TB cases per 100,000 in 2010 up from 650 per 100 000 in 2006. Case detection rate of new smear positive cases was 69%, in 2010, having increased from 34% in 2006. Of all detected cases in 2009, 68% successfully completed treatment in up from 42% in 2006.

## The National TB Programme

The NTP was established in 1986, and has been fully funded by the Government of Swaziland since 2001. At the national level, it operates under the Directorate of Health of Health Services (DHS) in the Ministry of Health, alongside other communicable and non-communicable disease control programs.

The program is headed by an NTP Manager under the responsibility of the Deputy Director Public Health (DDHS), who in turn reports to the Director of Health Services, who reports to the Principal Secretary in the ministry.

At the regional level, the Regional TB Coordinators directly supervises the TB focal points who are responsible for TB case registration and treatment in health facilities. At community level the community DOT supporter reports to the TB regional coordinators.

At community level, various stakeholders including CHWs, CSOs, NGOs, CBOs, TB Treatment Supporters and Traditional Healers etc in their varying capacities deliver TB care in close collaboration with the Regional Health Management Teams.

## The TB Control Strategy and framework for Swaziland

Swaziland adopted the Stop TB Strategy as the framework for TB Control in the country with emphasis on the pursuance of high quality DOTS expansion and enhancement, TB/HIV and MDR-TB. This is based on the Stop TB Strategy.

### Central Unit

The main roles of the National TB Programme at central level includes the following:

1. develop policies and plans, and secure budgets for the NTP
2. Coordinate the NTP, including all governmental and non-governmental organizations working in TB control
3. Plan for anti-TB drugs and supplies for patient management;
4. Prepare training programmes for health workers involved in the NTP
5. Monitor, procure and distribute supplies for the NTP (drugs, equipment, documentation, health education materials)
6. Prepare and develop reporting standards
7. Coordinate national TB surveillance activities
8. Supervise NTP activities at the Regional level
9. Conduct research for promotion of the NTP
10. Plan for TB laboratory equipment and reagents;

In order to effectively perform these roles, the central level is supported technically by WHO and other technical partners.

### Regional Level

The RHMTs are responsible health care planning, supervising health facility facilities (clinics and health centres) and the implementation of TB control activities through the regional TB coordinators. The regional TB control activities are essentially part of the regional health plan, which is coordinated through the Regional Health Management Teams (RHMT) with the regional TB Coordinators as focal points. However, the Central Unit of the National TB Programme provides technical support and capacity building to that level. The Regional coordinators are therefore responsible for planning and budgeting for specific TB Control activities including training of different cadres on TB. The central level as well as regional medical officers provide support in the facilitation of such trainings.

### Basic TB management units

Currently, there are 20 health facilities consisting of regional government hospitals, health centres, mission hospitals, industry health services as well as private practitioners providing TB diagnostic services in the country, while about 140 clinics provide only continuation phase treatment. Each of the diagnostic sites has a focal point referred to as the TB nurses who sees the majority of TB suspects and clients, requests for direct sputum microscopy, diagnose smear positive cases, and refer others as appropriate for confirmation of diagnosis by a medical doctor. A DOTS adherence officer, stationed in each diagnostic site and equipped with a motorbike is responsible for following up patients who interrupt treatment, and where community-based TB care has been supervising community DOT supporters.

### The National TB Hospital

The national tuberculosis hospital is responsible for specialized management of tuberculosis that includes drug resistant tuberculosis. It is equipped with highly skilled professionals and will be responsible for implementing the clinical components of the drug resistant tuberculosis guidelines. The admission criteria to the TB hospital are as follows:

All confirmed MDR cases will be admitted for a minimum of 4 weeks but maybe prolonged for up to even more than 6 months if clinically indicated. The referring health facility should inform the outpatient department of the TB hospital before transporting the patients for admission. Transport for clients referred to the TB hospital shall be arranged by the national TB referral hospital.

The main indications for hospitalization include the following:

* Initiation of treatment
* Adherence problems
* patient very sick (clinically and physically unfit)
* Severe adverse effects
* Immobility
* Vulnerable patients e.g. disadvantaged-orphan, mentally , socially or physically handicapped

***All confirmed XDR-TB patients will be admitted and managed in isolation until sputum culture conversion.***

### Community Level

The NTP currently works with community-based organizations (CBOs) wherever possible to assist in the early identification of persons with signs and symptoms of tuberculosis. The NTP also intends to engage traditional and non-traditional partners to assist with the provision of community-based TB care. The home-based care networks for HIV/AIDS have provided a unique opportunity to expand the control of tuberculosis in the community through the Rural Health motivators. Currently about 70% of the TB patients on treatment are being supervised by community treatment supporters.

### TB Laboratory services

Effective laboratory services are critical to a successful TB control programme. The national TB laboratory network consists of 16 sites under the leadership of the National TB Reference Laboratory (NRL), which operates under the overall national laboratory complex in the capital Mbabane.

The NRL has established collaboration with the Medical Research Council (MRC) and the National Institute for Communicable Diseases (NICD) laboratories in the Republic of South Africa (RSA) which serves as the Supra-National Reference Laboratory (SNRL).

The NRL has capacity for routine microscopy, mycobacterial culture and Drug Susceptibility Testing (DST) for first line anti-TB drugs (FLD), while the other 15 laboratories provide direct sputum smear microscopy services. The NRL is also responsible for maintaining national quality control as well as capacity development for all laboratory staff.

The national TB programme has established a strong collaboration with the NRL to facilitate quality TB diagnostic services.

### Intra-ministerial collaboration

The NTP and the National AIDS Programme (SNAP) are housed in separate locations at national level, hindering close collaboration in planning and implementation of collaborative programme activities. Both programmes should share their comparative advantages to their mutual benefit. E.g., the NTP’s experience in directly observed treatment, recording and reporting can be valuable to the SNAP in implementation and effective monitoring of the ART programme. The latter in turn can assist the NTP with its wealth of experience in advocacy, communication, education and multi-sectoral collaboration.

Since currently about 80% of TB patients are also co-infected with HIV, the NTP can significantly contribute to increasing access of ART by ensuring screening of all TB suspects and patients in all TB sites. Similarly, mainstreaming of TB activities in HIV/AIDS planning and management is essential, as is providing HIV/AIDS prevention, care and support activities to people with TB disease. To this end, the NTP should closely collaborate with NGOs, CBOs, FBOs and other organisations that provide home-based care services, which will in turn contribute to expanding community-based TB care. The national TB programme also has a functional collaboration with the National Malaria Control Programme (NMCP)

### NTP Partners

The national TB Programme collaborates with technical and financial partners within and outside the country. The technical partners include the World Health Organization, the University Research Corporation (URC), Italian Cooperation, Medicens sans Frontieres (MSF) and the Royal Netherlands Tuberculosis Foundation (KNCV). The NTP has numerous implementation partners who recently transformed into an umbrella body referred to as the Swaziland Stop TB Partnership. The members of the Swaziland Stop TB partnership include Private practitioners, Non-governmental organizations (NGOs), and Community-based organizations; while the MOH, NERCHA and WHO serve as ex-officio partners.

### NTP funding

The national TB Programme is funded mostly by the Swaziland Government with additional funds from the Global Fund (GFATM). The programme has an established budget line that covers human resources, first and second line anti-TB drugs and administrative costs. The WHO and PEPFAR also provides resources for closing funding gaps in the implementation of programme activities.

## Goals, Objectives and targets of the National TB Programme

The Goal of the SwazilandNational TB Programme is to reduce TB mortality, morbidity and disease transmission to a level that it no longer constitutes a Public Health Problem, while preventing the development of drug resistance.

### The Objectives:

To provide standardized short-course chemotherapy provided under strict supervision to at least all identified sputum smear positive cases.

### The targets:

Swaziland subscribes to the global initiative to eliminate TB as a public health problem within the context of the following agreed targets:

* **The World Health Assembly (WHA)targets** to cure at least 85% of newly detected cases of sputum smear-positive TB and to detect 70% of the estimated incidence of sputum smear-positive TB;
* **Millennium Development Goal (MDG) targets:**Target 8 under MDG Goal 6 (tocombat HIV/AIDS, malaria and other diseases), To have halted by 2015 and begun to reverse the incidence of malaria and other major diseases, with the following specific for TB:
  + **Indicator 23:** Prevalence and death rates associated with tuberculosis
  + **Indicator 24:** Proportion of tuberculosis cases detected and cured under DOTS
* **The Stop TB Partnership Targets:**
  + **By 2005:** At least 70% of people with infectious TB will be diagnosed (under the DOTS strategy), and at least 85% of these patients will be cured.
  + **By 2015:** The global burden of TB (disease prevalence and deaths) will be reduced by 50% relative to 1990 levels.

### Programme Goal

To reduce morbidity, mortality, disease transmission and socio-economic burden of TB including the TB/HIV co-infection while minimizing the risk of drug resistance to such an extent that the disease no longer a public health problem to the Swaziland nation.

### Objectives

The National TB Programme shall within the framework of the global Stop TB Strategy aim at achieving the following strategic results by 2015:

* Achieve universal access to high-quality care for all people with TB
* Reduce the human suffering and socioeconomic burden associated with TB
* Protect vulnerable populations from TB, TB/HIV and drug-resistant TB
* Protect and promote human rights in TB prevention, care and control

### Swaziland Stop TB Partnership targets

* Treatment success (cure + completion) rate increased from 68% to 85% for patients with smear-positive tuberculosis by 2015;
* Case detection of patients with smear-positive tuberculosis increased from 68% to 80% by 2014;
* HIV testing of 100% of TB patients;
* enrolment of 100% of HIV-positive TB patients on co-trimoxazole preventive therapy (CPT) and antiretroviral therapy (ART);
* provision of isoniazid preventive therapy (IPT) to all people living with HIV who are attending HIV care services and are considered eligible for IPT;
* testing of 100% of previously treated TB patients for MDR-TB, as well as testing of any new TB patients considered at high risk of having MDR-TB (estimated globally at around 20% of all new TB patients);
* enrolment of all patients with a confirmed diagnosis of MDR-TB on treatment consistent with international guidelines;
* Adequate capacity for operational research and epidemiological surveillance created for programme management by 2012;
* Improve the level of knowledge on tuberculosis disease and services for improved health-seeking behaviour and treatment adherence by 2014.

1. TB CASE FINDING AND REGISTRATION

## Importance of TB case finding and registration

The emphasis of the NTCP is on early TB case detection and provision of timely effective treatment. The NTCP is also responsible for ensuring that identified persons suspected of having tuberculosis are properly diagnosed, meet the definition for case or definite case, and are treated appropriately, and that outcomes are evaluated at the end of treatment.

## Identification of persons suspected of having pulmonary TB:

Every person presenting to a health facility with symptoms suggestive of tuberculosis should be considered a “person with presumptive tuberculosis”. The most common symptoms suggestive of pulmonary tuberculosis are:

* Any current cough
* sputum production which may be blood-stained
* shortness of breath, and chest pain
* loss of appetite and loss of weight
* a general feeling of illness (malaise)
* tiredness and loss of motivation
* night sweats and fever.

On clinical examination, there may be general signs, such as fever, tachycardia (fast pulse rate) and finger clubbing. Chest signs (heard through a stethoscope) may include crackles, wheezes, and bronchial breathing.

A patient presenting with these symptoms and signs who is, or was in contact with a person with infectious tuberculosis should be suspected of having PTB.

All TB suspects who present to health facilities should be recorded on a “Registry of TB suspects”.

All health facilities without microscopy should sent suspects sputa to the nearest accredited laboratory within the Regional.

### Sputum Collection, Labeling, Storage and Transport

At least two sputum specimens should be taken from a TB suspect.

Option A: : At the first encounter with the patient the first specimen is collected on the spot referred to as the**“ first spot specimen”** is collected and the patient should be provided with a sputum container for collection of the second Spot sample at least one hour apart (**Second Spot Specimen**)

Options B: At the first encounter with the patient the first specimen is collected on the spot referred to as the **“spot specimen”** is collected; the patient should be provided with a sputum container for collection of the second sample early morning at home **(‘early morning specimen’)**.

#### Sputum collection procedure

* Collection of sputum samples should be performed outside in an open place;
* The person should rinse the mouth with water;
* Explain the steps fully and slowly
* Demonstrate a deep cough from the bottom of the chest, beginning with deep breathing
* Ask the patient to be very careful to direct the sputum into the container not to contaminate the outside of the bottle
* Supervise the collection, but do not stand in front of the patient
* Do it in a well-ventilated area or outside without others watching
* Give the patient the container without the lid
* Hold the lid yourself, ready to replace it immediately
* Make sure that the lid is securely closed
* Wash hands after handling the sputum specimen
* The person must be encouraged to produce a specimen after deep coughing even if this is saliva.

#### Sputum labeling (Barcode reader?)

Correct labeling is essential and will save time and prevent errors.

Label the container first, very clearly with:

* Name of clinic/hospital
* Name of patient and clinic/hospital number
* Indicate whether the specimen is pretreatment, follow-up or end of treatment specimen
* Write clear instructions regarding what investigations are required
* Write the appearance of the sputum (e.g. mucoid, lumpy, green, offensive, etc)
* Date the specimen clearly and time of collection of the specimen

**Note: Labeling should always be done on the body of the container as the lids may easily be mixed up during specimen processing.**

#### Sputum storage

* Place the sputum bottle in a plastic bag if possible to prevent contamination
* Store sputum specimen in a fridge if transport is not available immediately. Do not store in a freezer
* Sputum specimens should not be kept in a fridge for more than a week before transportation, if possible send away as soon as possible
* Record the date on which the specimen has been sent to the laboratory in the “Suspect Register”

#### Transportation of sputum specimens

* For rural health facilities that are without laboratory services, sputum specimens have to be transported to laboratories at least on a weekly basis;
* The Regional TB Coordinator should organize a sputum collection schedule for all facilities in the Regional;
* Transportation of specimens to the laboratory should be in cool sputum transport boxes. High temperatures during transit will kill bacilli;
* During transportation, specimens should be protected from contact with direct sunlight;
* The driver should be properly informed of the reasons for transporting the specimens, thereby ensuring that specimens go direct to the laboratory.

**Note: Every working day, a responsible person should check the Suspects Register to confirm which results are pending and then contact the laboratory to find out where the results are.**

## Identification of persons suspected of having Extra-Pulmonary TB:

Symptoms of extra-pulmonary tuberculosis depend on the organ involved. Chest pain from tuberculosis pleurisy, enlarged lymph nodes and sharp angular deformity of the spine are the most frequent signs of extra-pulmonary tuberculosis.

Extrapulmonary tuberculosis is more strongly associated HIV infection than pulmonary tuberculosis. HIV-related extrapulmonary tuberculosis is a WHO clinical stage 4 (advanced AIDS) diagnosis, and patients often have disseminated disease and are at high risk of rapid clinical deterioration and death.

### Common types of Extra-pulmonary TB

The most common types of extra-pulmonary tuberculosis are:

* TB meningitis
* TB lymphadenitis
* Miliary tuberculosis
* TB Pleural effusion
* Tuberculous empyema
* Tuberculous pericardial effusion
* Ascites
* TB of the bones

Table 1: the usual clinical features and diagnostic tests of other forms of extrapulmonary TB

|  |  |  |
| --- | --- | --- |
| Site of disease | **Clinical features** | Recommended investigation |
| **Spine** | Back pain  Gibbus  Psoas abscess  Radicular pain  Spinal cord compression | Plain X-ray  Tissue biopsy |
| **Bone** | Chronic osteomyelitis | Tissue biopsy |
| **Peripheral joints** | Usually monoarthritis especially hip or knee | Plain X-ray  Synovial biopsy |
| **Gastrointestinal** | Abdominal mass  Diarrhoea | Barium X-ray |
| **Liver** | Right upper quadrant pain and mass | Ultrasound and biopsy |
| **Renal and urinary tract** | Urinary frequency  Dysuria  Haematuria  Loin pain/swelling | Sterile pyuria  Urine culture  Intravenous pyelogram  Ultrasound |
| **Adrenal gland** | Features of hypoadrenalism (calcification)  (hypotension, low serum sodium, normal/high potassium,  raised urea, low glucose) | Plain X-ray  (calcification)  Ultrasound |
| **Upper respiratory tract** | Hoarseness and stridor  Pain in ear  Pain on swallowing | Usually complication  of pulmonary disease |
| **Female genital tract** | Infertility  Pelvic inflammatory disease  Ectopic pregnancy | Pelvic examination  X-ray genital tract  Ultrasound pelvis  Tissue biopsy |
| **Male genital tract** | Epididymitis | Often evidence of  renal/urinary tract TB |

## Identification of Children with presumptive TB:

Children can present with TB at any age, but the most common age is between 1 and 4 years. Case notifications of childhood TB depend on the intensity of the epidemic, the age structure of the population, the available diagnostic tools, and the extent of routine contact tracing.

The diagnosis of TB in children should be based on careful and thorough assessment of all the evidence derived from a careful history, clinical examination and relevant investigations, e.g. Tuberculis Skin Test (TST), chest X-ray (CXR) and sputum smear microscopy.

Although bacteriological confirmation of TB is not always feasible, it should be sought whenever possible, e.g. by sputum microscopy for children with suspected pulmonary TB who are old enough to produce a sputum sample.

A trial of treatment with anti-TB medications is not recommended as a method to diagnose TB in children. The decision to treat a child should be carefully considered and established by a Medical Officer; and once such a decision is made, the child should be treated with a full course of therapy.

## Defining a case of tuberculosis

To ensure proper registration and notifications of detected TB cases, it is important to use the standard NTCP TB case definitions.

### The importance of defining a case

The standardized TB case definitions are important for the following reasons:

* proper patient registration and case notification;
* selecting appropriate standard treatment regimens (see Chapter 3);
* standardizing the process of data collection for TB control;
* evaluating the proportion of cases according to site, bacteriology and treat­ment history;
* cohort analysis of treatment outcomes;
* accurate monitoring of trends and evaluation of the effectiveness of TB pro­grammes within and across districts, countries and global regions.

### The TB case definitions

The case definitions which have been adapted from the WHO guidelines is based on the level of certainty of the diagnosis and on whether or not laboratory confirmation is available.

**Tuberculosis suspect**. Any person who presents with symptoms or signs sugges­tive of TB. The most common symptom of pulmonary TB is a productive cough for more than 2 weeks,1 which may be accompanied by other respiratory symptoms (shortness of breath, chest pains, haemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).

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

*Note*. Any person given treatment for TB should be recorded as a case. Incomplete “trial” TB treatment should not be given as a method for diagnosis.

**Definite case of tuberculosis**. A patient with *Mycobacterium tuberculosis* complex identified from a clinical specimen, either by culture or by a WHO-approved new diagnostic methods (e.g the Xpert MTB/Rif, or molecular line probe assay). A definite case can also be defined as a pulmonary case with one or more initial spu­tum smear examinations positive for acid-fast bacilli (AFB).

## TB patients registration groups

The diagnosis of TB refers to the recognition of an active case. Beyond the diagnosis of TB disease, the type of TB case should also be defined to allow appropriate treatment to be given and the outcome of treatment evaluated. Before initiating treatment, health care providers should register TB cases into the various registration groups based on the following determinants:

* Site of TB disease
* Bacteriology (result of sputum smear)
* History of previous treatment of TB
* HIV status

### Site of TB disease

**Pulmonary tuberculosis (PTB)** refers to disease involving the lung parenchyma. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of pulmonary TB. Miliary TB is classified as pulmonary TB because there are lesions in the lungs.

**Extra-pulmonary tuberculosis (EPTB)** refers to tuberculosis of organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. Diagnosis should be based on one culture-positive specimen, or histological or strong evidence consistent with active EPTB, followed by a decision by a clinician to treat with a full course of tuberculosis chemotherapy.

### Bacteriology (result of sputum smear) in pulmonary TB

Defining the smear result in pulmonary cases is important to:

* Identify smear-positive cases, because they are the most infectious cases;
* Record, report and evaluate programme performance (smear-positive cases are the cases for which bacteriological monitoring of treatment progress is most practicable).

**Case definitions by site and result of smear**

**Smear positive PTB case**

* At least 1 sputum smears positive for AFBs or
* 1 sputum smear positive for AFBs and chest x-ray abnormalities consistent with active TB or 1 sputum smear positive and culture positive for M. tuberculosis or
* One sputum smear examination positive for AFB and laboratory confirmation of HIV infection or strong clinical evidence of HIV infection

It is advisable that even if the first specimen is positive pre-treatment, another specimen should be taken. This will reduce the chances of a false-positive result as administrative errors may occur.

**Smear negative PTB case**

* At least two sputum smears are negative for AFBs and
* Chest x-ray abnormalities are consistent with active TB and
* Laboratory confirmation of HIV infection or
* Strong clinical evidence of HIV infection

**AND**

* Decision by by a clinician to treat with a full course of anti-tuberculosis chemotherapy

**OR**

* A patient with AFB smear-negative sputum which is culture-positive for Mycobacterium tuberculosis.
* Definition by GeneXpert (Molecular tests result)

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### History of previous treatment

Based on history of previous treatment with anti-TB drugs, detected TB patients can be assigned to two main registration groups namely:

* New cases
* Previously treated cases.

#### New patients:

These are patients that have never had treatment for TB, or have taken anti-TB drugs for less than 1 month. New patients may have positive or negative bacteriology and may have disease at any anatomical site.

**Previously treated cases:**

These are patients that have received 1 month or more of anti-TB drugs in the past, may have positive or negative bacteriology and may have disease at any ana­tomical site. Previously treated cases should be further classified by the outcome of their most recent course of treatment as follows:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| |  | | --- | | **Registration group**  **(any site of disease)** | | | **Bacteriology: Smear** | **Bacteriology: Xpert** | **Outcome of most recent prior treatment** |
| **New** | | + or – | + or - | - |
| **Previously treated** | Relapse | + | + | Cured |
|  | Failure | + | + | Treatment completed |
|  | Treatment interrupted | + | + | Treatment interrupted |
| **Transfer in:** A patient who has been transferred from another TB register to continue treatment | | + or – | + | Still on treatment |
| **Other** |  | + or – | + or \_- | All cases that do not fit the above definitions, such as patients   * for whom it is not known whether they have been previously treated; * who were previously treated but with unknown outcome of that previous treatment; and/or * who have returned to treatment with smear-negative PTB or bacteriologically negative EPTB |

1. DIAGNOSIS OF TB

## Approach to TB diagnosis

Detection of TB in health facilities should be an ongoing activity. Diagnosis of TB starts with identifying TB suspects through clinical symptoms and physical examination.

Diagnosis of tuberculosis should include assessment for drug resistance to ensure timely initiation on the most appropriate treatment regimen.

Sputum samples need to be collected for laboratory investigation.

The initial diagnostic tests for all persons suspected of tuberculosis should include

1. a microscopy preferably using the iLED; or,
2. ii) an Xpert MTB/Rif test.

The subsequent diagnostic tests which will include Line Probe Assay, Culture and DST to further confirm TB, MDR-TB diagnosis or determine resistance shall be applied based on the diagnostic algorithm (See figure ???).

## Bacteriological confirmation of pulmonary TB diagnosis

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### Microscopy

Microscopy remains an important screening test for persons with presumptive pulmonary TB which aims at demonstration of AFB in sputum.For microscopy to be reliable, consistent quality-assurance is required. The number of bacilli (AFB) seen in a smear reflects the patients infectivity (see 6.6.1). Two sputum samples are required for microscopy.

Two types of microscopy methods are available in Swaziland, namely:

* the direct smear light microscopy using the conventional Ziehl Nelsen’s staining technique; and
* the fluorescent-LED method where the AFB are visualised as fluorescence in a dark background.

The fluorescent LED microscopy has an advantage over the light microscopy in terms of ability to detect the bacilli easier and faster reducing time to diagnosis.

**The main uses of the microscopy are:**

* Initial diagnosis of pulmonary TB for TB suspects who do not have access to the GeneXpert.
* Follow up the smear status of patients during TB treatment.

Results for microscopy are given quantitatively according to the number of bacilli seen on each smear:

* A positive result is defined as one showing actual number to 3+;
* A positive result in one of the two samples submitted is considered a bacteriologically confirmed case of pulmonary TB;
* All positive sputum results should be recorded in both the laboratory and TB registers in red ink for ease of identification.
* The laboratory iden­tification number and the date the examination was performed should be entered in the column next to that for the result of the examination.

Table 2: Guide for grading results of smear microscopy

|  |  |  |
| --- | --- | --- |
| **Number of bacilli seen on a smear** | **Fields to examine** | **Results reported** |
| No AFB per 100 oil immersion fields | 100 | 0 |
| 1-9 AFB per 100 oil immersion fields | 100 | Scanty indicate number (1-9) |
| 10-99 AFB per 100 oil immersion fields | 100 | 1+ |
| 1-10 AFB per 1 oil immersion field | 50 | 2++ |
| >10 AFB per 1 oil immersion field | 20 | 3+++ |

The clinician and the laboratory personnel must always remember that there could be false positive or false negative sputum smear microscopy results. Therefore laboratory results should be examined in relation to the patients clinical condition.

The main causes of false positive or false positive smear microscopy results could be one or more of the following factors:

* Red staining of scratches on the slide
* Accidental transfer of AFBs from a positive slide to a negative one, usually in the laboratory
* Contamination of the slide or smear by environmental mycobacteria
* Contamination of the slide with food particles that are acid fast and stain red
* Mix up of specimens.
* Patient provides inadequate sample
* Sputum stored too long before smear microscopy, with overgrowth with other organisms
* Faulty sampling from specimen
* Faulty smear preparation and staining
* Inadequate time on examining the smear
* Incorrect labelling of specimens
* Mistakes in reporting

***Smear-positive pulmonary tuberculosis: diagnosed if:***

* Two sputum smears positive for AFB, **or**
* One sputum smear examination positive for acid-fast bacilli (AFB) with Chest X-ray abnormalities consistent with active TB **and**
  + Laboratory confirmation of HIV infection **or**
  + Strong clinical evidence of HIV infection.

***Smear-negative pulmonary tuberculosis diagnosed if:***

* At least two sputum specimens negative for AFB **and**
* Radiological abnormalities consistent with active tuberculosis **and**
* Laboratory confirmation of HIV infection **or**
* Strong clinical evidence of HIV infection.

**and**

* Decision by a clinician to treat with a full course of anti-tuberculosis chemotherapy

**OR**

* A patient with AFB smear-negative sputum which is culture-positive for *Mycobacterium tuberculosis*.

All positive sputum results should recorded in both the Laboratory and TB Regional registers in **red** ink for ease of identification. The laboratory iden­tification number and the date the examination was performed should be entered in the column next to that for the result of the examination.

**Note:**

The sensitivity of sputum smear microscopy can be increased by concentrating the specimen by centrifugation at 3000g after decontamination with 5% sodium hypochlorite for 30 minutes.

This method is highly recommended in diagnostic facilities with appropriate centrifuge machine as it gives better yield than the conventional methods

### Xpert MTB/Rif (Gene Xpert)

This is an automated cartridge-based rapid molecular method which was recently endorsed by WHO as an initial diagnostic test for pulmonary tuberculosis. The test also simultaneously detects rifampicin resistance conferring mutations directly from sputum providing both results within 2 hours for each sample using the multi-disease Gene Xpert platform. The Xpert MTB/Rif has increased sensitivity and specificity and useful in diagnosing TB in PLHIV who often have smear negative microscopy tests. A typical 4-module Gene Xpert can perform about 16 tests per a working day.

Xpert test should be performed for:

* For all persons suspected of having tuberculosis regardless of HIV status;
* For all persons suspected of drug resistant tuberculosis regardless of HIV status.

Xpert should not be used for bacteriological monitoring of TB treatment response.

#### Practical considerations for use of Xpert MTB/Rif

The Xpert should be applied as follows:

* Gene Xpert can be used at the peripheral level of the laboratory network as it has similar biosafety requirements to microscopy.
* Xpert should be used for testing of all persons suspected of having tuberculosis
* Ensure stable uninterrupted power supply, and use of UPS for each unit while in operation;
* Ensure adequate and secure storage space for Xpert Cartridges;
* There should be a dedicated staff to perform the Xpert tests;

Ensure calibration of the Xpert Module after every 2000 tests or one year, whichever comes first;

The use of Gene Xpert on other samples other than respiratory is not validated yet.

**Gene Xpert test should be requested for all patients with symptoms suspected of PTB as the diagnostic method of first choice (where the facilities are available)**

#### Use of Xpert MTB/Rif results

On receiving the Xpert results, treatment decisions should be made as follows:

* All patients whose diagnosis of TB has been confirmed by Xpert MTB/Rif but negative for Rifampicin resistance (i.e MTB +ve and Rif –ve) should be registered as bacteriologically confirmed tuberculosis (**Xpert MTB/Rif positive**), and started on first line anti-TB treatment;
* No additional microscopy is required for establishing baseline smear result in persons diagnosed using the Xpert;
* Xpert MTB +ve patients should be monitored while on treatment using smear microscopy at the recommended intervals until completion of treatment;
* Patients with TB and rifampicin resistance confirmed by Xpert should be registered as **Xpert MTB/Rif positive with Rifampicin resistance** considered as having MDR-TB and be placed on the standardized second line anti-TB treatment regimen;
* Xpert diagnosed MDR-TB patients should be monitored by sputum microscopy and culture as per the National MDR-TB management guidelines.

***Note: registration of diagnosed TB cases using conventional TB diagnostics remains unchanged if the results ofXpert MTB/Rif is not available*.**

#### Repeating Gene Xpert tests

Xxxxxxxxxxxx

### Use of interferon gamma tests:

The identification of genes in the M. tuberculosis genome that are absent from M. bovis BCG and most non-tuberculous mycobacteria has supported the development of more specific and sensitive tests for detection of M. tuberculosis.

These gene deletions including the region of difference 1 (RD-1) encodes for early secretory antigen target-6 (ESAT-6) and culture filtrate protein 10 (CFP-10), which are strong targets of the cellular immune response in patients with M. tuberculosis infection.

The presence of the ESAT-6 and CFP-10 trigger sensitized memory/effector T cells to produce interferon-gamma (IFN-gamma) in response to these M. tuberculosis antigens, thereby providing a biologic basis for T-cell-based tests such interferon-gamma release assays (IGRAs).

Research over the past decade on the basis of this has resulted in the development of two commercial IGRAs. Both assays work on the principle that the T-cells of an individual who have acquired TB infection will respond to re-stimulation with M. tuberculosis-specific antigens by secreting interferon-gamma.

The two tests include:

* The QuantiFERON-TB Gold (QFT-G, Cellestis, Australia) and the newer version QuantiFERON-TB Gold In-Tube (QFT-GIT, Cellestis, Australia) are whole-blood based enzyme-linked immunosorbent assays (ELISA) measuring the amount of IFN- produced in response to specific M. tuberculosis antigens (QFT-G: ESAT-6 and CFP-10, QFT-GIT: ESAT-6, CFP-10, TB7.7).
* The enzyme-linked immunospot (ELISPOT)-based T-SPOT.TB (Oxford Immunotec, UK) measures the number of peripheral mononuclear cells that produce INF- after stimulation with ESAT-6 and CFP-10.

Both IGRAs and the TST are surrogate markers of M. tuberculosis infection, indicating a cellular immune response to recent or remote sensitization with M. tuberculosis. Currently, there is no gold standard for the detection of M. tuberculosis infection, and neither the TST nor IGRAs can distinguish TB infection from active TB disease.

Due to insufficient data and low quality evidence on the performance of IGRAs in low- and middle-income countries, and especially high TB and/or HIV settings, IGRAs has not been endorsed by WHO.

This guideline therefore does not recommend the use of IGRAs in the diagnosis of TB in adults or children in the country.

### Use of Commercial sero-diagnostics

Serological tests for diagnosis of tuberculosis are tests developed on the basis of antibody recognition of antigens of Mycobacterium tuberculosis by the humoral immune response, as opposed to antigen recognition by the cellular immune response (e.g. interferon-gamma release assays).

Although and accurate serological test that could provide rapid diagnosis of TB and in a suitable format (e.g. point-of-care) would be particularly useful and desireable both as a replacement for laboratory-based tests and for extending TB diagnosis to lower levels of health services, especially those without on-site laboratories, so far WHO evidence review for these tests yielded inconsistent and imprecise findings resulting in highly variable values for sensitivity and specificity.

Currently, there is no evidence that existing commercial serological assays improve patient-important outcomes, and high proportions of false-positive and false-negative results adversely impact patient safety. Overall data quality was graded as very low and it is strongly recommended that these tests not be used for the diagnosis of pulmonary and extra-pulmonary TB. Sero-diagnostic tests for tuberculosis is therefore not endorsed by WHO.

This guideline does not recommend the use of sero-diagnostic tests for diagnosis of TB in adults or children in Swaziland.

## Diagnosis of drug resistant tuberculosis

### Line Probe Assay (LPA) method

The Line Probe Assay (LPA) is molecular method for rapid detection of resistance to both rifampicin and INH (MDR-TB) in a sputum sample. LPA indirectly detects presence of *Mycobacterium tuberculosis* by amplifying DNA present in the sputum by polymerase chain reaction (PCR), which can be subsequently be visualized on a strip by the presence or absence of bands. Results of LPA tests are obtainable within a 48 to 72 hours period, which will enable timely initiation of MDR-TB treatment.

The indications to send sputum samples for Line Probe Assay are:

* Smear positive diagnostic samples from facilities that do not have access to GeneXpert yet.
* Sputum from patients with a Xpert MTB +ve and Rif -ve

### Mycobacterial culture and drugs susceptibility testing (DST)

Mycobacterial culture method provides the most definitive diagnosis of tuberculosis, and therefore considered the gold standard. Culture significantly increase the number of TB cases found (often by 30–50%) and allow earlier detection of cases (often before they become infectious). Culture also provides the necessary isolates for conventional drug susceptibility testing (DST).

Two culture methods have been adopted in Swaziland namely:

* The conventional Solid Culture method (L-J techniques)
* Liquid culture using the Mycobactria Growth Indicator Tube (MGIT), which increases the case yield by 10% over solid media.

The MGIT method is an automated system, and reduces the diagnostic delay to days rather than weeks. However, the system is more prone to contamination, and the manipulation of large volumes of

infectious material. Good laboratory practice maintains a delicate balance between the yield of mycobacteria and contamination by other microorganisms.

Mycobacterial cultures should always be performed in containment laboratories with biosafety level BSL III.

Positive cultures must be identified to differentiate *M. tuberculosis* from non-tuberculous mycobacteria, which are more common in HIV-infected patients.

The culture method available in the National TB Reference Laboratory is the MGIT method (Mycobacterium Growth Indicator Tube). The method uses Middlebrook 7H9 broth (Liquid media), and the results can be reported as early as 10 days (if the culture is positive), or up to 42 days to report a culture-negative result.

The advantage of this culture method is its ability to give drug-sensitivity results to all the four major anti-TB drugs (Rifampicin, Isoniazid, Ethambutol and Streptomycin) and the short turnaround time.

#### Thin Layer Agar (TLA) culture method

Thin Layer Agar (TLA)uses solid media which is impregnated with isoniazid and rifampicin to allow bacilli to grow in their favourable environment, and few days later to observe the specimen under direct microscopy.

The growth of MTB in media containing Rifampicin or Isoniazid is then directly visualized, thereby giving DST results for R and INH.

The advantage of this method lies in its rapidity, with culture and DST results being reported simultaneously in 7-10 days, and it’s relatively low cost per test.

This method has been introduced in Nhlangano Health centre as a demonstration site, with the potential for scale up depending on its overall benefits in relation to other culture/DST tests available.

## Sputum transportation

The quality of sputum sample submitted for bacteriological examination for tuberculosis is critical in determining the correct outcome of the test.

The Xpert MTB/Rif is particularly sensitive, and require a very good quality sputum sample without particles to avoid error reading by the equipment. The sputum sample for Xpert MTB/Rif should be processed and read with 24 hours of collection.

The National Sample Transportation System should ensure collection of sputum samples from the requesting health facility to the referral laboratories, where the following takes place:

1. Samples for microscopy/Gene Xpert are processed at the referral laboratories and results are sent back to the clinics.
2. Samples that require culture and LPA will be sent to NTRL through DHL courier service.

NB: The triple packaging system should be strictly observed when transporting sputum samples

## Role of Other Investigations in TB Control

### Role of Chest x-rays

Chest X-rays are useful to suspect tuberculosis in routine screening and assessing the extent of complications of lung diseases. The common Chest X-ray findings associated with pulmonary tuberculosis include upper lobe infiltrates, bilateral infiltrates, cavitations, pulmonary fibrosis and shrinkage.

However, the sensitivity of Chest X-ray in the diagnosis of tuberculosis is low. Furthermore, there is NO Chest X-ray appearance that is typical for PTB as many other conditions mimic tuberculosis. These conditions include but are not limited to the following: bacterial pneumonia, lung abscess, fungal infection, bronchial carcinoma, connective tissue disease, occupational lung disease, sarcoidosis, and lymphoma. Additional specific tests might therefore be needed to rule out these diseases or conditions.

The use of Chest X-ray in the diagnosis of pulmonary tuberculosis is therefore relatively unreliable, but can be useful in diagnosing extra-pulmonary TB e.g miliary tuberculosis, pleural TB with effusion, pneumothorax, pericarditis, etc.

Chest X-ray is not necessary in a case where the sputum smear result is positive.

The absence of a chest X-ray should not be an obstacle to diagnose and initiate TB treatment.

Chest X-rays are not necessary for the routine follow-up of a patient on TB treatment.

They are not required to change to continuation phase or to stop treatment in patients who are clinically responding well to TB therapy.

Chest x-rays are contra-indicated in pregnancy especially during the first trimester.

## Revised diagnostic Algorithms according to existing TB diagnostic equipment in Swaziland

The National programme has adopted the Xpert MTB/Rif as the initial diagnostic test for all persons suspected of having tuberculosis in view of the high HIV and MDR rates among incident cases, while bacteriological monitoring of treatment will be through LED microscopy. However, the roll-out of the Xpert MTB/Rif and other new TB diagnostic tests described in 6.4.1 shall be phased until the ultimate goal is achieved.

Two algorithms are therefore currently recommended for use in Swaziland:

1. Algorithm 1: for health facilities without the Gene Xpert
2. Algorithm 2: for health facilities with Gene Xpert

Algorithm 1: Facilities without Gene Xpert

**Algorithm 2: Facilities having access to GeneXpert**

1. Includes MDR TB suspects

2. For discrepant results between genotypic and phenotypic tests refer to guidelines

Sputum microscopy / LED microscopy (2 smears)

Negative or smear not done

Positive

CXR (only if available)

Course of antibiotics

Asses HIV status

HIV +

R+/H+

R+/H-

R-/H+

LPA

Treat with FLD.

R-/H-

DST for FLD&SLD2 and adjust SLD regimen.

Follow up 2, 5 months with Sputum microscopy

Positive

Negative

Cont Rx

MGIT C/DST for FLD

INH and RIF Resistance

Susceptible or other resistance

Treat with SLD and send for SLD DST

Initiate appropriate treatment. Assess adherence

Follow up monthly with sputum microscopy and culture

Reassess for other HIV associated disease (PCP if less than CD4 200)

If no improvement consider starting empiric therapy

Modify R.Do FLD & SLD DST. Adjust regimen accordingly

HIV -

If no improvement consider anotherdiagnosis

HIV test and Xpert MTB/Rif2

Xpert MTB+/Rif+

Xpert MTB+/Rif-

Xpert MTB-/Rif-

Treat with Standard MDR TB Rx

IF HIV + initiate CPT and ART

Treat for TB with FLD

If HIV + initiate CPT and ART.

Further clinical assessment including:

* If HIV+ reassess for other HIV related diseases
* If HIV negative this might include broad spectrum antibiotics (medical doctor)
* Chest X Ray

DST for FLD&SL and adjust SLD regimen according to results

lts

Still considered TB suspect

No longer considered TB suspect

Inv for EPTB or other disease;

Initiate TB R on clinical grounds

Send for MGIT C/DST for FLD and adjust R accordingly

Exit algorithm.

Follow up according to follow up guidelines

Retest with Xpert

MTB+

MTB-

Send one specimen for LPA

R+/H+ or R+/H- 3

Modify R.Adjust R according to separate mono and poly resistant TB guidelines.

Send one specimen for DST for FLD & SLD drugs and adjust R2

R-/H+

R-/H-

Continue to treat with FLD R.

1. Includes MDR TB suspects

2. One sputum specimen

3. For discrepant results between genotypic and phenotypic tests refer to guidelines

## Confirming diagnosis of Extra-Pulmonary TB

Extra-pulmonary tuberculosis diagnosis is confirmed under the following situations:

* One specimen from an extra-pulmonary site smear positive for AFB or culture-positive for *M. tuberculosis;*

**OR**

* Histological or strong clinical evidence consistent with active extra-pulmonary tuberculosis **and**
* Laboratory confirmation of HIV infection **or**
* Strong clinical evidence of HIV infection;

**And**

* A decision by a clinician to treat with full course of anti-tuberculous chemotherapy.

### TB Meningitis

TB meningitis results from rupture of a cerebral tuberculoma into the subarachnoid space

orblood-borne. It is a life threatening condition with serious complications if not treated promptly. Diagnosis is confirmed by the demonstrating the relevant clinical signs backed with positive laboratory results:

**Clinical Features**

* + - * Patients present with gradual onset of headache and decreased consciousness.
      * Examination reveals neck stiffness and positive Kernig’s sign (flex one of the patient’s legs at hip and knee with the patient lying on back, and then straighten the knee - resistance to straightening the knee and pain in the low back and posterior thigh suggest meningeal inflammation).
      * Cranial nerve palsies resulting from exudates around the base of the brain.
      * Tuberculomas and vascular occlusion may cause focal neurological deficits and seizures.
      * Obstructive hydocephalus may develop.
      * Spinal meningeal involvement causes paraplegia (spastic or flaccid)

**Laboratory**

* Lumbar puncture to examine cerebrospinal fluid and the following features indicate a positive test:
  + Clear CSF
  + Elevated pressure
  + High levels of protein (>1g/ l)
  + High lymphocyte count (30-300/mm³)
  + Low glucose
  + AFBs on microscopy in a minority of cases.
  + Some of the CSF findings may be normal, especially in HIV-positive patients.

Patients with suspected TB meningitis should be referred to hospital without delay.

Table 3: Table showing symptom-based approach to the diagnosis of Extra-pulmonary TB

|  |  |  |
| --- | --- | --- |
| **TYPE OF EPTB** | **SYMPTOMS** | **DIAGNOSIS** |
| **TB Lymphadenitis (most common EPTB site)** | Fever, weight loss, fatigue and occasionally night sweats or no symptoms at all.  Enlarged lymph nodes (>2cm). They can break down due to the formation of caseous pus. Cervical LN are the most common.  Mediastinal lymph nodes or abdominal lymph nodes, if large may obstruct nearby organs thereby producing such symptoms as cough, dysphagia, intestinal obstruction, etc. | Lymph node aspiration of the caseous pus and send for microscopy, culture and DST.  If aspirate is dry then a lymph node biopsy should be taken, sending the material for anatomopathology and culture/DST. |
| **Pleural TB (Extrapulmonary TB)** | Acute or sub-acute illness varying from a few days to few weeks. Pleuritic chest pains, non-productive cough and dyspnoea, sometimes fever.  In an empyema, the patient is acutely ill with chest pains, breathlessness, and cough with expectoration, fever and toxaemia. Occasionally it may present as a chest wall mass or draining sinus tract. | By therapeutic/diagnostic tap and sending the fluid for microscopy and culture / DST .  If the patient has empyema, he must be admitted, the empyema drained and send the material for microscopy, culture and DST. |
| **TB meningitis** | Meningism (neck stiffness, kerning’s sign), irritability, anorexia, vomiting, fever and sometimes seizures.  Complete or partial loss of vision is a major complication of TBM. Without treatment the patient may descend into a coma and death would follow in five to eight weeks. Thus patient needs immediate admission. | Lumbar puncture for CSF (increased lymphocytes, increased proteins and decreased glucose).  CSF should be sent for microscopy and culture/DST.  If the patient is HIV + do also India ink and crptococcal antigen. |
| **Abdominal TB** | Symtpoms are non-specific and depend on the site and extent of the disease.  Loss of appetite, malaise, diarrhea, low grade fever, weight loss, night sweats, ascitis, masses or abscess, obstructive jaundice, etc | Diagnostic/therapeutic tap and send off for microscopy and culture/DST . |
| **Pericardial TB** | Fever, weakness, pericardial rub, vague chest pains, dyspnoea, cough, elevated jugular venous pressure, weight loss. | Clinical diagnose, cardiomegaly in the chest Xray and echocardiogram.  In case of pericardiocenthesis, liquid should be sent for microscopy and culture/DST. |
| **TB of the bones and joints** | Spinal TB (Potts disease) is the most common, usually constitutional symptoms (weakness, loss of appetite and weight, night sweats) will be present before any signs of spinal involvement (chronic back pain and gibbous deformity). If untreated, patient can develop neurological deficits and paraplegia.  TB of the joints affects the movement of the affected joints and produce pain. | X ray spine will show erosion of adjacent vertebral bodies and disc space narrowing.  These patients need to be referred to a specialist for treatment. |
| **Miliary TB** | Constitutional symptoms (fever, night sweats, loss of weight) and hepato-splenomegaly. They may also have a cough. | Chest X-ray: diffuse miliarynodules.  Sputum can be negative if not lung parenchyma is compromised. |

### Tuberculous Lymphadenopathy

Tuberculous lymphadenitis should be suspected in any patient with enlarged lymph nodes that are firm, asymmetrical, more than 2 cm in diameter, or where a node has become fluctuant or developed a fistula over several months. It most commonly affects the nodes in the neck(cervical region) and is difficult to distinguish clinically from other causes of enlarged nodes, such as reactive and/or HIV-related lymphadenopathy, malignancies and other lymph node infections, which are also common. Therefore,

needle aspiration using recommended techniques should be carried out at the first outpatient visit for all patients.

Diagnosis can be confirmed by biopsy and demonstration of histological evidence. Where the capacity for histology does not exist, the patient can be started early on anti-TB treatment based on the decision of a Medical Officer to treat as extra-pulmonary TB.

### Miliary TB

Miliary TB results from widespread blood borne dissemination of TB bacilli. This is either the consequence of a recent primary infection or the erosion of a tuberculous lesion into a blood vessel.

The patient presents with constitutional features (fever, night sweats and weight loss). Hepatosplenomegaly may be present and choroidal tubercles on fundoscopy. Miliary TB is an under-diagnosed cause of end stage wasting in HIV-positive individuals. Diagnosis should be established using Chest x-ray findingshowing diffuse, uniformly distributed, small miliary nodules (“miliary” means “like small millet seeds”) which is pathogneumonic of that form of the disease.

### Tuberculous pleural effusions

Inflammatory tuberculous effusions may occur in any of the serous cavities of the body, i.e. pleural, pericardial or peritoneal cavities. They are a common form of TB in HIV- positive patients.

* Patients usually have systemic and local features.
* Microscopy of the aspirates from tuberculous serous effusions rarely show AFB because the fluid forms as an inflammatory reaction to TB lesions in the serous membrane.
* Finding of a straw coloured fluid from the pleural tap is highly indicative of TB pleural effusion and should be treated as such.

### Tuberculosis of the spine

This is a severe form of tuberculosis when there are neurological sequelae. It is seen both in children, usually within three years following primary infection, and in adults. In many cases more than one intervertebral disc space is involved. As the disease develops, the vertebral body adjacent to the disc space is affected; an abscess is formed and spreads either forward towards the mediastinum or the retroperitoneal space, to the vertebral body with compression of the spinal cord, or back along the vertebral column eventually appearing as a subcutaneous “cold” abscess. Collapse of adjacent vertebral bodies affected by tuberculosis may lead to angulated kyphosis. The sites most commonly involved are the lower thoracic, lumbar and lumbo-sacral areas.

The main differential diagnoses are malignancy and pyogenic spinal infections. Malignant deposits in the spine tend to erode the pedicles and spinal bodies, leaving the disc intact. Pyogenic infection tends to be more acute than TB, with more severe pain. Diagnosis can be confirmed through X-ray of the spine revealing typical findings consistent with destruction of inter-vertebral disc.

1. QUALITY ASSURANCE OF LABORATORY SERVICES

## Importance of Laboratory Services in TB Control

A well-functioning laboratory is the first requirement for successful management of tuberculosis. This is in view of the fact that a reliable diagnosis and treatment follow-up is necessary to inform treatment decisions that ultimately leads to cure of infectious TB cases; thereby interrupting transmission of the disease. The laboratory also has a major role in surveillance of the TB situation in the community, incidence, prevalence, drug susceptibility patterns, etc).

TB diagnosis should be made as close as possible to the patient’s residence, while maintaining the proficiency of the testing procedures. Although sputum smear examination by Ziehl-Neelsen method remains the basic requirement for TB diagnosis, culture and drug susceptibility testing (DST) may be performed depending of the indication. For this reason, it is necessary for the entire population to have access to quality-assured TB laboratory services. Culture should be selectively used in the following circumstances[[3]](#footnote-3):

1. Surveillance of tuberculosis drug resistance as an integral part of the evaluation of control programme performance
2. Diagnosis of cases with clinical and radiological signs of pulmonary tuberculosis where smears are repeatedly negative
3. Diagnosis of extra-pulmonary and childhood tuberculosis
4. Follow-up of tuberculosis cases who fail a standardized course of treatment and why may be at risk of harbouring drug resistant organisms
5. Investigation of high-risk individuals who are symptomatic, eg. Laboratory workers, health care workers looking after multi-drug resistant patients

Drug susceptibility is mainly of value for epidemiological purposes. Testing of individual patients should be limited to:

* Patients who fail standardized treatment regimens
* High risk individuals who are found to have positive cultures, eg. laboratory workers, health care workers looking after multidrug resistant patients
* Close contacts of multidrug resistant tuberculosis patients who have signs and symptoms of tuberculosis
* Species identification

## TB laboratory Network in Swaziland

Tuberculosis laboratory services in Swaziland forms part of overall laboratory services in the country, and is organized according to the technical complexity, activities performed and functional roles as follows:

1. Central level (the National Reference laboratory )
2. Intermediate level (the Regional Laboratories/x
3. Peripheral laboratories (health centre and clinic laboratories)

### The National Reference laboratory

The National TB Reference Laboratory (NRL) is situated within the National Reference Laboratory and Blood Bank Complex in Mbabane. The NRL performs mycobacterial species identification, LPA, MGIT culture and first line drug susceptibility testing (FLD DST). Beside the core technical activities, the NRL should provide capacity building and training for laboratory staff, external quality assessment (EQA), contribute to surveillance of tuberculosis including drug resistance and participate in epidemiological and operational research. Establishment of tuberculosis culture facilities at in the country aims to achieve at least 1 centre per 500 000 population.

### The Regional laboratories

The regional laboratories, which are located within the hospitals, health centres and some clinics in the country primarily perform direct sputum smear microscopy using either the conventional Z-N technique or the LED microscopy. The national TB programme and the National clinical laboratory service aims to have at least one microscopy centre is serving about 50,000 population.

## Assuring Quality of Smear Microscopy

Results of TB laboratory investigations are critical for diagnosis and follow up of patients on treatment according to national guidelines. Hence, the credibility, success and sustainability of the programme depends on the capacity of TB laboratory network to produce reliable results.

Poor quality diagnosis results in failure to detect persons with infectious TB, who will continue to spread infection in the community, or unnecessary treatment of “non-TB cases.” Errors in the reading of follow up smears may result in wrong outcome of patients often with severe consequences to the community.

In order to achieve the required technical quality in laboratory diagnosis, a continuous system of quality assurance needs to be established. Intermediate laboratories should supervise the peripheral network, while the central or reference laboratory should supervise the intermediate network.

An effective quality assurance (QA) system of sputum smear microscopy network is of crucial importance for the programme. QA is a comprehensive system consisting of internal quality control (QC), assessment of performance using external quality assessment (EQA) methods, and continuous quality improvement (QI) of laboratory services. To optimize QA, the supervision and monitoring of the laboratory network is essential. This process requires the active support and participation of the NRL and regional laboratories. The definitions of QC, EQA and QI are explained below.

**Quality Control (QC)** or Internal Quality Control, includes all the ‘bench-top’ procedures by which the laboratory personnel performing TB smear microscopy control the process, including checking of instrument, new lots of staining solutions, smear preparation, grading etc. It is a systematic internal monitoring of working practices, technical procedures, equipment, and materials, including quality of stains.

**External Quality Assessment (EQA)** A process to assess laboratory performance. EQA includes ‘on-site evaluation’ (OSE) of the laboratory to review QC and evaluation of entire process of smear microscopy, and random blinded re-checking of routine smears. EQA also allows participant laboratories to assess their capabilities by comparing their results with those obtained in other laboratories in the network (intermediate and central laboratory) through panel testing and rechecking of patient slides, using both un-blinded and blinded procedures. EQA is also termed “Proficiency Testing” as described by IUATLD.

**Quality Improvement (QI)** A process by which all components of smear microscopy diagnostic services are carefully analyzed, periodically, 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. It involves continued monitoring, identifying defects, followed by remedial action including retraining when needed, to prevent recurrence of problems. QI mostly relies on effective on-site evaluation visits.

### External Quality Assessment (EQA)

External Quality Assessment is one of the most important components of a laboratory QA program.

The national TB reference laboratory should play an essential role in the organization and maintenance of the network in terms of developing guidelines, ensuring high quality and standardized smear microscopy, and therefore must have the capacity to provide training and External Quality Assessment, including providing panel testing and rechecking to intermediate and peripheral laboratories.

EQA should focus on identification of laboratories where there may be serious problems resulting in poor performance, and not on the identification of individual slide errors or the validation of individual patient diagnosis. It is also a very important tool for communication with and motivation of laboratory technicians who may otherwise feel isolated in their work. There are three methods that should be combined to evaluate laboratory performance:

• On-site Evaluation

• Panel Testing

• Blinded Rechecking

### On-site evaluation of Microscopy Centers:

The on-site evaluation includes a comprehensive assessment of laboratory safety, condition of the binocular microscope, adequacy of supplies as well as the technical components of sputum smear microscopy, including preparation, staining and reading of smears. On-site evaluation should always include macroscopic as well as microscopic examination of randomly selected 5 stained positive and 5 negative smears.

Checklists should be used to assist supervisors during the field visit and to allow for the collection and analysis of standard data for subsequent remedial action. The copies of the checklist, duly completed by the Supervisors, should be handed over to in-charge of the laboratory as well as the Hospital authorities. This will provide written documentation of the visit, its findings and proposed corrective actions for improvement.

The On-site Evaluation visits should be conducted to every regional and peripheral laboratory semiannually. A comprehensive checklist for on-site evaluation of Microscopy centers is provided as annexure.

## 

### Panel Testing

Panel testing is a method of EQA that evaluates a technician’s individual performance in staining and reading, and not the whole laboratory activities. Utilization of panel testing for EQA is considered to be less effective than random blinded rechecking of routine slides because it does not monitor routine performance.

Panels are to be prepared and distributed to all laboratories on a quarterly basis, which should be followed by analysis of results and feedback to facilities.

The panels should consist of a set of 10 panel slides, including negatives and covering all the positive grades of test smears. These slides should be read and graded within the normal routine programme conditions. Based on the results, gaps and remedial actions including training will be determined to address technical skill deficiencies and errors to achieve higher level of proficiency.

Insert paragraph on panel testing system

### Random Blinded Rechecking of Routine Slides

Blinded rechecking is a process of re-reading a statistically valid sample of slides from a laboratory to assess whether that laboratory has an acceptable level of performance. This method provides reliable assurance that NTP is supported by an efficient and reliable sputum microscopy laboratory network.

Random blinded rechecking involves selection of a representative sample of slides from a Microscopy Center (both positives and negatives). The results of the slides are blinded before being read by a supervisor (first controller) in an un-biased manner. The discrepant results are resolved by a higher supervisor (umpire reader). A timely feedback is provided every month to the laboratory staff heads of labs for improvement in the quality of microscopy.

The Central and intermediate laboratories would also be supervising the peripheral Microscopy Laboratories on a routine basis; and reports of their visits should be handed over to in-charges at all levels. Corrective measures should be implemented based on findings of these reports.

**Operation of the blinding rechecking using the IQLS system**

All regional and peripheral labs participate in blinded rechecking EQA and on a quarterly basis, each lab provides 40 slides for rechecking. A sample size of 40 slides per lab (microscopy centers) for the EQA per site was determined using the Lot Quality Sampling method basing on the annual volume of slides read. A blinded rechecking team of 8 lab technologists, was established to pick slides and re-read them. Each quarter, 40 slides are randomly picked at each participating lab and their results recorded on the IQLS blinded rechecking form. The form is sent for data capture into the IQLS system and filing a Data Analyst at the NRL while the slides are being re-read. The results of second reading are also recorded independently including details on the quality of stain on slide, thickness, evenness and stain grade. The results entered into the IQLS system will generate a comparison table for the two readings for each lab. The Data Analyst prints the comparison tables which are given to the rechecking team and discordant slides picked for a third reading. The slides are re-read by a different technologist and the result is recorded and captured as the tie-breaker and final. The final comparison list is now sent back to their original laboratories through rechecking teams who will also give feedback and technical assistance on the findings.

## Conducting visits to microscopy centres

Microscopy Laboratories are supervised by supervisors from the national and provincial level. The NTP will work with the Supervisors to make sure that tuberculosis-related laboratory services are performed according to national guidelines. Visits to the microscopy centres must be adequately planned, and a checklist should be used.

### Preparing for visits:

1. Supervisory visits to be planned in advance such that all laboratories are visited at least every quarter from National laboratory supervisor. Information should be given in advance about the visit to the laboratory.
2. Review the recommendations made during previous visits and the actions taken.
3. Ensure availability of an updated lab supervision checklist (Laboratory supervisory check-lists: given at annexure).

### Conducting the visit

Visiting the laboratory requires good time management to ensure a productive supportive visit without significantly disrupting the daily work schedule of the supervisee. The supervisor should be focused and be systematic in conducting the visit. The following techniques could be employed to check the laboratory operations:

* 1. Review the Tuberculosis Laboratory Register for completeness, consistency and accuracy of recording; and verify that monthly summaries are made correctly.
  2. Discuss with the laboratory technicians: to verify their understanding of the national guidelines concerning the correct number of sputum specimens required for diagnosis and follow up examinations; the importance of limiting administrative errors and accurately recording the results of sputum smear examinations on the Laboratory Form for Sputum Examination; and storing the examined sputum smear slides of all patients until the EQA purposes.
  3. Examine supplies: to determine if there are adequate numbers of sputum containers, slides, reagents, forms and other laboratory supplies for the expected patient turnover.

### Follow up Quality improvement

The findings of the supervision visit should be discussed with the supervisee with the view to finding solutions to problems detected. This should include on the job capacity building where required.

The supervisor should within one week produce a report of the supervisory visit and forward it to the higher authority. A copy of such a report should also be made available to the head of the Hospital and the laboratory visited.

Adequate follow up should be ensured concerning the recommendations of the report.

## Monitoring documentation related to microscopy examinations and other diagnostic methods

Every TB Microscopy laboratory must have a Tuberculosis Laboratory Register, which should be filled up completely and accurately to ensure that the results are entered for the right persons.

* In processing sputum sample for examination, the sputum containers and slides should be marked correctly with Laboratory Serial Number, and accurately record the results of sputum smear examinations on the form.
* Futhermore, all examined slides should be kept *serially* in the box without segregation of positive and negative slides, until the Laboratory Supervisor reviews them for quality assurance.
* During the on-site visit, the STLS should select five smear-positive and five smear-negative slides randomly and review them as per QA protocol.
* Ensure that the Microscopy laboratories and health facilities which collect and transport sputum are visited at least once every month. 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.

### Laboratory Request form

The laboratory request form is the first line of communication between the specimen submitting facility, agency, or physician and the laboratory. These forms are available upon request to the laboratory. Correctly completing this form will insure your patient and specimen are properly identified and matched, the requested procedures are performed in a timely manner, and the results get back to the facility, agency, or physician as requested. All results will be delivered by had electronically or faxed to the ordering facility, agency, or physician only.

The request form includes a place to enter many identifying elements. The national clinical laboratory service adopted a single the laboratory request form- **clinical laboratory services general request form** (see annex 16) , for all specimens including sputum testing for tuberculosis. It has a place for the ordering physician or agency, the patient information, specimen information, medical necessity justification, and procedures requested.

### Tuberculosis laboratory register

The Tuberculosis Laboratory Register is used to record the results of sputum smear examinations. The register should contain the patient’s personal data as well as name of the treatment facility, reason for examination and the results of the examinations. The following information about the patient is then recorded:

* Date of sputum smear examination
* Full name
* Sex
* Age
* Name of the health facility (e.g. primary health centre, private practitioner, NGO, etc.) that requested the examination
* Complete address
* Reason for examination (diagnosis, repeat diagnosis and follow-up of chemotherapy).
* Results of sputum smear examinations (results of specimens 1, 2 and 3 can be recorded).

The last two columns of the Tuberculosis Laboratory Register are for the Laboratory Technician’s (LT) remarks and signature.. The remarks column can also mention in brief the action taken for patients belonging to other treatment units or Regionals, e.g., “Referral.

Every week the in Charge of the MC should review the Tuberculosis Laboratory Register to ensure that correct numbers of sputum smear examinations (i.e. 3 per TB suspect) are being performed for diagnosis. Regional TB Coordinators should endeavour to compare sputum results mentioned in the

**Up to three-sputum specimen examination results can be recorded for each**

**patient on one line of the Tuberculosis Laboratory Register.**

Tuberculosis Laboratory Register with those mentioned in the TB Treatment Cards and TB Registers. This can be done by randomly selecting cases from the facilities to cross-check their results in the laboratories.

Laboratory staff should not use the Tuberculosis Laboratory Register to record the results of any other laboratory examinations. All results of sputum smear examinations done in a Microscopy Centre should be written only in one Tuberculosis Laboratory Register, and not in any other register.

The laboratory technician should summarize the information on sputum smear examinations done during that month. This information should be summarized in the monthly summary form (See annex) at the end of each month, printed in the Laboratory Register itself. Patients from the following month should be started from the next new page.

**Ensure that the patients for diagnosis had two sputum samples examined and follow-up cases had one sputum samples examined**

**Two samples for diagnosis is enough, as already WHO endorsed.**

**Reasons for False-negative Smear Results:**

* Improper storage of sputum specimens
* Inadequate sputum collection
* Too thin or thick smears
* Over-heating the slide while fixing
* Insufficient fixing
* Boiling carbolfuchsin
* Over decolorization with acid-alcohol
* Improper storage of stained slides
* Inadequate examination
* Using saliva for smears
* Reading and reporting errors

**Consequences of False-negative smear Results:**

* Patients with TB may be missed and thereby patient continues to spread the disease
* Wrong categorization
* Intensive phase treatment may not be extended for the correct duration, resulting in inadequate treatment
* Patients and the community may lose confidence in the programme
* Unwarranted repetition of investigations

**Reasons for False-positive Smear Results**

* Faulty sputum collection (presence of food particles or fibres)
* Using old scratched slides
* Using unfiltered carbolfuschin
* Insufficient decolorization with acid-alcohol
* 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 of False-Positive smear Results**

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

## The Ziehl–Neelsen staining procedure

1. Select a new unscratched slide and label the slide with the Laboratory Serial Number with a marking pencil.
2. Make a smear from yellow purulent portion of the sputum using a wooden stick. A good smear is spread evenly, 2 cms x 3 cms in size and is neither too thick nor too thin. The optimum thickness of the smear can be assessed by placing the smear on a printed matter. The print should be readable through the smear.
3. Allow the slide to air dry for 15–30 minutes.
4. Fix the slide by passing it over a flame 3–5 times for 3–4 seconds each time.
5. Pour 1% filtered carbolfuchsin to cover the entire slide.
6. Gently heat the slide with carbolfuchsin on it, until vapours rise. Do not boil.
7. Leave carbolfuchsin on the slide for at least 5 minutes.
8. Gently rinse the slide with tap water until all free carbolfuchsin stain is washed away. At this point, the smear on the slide looks red in colour.
9. Pour 3% acid-alcohol solution onto the slide.
10. Let the slide stand for 2–4 minutes.
11. Rinse gently with tap water. Tilt the slide to drain off the water.
12. A properly decolourised slide will appear light pink in color .If the slide is still red, reapply acid-alcohol for 1–3 minutes and rinse gently with tap water. Wipe the back of the slide clean with a swab dipped in acid-alcohol,
13. Pour 0.1% methylene blue onto the slide.
14. Leave methylene blue on the slide for 30 seconds.
15. Rinse gently with tap water.
16. Allow the slide to dry.
17. Examine the slide under the microscope using x40 lens to select the suitable area and then examine under x100 lens using a drop of immersion oil.
18. Record the results in the Laboratory Form and the Laboratory Register.
19. Store all positive and negative slides serially in the same slide-box until instructed by the supervisor.
20. Disinfect all contaminated material before discarding.

### Maintain an adequate supply of reagents and other materials

It is necessary to ensure availability of good quality laboratory reagents and consumable supplies for effective un-interrupted functioning of the laboratories.

Batch quality certification should be obtained for the purchased reagents and should be exhausted with in the expiry date. It is recommended that quality control testing slides (a set of at least ‘1+ positive’ and a good ‘negative’ unstained heat-fixed smears) should be used for each batch of new agents before they are used. It should be re-filtered by the laboratory technicians as and when required. Ensure that the binocular microscope is in good working condition and inspect and use the microscope.

The heads of the laboratories should determine monthly requirements of reagents and other materials.. The supervisors will make sure these supplies are distributed in a timely manner, usually on a monthly basis. The first in first out (FIFO) principle should also apply, hence the old supplies should be exhausted before starting to use the new ones. Old reagents should not be mixed with the new supplies. They should be kept in separate containers.

The following is a list of laboratory reagents, which should always be available in the laboratory:

* Carbolfuchsin (1%)
* Sulphuric acid (25%)
* Methylene blue (0.1%)
* Synthetic immersion oil
* Methylated spirit

The following is a list of other materials that should always be available in the laboratory:

* Glass slides for microscopy, and slide-boxes for storing slides
* Markers (for marking the slides) and marking pens or grease pencils (for marking the sputum containers)
* Wooden sticks (thick enough to make good smears)
* Transparent glass bottles for reagents (with self-adhesive labels stating date of preparation of reagents)
* Plastic tumblers/mugs
* Glass (or metal) rods (for holding slides during the staining process)
* Staining racks (for drying the slides)
* Sputum containers
* Spirit lamp or bunsen burner
* Lens paper (for wiping the oil immersion lens after examination of each slide)
* 5% phenol or 5% hypochlorite or bleaching powder / liquid bleach (for disinfection)
* Foot-operated bin (for disposal of contaminated materials)
* Timer (stop-watch)
* Laboratory Forms for Sputum Examination, Laboratory Register, “Referral for Treatment” Forms
* Filter Paper
* Fine Silk and Lint cloth

### Disposal of laboratory materials.

Sputum specimens examined in the laboratory are potentially infectious. Hence, after examination, they must be disinfected and destroyed so that the risk of infection is avoided. All disposable containers must be used only once.

Sputum cups which contain sputum can be disposed of by any one of the following methods:

* + - * **Disinfection:** After the sputum smears are examined, all sputum cups should be kept in a bucket containing 5% hypochlorite, or 10% bleach solution (freshly prepared), or 5% phenol solution. Caps of the sputum cups must be removed and the cups, caps and wooden sticks completely submerged in the solution in a secure place for at least 18 hours. After this, the solution, cups, caps and broom sticks can be discarded with other hospital waste. This bin/bucket should have a lid which is foot operated.
      * **Incineration:** Wherever incinerators exist, the type specified under Biomedical Waste Management & Handling Rules of the country, with combustion efficiency of 99%, it should be used. Sputum cups made of polypropylene should be used wherever available. (Note: If sputum cups are made of other varieties of plastic, they should be disinfected and destroyed as per the hospital waste management rules). Burning is not recommended.
      * **Autoclaving:** The sputum cups and lids, with the lids removed, along with wooden sticks can be autoclaved at the end of each day’s laboratory work. The autoclave cycle should have a holding time of 15 minutes at 121 °C HTAT (Holding time at temperature), 10 minutes at 126 °C HTAT or 3 minutes at 134 °C HTAT. The material can be discarded with other waste after proper cooling.

If none of the above is available, cotton and broom sticks can be disinfected and buried at a safe distance away from inhabited areas in a landfill site ensuring deep burial as specified by the infectious material disposal rules of the country.

Used slides should not be broken. They should be disposed through the hospital waste management system or in a secured pit for sharps in accordance to prevailing guidelines. Slides once used for sputum microscopy should not be reused.

1. TREATMENT OF TUBERCULOSIS

## The aims of TB treatment

The key to interrupting the spread of TB in the community is early detection and effective treatment of persons who are coughing up viable TB bacilli.

The National TB programme aims to provide timely and appropriate treatment for all forms of tuberculosis under standard case management conditions to cure the patient of active disease, prevent death from TB or its complications, decrease transmission of the disease to others, and to prevent the development of drug resistance. This requires that correct combination of anti-TB medications are prescribed and administered at the right doses for the correct duration.

## Essential anti-TB drugs

Anti-tuberculosis drugs have three main properties namely bactericidal, sterilizing activity and the ability to prevent resistance. For anti-TB treatment to be effective, a combination of these properties is required in a treatment regimen.

* Isoniazid and rifampicin are the most powerful bactericidal drugs, active against all populations of TB bacilli.
* Pyrazinamide and streptomycin are also bactericidal against certain populations of TB bacilli.
* Pyrazinamide is active in an acid environment against TB bacilli inside macrophages.
* Streptomycin is active against rapidly multiplying extra-cellular bacilli.
* Ethambutol is bacteriostatic and is effective in preventing development of resistance against other anti-TB drugs. The following are the recommended first line anti-TB drugs and the dose range.

### Fixed-Dose Combinations

Fixed-Dose Combination (FDC) tablets are tablets containing 2 or more anti-TB drugs combined in fixed doses. Their advantages and disadvantages compared to single formulation drugs are shown below.

### Advantages of FDCs compared to single formulation drugs

* Prescription errors are less likely or less frequent because dosage recommendations are more straightforward and adjustment of dosages according to patient weight is easier.
* The pill burden on the patient is smaller and may thus encourage patient adherence.
* If treatment is not supervised, the patient cannot be selective in the choice of drugs to ingest.

Table 4: Essential anti-TB drugs

|  |  |
| --- | --- |
| **Essential TB drugs** | **Recommended Daily Dose (Dose range in mg/kg)** |
| Isoniazid (H) | Adults :5 (4-6) |
| Children : 10 (10-15) |
| Rifampicin (R) | Adults:10 (8-12) |
|  | Children; 15 (10-20) |
| Pyrazinamide (Z) | 25 (20-30)  Children 35(30-40) |
| Streptomycin (S) | 15 (12-18) |
| Ethambutol (E) | Children: 20 (15-25) |
| Adults: 15 (15-20) |

## Standard TB Treatment Regimens for Adults and adolescents

Treatment of all forms of TB in Swaziland shall be based on the WHO-recommended treatment regimens for the respective case registration groups.

For the purpose of treatment, TB patients are grouped into two broad groups based on previous TB treatment history namely:

1. **New TB cases**(No history of prior treatment or received less than 1 month anti-TB treatment regardless of whether their smear or culture are positive or not)
2. **Previously treated TB cases**(with prior history of TB treatment lasting at least 1 month)
3. **MDR-TB Standardized regimen:** for treatment of all cases diagnosed with rifampicin, or both rifampicin and Isoniazid resistance using rapid molecular DST methods.

Standardised treatment regimens have been adopted for the first two groups of patients based on efficacy and feasibility, and the need to minimize prescription errors, reduce costs, enhance training of staff and improve drug estimation, purchasing, distribution and monitoring. The MDR-TB regimen is elaborated in the national MDR-TB management guidelines.

Treatment consists of two phases, an initial (or intensive) phase and a continuation phase.

The aim of the intensive phase in which 4-5 drugs are used is to ensure rapid killing of the bacilli, which could render an infectious patient non-infective within about 2 weeks period, convert most smear-positive patients to smear negative after 2 months of treatment.

The continuation phase, which usually consists of fewer drugs (2-3) is administered for a longer period in order to sterilise lesions and prevent relapse.

All medications in the Swaziland TB treatment regimens (in both intensive and continuation phases) are for **daily** administration.

The summary of the treatment regimens is as follows:

|  |  |  |  |
| --- | --- | --- | --- |
| **TB Registration** | **TB Patients** | **Treatment Regimens** | |
| **Intensive Phase**  **(daily)** | **Continuation Phase (daily)** |
| **New Cases** | * All new cases of TB, regardless of site, type or severity of disease | **2HRZE** | **4HR** |
| **Previously treated** | * 2HRZE (and then treat based on DST) |  | **4HR** |
|  | * Treatment failure | **Evaluate for MDR** |  |

**TB is curable, regardless of site of disease or HIV status.**

**This very important should always be communicated to patients.**

**DOTS and patient support should be strengthened at each visit**

Previously treated cases have a higher likelihood of harbouring drug-resistant TB. Sputum specimen should therefore be obtained from all previously treated patients for DST at or before initiation of TB treatment.

Fixed-Dose Combination (FDC) tablets are tablets containing 2 or more anti-TB drugs combined in a single tablet. FDCS have the advantage of easy of prescription and reduced pill burden, which may potentially enhance treatment adherence.

### Treatment of New tuberculosis cases – Adults and adolescents

All new TB cases (patients who have never been treated for TB in the past or who has taken anti-tuberculosis drugs for less than one month) should receive RHZE in the first 2 months initial phase; and RH in the 4 months of continuation phase.

TB treatment regimens have a standard code. Anti-TB drugs are abbreviated as shown below:

**2(RHZE) / 4(RH)**

The code indicates the following:

* both treatment phases (intensive and continuation) which are separated by a slash;
* the treatment duration in each phase in months denoted by the number preceding the bracket.
* anti-TB medications represented by the letters within the brackets
* brackets denoting that all drugs within it are in a fixed dose combination form.

The code includes both treatment phases, which are separated by a slash. A number is placed before a phase to indicate the duration of that phase in months. Letters enclosed in brackets indicate fixed-dose combinations.

Table 5: Recommended treatment regimen and anti-TB drug dosages for New TB cases

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Phase of treatment** | **Drugs** | **Weight in Kg** | | | |
| **30-39** | **40-54** | **55-70** | >70 |
| Intensive phase of 2 months | **(RHZE)\*** (150mg/75mg/400mg/275mg) | 2 | 3 | **4** | **5** |
|  | | | | | |
| Continuation phase of 4 months | (RH) (**150mg/75mg)** | **2** | **3** | **4** | **5** |

**\*Fixed-dose combination (FDC) drugs**

**Note:** It is important to note that the duration of treatment for TB Meningitis, Miliary TB, and TB of the Bones and Joints is **9 months**, whilst all other forms of TB are treated for a period of 6 months for new cases. In the context of HIV (HIV/TB – co-infection), CNS TB should be treated for 9 – 12 months.

### Treatment of previously treated cases

Previously treated TB cases should have DST at or before initiation of treatment and where available rapid DST with LPA or GeneXpert is recommended. The rapid DST test for at least rifampicin resistance as a proxy to MDR-TB using the Xpert, or for both rifampicin and isoniazid using the LPA should be requested immediately.

The patient’s treatment regimen should be determined by the results of rapid DST tests.

Conventional DST using the MGIT should immediately be requested for all patients diagnosed using the Xpert MTB/Rif and LPA at the start of treatment, and the regimen should be modified based on the full DST result(Refer to algorithms page??).

**Note: obtaining specimen for conventional DST should not delay initiation of treatment and ALL relapse patients should be initiated on 2HREZ. Previously treated patients returning after failure should be referred for empirical MDR-TB treatment as DST results are awaited.**

Patients whose treatment has failed or grouped under the Óther’group may have high likelihood of MDR-TB, and should be started on empiric MDR-TB treatment according to the National MDR-TB management guidelines.

Previously treated patients with evidence of resistance against Streptomycin but not having MDR-TB should be treated with 3RHZE / 5RHE

Table 6: Recommended treatment regimen and dosages for relapse and return after interruption cases

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Phase of treatment** | **Drugs** | **Weight in Kg** | | | |
| **30-39** | **40-54** | **55-70** | >70 |
| Intensive phase of 2 months | **(RHZE)** (150mg/75mg/400mg/275mg) | 2 | 3 | 4 | **5** |
| **S** (vial 1g) | 0.5 | 0.75 | 1 | **1** |
| Intensive phase of 1 months | **(RHZE)** (150mg/75mg/400mg/275mg) | 2 | 3 | 4 | **5** |
| Continuation phase of 5 months | (RHE)**(150mg/75mg/400mg)** | **2** | **3** | **4** | **5** |

**\* Streptomycin** should **NOT** be given during pregnancy and to those over 65 years.

### Treatment of extra-pulmonary tuberculosis

Pulmonary and extra-pulmonary disease should be treated with the same regimens. However, this guideline recommends 9–12 months of treatment for TB meningitis and other serious forms of EPTB given the serious risk of disability and mortality, and 9 months of treatment for TB of bones or joints because of the difficulties of assessing treatment response.

Provider-initiated HIV testing is recommended as part of the evaluation of all TB patients and patients in whom the disease is suspected. HIV testing is especially important in persons with or suspected of having EPTB because of the increased frequency of extra-pulmonary involvement in persons with immunosuppression. Extra-pulmonary TB is considered to be WHO clinical stage 4 HIV disease.

Unless drug resistance is suspected, adjuvant corticosteroid treatment is recommended for TB meningitis and pericarditis. Surgical intervention may be required in diagnosis of some EPTB, but mainly indicated in the 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 is beneficial.

### Important drug to drug interactions

Many TB patients have concomitant illnesses. At the start of TB treatment, all patients should be asked about medicines they are currently taking.

The most important interactions with anti-TB drugs are due to rifampicin. Rifampicin induces pathways that metabolize other drugs, thereby reducing the concentration and effect of those drugs. To maintain a therapeutic effect, dosages of the other drug(s) may need to be increased. When rifampicin is discontinued, its metabolism-inducing effect resolves within about 2 weeks.

Rifampicin substantially reduces the concentration and effect of the following drugs:

* **anti-infectives**(including certain antiretroviral drugs), mefloquine, azole antifungal agents, clarithromycin, erythromycin, doxycycline, atovaquone, chloramphenicol);
* **hormone therapy,** including ethinylestradiol, norethindrone, tamoxifen, levothyroxine (Rifampicin interacts with oral contraceptive medications leading to lowered protective efficacy. A woman receiving oral contraception may choose between two options while receiving treatment with rifampicin: following consultation with a clinician, an oral contraceptive pill containing a higher estrogen dose (50 μg), or another form of contraception); methadone; warfarin; cyclosporin; corticosteroids; anticonvulsants (including phenytoin);
* **cardiovascular agents** including digoxin (among patients with renal insufficiency), digitoxin, verapamil, nifedipine, diltiazem, propranolol, metoprorol, enalapril, losartan, quinidine, mexiletine, tocainide, propafenone; theophylline; sulfonylurea hypoglycaemics; hypolipidaemics including simvastatin and fluvastatin; nortriptyline, haloperidol, quetiapine, benzodiazepines (including diazepam, triazolam), zolpidem, buspirone.

### TB Treatment regimens in special circumstances

#### Treatment for pregnant women

The benefit of treating an active TB disease in a pregnant woman far outweighs and the risks that the drugs may pose to both the mother and the foetus. Most TB drugs are safe for use in pregnant women withthe exception of**streptomycin** which is ototoxic to the foetus and should therefore not be used in pregnancy.Every woman of child bearing age diagnosed with TB shouldbe asked of pregnancy status before starting TB treatment.

#### Treatment for breastfeeding women

A woman who is breastfeeding and has TB should receive a full course of TB treatment. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to the baby. ***All the TB drugs are compatible with breastfeeding and a woman taking them can safely continue to breastfeed her baby***. The mother and baby should stay together and the baby should continue to breastfeed in the normal way, but be given prophylactic isoniazid for at least six months (Isoniazid 5mg/ kg). BCG vaccination of the newborn should be postponed until the end of isoniazid prophylaxis.

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

#### Treatment for women taking the oral contraceptive pill

Rifampicin interacts with the contraceptive pill with a risk of decreased protective efficacy against pregnancy. A woman who is receiving contraception may choose between the following two options while receiving treatment with rifampicin. Following consultation with a physician, she could take an oral contraceptive pill containing a higher dose of oestrogen*(50* mcg), alternatively she could use another form of contraception.

#### Treatment for patients with liver disorders

Isoniazid, rifampicin and pyrazinamide are all associated with hepatitis. Of the three, rifampicin is least likely to cause hepatocellular damage, although the drug is associated with cholestatic jaundice, pyrazinamide is the most hepatotoxic. The patients with the following conditions can receive the usual short-course chemotherapy regimen provided that there is no clinical evidence of chronic liver disease: hepatitis virus carriage, a past history of acute hepatitis, excessive alcohol consumption. However, hepatotoxic reactions to TB drugs may be more common in these patients and should be anticipated.

Possible regimens include:

1. Two hepatotoxic drugs (rather than the three in the standard regimen):

* 9 months of isoniazid and rifampicin, plus ethambutol (until or unless isoniazid susceptibility is documented);
* 2 months of isoniazid, rifampicin, streptomycin and ethambutol, followed by 6 months of isoniazid and rifampicin;
* 6–9 months of rifampicin, pyrazinamide and ethambutol.

1. One hepatotoxic drug:
   * 2 months of isoniazid, ethambutol and streptomycin, followed by 10 months of isoniazid and ethambutol.
2. No hepatotoxic drugs:
   * 18–24 months of streptomycin, ethambutol and a fluoroquinolone.

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.

#### Treatment of patients with renal failure

Isoniazid, rifampicin and pyrazinamide are either eliminated almost entirely by biliary excretion or metabolized into non-toxic compounds. These drugs can, therefore, be given in normal dosage to patients with renal failure. In severe renal failure, patients should receive pyridoxine with isoniazid in order to prevent peripheral neuropathy. Streptomycin and ethambutol are excreted by the kidney. Where facilities are available to monitor renal function closely it may be possible to give streptomycin and ethambutol in reduced doses. The safest regimen to be administered in patients with renal failure is 2 HRZ/ 4 HR. All patients that fall under the category “special circumstances” should be referred to and managed by to a specialist.

## The Role of Adjuvant Steroid Treatment

Adjuvant steroid treatment is steroid treatment given in addition to anti-TB drug treatment. Studies in the pre-HIV era confirmed the benefit of steroids for TB meningitis and pleural and pericardial TB. Steroids arealso of benefit in HIV-positive patients with pericardial TB.

**Adjuvant steroid therapy is recommended in the following conditions:**

* TB meningitis (decreased consciousness, neurological defects, or spinal block).
* TB pericarditis (with effusion or constriction).
* TB pleural effusion (when large with severe symptoms).
* Hypoadrenalism (TB of adrenal glands).
* TB laryngitis (with life-threatening airway obstruction).
* Severe hypersensitivity reactions to anti-TB drugs.
* Renal tract TB (to prevent ureteric scarring).
* Massive lymph node enlargement with pressure effects.

Rifampicin being a potent inducer of hepatic enzymes that metabolize steroids,the effective dose of prednisolone is half the prescribed treatment dose given to the patient. The suggested treatment doses of prednisolone depending on the condition is as follows:

Table 7: Prednisolone indication and recommended doses in TB management

|  |  |
| --- | --- |
| **Indication** | **Prednisolone treatment**  **(dose for children in brackets)** |
| **TB meningitis** | 60 mg (1–2 mg/kg) daily for weeks 1–4,  then decrease over several weeks |
| **TB pericarditis** | 60 mg (1–2 mg/kg) daily for weeks 1–4  30 mg (0.5–1 mg/kg) daily for weeks 5–8, then  decrease over several weeks |
| **TB pleural effusion** | 30 mg (0.5–1 mg/kg) daily for 1–2 weeks |

Steroids are immunosuppressants. Steroids may further depress immunity and increase risk of opportunistic infections in HIV-positive patients. However, on balance, TB/HIV patients are still likely to benefit from the use of steroids in the presence of the above conditions.

1. PATIENT SUPPORT AND DOT PROVISION

## Importance of patient support

The public health priority for TB control is to cure the patients and ultimately interrupt transmission of the disease within communities. A patient-centred approach to Directly observed therapy (DOT), and measures to prevent interruption of treatment that are important to support patients on treatment are critical to ensure adherence to the prescribed anti-TB treatment regimen.

Adherence to TB treatment is crucial to achieving cure while avoiding the emergence of drug resistance. Regular and complete intake of medications gives the individual TB patients the best chance of being cured; and results in the reduction of spread of TB within the community.

The emergence and spread of MDR- and XDR-TB further reinforces the absolute necessity of supporting TB patients to not miss any drug doses. Standardized treatment including patient support remains a critical core element of high quality DOTS enhancement in the Stop TB Strategy to achieve the treatment success target of 85%.

In addition to supervised treatment (or DOTS), measures to support patient adherence to regular and complete treatment include:

* A regular supply of drugs
* Accessible, high-quality, continuous ambulatory TB cares
* Positive action to remove barriers to treatment and care
* Availability of hospitalization

Hospitalization is essential for severely ill patients and for those with complications or associated conditions requiring closer clinical monitoring

## Community Based DOTS (CB DOTS)

Patients should be able choose to come to the health facility for their daily DOT or they can take their treatment at home with a treatment supporter of their own choice (community-based DOTS). The supporter needs to collect the drugs at monthly intervals from the health facility, to ensure that the patient takes the drugs as prescribed and to keep record of the daily intake of drugs.

### Identification of treatment supporter

The first step is to assist the patient in identifying a treatment supporter that is acceptable to him or her. For TB patients who live close to a health facility, the treatment supporter will be one of the staff in the health facility, and this is the ideal choice if convenient to the patient. For TB patients who live in a distant location from a health facility, the treatment observer could be a community health worker or a trained and supervised local community member. ART community care providers can observe TB treatment. The treatment observers should receive training according to the NTCP protocols.

The treatment supporter should:

* Remind and watch the patient take their drugs everyday
* Mark the Identity card after the drugs are taken
* Collect the drugs every week from the health facility
* Inform the health worker of any problems encountered
* Accompany the patient to the health facility when needed

### Orient the supporter

* Carefully explain the tasks above to the supporter.
* Check that the supporter can carry out the tasks.
* Demonstrate how to provide DOT and how to mark the drug intake.
* Explain possible side-effect and what needs to be done.
* Make sure that the supporter fully understand the tasks.

### Provide enough drugs to last until the next visit.

* Cut up the blister pack to prepare daily blister strips, which contain the exact number of tablets that a patient needs to take each day.
* Explain how many tablets the patient should take each day.
* Agree on the date of the next visit and note this on the Identity and treatment cards.
* Ask patients to bring back the empty blister packs and Identity card during each visit to the health facility.
* Draw a horizontal line in the TB treatment card to cover the number of days drugs have been supplied

### Keep regular contact with the patient and supporter

* Ask the supporter and patient to return every week to collect more drugs in the intensive phase and every two weeks in the continuation phase.

##### What to do during the visit of the supporter / patient to health facility?

* Take the time to talk to the supporter and patient on each visit.
* Help them to resolve any problems that they have encountered
* Check the daily treatment record when re-supplying drugs.
* Check that the TB Identity card record corresponds to the empty blister packs.
* Discuss any problems in filling out the treatment record.
* Check and put “X” on the horizontal line of the TB treatment card where patient did not swallow the drugs
* Provide the supporter with enough drugs until the next scheduled visit

## Prevention of treatment interruption

Promoting adherence through a patient-centred approach is probably more effective in preventing treatment interruption than devoting resources to tracing patients who default.

Whenever the patient visits the health facility, the need for regular and complete intake of treatment should be reinforced and any problems that may cause interruption should be identified.

At registration, sufficient time should be set aside for meeting with the patient (and preferably also the patient’s family members or a designated treatment supporter). This initial meeting provides an important opportunity to inform the patient about the duration of treatment. During the meeting, it is vital to record the patient’s address and other relevant addresses (e.g. partner or spouse, parents, place of work or study, or private doctor who may be consulted) as well as explain the need to consult ahead of time in case of a change of address. This maximizes the likelihood of locating patients who interrupt treatment. Recording mobile telephone numbers for the patient and family has proved valuable in many settings.

### Role of Adherence Officers

The Adherence Officers have a special role in providing support in ensuring continuation of treatment for all patients who happen to interrupt treatment. In such situation, the Clinic staff or treatment supporter should liaise with the Adherence Officer in order to trace the patient and encourage him/her to resume treatment.

## Nutritional support to TB patients

Although conclusive evidence that nutritional support reduces mortality is lacking, it is known to speed client’s recovery of health after initiating ART and or TB treatment and to improve the nutritional health of the client.

### Food by prescription

This is a joint initiative of the NTCP, the Swaziland Nutritional Council, WFP, WHO and other partners to provide food by prescription to TB clients.

The food by prescription programme was necessitated by the nutritional challenges resulting from the high HIV and TB prevalence. It seeks to improve treatment adherence, contribute to meeting the body’s increased demand for nutrients and compensate for the deleterious effects of diseases and medication on nutrient absorption.

The overall objectives of the food by nutrition includes:

* Increase adherence to treatment of malnourished members of the target populations.
* Improve the nutritional status of malnourished members of the target populations and their families.

Malnourished individuals will be identified based on assessment of their body mass index (MBI), mid upper arm circumference (MUAC), and weight measures, using internationally accepted baseline measurements.

* The beneficiary TB patients should be:
* Acutely malnourished adults on ART and or TB patients
* Adults on ART and TB treatment
  + BMI> 18.5 and MUAC > 23cm for two consecutive monthly visits
  + Weight must also be stable or increasing for two consecutive visits.

**NOTE: Acutely malnourished children should be referred to the nearest IMAM site**

Admission criteria for food by prescription vary based on the treatment programme which refers the client, according to:

Admission criteria:

* Adults on ART and or TB Treatment:
  + BMI≤ 18.5 or
  + MUAC≤ 23cm or
  + Loss of weight/BMI of ≥ 10% in the previous month.

The criteria used for admission is due to the fact that BMI and MUAC do not identify a 100% congruent set of clients as malnourished. It could easily happen that a client is malnourished according to one criterion but not according to another.

All clients who come to participating health facilities will be screened for malnutrition according to the standard procedure (See below).

If found to be malnourished, they will be eligible to receive the services described in stage three and four below.

### Food Prescription Initiation procedure

**Stage 1: screen**

1. During the physical examination, the appropriate person (nurse or expert client, depending on procedure at the facility) should measure the client’s weight, height and MUAC. This person should also find the client’s BMI chart.If the client is an adult ART client, adult TB client or adult Maternal and Child Health Nutrition client, the clinician should admit them if any or all of the following three conditions apply
2. Their BMI is less than or equal to 18.5
3. Their MUAC is less than or equal to 23
4. They have lost 10% or more of their weight (or BMI) in the previous month.
5. If the client meets any of the malnutrition criteria above, proceed to stage 2.

**Step 2: Admit**

1. The examining clinician should fill in the client card carefully and give it to the client.

**Stage 3: provide nutritional treatment**

1. Each client should also be registered in the registration book in the food room. This is important because it enables the client’s admission and exit status to be tracked, and allows for home visits by the food by prescription organizations. **The client must sign against the NUMBER OF KILOGRAMS received**. It is not sufficient to say simply “one family ration” or “one individual ration”

**Stage 4: health education and follow up**

1. Be sure the client understands the roles of the foods they are receiving (the individual ration is their medicine, and the family ration is the food security of their family), the goal of the programme, and the reasons for admission. Provide the client with an information pamphlet about the programme for them to take home. Inform the local treatment supporters of the client’s enrolment and ask them to follow up. This should be encouraged most strongly if the client is malnourished.

**Stage 5: Make next appointment**

1. Before the client returns home, the next appointment should be emphasized (the same date as the next monthly ART and or TB review). The importance of adherence should be stressed, and clients who are admitted should receive a note in their files as well. This note will guard against the danger of clients losing the card and against the possibility that the client may forget to take their food.
2. **Discharge procedures:**

The procedure for discharging a client as cured starts in the month before the actual discharge. If the client’s anthropometrics are above the programme admission criteria for the first month, they should be informed that their condition has improved significantly. The client should receive food for this month, but must be informed that after the next month, food supplementation will cease.

**Lost to follow up:**

A client who has missed two consecutive monthly visits is considered in default. The following procedure should be used if a Food by prescription client defaults:

1. Standard procedure for follow up from community health workers should be followed, according to the procedure of the unit initiating the client. If the client cannot be found or refuses to return after counseling, proceed to step 2.
2. Any client who is declared Lost to follow up under the criteria of the unit referring them to Food by prescription should also be discharged from Food by description. “Lost to follow up” entry for the client should be recorded in the “discharge status” field of the registration book entry for the client.
3. If a client is discharged as a defaulter returns to the health facility in the future and is eligible to be initiated on food by prescription again, he/she may rejoin the programme.

**Death:**

If a client passes on while enrolled on the programme, the client should be removed from the register of beneficiaries on account of death.

1. MONITORING TUBERCULOSIS TREATMENT

## Basis for monitoring TB treatment

Monitoring patient’s clinical as well as bacteriological response to anti-TB therapy is an essential element of TB treatment and care. Regular monitoring of patients also facilitates treatment completion and allows the identification and management of adverse drug reactions.

All patients on anti-tuberculosis treatment should be monitored systematically throughout the duration of treatment. Patients, their treatment supporters and health workers should be instructed to report the persistence or reappearance of symptoms of TB (including weight loss), symptoms of adverse drug reactions, or treatment interruptions.

### Clinical monitoring:

Monitoring the improvement in the patients’ clinical state provides a guide to treatment response. During regular follow up visits, clinical assessment in the form of focused history and physical examination should be conducted and the results documented in the patient’s treatment card.

Smear-negative pulmonary TB patients or those enrolled without sputum whose sputum smears are negative at 56th dose need no further sputum monitoring. They should be monitored clinically; and their body weight should be taken and recorded monthly.

Evidence of clinical improvement includes reduction or disappearance of symptoms including cough, fever, tiredness and weight gain. A sudden unexplained drop in the patient’s weight should be investigated by the clinician.

#### Monitoring Extra-pulmonary TB treatment

Response to treatment is usually monitored clinically and depending on the organ affected, radiology may play an important role. As in pulmonary smear-negative disease, the weight of the patient is also a useful indicator in monitoring clinical response in extra-pulmonary disease.

### Bacteriological monitoring:

Patients with sputum smear-positive PTB or positive Xpert MTB/Rif tests should be monitored by sputum smear examination. These are usually adults and sometimes older children.

Xpert MTB/Rif test should not be requested for the purpose of monitoring patients on treatment.

Routine monitoring of treatment response by CXR is also not recommended.

Serial sputum smear examinations should be performed at the recommended intervals to verify the effectiveness of the treatment in killing the bacilli.

One sputum sample should be obtained from the patient for examination at the end of the second and fifth month and at the end of treatment for all sputum smear positive TB patients. The sample should be collected as ‘**spot or early morning samples’.**

* Sputum specimens should be collected without interrupting treatment and transported to the laboratory as soon as possible thereafter;
* In the event of an unavoidable delay, specimens should be refrigerated or kept in as cool a place as possible.

Table 8: Recommended Schedule for follow up sputum examinations for PTB patients

|  |  |  |
| --- | --- | --- |
| **When to monitor** | **Regimen for New TB cases**  **6-month treatment regimen** | **Regimen for Previously treated Casess** |
| **At time of diagnosis** | sputum smear microscopy or  Xpert MTB/Rif test | **sputum smear microscopy or**  **Xpert MTB/Rif test** |
| **At end of initial phase** | sputum smear (end month 2) | **sputum smear (end month 3)** |
| **In continuation phase** | sputum smear  (end month 5) | **sputum smear**  **(end month 5)** |
| **During last month of treatment** | **sputum smear**  **(end month 6)** | **sputum smear**  **(end month 8)** |

#### New sputum smear-positive pulmonary TB patients

Follow up sputum smears should be performed at the end of the second and fifth months, and in the last month of treatment.

* If the sputum smear result is positive at the end of the second (2nd) month, a DST should be performed immediately, and treatment should be modified based on the results. A rapid DST method e.g the LPA should be used.
* If the sputum smear result is still positive at the end of the fifth (5th) month, this constitutes treatment failure. The treatment should be discontinued, and the patient’s sputum sample should be obtained for culture and drug susceptibility testing. A rapid DST method e.g the LPA should be used.

#### Previously treated pulmonary sputum smear-positive patients

Sputum smear examination is performed at the end of the initial phase of treatment (at the end of the third month), at the end of the fifth month; and at the end of treatment.

If the patient is sputum smear-positive at the end of the third month, the initial phase of treatment with 4 drugs, DST should be performed immediately, and treatment should be modified based on the results. A rapid DST method e.g the LPA should be used.

Positive smears at the end of the fifth (5th) month indicate failure of treatment and, the patient should have their sputum examined by culture and DST. Treatment should be guided by the results of DST.

#### New sputum smear-negative pulmonary TB patients

Sputum smear-negative patients should be monitored clinically; body weight is a useful progress indicator.

Sputum smears should be checked at the end of the second month in case of the following possibilities:

* disease progress due to non-adherence to treatment, or
* an error at the time of initial diagnosis (i.e. a true smear-positive patient misdiagnosed as smear-negative) plus
* drug resistance.

A patient initially diagnosed as sputum smear-negative and becoming positive at the second month should be investigated for MDR-TB using the rapid DST methods Xpert MTB/Rif and LPA. A full conventional DST should also be requested.

* In case of any MDR result, the treatment is declared “failure” and the patient is referred to DR unit.
* In case of any positive smear result during the treatment, follow the steps described in the box above.

Table 9: Sputum follow-up algorithm for patients on anti-TB treatment

Pulmonary TB patient

Positive

**(+)**

**(-)**

Continue treatment till end of 6 months

**(-)**

* Continue treatment
* Collect sputum at end of 5 months

**(+)**

* Declare treatment failed
* Collect sputum for culture/DST

**(-)**

* Continue treatment
* Collect sputum at end of 6 months

**(-)**

**(+)**

* Declare treatment failed
* Collect sputum for culture/DST

Negative

* Send sample to LPA or Gene-Xpert
* Start 2HREZ/4HR
* Collect sputum at end of 2 months
* Start 2HREZ/4HR
* Collect sputum at end of 2 months
* Collect sputum for culture/DST
* Continue the treatment of RHEZ for one month then continue with ?3RH or as directed by DST results

Declare cured

## Management of treatment interruption

When a patient misses an arranged appointment to receive treatment, such a patient should be contacted immediately to ensure that the treatment can be continued.

The NTCP adherence officer should ensure that the patient is contacted within a day after missing treatment during the initial phase, and within a week during the continuation phase.

The patient can be traced using the locating information previously obtained. It is important to find out the cause of the patient’s absence so that appropriate action can be taken and treatment can continue. The management of patients who have interrupted treatment takes into consideration several factors, such as the time at which the treatment was interrupted, the length of treatment interruption, the smear and LPA/Gene Xpert status after return, as shown in Table 26.

Culture and DST should be performed upon return of patients who interrupted treatment for more than 2 consecutive weeks.

A simple decision matrix is suggested in Table below:

Table 10: Management of TB treatment interruption

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Length of treatment** | **Length of**  **interruption** | **Sputum status upon return** | **Actions to be taken** | | |
| **Treatment**  **outcome** | **DST** | **Registration and further**  **treatment** |
| < 1  month | <2 weeks |  |  |  | Continue treatment started at the point it was stopped |
| 2-7 weeks |  |  |  | * Restart treatment without new registration |
| > 7 weeks |  | Defaulter | Perform (GeneXpert or LPA)  **AND** culture/DST by MGIT | * If no resistance, register again as new case of TB and start Cat I |
| > 1  months | <2 weeks |  |  |  | * Continue treatment started at the point it was stopped |
| 2-7 weeks | (-) |  |  | * Continue treatment started, at the point it was stopped |
| (+) |  | Perform (GeneXpert or LPA)  **AND**  culture/DST by MGIT | * If no resistance, continue treatment started |
| > 7 weeks |  | Defaulter | * If no resistance, register again as Treatment after defaulter and start treatment for cases previously treated with FLD |

* In any case of drug resistance detected by LPA or Gene-Xpert, refer the patient to DR treatment unit.

### Monitoring of TB Patients for Adverse Effects of Anti-TB Drugs

Most TB patients complete their treatment without any significant adverse effects of drugs. However, a few patients do experience adverse effects. It is therefore important that patients be clinically monitored during treatment so that adverse effects can be detected promptly and managed properly. Routine laboratory monitoring is not necessary.

Health personnel can monitor adverse effects of drugs by teaching patients how to recognize symptoms of common adverse effects and to report if they develop such symptoms, and by asking about symptoms when patients report to collect drugs or on follow-up visit.

#### Prevention of adverse effects of drugs

Health personnel can prevent some drug-induced side-effects, for example Isoniazid-induced peripheral neuropathy. This usually presents as a numbness, tingling or burning sensation of the feet and occurs more commonly in pregnant women and in people with the following conditions: HIV infection, alcoholabuse, malnutrition, diabetes, chronic liver disease. These patients should receive preventive treatment with pyridoxine, 10 mg daily, along with their anti-tuberculosis drugs.

#### Adverse effects of anti-tuberculosis drugs

Adverse effects associated with anti-TB are classified as minor or major. In general, a patient who develops minor adverse effects should continue the TB treatment, sometimes at a reduced dose. The patient also receives symptomatic treatment. If a patient develops a major side-effect, the treatment or the offending drug is stopped. Further management depends on the nature of the adverse reaction. Patients with major adverse reactions should be managed in a hospital. Table below provides a symptom-based approach to the management of adverse effects.

#### Symptom-based approach to management of drug side-effects

Table 11: Guide to Management of side effects of first-line anti-TB drugs



Note that first line drugs cannot be substituted with any secondline drug or any other in the event of adverse reaction management.

*When to stop anti-TB drugs*

|  |  |
| --- | --- |
| **Reaction** | **Drug Responsible** |
| **Hearing loss or disturbed balance** | Streptomycin |
| **Visual disturbance (poor vision and colour perception)** | Ethambutol |
| **Renal failure, shock, or thrombocytopenia** | Rifampicin |
| **Hepatitis** | Pyrazinamide |

#### Management of skin itching and rash

In case of skin itching, it is necessary to determine if the reaction was present before initiation of anti-TB treatment, as many HIV-positive patients have itchy skin lesions as a result of HIV infection.

Other causes of itching should also be excluded, give antihistamines, continue anti-TB treatment and observe closely. In the event that rash develops, anti-TB drugs should be stopped until the rash resolves. In case of severe reaction, supportive treatment should be provided as appropriate.

#### Reintroduction of anti-TB drugs following drug reaction

Drug challenge should be done to identify the drug responsible for the reaction. The process should start with the anti-TB drug least likely to be responsible for the reaction (i.e.isoniazid). The initial challenge should start with a small dose of the drug. If a reaction occurs to a small challenge dose, it will not be such a severe reaction as to a full dose. Gradually increase the dose over 3 days. Repeat the procedure, adding in one drug at a time. A reaction after a particular drug is added identifies that drug as the one responsible for the reaction.

Table 12: Guide to performing anti-TB drug challenge and re-introduction

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Likelihood of causing a reaction** | Challenge doses | | |
| Drug |  | **Day 1** | **Day 2** | **Day 3** |
| **Isoniazid** | Least likely | 50 mg | 300 mg | 300 mg |
| **Rifampicin** |  | 75 mg | 300 mg | Full dose |
| **Pyrazinamide** |  | 250 mg | 1 gr | Full dose |
| **Ethambutol** |  | 100 mg | 500 mg | Full dose |
| **Streptomycin** | Most likely | 125 mg | 500 mg | Full dose |

If the drug responsible for the reaction is pyrazinamide, ethambutol, orstreptomycin, resume anti-TB treatment without the offending drug. If possible, replace it with another drug. It may be necessary to extend the treatment regimen. Consider the start of the resumed regimen as a new start of treatment. This prolongs the total time of TB treatment, but decreases the risk of recurrence.

## Determining TB Treatment Outcomes

. The table below (Table 7.3) shows the definitions of standardized treatment outcomes.

Table 13: Definitions of TB treatment outcomes

|  |  |
| --- | --- |
| **Outcome** | **Definition a** |
| **Cure** | A patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear- or culture-negative in the last month of treatment and on at least one previous occasion. |
| **Treatment completed** | A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and in at least one previous occasion b |
| **Treatment failure** | * A patient whose sputum smear or culture is positive at 5 months or later during treatment. * Patients found to harbour a multidrug-resistant (MDR) strain at any time during the treatment, whether they are smear-negative or –positive. * Smear negative or extra-pulmonary patients with clinical condition not improving or worsening (clinically judged) |
| **Died** | A patient who dies for any reason during the course of treatment |
| **Default** | A patient whose treatment was interrupted for 2 consecutive months or more |
| **Transfer out** | A patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown |
| **Treatment success c** | Sum of cured and completed treatment |
| (a) These definitions apply to pulmonary smear-positive and smear-negative patients, and to patients with extra-pulmonary disease.  (b) The sputum examination may not have been done or the results may not be available  (c) For smear or culture positive patients only | |

1. MANAGEMENT OF CHILDHOOD TUBERCULOSIS

## Importance of childhood TB

Childhood TB accounts for almost 15-20% of all TB cases. It represents active TB transmission in the community, mainly from adult sources. Usually children become infected with TB after household exposure to a sputum positive adult or adolescent, although smear negative cases can also transmit TB. Children (especially <10 years of age) rarely develop lung cavities and they are therefore less likely to transmit the TB organism. However, the absence of a potential source case does not exclude childhood TB especially in a high prevalence setting like Swaziland as infections may occur outside the household. This, usually coupled with inadequate capacity for effective paediatric TB diagnosis, often results in under-detection and treatment of childhood TB, leading to high morbidity and mortality.

These guidelines outlines:

* the approach to diagnosis of paediatric TB
* TB treatment of childhood TB
* diagnosis and treatment of resistant TB in children

## Approach to diagnosis of TB in children

Diagnosis of active TB disease in children is often difficult, and should be made based on careful and thorough assessment of all the findings from a careful history, clinical examination and relevant investigations, e.g. TST, chest X-ray (CXR) and sputum smear microscopy. As most children with TB have pulmonary TB, bacteriological, confirmation of TB should be sought whenever possible, e.g. by sputum microscopy for children with suspected pulmonary TB who are old enough to produce a sputum sample.

The decision to treat a child should preferably be made by a Medical Officer after careful consideration; and once such a decision is made, the child should be treated with a full course of therapy. Diagnosis can be done at any level of care, even when X-Rays are not available.

However, a trial of treatment with anti-TB medications is not recommended as a method to diagnose TB in children.

**Clinical symptoms and a positive TB contact can be enough to start TB treatment.**

The key risk factors for TB include:

* household contact with a newly diagnosed smear-positive case
* age less than 5 years
* HIV infection
* severe malnutrition.

The key features suggestive of TB are:

* chronic symptoms suggestive of TB
* physical signs highly of suggestive of TB
* a positive tuberculin skin test
* chest X-ray suggestive of TB.

The approach to diagnose TB in children follows the usual standard protocol in clinical practice. This includes:

* Careful history (including history of TB contact and symptoms consistent with TB)
* Clinical examination (including growth assessment)
* Tuberculin skin testing
* Bacteriological confirmation whenever possible
* Investigations relevant for suspected pulmonary TB and suspected extra-pulmonary TB
* HIV testing (in high HIV prevalence areas)

**Note:** In most immune-competent children, TB presents with symptoms of a chronic disease after they have been in contact with an infectious source case. TST can be used to demonstrate infection with *M. tuberculosis* in most cases. The presentation in infants may be more acute, resembling acute severe pneumonia and should be suspected when there is a poor response to antibiotics. In such situations, there is often an identifiable source case, usually the mother.

### Evaluation for paediatric TB disease

The clinician should ensure that careful history is taken including history of TB contact and symptoms consistent with TB.

***a. Contact***

This refers to a child living in the same household as or in frequent contact with a source case

(e.g. the child’s caregiver) with sputum smear-positive pulmonary TB or sputum

smear-negative but culture-positive TB.

The following actions concerning contact are of importance for diagnosing TB in children.

* All children aged 0–4 years and children aged 5 years and above who are symptomatic, who have been in close contact with a smear-positive TB case, must be screened for TB.
* Effort should be made to detect the source case (usually an adult with sputum smear-positive pulmonary TB) and any other undiagnosed cases in the household when any child (aged less than 15 years) is diagnosed with TB.
* If a child presents with infectious TB, child contacts must be sought and screened, as for any smear-positive source case. Children should be regarded as infectious if they have sputum smear-positive pulmonary TB or cavitary TB on CXR.

All children with a negative screening for PTB should receive IPT for 6 months if:

* They are under 5 years old, irrespective of their HIV status, when there is a documented exposure to PTB. For every new TB contact, IPT should be repeated.
* They are HIV positive and more than 1 year old, even if there is no contact (if no prophylaxis in the previous 2 years).
* Newborn babies born to a mother with tuberculosis in pregnancy. Vertical transmission of TB (Congenital TB) can happen, especially if the mother is diagnosed in the last 3 months of pregnancy and is sputum smear-positive. In these cases, if *there are no TB symptoms in the newborn*, INH prophylaxis for 6 months is recommended for the newborn. These children should withhold BCG vaccination until completion of IPT.

***b. Symptomatic children***

Children with symptomatic TB often have already developed chronic disease. The commonest symptoms to be considered are as follows:

Clinical symptoms:

* Persistent and unremitting cough (with or without previous antibiotic treatments).
* Weight loss or failure to thrive (absence of appropriate weight gain for infants). Malnutrition can be the first sign of TB in children, especially if there is poor response after 1 week of nutritional support.
* Persistent fever
* Drenching night sweats
* Fatigue, reduced playfulness, decreased activity.
* Enlarged liver and spleen (disseminated TB).
* Enlarged LN.

A child should start TB treatment when there are TB symptoms not responding to adequate antibiotic therapy, even in the absence of a CXR. This is especially important in infants and young children, as symptoms are less specific and the mortality is higher.

### Clinical examination (including growth assessment)

There are no specific features on clinical examination that are typical of TB in children or can confirm that the presenting illness is due to pulmonary TB. Some signs, although uncommon, are highly suggestive of extra-pulmonary TB (i.e. TB of organs other than the lungs). Other signs are common and should prompt an investigation into the possibility of childhood TB. Important physical signs are:

*a. physical signs highly suggestive of extra-pulmonary TB:*

* gibbus, especially of recent onset (resulting from vertebral TB)
* non-painful enlarged cervical lymphadenopathy with fistula formation;

*b. physical signs requiring investigation to exclude extra-pulmonary TB:*

* meningitis not responding to antibiotic treatment, with a sub-acute onset or raised intracranial pressure
* pleural effusion
* pericardial effusion
* distended abdomen with ascites
* non-painful enlarged lymph nodes without fistula formation
* non-painful enlarged joint
* signs of tuberculin hypersensitivity (e.g. phlyctenular conjunctivitis, erythema nodosum).

**Note:** Documented weight loss or failure to gain weight, especially after being treated in a nutritional rehabilitation programme, is a good indicator of chronic disease in children, of which TB may be the cause.

## Special Investigations for paediatric TB

### Chest X-ray

Chest X-ray in children is a useful tool to assist in the diagnosis. Lateral X-rays should be routinely done in children.

The most common signs are:

* Enlarged lymph nodes in the hilar region or compression of the airway.
* Lateral X-rays can identify lymph nodes in the hilar region or posterior pneumonias.
* Opacification of the lung tissue, with or without cavities.
* Miliary pattern.
* Pleural effusion in older children.

***False negatives:***

**A normal chest X-Ray in a child does not rule out active TB disease:** this is a very frequent presentation in HIV positive children with a low CD4 count and/or malnourished children.

***False positives:***

HIV-infected children can present with lymphoid interstitial pneumonia (LIP) and bronchiectasias, which can mimic TB in an X-ray.

### Role of a Tuberculin Skin Test

The tuberculin skin test (TST) is a tool for detection of latent TB infection (LTBI). The test involves intradermal injection of purified protein derivative (PPD), a crude mixture of mycobacterial antigens, which stimulates a delayed type hypersensitivity response and causes induration at the injection site within 48 to 72 hours.

However the **TST detects only infection with MTB, not necessarily active disease** (See Annex ??).

* A positive test indicates infection with TB, but not necessarily TB disease.
* In a child under 5 years, a strongly positive skin test indicates recent (6 weeks or more) infection that is a risk factor for progression to disease. In the presence of other features, i.e. history of TB contact, signs and symptoms of TB and x-ray changes, a positive tuberculin skin test is suggestive of TB disease in children.

A positive reaction occurs after previous BCG immunization and should remain positive for several years thereafter. This reaction is usually weaker than the reaction to natural infection with *M. tuberculosis*. A positive reaction is only one piece of evidence in favor of the diagnosis in children.

A negative tuberculin skin test does not exclude TB. Various conditions may cause a negative reaction even if a child has TB.

If the chest x-ray is suspicious of TB and the skin test is negative, TB can be diagnosed in children. Conditions that may suppress the tuberculin skin test and give a false negative result include: HIV infection, malnutrition, severe viral infections (e.g. measles, chicken pox), cancer, immuno-suppressive drugs (e.g. steroids), severe disseminated TB.

A positive result is 5mm of induration in HIV positive children or 10mm of induration in HIV negative children.

False negative results can be found in severely malnourished children, those with low CD4 count, in meningitis or miliary TB and in cases of recent TB infection (less than 10 weeks).

False positive results can be found in mycobacteria other than tuberculosis (MOTT), BCG vaccination and due to an incorrect interpretation of the TST.

TST should not be used routinely. It should be used to assist with diagnosis of MDR TB (where it is not always possible to obtain a sample for culture) and in research settings.

TST should be done using 2 TU of tuberculin PPD RT23. A TST should be regarded as positive as follows:

* in high-risk children (includes HIV-infected children and severely malnourished children, i.e. those with clinical evidence of malnutrition): >5 mm diameter of induration;
* in all other children (whether they have received a Bacille Calmette–Guérin (BCG) vaccination or not): >10 mm diameter of induration.

**Note:** There can be false-positive as well as false-negative TSTs. Sometimes it is useful to repeat the TST in children once their nutritional status has improved or their severe illness (including TB) has resolved, as they may be initially TST negative, but positive after 2–3 months on treatment. A negative TST never rules out a diagnosis of TB in a child.

### Bacteriological confirmation of childhood TB

Diagnosis of TB in a child should be confirmed using whatever specimens and laboratory facilities are available. Bacteriological confirmation is especially important for children who have:

* suspected drug-resistant TB
* HIV infection
* complicated or severe cases of disease
* an uncertain diagnosis.

Pulmonary TB in children tends to be smear negative and obtaining samples for laboratory investigations can be challenging. However, Children older than 5 years old may produce sputum, which should be examined preferably using the Gene Xpert.

Appropriate specimens from the suspected sites of involvement should be obtained for microscopy and, where facilities and resources are available, for culture (and also histopathological examination). Appropriate clinical samples include sputum, gastric aspirates and certain other material (e.g. lymph node biopsy or any other material that is biopsied). Fine-needle aspiration (FNA) of enlarged lymph glands – for both staining of acid-fast bacilli and histology – has been

shown to be a useful investigation, with a high bacteriological yield.

#### Techniques for obtaining specimens from children

Common ways of obtaining samples for smear microscopy include the following.

***With the increased rates of DR TB, routine culture should be requested for all children starting TB treatment whenever possible***

The main 3 available techniques used to obtain respiratory samples are: gastric aspirate, nasopharyngeal aspirate (NPA) and induced sputum (See Annexes 5 and 6).

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Gastric Aspirate** | **Nasopharyngeal Aspirate** | **Induced Sputum** |
| **Yield** | 30-40% for 3 GA, increased in younger and sicker children | Similar yield reported to induced sputum | 1 sputum same yield as 3 GA |
| **Specimen collected** | Gastric fluid | Upper secretions (lower secretions can be obtained if the child coughs) | Lower respiratory secretions |
| **Characteristics** | Invasive, doesn’t need special equipment | Simple, non-invasive, but needs special equipment | Needs special equipment and well ventilated areas |

*When DR TB is suspected, the child should be referred for evaluation and to assure a specimen collection.*

***a. Expectoration***

Sputum should always be obtained in adults and older children (10 years of age or older) who are pulmonary TB suspects. Although it is difficult to obtain sputum from younger children under 5 and most of them are sputum smear-negative, for those who are able to produce a specimen, it is recommended to send it for smear microscopy (and mycobacterial culture if available).

As with adult TB suspects, two sputum specimens should be obtained: an on-the-spot specimen (at first evaluation) and an early morning specimen (at a follow-up visit).

***b. Gastric aspiration***

Gastric aspiration using a nasogastric feeding tube can be performed in young children who are unable or unwilling to expectorate sputum. The procedure can be done by nurse or doctor. . Gastric aspirates should be sent for smear microscopy and mycobacterial culture. A gastric aspirate can be obtained on the same day 4 hours apart. For in patients, two gastric aspirates should be obtained on each of two consecutive mornings.

***c. Sputum induction***

Several recent studies have found that sputum induction is safe and effective in children of all ages and the bacterial yields are as good as or better than for gastric aspirates. However, training and specialized equipment are required to perform this procedure properly.

***d. Fine needle aspiration***

Fine needle aspiration is a useful technique to collect samples from an enlarged lymph node for both histology and staining for acid-fast bacilli (AFB). It should be mainly use for children with persistent LN not responding to adequate TB treatment (See Annex 6).

## Paediatric Extrapulmonary TB

Young children (<2-3 years of age) with immature cellular immune responses are at highest risk of developing extra-pulmonary forms of disease.

A review of the natural history of TB disease in children demonstrated that up to 50 % of infants progress to active TB disease after primary TB infection (in the first few months), with 10 to 20 % developing miliary TB and/or TB meningitis (TBM).

Extra-pulmonary disease may also develop years later (e.g. osteo-articular or renal involvement) following reactivation of organisms sub-clinically disseminated during primary infection.

### TB meningitis

TB meningitis is a very severe form of TB disease, which is more common in children under 5 years.

Symptoms are very nonspecific and include: headache, early morning vomiting and convulsions, neck stiffness, reduced consciousness and cranial nerve palsies. Hydrocephalus frequently develops as a complication of TB meningitis (TBM), and needs urgent referral to a referral hospital.

Clinical diagnosis can be made whenever a child with meningitis is not responding to standard therapy (especially in HIV positive children). Diagnosis can be supported by a lumbar puncture where specific findings are: raised proteins, low glucose and lymphocytosis.

Any CSF sample needs to be sent for smear and culture/DST.

**Due to its poor prognosis treatment for TB meningitis has to be initiated as soon as it is suspected.**

### Lymph node TB

This type of tuberculosis represents the most common extra-thoracic manifestation of TB. Lymph node TB presents with persistent painless glands for more than 2 weeks, with no response to antibiotics. Glands may become fluctuant prior to spontaneous drainage and sinus formation (scrofula). Laboratory confirmation is not needed to start treatment. However, if there is no adequate response to TB treatment, additional laboratory tests (FNA and/or biopsy) can be performed to rule out other less common conditions.

### Abdominal TB

May present as peritonitis, malnutrition, abdominal distension with ascites, or bowel, biliary or lymphatic obstruction due to the compressive effects of enlarged intra-abdominal nodes.

Whenever possible, an abdominal ultrasound should be done, as **abdominal lymph nodes in a child are highly suggestive of abdominal TB.**

### Bone and joint disease

Most cases arise in older children who may present with painful limbs or joints or a limp frequently misattributed to trauma. Spinal TB represents 50% of all osteo-articular TB and can present as a backache of a few weeks duration, with spine deformity.

### BCG disease

Currently there is one attenuated vaccine for TB (M.bovis BCG), which has proven to offer a significant protection against disseminated TB (miliary and TBM) in HIV-uninfected children. In HIV-infected children, there are concerns regarding the possible complications related to the vaccine.

Due to the high TB prevalence in Swaziland, BCG Vaccination is recommended in all children at birth.

A normal reaction to the BCG vaccine includes a small area of redness, followed by a raised papule and a shallow ulcer that will heal up to around 14 weeks after vaccination.

BCG disease can present (especially in HIV infected children) as:

* **Local BCG disease**: abscess at the site of injection more than 10mm or ulceration that lasts more than 14 weeks.
* **Regional BCG disease:** Involvement of regional lymph nodes (ipsilateral axillary, supraclavicular, cervical and upper arm glands) more than 15mm. (Ipsilateral axillary LN in infants are likely BCG disease).
* **Distant BCG disease:**  Involvement of any site beyond a local or regional ipsilateral process (BCG confirmed from sputum, CSF, urine, bone or distant skin lesion). Clinical relevant symptoms may be present.
* **Disseminated disease:**  BCG confirmed from more than 1 remote site and/or from at least one blood or bone marrow culture.

BCG disease can also present as IRIS during the first 3 months after initiation of ART therapy.

*If BCG disease is suspected, refer the child to a hospital or specialized center, as full TB treatment may be needed in severe forms.*

The decision to treat BCG disease depends on the immune system of the child and the extent of the disease.

***HIV-uninfected children*:** Usually they do not require treatment and therapeutic FNA can be considered if the node is fluctuating. They need to be followed up every 3 months until it has been totally cured.

***HIV-infected children*:** Treatment is recommended. As M.Bovis is resistant to pyrazinamide, a Fluorquinolone (Levofloxacine 7.5-10mg/kg or Ofloxacine 15mg/kg) has to be added. Co-infection with MTB has been reported, so children who need treatment should start with a five-drug regimen (RHZE + Fluorquinolone) for 2 months and complete further 7 months with RH.

Mortality in HIV positive children with BCG disease is very high, so prompt initiation of HAART is strongly recommended.

## Paediatric DR-TB

DR-TB can also affect children, but due to the difficulty in obtaining samples, they are rarely diagnosed. It is crucial that we make all possible efforts to collect a specimen for Gene Xpert/culture and DST and refer the children for further assessment.

DR-TB is suspected if:

* A positive MDR-TB contacts exists.
* There is poor response to DS TB treatment-persistent symptoms or failure to gain weight.
* It is a retreatment case.

## PadediatricTB treatment

### Treatment of susceptible paediatric TB

Due to the high HIV prevalence and INH resistance, all children starting TB treatment need to receive a four-drug regimen (HRZE) during the initial phase, followed by a continuation phase of 2 drugs (RH) for a minimum period of 4 months.

|  |  |  |
| --- | --- | --- |
| **Drug** | **Doses (mg/kg)** | **Range (mg/kg)** |
| **Rifampicine (R)** | 15 | 10-20 |
| **Isoniazid (H)** | 10 | 10-15 |
| **Pyrazinamide (Z)** | 35 | 30-40 |
| **Ethambuthol (E)** | 20 | 15-25 |
| **Streptomycine (S)** | 15 | 12-18 |

**All children starting TB treatment should be initiated on:**

**2RHZE / 4RH**

**Children with severe immune-suppression and severe forms of TB disease need to complete 9 months of treatment on:**

**2RHZE / 7RH**

**Severe immunosuppressed children (CD4 < 750/25% if less than 5 years old and CD4 < 350 in 5 years old or older)**

**and**

**Severely sick children (severe malnutrition/failure to thrive, chronic/recurrent fevers, severe dyspnoea) need to complete 9 months of treatment**

**2RHZE / 7RH**

Table of severe immunosuppression in children:

|  |  |  |
| --- | --- | --- |
|  | Under 5 years old | 5 years and up |
| **CD4%** | ≤25% | ≤350 cells/mm3 |
| **Absolute CD4** | ≤750 cells/mm3 |

**Children with TBM and osteoarticular TB should complete 1 year of treatment on**

**2RHZE / 10RH**

In all children previously treated for TB, **all efforts will be put in place to assure a sample is obtained for culture and DST**.

In case resistant TB is suspected, the child has to be referred to a facility where MDRTB treatment is available for evaluation.

### Use of Steroids in Pediatric TB forms

1-2mg/kg of prednisone is recommended in severe forms: TB meningitis, TB pericarditis, obstruction of the airway and sick children with miliary TB.

Corticoids should be given for 4-6 weeks, with tapering over 2 weeks.

### Paediatric anti-TB drugs dosage

Children less than 11kg will receive RHZ (60/30/150), Ethambuthol 100mg and H (100mg)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **WEIGHT BANDS** | **INITIAL PHASE** | | | **CONTINUATION PHASE** | |
| RHZ (60/30/150) | INH 100mg | Ethambuthol 100mg | RH (60/30) | INH 100mg |
| **3 - 5.9 kg** | 1 | ½ | 1 | 1 | ½ |
| **6 - 7.4 kg** | 1.5 | 1.5 |
| **7.5 - 8.9 kg** | 2 |
| **9 -10.9 kg** | 2 | 2 |

**Children less than 11 KG:**

RHZ (60/30/150), Isoniazid 100mg and Ethambuthol 100mg

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **INITIAL PHASE** | | | **CONTINUATION PHASE** | |
| **Weight bands** | RHZ (60/30/150) | INH 100mg | Ethambuthol 100mg | RH (60/30) | INH 100mg |
| 3 - 5.9 kg | 1 | ½ | 1 | 1 | ½ |
| 6 - 7.4 kg | 1.5 | 1.5 |
| 7.5 - 8.9 kg | 2 |
| 9 -10.9 kg | 2 | 2 |
| All children on TB treatment should receive 1 tablet of pyridoxine per day (12.5mg) | | | | | |

**Children above 11 to 34.9kg:**

RHZE (150/75/400/275) and Isoniazid 100mg

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **INITIAL PHASE** | | **CONTINUATION PHASE** | |
| **Weight bands** | RHZE (150/75/400/275) | INH 100mg | RH (150/75) | INH 100mg |
| 11 - 15.9 kg | 1 | 1 | 1 | 1 |
| 16 - 20.9 kg | 1.5 | 1 | 1.5 | 1 |
| 21 - 25.9 kg | 2 | 1 | 2 | 1 |
| 26 - 29.9 kg | 2.5 | 2 | 2.5 | 2 |
| 30 – 34.9 kg | 3 | 2 | 3 | 2 |
| 35 – 39.9 kg | 3.5 | 2 | 3 | 2 |
| All children on TB treatment should receive 1 tablet of pyridoxine per day (25mg) | | | | |

## Paediatric MDRTB treatment

Children diagnosed with MDRTB will be initiated following the same regimen as for adults.

If there is a known contact case, the child will be put on the same regimen as the contact case, while waiting for his DST result. Any child suspected of having MDRTB has to be referred to a MDRTB site, where empiric treatment will be considered.

Before initiating treatment, other possible causes for poor response to therapy need to be investigated:

* + Severe immune-suppresion.
  + Poor adherence, due to lack of adequate support.
  + Treatment failure of ARVs.
  + IRIS

## Follow up of children on TB treatment

For children starting TB treatment, the first follow up is recommended at 2 weeks, 4 weeks and monthly thereafter. To assure a good outcome, on each visit the following should be monitored:

* Weight: It has to be checked each visit and documented in the TB card. An increase in the weight is one of the best indicators we have of successful treatment.
* Doses: They need to be adjusted every visit, according to the weight.
* Adherence: Good adherence is essential to assure good treatment outcomes. The HCW need to asses in each visit:
  + Who is the main caregiver.
  + Who is in charge of giving the tablets (DOTS is highly encouraged).
  + What happens when the main caregiver is not at home.
  + If there is any other problem compromising the adherence.

Orphans are especially vulnerable, and they need special attention to assure good adherence. If adherence is compromised due to the social situation, we can consider long term hospital admissions while the social situation is solved together with the child welfare services.

CXR is not required routinely in the follow up of a child if there is good clinical response to anti-TB treatment, as they can have slow radiological response.

## TB-HIV COINFECTION

All children on TB treatment should be tested for HIV. ***Consent for paediatric testing can be given by any parent, guardian, caregiver, health care worker or social worker when it’s in the best interest of the child.***

### Anti-Retroviral Therapy

All HIV positive children diagnosed with TB are clinically eligible for ART initiation.

High pill burden, poor supervision, inadequate social support and lack of disclosure can jeopardize the adherence of children on TB and HIV medication. To assure a good long-term outcome on ARVs, a thorough social assessment needs to be done before starting ARVs, identifying 2 caregivers whenever possible and disclosing the HIV status of the child if they are more than 10 years old.

#### Recommended regimens for HIV+ pediatric patients on TB treatment:

For children who are treatment naïve or on any first-line ART regimen:

Table 15:Recommended Regimens for Pediatric Patients Naive to Treatment

|  |  |
| --- | --- |
| **under 3 years of age** | **Age 3 and over** |
| AZT–3TC–NVPa | AZT–3TC–EFV |
| aIf patient is on TB therapy and is ART naïve, NVP should be initiated at twice-daily dosing. Due to enzyme induction by rifampicin, lead-in dosing is not indicated (and will increase the risk of developing NVP resistance). | |

#### Alternative ART regimen options for special situations requiring TB/HIV co-treatment:

Table 16: Alternative Paediatric Regimens for Special Situations

|  |  |  |
| --- | --- | --- |
| Special Situation | Alternative Regimen | Comments |
| **Child is currently on or qualifies for an LPV/r-based first-line regimen** | May use LPV/r  boosted 1:1 with ritonavir,  if available | Only use if ritonavir availability can be ensured for the duration of TB treatment. |
| **Child is on second-line therapy** | If current regimen contains  LPV/r, continue with  1:1 ritonavir-boosting | Consult a TB or HIV specialist if ritonavir is not available. |
| **Children > 3 years old already on NVP-based regimen before initiating  TB treatment** | AZT–3TC–NVP | Studies in adults show  that NVP-based regimens maintain viral suppression  as well as EFV-based regimens in this situation. |
| **NVP or EFV toxicity** | AZT–3TC–ABC | Immediately switch to  an LPV/r-based regimen when TB therapy is completed. |
| **Severe anaemia*(Hb<8 g/dl)*** | Use d4T instead of AZT | Switch to AZT when stable |

To reduce pill burden and facilitate adherence children should be switched from EFV to NVP once TB treatment is complete (no leading dose of NVP is needed in these cases).

### Cotrimoxazole Prophylaxis

Cotrimoxazole has been shown to reduce HIV related morbidity and mortality. Therefore, all HIV positive children should receive life long prophylaxis with cotrimoxazole.

Table 17: Dosing for Cotrimoxazole Given Once Daily (TMP/SMX.CTX,Bactrim,Cotrim,Cozole)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Age** | **Weight of child** | **Suspension 5ml (200mg/40mg)** | **Pediatric Tablet (100mg/20mg)** | **Dose** |
| **< 6 months** | <5kg | 2.5ml | 1 tablet | 120mg |
| **6m – 5yr** | 5 - 15kg | 5ml | 2 tablets | 240mg |
| **6yr – 14 yr** | 15 - 30kg | 10ml | - | 480mg |
| **>14yr** | >30kg | - | - | 960mg |

### Administering treatment and ensuring adherence

Treatment of TB in children should be administered on an ambulatory basis. Children, their parents and other family members, and other caregivers should be educated about TB and the importance of completing treatment. The support of the child's parents and immediate family is vital to ensure a satisfactory outcome of treatment.

Children with severe forms of TB should be hospitalized for intensive management where possible e.g. in:

* respiratory distress,
* Spinal TB, and (iv) severe adverse events, such as clinical signs of hepatotoxicity (e.g. jaundice).

If it is not possible to ensure good adherence and treatment outcome on an outpatient basis, some children may require hospitalization for social or logistic reasons.

## Prevention of Paediatric TB

Early diagnosis and treatment of adults (especially for smear-positive cases) is essential to reduce the number of TB infections in children. In addition, isoniazid preventive therapy (IPT) for children exposed to tuberculosis infection but without disease has been proven effective to prevent TB in HIV positive and negative children.

### Paediatric Isoniazid Preventive Therapy

All children *with a negative screening for PTB* should receive IPT for 6 months if:

* They are under 5 years old, irrespective of their HIV status, when there is a documented exposure to PTB. For every new TB contact, IPT should be repeated.
* They are HIV positive and more than 1 year old, even if there is no contact (if no prophylaxis in the previous 2 years).
* Newborn babies born to a mother with tuberculosis in pregnancy. Vertical transmission of TB (*Congenital TB*) can happen, especially if the mother is diagnosed in the last 3 months of pregnancy and is sputum smear-positive. In these cases, *if there are no TB symptoms in the newborn*, INH prophylaxis for 6 months is recommended for the newborn.This children should withhold BCG vaccination until completion of IPT.

Table 18: Dosage of INH for prophylaxis in Children

|  |  |  |
| --- | --- | --- |
| **Dosing of Isoniazid**  **INH should be given at a dose of 10mg/kg together with Vitamin B6.** | | |
| **Weight range (Kg)** | **Number of 100mg tablets of INH to be administered per dose** | **Dose given (mg)** |
| **<5** | ½ tablet | 50 |
| **5.1 – 9.9** | 1 tablet | 100 |
| **10 – 13.9** | 1½ tablets | 150 |
| **14 - 19.9** | 2 tablets | 200 |
| **20 – 24.9** | 2 ½ tablets | 250 |
| **>25** | 1 ADULT dose | 300 |

FOR ANY QUESTION REGARDING PEDIATRIC TB/HIV, PLEASE CONTACT THE FREE BAYLOR HOT LINE

24048569

1. COLLABORATIVE TB AND HIV ACTIVITIES

## TB/HIV interaction

TB and HIV are inextricably linked. While TB is the leading cause of mortality among people living with HIV virus, HIV remains the most powerful risk factor for developing TB.

TB can occur at any point in the course of progression of HIV infection and the risk of developing TB rises sharply with worsening immune status. A person infected with HIV has over 20 times increased risk of developing TB disease. Mortality in HIV+ TB patients is 2-4 times higher (6% to 39% in SSA) than in HIV- TB patients. In SwazilandHIV is considered to be the major factor fueling the TB epidemic. Currently 83% of incident TB cases are also co-infected with HIV.

Early detection and effective treatment of TB among HIV-infected patients is critical to prolong the lives of people living with HIV/AIDS.

Swaziland has made significant progress in implementation of the WHO interim policy on TB/HIV collaborative activities. Current HIV testing rate among TB patients is at 94%, 95% of registered patients are on CPT, and about 50% of co-infected patients have been initiated on ART.

This guideline emphasizes the need to ensure early ART initiation in co-infected TB patients within 8 weeks of staring anti-TB treatment.

***Note: Same tuberculosis treatment should be administered to both HIV + and HIV – TB patients. HIV positive patients can be completely cured of tuberculosis.***

## HIV Testing and Counseling (HTC)

TB is often the first clinical indication that a person may have an underlying HIV infection; hence the importance of TB services as an entry point to HIV prevention, care and treatment.

HIV testing and counseling should be offered to all patients of all ages who present with signs or symptoms suggestive of tuberculosis or have confirmed TB (Standard 14 of the ISTC).

The family-centered approach to HIV testing should be employed such that once a family member is identified as having HIV, health workers should encourage and actively facilitate HIV testing for other family members.

Appropriate post-test counseling should be ensured, with a strong focus on HIV prevention; as this will also help prevent the spread of TB.

Results of HIV testing should be properly documented in the appropriate columns of the Tuberculosis register.

## HIV prevention in TB patients

The HIV prevention package in Swaziland includes behavior change campaigns; promotion of the ABC Strategy (i.e Abstinence, Being faithful to one partner, and Condom use); as well as Male Circumcision (MC). Provision of health promotion messages and distribution of condoms should be reinforced to all TB patients regardless of their HIV status. Similarly information on Male circumcision should be offered to all male patients who test negative.

## TB treatment in people living with HIV

Treatment of tuberculosis is essentially same for HIV co-infected and HIV negative TB patients.

All drug-sensitive HIV positive TB cases should be treated with the standard 6-month regimen as outlined in the Treatment section of this guideline page???

All central nervous system (CNS) related tuberculosis cases should have treatment extended to 9 months as outlined in the treatment section ???

Drug resistant disease should be treated by the specialized centres in line with the MDR-TB treatment guidelines.

## Co-trimoxazole preventive therapy

Co-trimoxazole preventive therapy substantially reduces morbidity in HIV-positive TB patients by reducing the risk for recurrent bacterial infections, malaria and Pneumocystis jirovecii.

All TB/HIV co-infected patients should receive co-trimoxazole preventive therapy throughout the duration of the anti-tuberculous therapy and continue lifelong thereafter.

## Antiretroviral therapy

Antiretroviral therapy improves survival in HIV-positive patients. In addition, antiretroviral therapy reduces TB rates by up to 90% at an individual level, by 60% at a population level and it reduces TB recurrence rates by 50%.

ART should be initiated for all people living with HIV with active TB disease irrespective of CD4 cell count.

TB treatment should be initiated first, followed by ART as soon as possible preferably within the first 8 weeks of starting TB treatment.

### Interactions with ART Regimens

Standardized, simplified ART regimens are used to support HIV treatment programmes so they can reach as many people living with HIV as possible.

Guidance for concomitant administration of first-line anti-retrovirals is given below. There are few long-term clinical outcome data to support use of these TB/HIV drug combinations.

Table 19: TB Medicine/ARV Drug Regimen Recommendations

|  |
| --- |
| Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)  **There are no major interactions between rifampicin and lamivudine (3TC), emtricitabine (FTC), tenofovir, abacavir, zidovudine (AZT) or didanosine (ddI).**  **Stavudine (d4T) should not be given because of the increased risk of peripheral neuropathy with concomitant TB therapy.** |
| Non-nucleoside reverse transcriptase inhibitors (NNRTIs)  **The preferred regimen for patients who have no contraindication is:**  **Rifampicin + Efavirenz - Use standard dose 600mg/day in patients**  **Other regimens include:**  **Rifampicin + Nevirapine - Not recommended, but if given then use standard doses and perform Nevirapine therapeutic drug monitoring** |
| Protease inhibitors (PI)  **Rifampicin + unboosted PI - DO NOT USE**  **Rifampicin + boosted PI - Not recommended due to evidence of poor pharmacokinetics and high rates of hepatotoxicity seen in studies with healthy volunteers.** |

Swaziland HIV treatment guidelines (2010) recommend as first line TDF+3TC+EFV, with alternatives being AZT+3TC+EFV (for those who cannot tolerate TDF).

For patients who cannot use Efavirenz (1st trimester pregnant women, patients with mental health disease), it is substituted with Nevirapine.

Alternatives for patients who are intolerant to efavirenz or are infected with a strain of HIV that is resistant to NNRTIs, a triple NRTI regimen (AZT+3TC+ABC or AZT+3TC+TDF) may be used for the duration of the anti-tuberculosis treatment and patient MUST be switched back to their original regimen.

In individuals who need TB treatment and who require an ART regimen containing a boosted protease inhibitor (PI), it is recommended to give a regimen containing lopinavir or saquinavir with additional ritonavir dosing ; this regimen should be closely monitored as the PI serum concentration is very much reduced by the rifampicin. Patients should be monitored for treatment failure.

### When to start ART?

Currently available evidence suggests that early provision of ART reduces morbidity and mortality in TB/HIV co-infected patients. However, starting ART during TB treatment may be complicated by overlapping toxicities, drug-to-drug interactions, immune reconstitution disease, as well as high pill burden, which may negatively affect adherence. On the other hand, delaying ART may lead to prolonged or worsening immune suppression. Clinicians need to balance these risks when deciding when to initiate concomitant HAART and TB treatment. The revised

* START All TB patients with HIV on antiretroviral therapy (ART) as soon as possible (and within the first 2 weeks of starting anti-TB treatment) regardless of immune system measurements and not later than 8 weeks of starting anti TB treatment.

## Drug susceptibility testing

High mortality rates have been reported among people living with HIV who have drug resistant-TB, and death rates can exceed 90% in patients co-infected with extensively drug-resistant TB (XDR-TB) and HIV.

Prompt initiation of appropriate TB treatment (and subsequent initiation of ART) can reduce mortality among people living with HIV who have drug-resistant TB.

A drug sensitivity testing (DST) should be requested at the start of TB therapy for all HIV-positive TB patients, to avoid mortality due to unrecognized drug-resistant TB. (refer to Chapter 4: Diagnosing TB).

## Dealing with TB diagnosed in patients already on ART

Patients receiving any HIV care including ART should be continuously screened for TB using the standard screening tool, and if positive on screening should be properly investigated to establish TB diagnosis.

When TB is diagnosed in patients already receiving ART, ant-TB treatment should be started immediately.

There are two issues to consider in such cases:

* Whether ART needs to be modified because of drug–drug interactions or to reduce the potential for overlapping toxicities (see section on ART)
* Whether the presentation of active TB in a patient on ART constitutes ART failure that requires a change in the ART regimen. (Refer Swaziland HIV Treatment guidelines section on Diagnosis and management of ART failure)**.**

## HIV-related prevention, treatment, care and support

The recommended package of HIV-related prevention, treatment, care and support services and support for people living with HIV as outlined in the Swaziland HIV Package of care guideline should be provided either by TB clinics or by referral to HIV/AIDS programmes.

To improve treatment success, the special needs of particular groups (e.g. drug users, prisoners, migrant populations and other marginalized groups) should be assessed and addressed; their care should be integrated with other services.

#### Managing side effects in concurrent TB/HIV treatment

Patients on concurrent anti-tuberculous therapy and ART may experience overlapping toxicities due to both treatments.

These patients should therefore be closely monitored especially for evidence of hepatic damage through monthly ALT assay.

Due to the high risk of peripheral neuropathy associated with the use of INH, and D4T regimens, it is recommended that patients be placed on pyridoxine (vitamin B6) as a routine part of anti-tuberculous therapy in co-infected patients using the following dosages:

***Pyridoxine:***

*Adults and Children > 3 years of age:* 25mg po daily

*Children < 3 years of age:* 12.5mg po daily

#### Directly Observed Therapy for concomitant TB/HIV treatment

Due to the difficulties of taking anti-tuberculous therapy and ART as well as the risk of developing drug-resistance, it is recommended that all patients receive directly observed therapy (DOT) during the course of their TB treatment.

DOT should be provided by a paid treatment supporter who fills out the DOT card. The importance of patient education and empowerment around medication taking is a key part in improving adherence as is addressing socioeconomic barriers.

#### Monitoring patients on concurrent ART and DOTS

**Clinical Monitoring**

Clinical assessment should be the primary tool for monitoring adults both before and after initiation of ART.

After starting ART, clinical assessments should take place by a doctor or nurse at 2 weeks, 1 month, 2 months, 3 months, 6 months, and at least every 6 months thereafter

A focused history and physical should be performed during routine visits. Important features of regular clinical assessments should include:

* monitoring of
  + weight (done at every visit)
  + height (in children, done every 3 months)
  + head circumference (in children < 3 years of age, measured every 3 months)
  + developmental status in children;
  + nutritional status in children;
* diagnosis and management of interim or new illnesses
  + OIs that may suggest immune reconstitution syndrome or treatment failure;
  + other co-morbidities, including STIs, Hepatitis B, substance abuse, psychiatric illness
* medication review
  + side effects
  + adherence and dosing
  + other medications, including traditional medicines and other medications that may interact with ARVs
* early diagnosis of pregnancy
* changes in social situation that might affect adherence to ART

**Laboratory Monitoring**

Laboratory monitoring should complement the clinical assessments. Baseline laboratory tests will help to determine which regimen a person should be initiated on. However, the absence of the capacity to perform laboratory testing should not preclude a person from starting ART.

**Baseline Laboratory Investigations**

Where possible, the following baseline laboratory investigations should be obtained prior to starting ART:

* CD4 count, or percentage (in children < 5 years)
* Full blood count (FBC)
* ALT
* Serum Creatinine when Tenofovir (TDF) is being considered in adults, followed by calculation of the rate of Creatinine Clearance *(for details of calculation method for Creatinine clearance, please refer to the National ART guidelines)*
* Pregnancy test in all women of child-bearing age

**Routine Laboratory Investigations**

The following laboratory tests should be performed routinely depending on the specific ARVs that are included in the patient's regimen:

* If on AZT, Haemoglobin (Hb) should be checked at 1 month, 2 months, 3 months, 6 months, and every 6 months thereafter.
* If on NVP, ALT should be checked at 1 month, 2 months, 6 months, and every 6 months thereafter. If the CD4 count at initiation is between 250-350, there is an increased risk of hepatotoxicity, so additional ALT testing is recommended at 2 weeks and 3 months.
* If on Tenofovir (TDF), serum creatinine (and rate of Creatinine Clearance) should be checked 6 months after initiation, and every 6 months thereafter.
* CD4 counts should be checked every 6 months, to help determine efficacy of treatment

Additional laboratory tests can be requested depending on the results of the clinical assessments, but should only be done if the result is required to further guide management. These include, but are not limited to:

* Lactate measurement, if the patient is on a NRTI (especially d4T or ddI) for > 4 months and losing weight, and/or having other symptoms that suggest hyperlactatemia[[4]](#footnote-4)
* Glucose and lipid measurements, if the patient is taking a Protease Inhibitor, such as Lopinavir/ritonavir (Kaletra) or Atazanavir/ritonavir

#### Immune Reconstitution Inflammatory Syndromeamong patients with HIV-related TB

* Fever
* New or worsening adenitis - peripheral or centralnodes
* New or worsening pulmonary infiltrates, includingrespiratory failure
* New or worsening pleuritis, pericarditis, or ascites
* Intracranial tuberculomas, worsening meningitis
* Disseminated skin lesions
* Epididymitis, hepatosplenomegaly, soft tissueabscesses

Table 20: Overlapping Side effect adverse reactions to First-line anti-TB and ART drugs

|  |  |  |
| --- | --- | --- |
| **Side Effects** | **Possible causes** | |
| **Anti-TB Drugs** | **ARV Drugs** |
| Skin rash | PZA, RIF, INH | NVP, EFZ, ABC |
| Nausea, vomiting | PZA, RIF, RBT, INH | ZDV, RTV, AMP, IDV |
| Hepatitis | PZA, RIF, RBT, INH | NVP, PIs, Immune  reconstitution |
| Leukopenia, anemia | RBT, RIF | ZDV |

1. INFECTION CONTROL

## Rationale

Persons with undiagnosed, untreated and potentially contagious TB are often seen and managed in Health care settings; and such frequent exposure to patients with infectious TB disease may put the health worker at risk. Furthermore Health care workers and staff may themselves be immunosuppressed due to HIV infection and be at higher risk of developing TB disease once infected.

Nosocomial transmission of M. tuberculosis has been linked to close contact with persons with TB disease during aerosol-generating or aerosol-producing procedures, including bronchoscopy, endotracheal intubation, suctioning, other respiratory procedures, open abscess irrigation, autopsy, sputum induction, and aerosol treatments that induce coughing.

All health facilities should be made aware of the need for preventing transmission of M. tuberculosis especially in settings where persons infected with HIV might be encountered or might work. All HCWs should be sufficiently informed regarding the risk for developing TB disease after being infected with M. tuberculosis.

All health-care settings should develop a TB infection-control plan designed to ensure prompt detection, airborne precautions, and treatment of persons who have suspected or confirmed TB disease. TB infection control measures can be divided into three categories namely: Administrative, Environmental (or engineering) and Personal respiratory protection controls.

## Administrative Controls

The first and most important level of infection control is the use of administrative measures to prevent droplet nuclei from being generated, thus **reducing the exposure** of HCWs and patients to *M. tuberculosis*. These measures include:

* Each health facility implementing effective written policies and protocols to ensure the rapid identification, isolation, diagnostic evaluation, and treatment of persons likely to have TB;
* Designating an Infection Control Officer in key health facilities with responsibility and authority for the implementation of the infection control plan.
* Risk assessment for TB transmission in the facility should be conducted periodically,
* Ensuring the timely processing of patients screening, laboratory testing, and reporting of results to the ordering clinician;
* Implementing effective work practices among health care workers (HCWs) for the management of patients with suspected or confirmed TB disease
* Educating, training, and counseling HCWs about TB, with specific focus on prevention, transmission, and symptoms
* Screening and evaluating HCWs who are at risk for TB disease or who might be exposed to M. tuberculosis for TB infection and disease.
* Ensuring that HIV-positive HCWs do not work in areas of high TB transmission or with MDR-TB patients

## Environmental control measures

The following environmental control methods should be used in the above-mentioned high-risk areas to prevent the spread and **reduce the concentration of droplet nuclei in the air**.

* Maximising natural ventilation e.g., keeping windows open (even in winter and at night)
* Controlling the direction of airflow e.g. strategically placed fans

Ventilation maintains air quality by both air dilution and removal of airborne contaminants. Uncontaminated supply air mixes with contaminated room air (dilution), and air is subsequently removed from the room.

## Personal respiratory protection

**HCWs need to be protected from inhaling infectious droplets** by the use of personal respiratory protective devices designed to fit over the mouth and nose and filter out infectious TB particles. The emphasis of infection control rests on maximising the environmental control and personal caution. Therefore, personal respiratory protection using **N95** is only indicated in specialized settings, e.g., referral facilities nursing MDR-TB and XDR-TB patients, and only when all other infection control measures have been fully implemented

10.4 Control of TB Transmission in Prisons

Tuberculosis occurs up to 100 times more commonly in prisons than in civilian populations.

* The spread of tuberculosis is worsened by late diagnosis and treatment of infectious cases, and poor prison living conditions such as overcrowding
* The main strategies for achieving these goals of TB control are the early diagnosis of TB cases and their prompt and effective treatment.
* It is thus vitally important to screen new inmates by history and sputum smear microscopy if the inmates are symptomatic for TB.
* Penal reforms and improvement in prison living conditions are also important strategies for early case detection, rapid effective treatment which will reduce morbidity and mortality in prisons and so interrupt the chain of transmission
* There should be “Equivalence” of care in the prisons, i.e., all prisoners have the right to the same standard of health care as the state provides for the general community
* There should be particular attention on integrating prison and civilian TB services

# 

1. MANAGEMENT OF MULTI-DRUG AND EXTENSIVELY RESISTANT TUBERCULOSIS

## Definitions

Multi-Drug-resistant TB is said to be present only through laboratory confirmation of in-vitro resistance to one or more first-line anti-tuberculosis drugs.

The national TB drug-resistance survey conducted in 2009-2010, revealed high 7.7% prevalence of MDR among new TB cases (never treated before); and 33.9% among previously treatment cases. In general, it can be projected that more than 41% of all TB patients enrolled on treatment would require a modification of their treatment due to the problem of drug resistance.

Based on the number and classes of anti-TB drugs to which the bacilli are resistant to, the various forms of anti-TB drug resistance are defined as follows:

* **Mono-resistance**. Tuberculosis in patients whose infecting isolates of *M. tuberculosis* are confirmed to be resistant in vitro to one first-line anti-tuberculosis drug.
* **Poly-resistance**. Tuberculosis in patients whose infecting isolates are resistant in vitro to more than one first-line anti-tuberculosis drug, other than both isoniazid and rifampicin.
* **Multi-drug resistant tuberculosis(MDR-TB)**. Tuberculosis in patients whose infecting isolates are resistant in vitro to at least isoniazid and rifampicin.
* **Extensively Drug resistant tuberculosis(XDR-TB).**A case where in addition to the existence of MDR-TB, there is established resistance to any fluoroquinolone, and at least one of injectable second-line drugs (capreomycin, kanamycin, and amikacin).

The emergence of multi-drug resistant (MDR) TB and lately extensively drug resistant (XDR-TB) is the most serious aspect of the TB epidemic. MDR TB is difficult and expensive to treat, whilst XDR-TB is almost untreatable.

It is therefore essential to prevent the development of MDR TB. As with other forms of drug resistance, MDR TB is a largely man-made problem, being the consequence of human error in any of the following:

* prescription of chemotherapy
* management of drug supply
* patient management
* patient adherence.

## Causes of MDR-TB

From a microbiological perspective, resistance is caused by a genetic mutation that makes a drug ineffective against the mutant bacilli. From a clinical and programmatic perspective, it is inadequate or poorly administered treatment regimen that allows a drug-resistant strain to become the dominant strain in a patient infected with TB. **Table 28** summarizes the common causes of inadequate treatment.

Primary resistance to anti-TB drugs is also common, where the patient is infected with resistant strains from a DRTB patient. The genotypic analysis of the samples collected during the National Drug Susceptibility Survey showed that MDR epidemic in Swaziland is largely driven by recent transmission of resistant strains.

Table 21: Causes of DRTB

|  |  |  |
| --- | --- | --- |
| Health-care providers: - Inadequate regimens  - Inappropriate guidelines or  - Non-compliance with guidelines  - Absence of guidelines  - Poor training  - No monitoring of treatment  - Poorly organized or funded TB control programmes | Drugs: inadequate supply or quality - Poor quality  - Unavailability of certain drugs (stock-outs or delivery disruptions)  - Poor storage conditions  - Wrong dose or combination of drugs | Patients: inadequate drug intake - Poor adherence (or poor DOT) - Lack of information on treatment , - Adverse effects of treatment; - Social barriers (stigma, restrictions) - Malabsorption due to other causes - Substance dependency disorders - Mental disorder; - Non-cooperative |

## When to Suspect MDR TB

The occurrence of MDR should be suspected clinically in the following situations:

* Without prior history of TB treatment
  + Health care worker with new tuberculosis
  + Household contact of known MDR-TB case
  + Patients who have a history of migrant work
* With prior history of TB treatment:
  + Treatment after relapse or default
  + Treatment failure in HIV-negative patients (sputum smear positive after five months of therapy)
  + Treatment failure in HIV-positive patients (sputum smear positive or lack of clinical improvement after two months)
  + Patients with history of multiple previous treatments in public or private sectors

The above cases should be investigated by *M. TB* Culture and Drug Susceptibility Testing (DST).The clinician should obtain two new sputum samples form the suspect using standard operating procedures and send a request for culture and DST. See Annex for the Request Form for Smear, Culture and DST.

Two sputum samples are needed in view of high contamination rates when transporting raw sputum samples over long distances.

The clinician may initiate treatment with second-line anti-tuberculosis drugs in some of while DST results are being awaited.

## Laboratory Confirmation of MDR

Drug-resistant tuberculosis is confirmed through laboratory tests that demonstrate growth in-vitro of infecting isolates *of Mycobacterium tuberculosis* in the presence of one or more anti-tuberculosis drugs. This is known as **drug-susceptibility testing**.

DR-TB can be diagnosed using one of the following diagnostic methods (the last three are available in Swaziland)

* Conventional Solid(Lowenstein Jenssen – LJ)
* Liquid culture medium (MGIT)
* Xpert MTB/Rif (GeneXpert)
* Line probe assay

A summary of TB patients who should have access to drug-susceptibility testing (MGIT; Gene-Xpert or LPA) is presented in the algorithm in Chapter 4 of this guideline.

## Management of MDR TB

The management of MDR should focus both on improving the quality of case management for TB patients on first line treatment to prevent emergence of resistance as well as appropriate management of the diagnosed resistant cases.

Reference should be made to the National MDR-TB management guidelines for details of case management. However, the following basic principles should be observed in the treatment of MDR cases:

* A ‘consent to treatment’ should be obtained prior to initiation of treatment;
* Treatment regimen should consist of at least 5 drugs anti-TB drugs (both first and second line) to which the organisms have proven susceptibility.
* The drugs should be administered for at least 6 days per week, usually twice daily to minimize side effects,
* The treatment should be started preferably with the high ended recommended doses;
* Total duration of treatment should be at least 20 months including an 8-month intensive phase when injectables would be administered.
* Each dose must be given under direct observation by a treatment supporter;
* All treatment records should be properly documented and preferably kept in a database.
* Patients should not be admitted with other normal TB patients at all or admitted in general medical wards.
* When necessary and especially in very sick patients, hospitalization can be indicated for two (2) months to stabilize clinical condition as well as HIV testing and counseling and other baseline investigations;

Treatment of PDR-TB ranges between 9-18 months, and XDR (please refer to the national DR guideline for details).

The Main referral centre for MDR TB in Swaziland will be based in National TB Hospital.

A specialized management team comprising of a physician or specially trained medical officer, a dedicated MDR TB trained nurse, and a social worker should be established. The purpose of this team is to oversee all aspects of management including counseling of the patients.

A community-based care approach for MDR management should be considered where feasible and with adequate steps taken to ensure infection control.

It must be emphasized that the priority of the programme is to ensure that all new patients complete their first line TB treatment. “**With good standard treatment meticulously prescribed and meticulously administered, multidrug resistance should not occur”**(pg 14 of the “Guidelines for the Management of Drug-Resistant Tuberculosis. WHO:TB:96.210(Rev1) 1997, World Health Organization”).

The key to this approach includes:

* use of the approved standardized regimen
* rational drug susceptibility testing of specimens from MDR tuberculosis patients
* provision of a social worker for counseling and support
* provision of key nursing staff to provide continuity during the treatment period
* direct observation of treatment throughout the course
* keeping updated registers
* monitoring compliance
* developing measures for rapid recall if patients interrupt their treatment
* increasing education and motivation of patients
* tracing and evaluating contacts rapidly.

### DR-TB treatment

For the treatment of DR-TB, first and second line anti-TB drugs are grouped into 5 classes from which a treatment regimen can be built. The different groups are shown in **Table ??**. Note that: not all drugs in the same group have the same efficacy, tolerability or safety profile.

Table 0.22: Classification (groups) of second line anti-tuberculosis drugs

| **Grouping** | **Drugs** | **Remarks** |
| --- | --- | --- |
| **Group 1  First-line oral agents** | isoniazid (H); rifampicin (R); ethambutol (E); pyrazinamide (Z); rifabutin (Rfb)a | These are the most potent and best tolerated, and should be used  If there is good laboratory evidence and clinical history to suggest that a drug from this group is effective. |
| **Group 2 Injectable agents** | kanamycin (Km); amikacin (Am); capreomycin(Cm); | All patients should receive at least one of these injectable agents so long as there is documented or suspected susceptibility. |
| **Group 3 Fluoroquinolones** | levofloxacin (Lfx); moxifloxacin (Mfx);  Gatifloxacin (Gfx)  Ofloxacin (Ofx) | All patients should receive one of the fluoroquinolones if the strain is susceptible or if the agent is thought to have efficacy.  Levofloxacin is the recommended fluoroquionolone for used in the standardized MDR-TB regimen. |
| **Group 4  Oral bacteriostatic second-line agents** | ethionamide (Eto); protionamide (Pto); cycloserine (Cs); terizidone (Trd); *p*-aminosalicylic acid (PAS) | Medications from this group are added based on estimated susceptibility, drug history, efficacy, side-effect profile and cost. |
| **Group 5  Agents with unclear role in DR-TB treatment (not recommended by WHO for routine use in DR-TB patients)** | clofazimine (Cfz); linezolid (Lzd);  amoxicillin/clavulanate (Amx/Clv); thioacetazone (Thz); imipenem/cilastatin (Ipm/Cln); high-dose isoniazid (high-dose H);b clarithromycin (Clr) | These drugs are not recommended by WHO for routine use in DR-TB treatment because their contribution to the efficacy of multidrug regimens is unclear. |

When the results of DST are available, a definitive individualized treatment regimen (ITR) can be designed for the patients. If the resistance pattern does not prove the existence of MDR TB, the regimen should be designed based on the treatment of mono or poly-resistant TB. If the DST reveals MDRTB, the regimen can be designed using the following approach.

**Discontinuation of the injectables**

The decision to stop the injectable should be made upon review of the cultures, smears, X-rays, and clinical status of the patient. The following criteria are used to consider cessation of the injectable agent:

* Patient has completed a minimum of six months of documented culture-negativity.
* Surgery is not planned.
* There are four remaining drugs to which the isolate has documented sensitivity.

### Completion of MDR therapy

Bacteriological, clinical, and radiological data are all considered when determining the duration of therapy for MDR TB. The guidelines are:

* A minimum of 18 months of negative cultures past conversion.
* For patients with extensive damage on chest X-ray, therapy may be extended to 24 months negative cultures past conversion.

The final outcome of treatment should be recorded in the MDRTB registry. Final outcomes consist of cure, treatment completed, death, treatment default, treatment failure, and transfer out.

### Follow-up after completion of MDR therapy

Treatment follow-up should be done for a minimum of two years after cure. The following are guidelines for surveillance of the cured MDR TB patient:

* Follow-up visits (months 6, 12, and 24) to assess for symptoms and signs of relapse.
* Smear and culture every three months for the first year, and then every six months for the second year.
* Clinical and radiographic evaluation as needed for development of respiratory symptoms.

Due to the high prevalence of residual lung disease, it may be helpful to continue ancillary medicines, such as bronchodilators in patients after anti-tuberculosis therapy is completed.

### Interruption and re-initiation of treatment

The clinician should reinitiate treatment in patients for whom therapy has been suspended due to non-compliance or in patients who have defaulted during therapy. The following is recommended:

Have the patient sign a new adherence contract.

* Perform a full history and physical exam.
* Obtain a smear and culture.
* If positive, culture should be sent for DST.
* Obtain a radiograph and repeat the initial laboratory data.

The treatment regimen and duration to be used for patients restarting therapy should be based on the month at which the patient abandoned therapy and the clinical state at which the patient returns to therapy (see MDR management guidelines).

Patients who have been off therapy for longer than six months should be evaluated for active disease, and, if it is present, the patient should be started on a completely new course of treatment.

If no active disease is present, clinical judgment should be used to decide whether to reinitiate therapy. If therapy is not restarted, the patient should be followed regularly for signs of relapse.

### MDR TB Treatment in Special Situations.

#### MDR-TB treatment in Children:

Children with MDR TB generally have primary resistance transmitted from an adult contact with MDR TB. Specific data regarding pediatric MDR-TB situation in Swaziland is limited by the inadequate diagnostic capabilities. However, since the rates of childhood TB is generally a reflection of the rates of adult disease at the community level, a high childhood MDR-TB rate can be expected given the current adult MDR-TB prevalence.

Gene Xpert should be used to diagnose pulmonary TB in children whenever possible, for early detection of MDR-TB and provision of early and effective treatment.

In a case where extra pulmonary DR TB is suspected, any specimen obtained should be sent for culture (e.g., cerebrospinal fluid for TB meningitis, biopsy of a lymph node and swabs in draining sinus)

Lack of a positive DR TB sample does not exclude DR TB. If clinical suspicion remains, refer the patient to DR treatment unit.

In culture-negative children who have clinical evidence of active TB and a contact with documented MDR TB, the child’s treatment should be guided by results of DST of the contact.

Careful consideration of the risks and benefits of each drug should be made in designing a regimen. Frank discussion with the patient and family members is critical, especially at the outset of therapy. Given the life-threatening aspects of MDR TB, there are no drugs that are absolutely contraindicated in children. Drugs should be dosed according to the child’s weight (see MDR clinical management guidelines).

Monitoring monthly weights is therefore especially important in pediatric cases, with adjustment of doses as the child gains weight.

**Any respiratory sample (sputum, nasopharyngeal or gastric aspirate) from pediatric cases of TB should be sent for Gene-Xpert and culture/drug susceptibility testing (DST) to detect drug resistance to first line anti-TB drugs**

#### MDR TB treatment and pregnancy

All female patients of childbearing age should be tested for pregnancy upon initial evaluation; birth control is strongly

recommended for all women receiving MDR TB therapy. The efficacy of oral contraceptives may be decreased due to potential drug interactions, and therefore other contraceptive options should be considered. All patients are encouraged to use condoms to protect against sexually transmitted diseases.

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

* Since the majority of teratogenic effects occur in the first trimester, therapy may be delayed until the second trimester unless life-threatening symptoms occur.
* Patients in the third trimester have reduced risk of teratogenicity, although aminoglycosides may still damage the fetal ear. For the most part, aminoglycosides are not used in the regimens of pregnant patients.
* If possible, begin treatment in the second or third trimester with three or four oral drugs with demonstrated efficacy against the infecting strain, and then reinforce the regimen with an injectable agent and possibly other drugs immediately postpartum.

Newborn infants are at high risk of developing disseminated tuberculosis. If possible, smear-positive mothers should avoid close contact with infants, leaving the care of the infant to a family member until the mother is smear-negative.

#### MDR TB treatment and diabetes

The treatment of TB in the diabetic will result in poorer outcomes if glucose is not well controlled. The responsibility often

falls on the physician treating the patient for tuberculosis to ensure proper diabetic care. In addition, diabetes may potentiate adverse effects, especially renal dysfunction and peripheral neuropathy. The following guidelines are suggested to assist in the management of the diabetic with MDR TB.

#### MDR TB and renal insufficiency

Renal insufficiency due to longstanding tuberculosis disease is not uncommon. Great care should be taken in the administration of second-line drugs in patients with renal insufficiency, and the dose and/or the interval between dosing should be adjusted according to recommended guideline (See guidelines on MDR clinical management).

### Extensively Drug Resistant Tuberculosis (XDR-TB)

XDR-TB is defined as resistance to at least Isoniazid and Rifampicin (which is the definition of MDR TB), in addition to any fluoroquinolone, and at least one of the three following injectable used in anti-TB treatment: Capreomycin, Kanamycin and Aminkacin[[5]](#footnote-5).

1. SUPERVISION, MONITORING AND EVALUATION

## Importance of SME

A key element of the DOTS Strategy is the establishment and maintenance of a system to monitor case detection and treatment outcomes. It is essential for efficient programme management since it provides a basis for evaluating the progress made in achieving programme targets, supervision of staff and for monitoring and surveillance.

A successful monitoring and evaluation of TB prevention and control activities assumes a clear definition of roles and responsibilities (tasks) of the TB staff at all levels, e.g. national, regional, and peripheral levels. This means that each staff is expected to perform a set of activities over a defined period of time and to report progress to his/her immediate supervisor on a regular basis.

## Programme supervision

Supervision is a systematic process for increasing the efficiency of health workers by developing their knowledge, perfecting their skills, improving their attitudes towards their work, and increasing motivation, and not merely the observation of health workers to ascertain whether activities are carried out to recommended standards.

The Swaziland NTP should ensure sustenance of task-oriented supervision at all levels to increase the efficiency of health workers by developing their knowledge, perfecting their skills, improving their attitudes towards their work and increasing motivation. The NTP Central Unit should provide technical supervision support to the Regional level, while the Regionals provide same to the health facility level.

Supervision The TB Central unit team, TB laboratory coordinator, and the M&E officer should visit each TB diagnostic facility at least once in a quarter.

The emphasis of supervision to the regional level should be on supporting the Regional TB Coordinators in the discharge of their technical and managerial functions, while that of health facilities should focus on identification of TB cases and administration of treatment including follow up of cases according to national guidelines.

**Supervisory visits must be planned carefully.** Before each visit the supervisor should review the health centre’s reports, the correspondence about the reports, the findings of the last supervisory visit and corrective actions already taken.

Supervision should be conducted using the appropriate supervision tool that assesses the relevant tasks. The facilities to be visited should be notified in advance of the date and purposes of the supervisory visit. The number of supervisory visits should be planned before the start of the fiscal year, for inclusion in the annual-programme budget.

The team together with the Regional TB coordinator should:

* **Observe performance of tasks** and general adherence to national guidelines in diagnosis and managemnent of TB;
* **Review records** e.g suspect registers, treatment cards andTB Registers etc for accuracy, completeness, consistency. Pay attention to results of sputum examinations that were not recorded or sputum examinations that were not carried out at the correct intervals, omission of age of patients or treatment outcomes, misclassification of previously treated cases etc.
* **Examine supplies**e.g anti-TB drugs stock management, expiry, storage conditions etc; also treatment related supplies and forms
* **Discuss with health care staff;** e.g, training needs
* **Discuss with patients:** e.g how they feel about the services they receive, their understanding of cause of TB, treatment duration, the need for adherence etc.

At the end of the visit, the team should summarize their observations, and discuss them with the TB supervisor.

The Regional coordinator should visit the TB diagnostic facilities and the clinics at least every month. At the clinics, the regional coordinator should also assess their case holding practices.

### Monitoring tools

Monitoring and evaluation are key activities for assessing the performance of the programme. Recording and reporting are part of the monitoring and evaluation process. Key elements of a Recording and Reporting System include:

* 1. Collection of individual, patient-based data
  2. Region-based cohort analysis on a quarterly basis, using standardized formats and definitions
  3. Interim reports (smear conversion) and treatment outcome reports based on quarterly diagnosis
  4. Calculation and analysis of key performance indicators
  5. Use of data at facility and region-levels for performance assessment and improvement.

Standardized forms are necessary to capture all relevant data. The following is the complete list of forms:

* 1. Suspect Register, to record patients with a positive chronic history and measure the quality of diagnosis
  2. Laboratory Sputum Request Form, to indicate the examinations requested;
  3. TB Laboratory Register, kept at laboratories performing bacteriology tests;
  4. Patient Treatment Card, a patient-held card to record key patient information, replicating the Clinic/Hospital Card
  5. TB Treatment Card, the key data collection tool to record characteristics of the patient, the episode of TB disease, treatment progress and outcome; this is kept at the facility where the TB patient is registered
  6. TB Register is used to record key diagnostic and treatment information on each registered patient. It includes basic demographic and treatment information as well as treatment outcome. It forms the basis for cohort analysis.
  7. Transfer Form, used to ensure that vital patient information is communicated from one facility to another in an effort to improve continuity of care.
  8. Daily Treatment Supporter Card (yellow card), used by community-based treatment supporter to record directly observed treatment.
  9. Defaulter Tracing Form (pink card) used for tracing defaulters
  10. Referral form

## Programme monitoring

**Monitoring** programme performance to ascertain whether activities are accomplished as planned, and identification of problems should be conducted periodically in collaboration with partners. It aims to identify problems quickly so that they can be solved without delay.

### Programme indicators:

The programme indicators are basically categorized as follows:

**Impact indicators:**

The three impact indicators include:

1. TB Incidence
2. TB Prevalence
3. TB Mortality

**Outcome indicators**

These include:

1. TB Case notification for all cases
2. TB case notification rate for new
3. TB treatment success rate

**Output indicators:**

As may be dictated by the various activities in the National TB Control Programme annual operational plans.

#### Cohort Analysis

Each group of patients diagnosed and registered for treatment during a particular period of time (e.g., a quarter) is called a cohort. The case detection and outcome of treatment of each cohort is recorded every quarter. The most important cohort to monitor is that of sputum smear-positive cases, which is used as the major indicator of the programmer’s quality. It is also useful to monitor the outcome of other forms of TB such as smear-negative PTB and EPTB. These patients tend to have much higher mortality than smear-positive PTB. With the advent of ARVs, it is expected that mortality in these patients will decrease.

Cohort analysis is the key management tool for evaluating the effectiveness of NTCP performance. By identifying problems, it allows corrective measures to be taken. Evaluation of treatment outcomes and trends must be done peripheral, regional and central levels so that appropriate measures can be taken at the appropriate level. The regional TB coordinator should perform cohort analysis every three months and at the end of every year.

#### Reports

The information collected by cohort analysis is in the form of quarterly reports. The electronic TB register is in place in all the TB diagnostic facilities. It has a built-in analysis programme that automatically produces the whole cohort analysis (case finding and treatment outcome). It is important to note that the information that is entered into the electronic TB register is obtained from the manual TB registers, which must therefore be correctly and completely filled. All reports prepared from the Tuberculosis Register are only as accurate as the information recorded in the manual TB register.

#### Quarterly Report on Case Finding

This report is completed by systematically counting the number of cases recorded in the Tuberculosis Register within the quarter that has just ended. Any case classified as “Transfer in” or “Other” is not reported. New tuberculosis cases (all forms) should be analysed separately from previously treated cases. Likewise, new smear-positive PTB cases should be analyzed separately from previously treated cases, and should be recorded by age groups and sex.

#### Quarterly Report on Treatment Outcome

Evaluation of outcome at the end of treatment should be done three months after all patients in the cohort have had time to complete treatment, a period of about 15 months. The treatment outcomes of interest are those of sputum smear positive cases. Smear positive PTB cases are analyzed by category: new cases and retreatment cases (relapse, treatment after default and treatment after failure). Those cases recorded, as “Transfer in” must not be included in the report, as the results of treatment of such cases should be sent to the unit from which the patient was transferred and reported in that unit.

The total number of cases evaluated within each category (according to the type of case and treatment regimen) should be equal to the number entered in this section, obtained from theQuarterly Report on Case-finding. Where the number is different, an explanation must be provided.

In completing the report, the information should be obtained from the Tuberculosis Register under the section entitled “Results of treatment”. The result for every case should have been recorded at this point. Where more than one result occurs for a single patient, the result that will be recorded is that event which occurs first. That is to say, if an. individual remained smear positive at 5 months but subsequently died (or defaulted or was transferred) the patient must be evaluated as smear positive (failure).

At the time of preparation of the report, if no other result is recorded, the patient must be evaluated as having defaulted. When a patient has been transferred to another unit to continue treatment, the outcome of the treatment at the unit to which the patient was transferred should be obtained and entered into the register at the referring unit. Patients should only be recorded as “Transferred” only when their treatment outcome is not known.

#### Information Flow

The TB supervisor compiles the quarterly reports including cohort analysis, which is transmitted to the regional TB coordinator. Peripheral quarterly reports should be transmitted to the regional TB coordinators, who should ensure that they are correct, complete and consistent. The regional TB coordinator should then compile cohort analysis for the region, give feedback to the peripheral units and transmit this report to the national level. The NTCP central unit should then compile a national cohort analysis from these data and provide feedback to all programme levels.

Regular supervisory visits and annual impact assessment meetings are also crucial for monitoring programme performance. Reports must be compiled to document all the meetings and field visits, using a standard supervisory checklist.

## Programme evaluation

**Programme Evaluation should be conducted at the end of a plan period to** assess progress towards operational targets and epidemiological objectives. The evaluation should ensure measurement of all programme indicators, such as percentage of patients cured, to assess progress in achieving targets and objectives.

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## Reporting and Recording system

The adequate care of tuberculosis cases requires that records be kept on each individual patient, with periodic reporting of the results of case-find­ing and of treatment. This is essential to ensure that the patient is correctly treated and that adequate supplies of essential materials are provided. In addition, the information that is routinely collected and reviewed allows problems that may arise with the management of the patients and of the system to be identified. The documents used to record and report the care of the patients should be simple, clear and kept to the absolute minimum that is required for adequate care. The following description provides a guide for the recording of patients as they appear to the health facility, and comprises the minimum number of records and reports necessary to ensure the proper care of the patients.

Table 23: Recording and reporting formats used in the National TB Programme

| S/No. | **M&E format** | **Data requirement** | **Level** | **Responsible** | Frequency of entry |
| --- | --- | --- | --- | --- | --- |
| **1** | TB Suspects register | Records of patients presenting with chronic cough | Health facility | General Health Care staff | Daily |
| **2** | General Laboratory request form that includes the Sputum Examination request section | Results of AFB smear microscopy  Request for DST | Health facility | General Health Care staff | Daily |
| **3** | TB Laboratory register | Results of AFB smear microscopy | Laboratory | Laboratory Scientist or technician | Daily |
| **55a** | TB Treatment Card | Patients treatment records and progress | Health facility | General Health Care staff | Daily |
| **5b** | Childhood TB monitoring card | Child’s treatment records and progress | Health facility | General Health Care staff | Daily |
| **6** | TB appointment Card | Daily patient’s treatment records | Health facility Home | General Health Care staff | Daily |
| **7** | TB referral/ Transfer Form | Patient’s up to date treatment status | Health facility Home | General Health Care staff | Based on need. |
| **8** | TB Treatment Register | Patient’s daily treatment records | Health facility | General Health Care staff | Daily |
| **9** | TB screening Form | Records symptom screening among populations vulnerable to tuberculosis | Facility | General Health Care staff | Daily |
| **10a** | Quarterly Report on TB Intensified Case finding form | Report on suspected TB cases among PLWA/vulnerable groups in a quarter by category. | BMU/National | Regional TB Coordinator | Quarterly, Annual |
| **10b** | Quarterly Report on TB Case finding form | Report on TB cases detected in a quarter by category. | BMU/Regional/National | Regional TB Coordinator | Quarterly, Annual |
| **11** | Quarterly Report on Sputum Conversion form. | Report on treatment outcome of TB cases started on treatment 3-6 months earlier. | BMU/Regional/National | Regional TB Coordinator | Quarterly, Annual |
| **12** | Quarterly TB Cohort Report form. | Report on treatment outcome of TB cases started on treatment 12-15 months earlier. | BMU/Regional/National | Regional TB Coordinator | Quarterly, Annual |
| **13** | TB drugs Returns form. | Quarterly Regional or State drug utilization and request | Health facility/ Regional/National | Pharmacist | Quarterly, Annual |

# ADVOCACY, COMMUNICATION, SOCIAL MOBILISATION

## Introduction

Advocacy, communication, and social mobilization (ACSM) strategies can be most effectively concentrated to help address four key challenges to TB control **at country level**:

* Improving case detection and treatment adherence
* Combating stigma and discrimination
* Empowering people affected by TB
* Mobilizing political commitment and resources for TB.

## Communication as an overarching theme

The term “communication” is overarching one meaning the processes people use to exchange information about TB. All communication activities make use of some form of mediator channel of communication (e.g. mass media, community media, interpersonal communication). While much of the communication effort on TB is concerned with transmitting series of messages to people affected by TB, nearly all communication practitioners stress that to be effective, communication should be understood as a two-way process, with “participation” and “dialogue” as key elements.

***Programme communication to inform and empower***

In the context of TB control, *programme communication* is concerned with informing and creating awareness among the general public or specific populations about TB, and empowering people to take action. Programme communication also works to create an environment through which communities, particularly affected communities, can discuss, debate, organize, and communicate their own perspectives on TB. It is aimed at changing behaviours (such as persuading people with symptoms to seek treatment) but can also be used to catalyze social change(such as supporting community or other communication-for social-change processes that can spark debate, and other processes to shift social mores and barriers to behavior change).

## Advocacy to change political agendas

Advocacy denotes activities designed to place TB control high on the political and development agenda, foster political will, increase financial and other resources on a sustainable basis, and hold authorities accountable to ensure that pledges are fulfilled and results achieved.

*Policy advocacy* includes data and approaches to advocate to senior politicians and administrators about the impact of TB at the national level, and the need for action.

*Programme advocacy* is used at the local, community level to convince opinion leaders about the need for local action.

*Media advocacy* generates support from governments and donors, validates the relevance of a subject, put issues onto the public agenda, and encourage the media to cover TB-related issues regularly and in a responsible manner*.*

## Social mobilization to build partnerships

Social mobilization is the process of bringing together all feasible and practical intersectoral allies to raise awareness of and demand for a particular programme, to assist in the delivery of resources and services and to strengthen community participation for sustainability and self-reliance.

“Allies” include decision - and policy - makers, opinion leaders, nongovernmental organizations (NGOs) such as professional and religious groups, the media, the private sector, communities and individuals. Social mobilization generates dialogue, negotiation and consensus, engaging a range of players in interrelated and complementary efforts, taking into account the needs of people.

To achieve TB control advocacy objectives, the main obstacles to TB control and the tools available for overcoming them should be identified. Some of the constraints in Swaziland are:

* The DOTS strategy is not being implemented
* Financial and human resources are lacking
* Prevalence of MDR TB is increasing
* Prevalence of HIV/AIDS is increasing and directly affecting TB morbidity and transmission of TB infection.

There is a need to identify ways of overcoming these constraints and why do they exist?

## Selection of Advocacy Strategies and Tactics

**According to the WHO[[6]](#footnote-6); there are four priority advocacy strategies. They are:**

* A media strategy
* A publications strategy
* Coalition-building and working with NGO’s
* An insider strategy

Deciding which strategy or which combination of strategies to use should take into account the benefits and risks, the time frame, and the expertise and financial resources needed for effective implementation.

### Media strategy

Media coverage should focus on the country’s most important media (press, radio and television). Tactics might involve:

* Using World TB Day as an opportunity for a media event;
* Holding news conferences
* Conducting media tours to DTDs.
* Developing background materials for the media such as fact sheets
* Purchasing advertising space and placing newspaper supplements
* Using articulate and eloquent TB patients as speakers in media interviews and visits.

### NTP Publications strategy

Activities should include:

* Publishing quality and informative TB programme reports;
* Publishing TB programme brochures including reading materials for the community
* Producing a newsletter
* Disseminating WHO TB reports
* Developing and distributing Information, Education and Communication (IEC) materials for the community and patients

### Coalitions and working with NGOs

**Activities could include:**

* Encourage grassroots participation in TB control efforts
* Involve community organizations
* Coordinate education, communication, training and advisory activities with those of organizations working on related issues such as AIDS, asthma, anti-smoking and diabetes;
* Approach corporations, professional associations and workers unions for political and financial support for TB control;
* Conduct a preparatory World TB Day workshop for NGOs and professional associations;
* Request prestigious personalities from scientific circles and performing arts celebrities to serve as advocates.
* Establish an advocacy steering committee that should include representatives from the Health Education Unit.

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### Insider strategy

The “Insider strategy” refers to making direct contact with the principal “targets” of advocacy activities, particularly politicians, government officials at decision making level.

Activities should include:

* Networking and lobbying
* Arranging meetings, workshops and seminars to reach key people
* Maintaining regular and frequent communication with international cooperation and technical agencies.

## Message Development and Presentation

Messages should take into account the audience, i.e. the key persons for whom they are intended.

**Message content:**

* Ensure that the message is technically sound and defensible;
* Always emphasize the severity of the TB problem and that DOTS is the best solution;
* Provide examples of DOTS successes and demonstrate its advantages;
* Emphasize the threat of MDR TB

**Resource mobilization**

Advocacy implies some budgetary risk. But failure to undertake any advocacy activity will probably mean that the NTP continues to operate at the same or even a lower level of funding.

In order to secure financial resources:

* Assign regular budget funds for advocacy activities;
* Investigate and understand potential donors.

In order to secure human resources:

* Involve those MOHSW departments (e.g. AIDS programme, Health Education) that have expertise in advocacy and related issues;
* Use WHO to guide the programme

## Role of NGOs , Private Sector and communities in TB control and involvement in social mobilisation

The government of Swaziland encourages Public-Private Partnership (PPP) especially in the health sector with the aim of complementing the government efforts to expanding access to quality health care to the population. The guiding principle for the partnership and collaboration is to strengthen ownership, ensure transparency and social responsibility. The involvement of the private sector and NGO’s in TB control activities is very crucial. However, there is need for strong coordination to ensure synergy and complimentarity in implementation of activities. It is necessary to ensure that partners are adequately oriented in the Stop Strategy, follow the national policy with respect to standard case management as well as the NTP information system.

Stakeholders in diagnosis and treatment of TB patients should also be involved in all activities of tuberculosis control, including training, monitoring and evaluation. The main output indicators of the involvement of other partners is the number and proportion of private hospitals, clinics and individual doctors, who notify new cases, implement DOTS and report treatment outcomes in a collaborative agreement with the MOH.

At the community level, Community-based organizations (CBOs) have a significant role to play with respect to:

1. Supporting patients throughout treatment until cure
2. Patient, family and community education
3. Case finding
4. Lobbying for government commitment to TB control
5. Increasing accountability of local health services to the community.

Based on the available information on the key lessons learned from community contribution as documented by by WHO[[7]](#footnote-7), the determinants for success includes:

1. Good collaboration between the general health services, NTP and the community groups;
2. Good education of the TB patients and their family members;
3. Training of community members and the health services staff;
4. A system of regular supervision of community members by NTP staff.

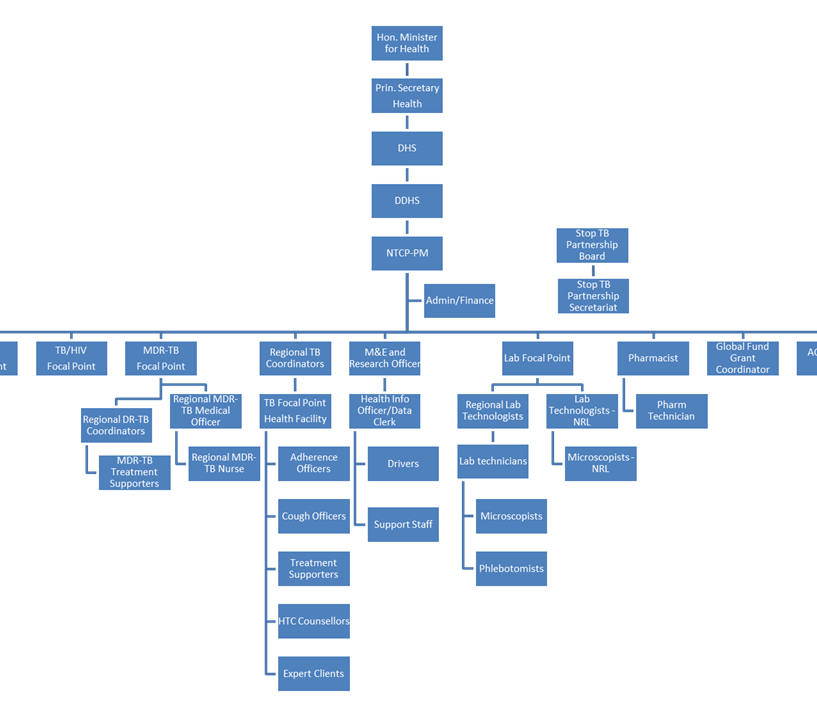
The main challenges identified include: identification of the leadership responsible for managing the change process and of the appropriate community group; maintaining adequate level of community motivation; and ensuring good communication links between the different elements of service provision.

NGOs often play an important role in mobilizing community contribution, as they are usually closer to the community than the formal health care sector. However, regular supervision and monitoring is still required to achieve the desired impact. Before the programme decides to involve the community in TB care, it is necessary to ensure that a system of follow-up is established. Regular monitoring and evaluation of treatment outcomes needs to be conducted. The key areas that communities can contribute in TB care are:

* Direct Observation of Treatment
* Support and motivation of patients
* General support and home visits
* Case detection
* Default tracing
* Increasing community awareness

# ANNEXES

## ANNEX 1: TB Programme Organogram

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## ANNEX 2: Stop TB Partnership Organogram

## ANNEX 3: SPUTUM COLLECTION

Clean containers that are free from paraffin and other waxes or oils should be used for sputum collection. The containers should have an opening that is 2 cm or more across and have at least 50 ml capacity. They should be leak proof and rigid to avoid crushing during transport to the laboratory. An identification label must be placed on the side of the container and should include the *patient’s name number*, the *date of specimen collection*, the *name of the health facility* sending the specimen, and the *test requested*. Fill in the relevant details on the label before the specimen is submitted.

Sputum collection should be conducted in open air and away from other people. The following instructions should be given to the patient in order to obtain sputum of good quality:

* Rinse the mouth before producing the specimen.
* Take two deep breaths, holding the breath for a few seconds after each inhalation and then exhaling slowly.
* Breathe in a third time and forcefully blow the air out.
* Breathe in again and then cough.

Specimens must be sent to the laboratory as soon as possible after collection. If this is not possible, specimens should be refrigerated but not frozen. During transport, specimens should be surrounded by absorbent packing and should be kept cool. Exposure to sunlight should be avoided because mycobacteria are killed by ultraviolet light. For each sputum specimen collected, a laboratory request form should be filled to accompany the specimen.

## ANNEX 4: Prerequisites for implementation of XPERT MTB/Rif

|  |  |
| --- | --- |
| **1. Key prerequisites before country implementation of the Xpert MTB/RIF assay Prerequisite** | |
| **Epidemiological**  **data** | 1. Data available on prevalence of MDR-TB and HIV-associated TB to allow for decision making on **prioritizing** placement of the technology and **optimising** use of Xpert MTB/RIF in high-risk patient groups |
| **Diagnostic policy reform** | 2. Plan to modify existing diagnostic algorithms as part of the NTP strategy to introduce Xpert MTB/RIF testing. |
| **Laboratory network** | 3. Existing capacity and referral network to provide quality assured laboratory services with: **a)** culture and DST to determine resistance to first- and second-line drugs at central level (at least), quality assured through an established link with a Supranational Reference Laboratory; **b)** sputum smear microscopy for TB testing and treatment response monitoring; **c)** culture to monitor response to MDR-TB treatment. |
| **Laboratory workload** | 4. Potential number of samples from high-risk groups for Xpert MTB/RIF testing in the facility where implementation is intended ranges 10-20 a day or 2000-4000 annually, in order to ensure optimal efficiency3 |
| **Infrastructure** | 5. Stable electricity supply in the facilities where implementation is intended or sufficient measures to ensure uninterrupted supply (generator, solar panels, battery/UPS backup, etc.) |
| 6. Secure premises for the equipment to prevent theft of the GeneXpert unit and the computer/laptop. | |
| 7. Adequate storage of cartridges at recommended temperature range (2-28°C). | |
| 8. Appropriate measures to prevent ambient temperature exceeding 30°C in the room where equipment will be installed (e.g. ventilation, air conditioning). | |
| **Bio-safety** | 9. Bio-safety requirements similar to sputum smear microscopy. |
| **Personnel** | 10. 1-2 staff per site with basic computer literacy and knowledge of laboratory registers who can be trained to perform the testing and equipment maintenance. |
| **Treatment capacity** | 11. Sufficient capacity for treatment of identified TB and MDR-TB patients is available and is in line with international recommendations. |
| **Financing** | 12. Secure funding from national budget or donors/partners |
| **Procurement** | 13. Country importation procedures allowing for procurement of both equipment and consumables (regulatory registration or waiver) and exchange of modules for annual calibration. |

## ANNEX 5: Key recommended actions at country level for Xpert MTB/Rif implementation

|  |  |
| --- | --- |
| **2. Key actions necessary at country level for implementation of Xpert MTB/RIF assay Action** | |
| **Policy reform update** | 1. Incorporate Xpert MTB/RIF testing in the NTP diagnostic strategy and algorithms, including identifying placement of Xpert MTB/RIF at the appropriate level of diagnostic network. Identify appropriate pre-test screening strategies where necessary. |
| **Logistics** | 2. Identify adequate premises for the equipment (as per prerequisites 5,6) |
| 3. Allocate storage for cartridges (as per prerequisite 7) | |
| 4. Identify procedure for cartridge disposal (for example, incineration) as part of current laboratory waste disposal plan. | |
| **Procurement** | 5. Register the GeneXpert system and Xpert MTB/RIF assay OR obtain waiver for importation |
| 6. Forecast needs based on expected demand and period of implementation | |
| 7. Calculate first and subsequent orders for the period of implementation | |
| 8. Quantify buffer stock (at least to cover 3 months of expected workload) taking into account the shelf life of cartridges. | |
| 9. Place order for equipment and cartridges to manufacturer directly or certified distributor insisting on preferential pricing where relevant. | |
| Financing | 10. Secure sustainable funding from national budget or donors/partners to ensure continued use of the Xpert MTB/RIF testing. |
| **Training** | 11. Identify and train staff to perform Xpert MTB/RIF assay |
| 12. Train staff to ensure timely referral and/or proper treatment, infection control measures and contact tracing. | |
| **Reporting** | 13. Adapt request and reporting forms to include Xpert MTB/RIF result |
| 14. Develop system for reporting to the clinic on the same day when results are available | |
| 15. Develop system for regular reporting to WHO (quarterly or semi-annual) | |
| **Validation** | 16. Use GLI (Global Laboratory Initiative) validation kit provided by Cepheid after first installation and after each module calibration. Report results to WHO/GLI. |
| **Maintenance** | 17. Send each module for annual calibration or after performing 2,000 tests on the same module. |

## ANNEX 6: BASIC GUIDE TO CXR READING

To evaluate a CXR properly the following needs to be done:

1. Name of the patient and date should be double checked to ensure one is reading the right xray.
2. Locate the right and left sides of the xray
3. Assess the quality of the x-ray by commenting on the exposure – one should be able to see the thoracic vertebrae and vessels behind the heart shadow.
4. Ensure that there is correct positioning, by assessing whether both left and right clavicles and scapulae are symmetrically located i.e. in line with each other.
5. Make sure there is good inspiration – one should see the posterior 5 posterior ribs in the film.
6. Then with a good knowledge of the normal anatomy and bearing in mind that air is black on xray and solid organs, fluid and bones appear white; one proceeds to look at :
   * The heart – the central white shadow, assess it for its size relative to the size of the chest, its shape, as well as its location (most of the heart should be in the left lung field normally).
   * The lungs – on each side of the heart, normally are black on the xray. One should assess them for good inspiration, any abnormal white shadows (infiltrates) bearing in mind that the blood vessels at the hilum appear white as well. One should also assess the angle between the chest wall and the diaphragm, it should be an acute angle, if it is fuzzy or filled with white shadows there may be effusion. If the lung field is too black with no blood vessels visible, there may be the possibility of a lung collapse or no lung at all.
   * The bones – comment on the number of posterior ribs present as it gives an indication of the inspiratory effort, as well as hyperinflation (as in COPD). Then comment on the appearance of the bones themselves i.e. any undue dark lesions (osteolytic lesions) or white lesions (osteoblastic lesions); any fractures present.
   * Trachea and main bronchi for any obstruction or deviation.
   * Soft tissue – breast shadows, axillae and the skin shadow for any masses or fluid filled cavities.
   * The gastric bubble is usually on the left. And also assess for air under the diaphragm, between diaphragm and liver/stomach. Note that the right diaphragm is slightly higher than the left due to the underlying liver.

## ANNEX 7: TUBERCULIN SKIN TEST (TST)[[8]](#footnote-8)

Thetuberculin skin test (TST) is administered to detect the presence of Mycobacterium tuberculosis, the bacterium that causes tuberculosis (TB). It’s sometimes call Mantoux or PPD.

Material needed:

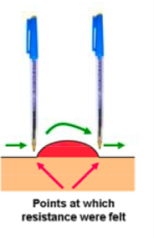
* 1 vial of purified protein derivative (PPD). Once the vial is open, it lasts for one month, so make sure you write on the label date you open the vial and expiry date.
* 1ml syringe
* A pen

Procedure:

1. Use a 1mL syringe to aspirate out 0.1mL of PPD
2. Inject PPD intradermally on the volar surface of the forearm (the bevel is visible under the skin). Position the syringe at a 10-15° to the forearm and insert just below the epidermis (about 2 mm).



1. Remove the needle quickly. Do not massage or use dressing. A well-defined bleb of 6-10mm in diameter should be formed if injected correctly. If the bleb is <6mm, repeat the process 2.5cm from the first site.
2. Mark down the site, date and time of injection, both on the forearm and in patient’s record.
3. After 48 to 72 hours, read the test result by marking down the transverse diameter of the induration, not erythema, by Sokal’s ballpoint method.



1. Measure the largest transverse diameter of induration (palpable, raised, hardened area of swelling) and note down in millimeters (mm). Do not just write test result positive or negative.

**A *positive result* is *5mm of induration in HIV positive children* or *10mm of induration in HIV negative children*.**

## ANNEX 8: FINE NEEDLE ASPIRATION (FNA)

Fine needle aspiration is a very useful way of diagnosing tuberculosis when enlarged lymph nodes are present.FNA is a rapid, safe and cost-effective diagnostic test to diagnose EPTB. It’s recommended especially in children with persistent LN not responding to DS treatment. If pus or necrotic material is aspirated, it should be sent for culture/GenXpert**.**

Material needed:

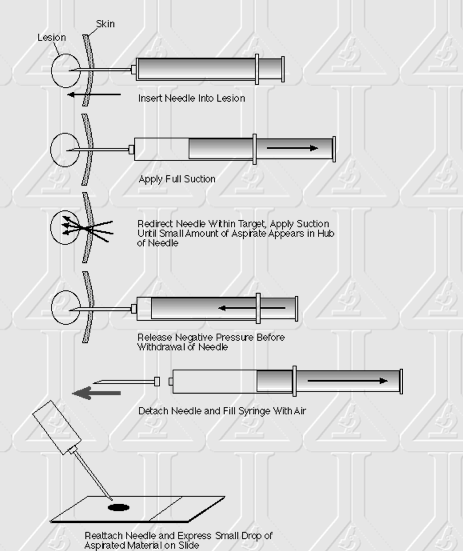
* 10ml syringe
* 22 or 23 gauge needle
* Cytology slides labeled with the patient’s name and surname
* Fixative spray
* Adequate laboratory form
* Specimen cup in case we send for culture.

Perform as follows:

Site preparation

* Wash hands and aseptically put on sterile gloves.
* Sterilize a wide area surround the puncture site with either 0.05 percentchlorhexidine or 10 percentpovidone-iodine solution.
* Allow adequate time for the skin preparation to dry.

Procedure:

1. Immobilize the mass with one hand and insert the needle into the mass
2. Pull back the plunger to create a vacuum of no more than 1 ml
3. Aspirate the mass by moving the needle in a fan-like fashion throughout the mass.
4. When there is material in the hub, release the suction and withdraw the needle
5. Remove the needle from the syringe, pull 8-10ml of air into the barrel, reattach the needle and push the plunger down while placing the tip of the needle in the slide[[9]](#footnote-9)

## ANNEX 9: GASTRIC ASPIRATE PROCEDURE FOR CULTURE OFM. *tuberculosis[[10]](#footnote-10)*

It is a simple procedure to obtain gastric material in order to perform smear and culture/GenXpert for children who can’t produce sputum.

Ideally 3 gastric aspirates should be collected whenever possible for culture (to obtain the highest yield). If the child is admitted, samples can be collected on 3 consecutive days. If the child is not admitted, 1 or 2 aspirates can be done on the same day, at the clinic, with 5-6 hours of difference and repeated the following visit.

Material needed:

* N95 masks
* A sheet to wrap the child
* 8-10 french or larger feeding tube with a 20ml syringe
* Pen/marker
* Sterile water with a 20 ml syringe
* Specimen cup
* Sodium Bicarbonatum 8,5% (IV from the pharmacy) with a needle and a 10ml syringe
* Culture request form

Procedure:

1. Describe the procedure to the family beforehand. Explain the procedure is brief, uncomfortable but not painful. Advise that a negative result does not exclude TB and that the results can take up to 6-8 weeks.
2. Patient should be NPO at least 5-6 hours. If the child is admitted, the procedure should be done in the AM before he starts ambulating.
3. All HCW involved in the procedure are encouraged to wear a N95 mask and good ventilation is advisable in the room.
4. Measure the expected distance from nose to stomach. Strech the tube from the tip of the nose, around the ear and down to the stomach. This is the distance the tube should be inserted into the stomach. Mark the spot on the tube.
5. Immobilize the child with a sheet or with his own upper clothes.
6. Moisten the tube in the child’s mouth to avoid bacteriostatic lubricants.
7. Pass the tube through the child’s nose to the stomach. (If the child does not swallow the tube, take a breath, pull your mask away, puff in the child’s face and replace your mask. This maneuver frequently elicits a swallow-look to make sure that the tube is not coiled in the mouth. Children frequently vomit at this stage, so be prepared to collect any emesis in a specimen cup. It may contain the mucous you’re looking for!)
8. Once the child swallows the tube, pass the tube quickly down into the stomach. Stop when the pen mark on the tube reaches the tip of the nose. *RARELY, the tube will pass into the airway. If the child has any respiratory distress or a muffled cry, the tube is misplaced. Remove the tube immediately*
9. When the tube reaches the pen mark, aspirate the stomach contents with the syringe and place the gastric aspirate in the specimen cup.
10. If less than 5-10cc of mucous returns, re-position the tube and/or the child in order to look for the pool of mucous. While continuing to gently aspirate with the syringe, pass the tube further along several centimeters and try rolling the child up onto his/her side.
11. If still < 5-10cc of gastric contents have been aspirated, instill 20-30cc sterile water into the tube. *BEFORE instilling anything into a nasogastric tube, always check the position on the tube inserting 10cc of air quickly while listening with a stethoscope directly over the stomach. If there is doubt of the positioning, withdraw the tube.*
12. Re-aspirate the contents of the stomach. If still there is no significant yield, try advancing or withdrawing the tube and changing the child’s position in order to find mucous. Continue to aspirate as you withdraw the tube.
13. Place the material obtained in the cup.
14. Insert the same quantity of sodium bicarbonate as gastric material you have, to neutralize the sample.

## Assure sample is well labeled and all forms correctly filled before sending the material to the laboratory.ANNEX 10: INDUCED SPUTUM IN CHILDREN[[11]](#footnote-11)

**Sputum Induction in Children**

**Precautions:** *Only HCW who have been trained in proper, safe technique should perform sputum induction.* Patients must be observed at all times during sputum induction

Sputum induction should not be performed in children with:

* Acute (active) asthma
* Any signs of moderate to severe respiratory distress
* Wheezing
* Abnormal vital signs
* Epistaxis
* Pneumothorax
* Fractured ribs or other chest trauma
* Recent eye surgery

**Infection control:**

Sputum induction produces coughing so it is likely that infectious droplets, if present, will be expelled into the room air. *Sputum induction must be performed in a well ventilated area.* The HCW must wear an N95 respirator throughout the procedure and disposable gloves when handling the sample.

If outside, determine the wind direction before beginning the procedure. The patient must always be located downwind of the HCW. If inside, open doors and windows and use fans to direct airflow away from the HCW

Nebulizers and tubing must be sterilised after every use with (precept or glutaraldehyde) for 15-20 minutes

Material needed:

* N95 respirator for the HCW
* Nebuliser machine
* Sterile hypertonic saline (3-5%)
* Salbutamol and 0.9% NaCl solution (normal saline)
* Suction machine and catheter or Yankaeur
* Pulse oximetry machine (if available)
* Oxygen cylinder
* Goggles
* Small volume nebuliser
* The compressor
* Infra-red light
* Sputum traps (mucous extractor)
* Disinfectant (precept or glutaraldehyde)
* Disposable gloves
* Completed laboratory request form with patient details
* Sterile sputum collection container identified with the patient details and culture form adequately filled

Procedure:

**NPO requirements:** The child should be NPO for 6 hours prior to the procedure. Do not perform sputum induction if the child has eaten within 3 hours prior to the procedure. Medication with a small amount of liquid is acceptable.

**Preparations:**

* Set up area ahead of time to minimize the anxiety level of the child
* Keep syringes and needles out of sight
* Preload the equipment with salbutamol and normal saline
* Keep a suction catheter or Yankaeur nearby in case of vomiting
* Fill out laboratory request forms
* Have the caregiver hold the child during the procedure. If this is not possible, an assistant should hold the child.
* Position the child in the upright or semi-upright position
* Hold infants supine in the feeding position
* Stand or sit where you can clearly observe the child and all of the equipment

**Induction procedure:**

1. Run correct dosage of Salbutamol in normal saline (0.9% NaCl solution) for 3-5 minutes.
2. Add hypertonic saline (3-5% NaCl solution) to the solution and continue nebulisation for at least 10 minutes:
   1. If the child coughs during this time and produces a sputum, you’re done.
   2. If the child does not produce a specimen within 10 minutes, insert the suction catheter, nasopharyngeal airway (NPA), or oropharyngeal airway (OPA) to stimulate cough.
3. When there is adequate sputum in the oronasopharyngeal area, insert the catheter from the sputum trap (either alone or through an airway).
4. Apply vacuum until at least 2 ml of sputum is collected in the sputum trap. Start at 15-20kPa pressure and increase only if needed.
5. Ensure that the sputum collection container is tightly sealed and labeled.

**Stop induction if:**

* Respiratory distress including increased respiratory rate, wheezing, laboured breathing, chest wall retractions, nasal flaring or cyanosis
* Profuse sweating
* Nausea or vomiting
* Light-headedness, dizziness or loss of consciousness

**After induction:**

* Monitor the child for several minutes. If pulse oximetry is available and is below baseline or there are signs of respiratory distress give oxygen and suction excess sputum from the airway.
* Educate the caregiver that coughing may be more frequent within 24 hours of the procedure.
* Assure all samples are labeled and the forms for culture correctly filled.
* Keep samples out of direct sunlight.

In case there is no nebuliser machine available, nasopharyngeal aspirates can be done without nebulisation. In this case, clapping of the patient for 10 minutes is recommended, to facilitate the secretion of the mucous. The rest of the procedure is the same as the same as indicated above.

The committee should meet monthly.

## ANNEX 11: PERFORMINGTHORACENTESIS

INDICATION

Perform thoracentesis on all patients with pleural fluid unless;

- There is a small amount of pleural fluid

or

- Patient has clinically obvious congestive heart failure without atypical features.

Atypical features (implying additional complications to the CHF or an incorrect diagnosis) that would justify a thoracentesis include:

- A unilateral effusion, especially if it is left-sided

- Bilateral effusions that are of disparate sizes

- Pleurisy

- Fever

- Normal cardiac silhouette on chest radiograph

- An effusion that does not resolve with heart failure therapy

- Known chronic kidney failure

CONTRAINDICATION

- Active skin infection at the site of needle insertion

- Patient is actively bleeding or has received anticoagulation

- Very small amount of pleural fluid

MATERIAL

- Lidocaine 1 percent

- Sterile syringe with 25-gauge needle for lidocaine injection

- 50 mL syringe for fluid collection

- Sterile gloves

- Sterile drapes

- Povidone-iodine solution

- Sterile sponges or 4 x 4s for preparing puncture site

- 20 or 22-gauge needle 1.5 inches in length.

PROCEDURE

1. Patient positioning

- Patient should be sitting upright with their arms on a solid surface (such as a table with a pillow on it). If unable to sit, patient can assume a lateral recumbent position.

2. Site selection

The site of needle insertion must meet all of the below criteria:

- One to two interspaces below the level at which breath sounds decrease or disappear on auscultation, percussion becomes dull, and fremitus disappears

- Above the ninth rib, to avoid subdiaphragmatic puncture

- Midway between the spine and the posterior axillary line, because the ribs are easily palpated in this location.

3. Site preparation

- Wash hands and aseptically put on sterile gloves.

- Sterilize a wide area surround the puncture site with either 0.05 percentchlorhexidine or 10 percentpovidone-iodine solution.

- Allow adequate time for the skin preparation to dry.

- Using a 25-gauge needle sterilize the area with local anesthetic . Advance towards the rib, and direct towards the superior edge of the rib , intermittently pull back on the plunger of the syringe as the needle is advanced to make sure you are not hitting a vessel. Pleural fluid return indicates needle is inserted in the pleura. Inject more anesthetic into the border of the rib and the pleural space and remove the needle.

4. Needle insertion and aspiration

Add 1 mL of 1:1000 heparin to a 50 mL syringe . Attach the syringe to a 22-gauge needle. Advance through the anesthetized region until reaching pleural space, trying to passing on the superior edge of the rib. Remove 30 to 50 mL of pleural fluid. Send to the laboratory for cell count, chemistry, AFB and culture, if applicable.

• No fluid return, “dry specimen”, signifies incorrect needle placement, thick pleural fluid, or use of an inappropriately short needle. The needle can be withdrawn and reinserted in a slightly different angle if the patient tolerated the initial dry tap.

• Aspiration of air means the lung was punctured. Obtain a chest x-ray to rule out pneumothorax. Consideration insertion of chest tube if pneumothorax is severe.

• Aspiration of small amount of blood implies the needle was inserted inferior to the effusion.

5. Clean the area with betadine and apply sterile dressing.

COMPLICATIONS

Pneumothorax, infection and empyema, allergic reaction to the anesthetic, liver or spleen puncture, seeding of needle tract with tumor.

## ANNEX 12: PERFORMING LUMBAR PUNCTURE IN ADULTS

INDICATIONS

Non-Urgent diagnosis:Tuberculous meningitis

CONTRAINDICATION

- Patients suspected of having an epidural abscess in the lumbar area.

- Patients with known bleeding disorders

MATERIAL

- Lidocaine 1 percent without epinephrine

- Sterile 3 mL syringe with 25-gauge needle for lidocaine injection

- Four sterile collecting tubes

- Sterile gloves

- Sterile drapes

- Povidone-iodine solution

- Sterile sponges or 4 x 4s for preparing puncture site

- Manometer (typically used in patients older than two years of age)

- 20 or 22-gauge styleted spinal needle.

PROCEDURE

1. Patient positioning

Preferred position is the lateral recumbent. It can also be performed when patient is sitting upright. If in lateral recumbent, instruct the patient to remain in fetal position with the neck, back and limbs held in flexion. The lower lumbar spine should be flexed with the back perfectly perpendicular to the edge of a bed or examining table. The hips and legs should be parallel to each other and perpendicular to the table. Pillows placed under the head and between the knees may improve patient comfort.

2. Site selection

- Locate the highest point of iliac crest bilaterally and confirm by palpation.

- A direct line joining these points passes across 4th lumbar vertebral body.

- Locate the spinous processes of L3, L4 and L5 by palpation.

- Identify the interspaces of L3/L4 and L4/L5. Needle can be inserted in either of these two sites.

3. Site preparation

- Wash hands and aseptically put on sterile gloves.

- Clean the overlying skin using alcohol, and disinfect (e.g. povidone iodine)

- Place a sterile drape with an opening over the lumbar spine.

- Allow adequate time for the skin preparation to dry.

- Anesthetize only the skin and the underlying soft tissue, using anesthetic. Intermittently pull back on the plunger of the syringe as the needle is advanced to make sure you are not hitting a vessel.

4. Needle insertion

Prepare a 20 or 22 gauge spinal needle containing a stylet. The bevel of the needle should be facing up for the patient in the lateral decubitus position and sideways for the patient in the sitting position . Advance the needle slowly, angling slightly toward the head, as if aiming towards the umbilicus.

The stylet can be cautiously removed from time to time as the needle is advanced to look for CSF. A "pop" often is perceived as the needle penetrates the dura and enters the subarachnoid space. Flow of CSF confirms correct insertion of the needle.

5. Fluid collection

Instruct the patient to slowly straighten or extend the legs to allow free flow of CSF within the subarachnoid fluid. Opening pressure can now be measure using a manometer if available. If manometer is not available, use IV tubing attached to the back of the spinal needle and held vertically up in the air. Up to 40 mL of fluid can be removed, however, 8 to 15 mL is the amount most commonly collected in routine LP. Once CSF has been collected, the stylet should be replaced and the needle removed. Clean the area with betadine and apply sterile dressing.

COMPLICATIONS

- Post-LP headache; 10-30% of patients, 24-48 hours post procedure, exacerbated in an upright position and improved in the supine position. Can be associated with nausea, vomiting, dizziness, tinnitus, and visual changes. Treat with paracetamol, fluids and rest.

- Infection;

1. Meningitis, usually due to contaminated instruments or bad technique.

2. Osteomyelitis (rare)

- Bleeding, 1-2% can develop serious bleeding due to thrombocytopenia or clotting factor abnormalities.

- Cerebral herniation; neurologic decline either immediately or within 12 hours of LP

- Minor neurologic symptoms such as radicular pain or numbness

- Late onset of epidermoidtumors of the thecal sac

## ANNEX 13:PERFORMING LUMBAR PUNCTURE IN CHILDREN

INDICATIONS

Urgent diagnosis:Tuberculous meningitis,

CONTRAINDICATION

- Confirmed or suspected increased intracranial pressure (ICP) .

- Patients suspected of having an epidural abscess in the lumbar area.

- Patients with coagulation defects who are actively bleeding, have severe thrombocytopenia (eg, platelet counts <50,000/µL), or an INR >1.4.

MATERIAL

- Lidocaine 1 percent without epinephrine

- EMLA cream only if available

- Sterile 3 mL syringe with 25-gauge needle for lidocaine injection

- Four sterile collecting tubes

- Sterile gloves

- Sterile drapes

- Povidone-iodine solution

- Sterile sponges or 4 x 4s for preparing puncture site

- 22-gauge styleted spinal needle. The following guidelines for the appropriate length needle are based on the child's age (although a longer needle may be necessary for children who are large for their age, particularly for those closer to 12 years):

o Under two years, 1.5 inches (3.75 cm)

o Between 2 and 12 years, 2.5 inches (6.25 cm)

o Over 12 years, 3.5 inches (8.75 cm)

PROCEDURE

1. Patient positioning

The lateral recumbent or the sitting position can be used. The lateral recumbent position can be achieved by the help of an assistant placing one arm around the posterior aspect of the child's neck and the other arm under the child's knees, flexing the neck and drawing knees upward. The child's hips and shoulders should be kept perpendicular to the examining table in order to maintain spinal alignment without rotation. The gluteal crease must be aligned with the spinous processes.

Sitting position is best in children in respiratory distress, particularly infants and small children. Hold the infants in the sitting position by the help of an assistant grasping one of the infant's arms and one of the legs in each hand, while supporting the head to prevent excessive flexion at the neck. Older children should be asked to sit with their legs hanging over the edge of the examining table. They can then be flexed over a pillow with the elbows resting on the knees. An assistant should maintain alignment throughout the procedure (even in a cooperative child).

2. Site selection

- Locate the highest point of iliac crest bilaterally and confirm by palpation.

- A direct line joining these points passes across 4th lumbar vertebral body.

- Aim for the L3-L4 and L4-L5 interspaces accordingly.

3. Site Preparation

Apply EMLA cream if adequate time (30-60 min) is available for the cream to be effective. Otherwise proceed;

- Wash hands and aseptically put on sterile gloves.

- Clean the overlying skin using alcohol, and disinfect using povidone iodine. Clean a large area, including the posterior superior iliac spine.

- Allow adequate time for the skin preparation to dry.

- Place a sterile drape with an opening over the lumbar spine.

- Anesthetize the skin and the underlying soft tissue, using lidocaine. Intermittently pull back on the plunger of the syringe as the needle is advanced to make sure you are not hitting a vessel.

6. Needle insertion

Prepare a 20 or 22 gauge spinal needle containing a stylet. The bevel of the needle should be facing up for the patient in the lateral decubitus position and sideways for the patient in the sitting position . Advance the needle slowly, angling slightly toward the head, as if aiming towards the umbilicus.

The stylet can be cautiously removed from time to time as the needle is advanced to look for CSF. A "pop" often is perceived as the needle penetrates the dura and enters the subarachnoid space. Flow of CSF confirms correct insertion of the needle. Alternatively you can remove the stylet once penetrating the skin. This improves CSF fluid collection in infants.

7. Fluid collection

Slowly straighten the child's legs to increase fluid flow. 8 to 15 mL is the amount most commonly collected in routine LP. Once CSF has been collected, the stylet should be replaced and the needle removed. Clean the area with betadine and apply sterile dressing.

COMPLICATIONS

- Post-LP headache; 18-40% of children.

- Infection;

3. Meningitis, usually due to contaminated instruments or bad technique.

4. Osteomyelitis (rare)

- Bleeding, spinal hematoma

- Cerebral herniation; neurologic decline either immediately or within 12 hours of LP

- Minor neurologic symptoms such as radicular pain or numbness

- Late onset of epidermoidtumors of the thecal sac

## ANNEX 14: INFECTION CONTROL RISK ASSESSMENT TOOL

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **INFECTION CONTROL RISK ASSESSMENT TOOL** | | | | |
| DATE:\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_ | Risk for TB in the setting (0=negligible, 1=Low, 2=High, 3= Very High) | Likelihood of event occurring. 0= not likely, 1=remotely possible, 2=likely, 3= highly likely | Total  = a+b | Assessment  4-6=Very high risk; 2-3= High risk; 1= Low risk; 0=No risk |
| Exposure of HCW to a potentially infectious TB case |  |  |  |  |
| Exposure of other patients to a potentially infectious TB case |  |  |  |  |
| Inadequacy of ventilation |  |  |  |  |
| Duration of exposure to a potentially infectious case |  |  |  |  |
| Exposure of a person living with HIV (PLHIV) to a potentially infectious TB case |  |  |  |  |
| Contamination of the environment with infectious material from a TB case |  |  |  |  |
| Generation of infectious aerosol containing *M. tuberculosis* |  |  |  |  |
| Accumulation of potentially hazardous infectious waste material |  |  |  |  |

## ANNEX 15: HIV TESTING MODELS



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Annex 15 HUMAN RESOURCE DEVELOPMENT

The purpose of DOTS training sufficiently build capacity of programme as well as general health care staff to effectively deliver quality TB care to patients. Detailed planning is crucial if sufficient public and private sector personnel are to be trained effectively and within the time frame needed. Central and Regional staff must be trained in both technical and managerial aspects of TB control to equip them with the necessary skills to adequately support the general health care staff. To this end, a well articulated Human Resource Development (HRD) plan based on the needs at various levels is required. One of the strategies to strengthen HR is through in-service training.

## Planning Issues

The planning of training should cover a number of issues:

* How to organize training activities;
* Who should be trained (i.e. the many different types of staff to be trained and their training needs;
* How many staff to be trained;
* Training methods and materials;
* Selection of trainers and training sites
* The schedule of training activities
* Supporting and maintaining training activities
* Monitoring and evaluation of training activities
* Introducing the revised national policy on TB control into the curricula of laboratory, nursing and other health-related schools.

## 2How to Organize Training

At the central level, an HRD focal point should be identified and assigned the responsibility of preparing the plan for training, coordinating with other programmes and institutions, and evaluation of training activities. The HRD focal point is also responsible for identifying all resources required for the training sites (overhead projectors, slide projectors, flip charts, course and facilitators guides) and for the workshop participants (modules, answer sheets, recording and reporting forms, manuals.

To estimate the cost of training, basic information is needed on:

* Per diem and travel of participants;
* Per diem and travel of facilitators
* Quantity and cost of printed materials, stationery and refreshments

The decision on the staff to be trained should take into account the calibre of staff required to implement the revised strategy. This should include managerial staff, the private sector, CHAL, the leadership of professional health associations, and individual private practitioners who can provide care for TB patients.

Table 24: Analysis of training needs at various levels of the NTP

|  |  |  |
| --- | --- | --- |
| **Level** | **Type of personnel** | **Training Needs** |
| **Central** | TB Central Unit Staff | Basic TB epidemiology. How to plan, provide, support and evaluate the programme, how to coordinate with other programmes and training institutions, assist and supervise the Regionals, establish linkages with NGOs and health institutions and undertake advocacy |
| **Regional** | Regional TB Coordinator | Information about the revised NTP strategy and goals so that s/he can support its implementation.  How to establish DTDs, how to use the reporting and recording system, evaluate quarterly Regional reports, and supervise health centre staff. |
| **Regional hospitals, health centres,**  **Private sector and NGO hospitals** | Doctors, nurses, community health workers | Knowledge and skills regarding how to:   * Identify TB suspects * Collect, handle and transport sputum specimens * Prescribe TB treatment * Provide DOT * Provide health education to patients and families * Register and report data * Examine contacts of infectious cases * Manage TB/HIV/AIDS |

## Monitoring and evaluation of training activities

Training activities should be monitored in terms of quantity and quality. The quantity of training should be guided by training targets, while the quality should be assessed with respect to the corresponding quality of service delivery at the health facility level. In particular, programme managers should monitor:

* The number of health staff of different categories who have been trained as a percentage of the training target for each Regional;
* The number of health centres and laboratories of each category that have sufficient trained staff
* Completion of training activities in relation to the training schedule
* The number of health units that have at least 1 staff member trained in the DOTS strategy.
* The number of staff at health units who are trained in the DOTS strategy.
* The number of laboratories that have at least one technician trained in microscopy.
* The number of doctors in the public sector that have been trained on the DOTS strategy
* The number of private practitioners who are able to provide correct TB diagnosis and treatment.

The immediate assessment of quality of training should be conducted by comparing participants knowledge at the beginning and end of each course through pre and post tests. It should be recognized that the impact of a training course on TB control is limited unless it is reinforced by supervision where performance is evaluated and support provided to ensure optimum quality of care. Howver, evaluation of performance should also take note of the context (logistics, supervision and communication) within the trainees work.

ANNEX 15:SUPPLIES AND LOGISTICS MANAGEMENT

## Rationale

Availability of TB drugs and other supplies is essential for provision of effective TB services on a continual basis, and hence must be procured and distributed in adequate quantities, at the appropriate time. Within the context of TB control, supply and logistics referstothe maintenance of a system that guarantees un-interrupted supply of drugs, laboratory materials and reporting and recording forms.

### Estimating Drug Needs and Preparing Procurement Plan

Before estimating drug requirements, the lead time (length of time between placing an order and receiving it) must be known. If the lead time is 6 months or more, the procurement plans should cover the drug needs for one year plus the reserve stock. Estimates of drug requirements are based on the expected number of cases to be treated vis-à-vis the recommended standard regimen for chemotherapy.

### Estimate the expected number of cases in each treatment category and the drugs needed next quarter

Sufficient stock of drugs should be available in the country for all TB cases expected to started on treatment during a whole year. Drug supply to the Regional level will be carried out on quarterly basis based on need. The number of patients detected in a particular quarter is used to determine the requirements for the next.

The Regional TB Coordinator will determine these numbers from records of current cases and will order drugs to be sent to your health facility to meet the expected need including a provision for buffer stock. The reserve stock allows for possible increases in the number of cases and extra supplies in case of delay in drug delivery. These regimens are packaged in patient drug boxes (patient kits), which makes calculation and accounting easier.

## Logistics for laboratory materials

The health units require an adequate supply of sputum containers to collect and transport sputum specimens to microscopy service. **All health facilities that see TB suspects should have sputum containers.** The laboratories themselves need a regular supply of slides, reagents and other materials to perform the tests required.

### Estimating Laboratory Materials Requirements

The sputum containers and laboratory supplies required for microscopy examinations are estimated on the basis of the expected prevalence of TB among the respiratory symptoms who attend Health Care facilities. Generally, prevalence of smear-positive cases among respiratory symptomatics at health facilities ranges from 5-15%.

A large number of sputum containers are needed to identify and investigate TB suspects and to follow up patients. A shortage of sputum containers can constitute a major barrier to the TB diagnostic process; and must be avoided.

Estimation of the quarterly requirements for sputum containers should be based on the expected number of sputum examinations to be done for diagnosis plus the expected number to be done for follow-up. Estimates can be based on the number of new cases treated in the previous quarter.

**Example methodology for calculating the number of sputum containers needed**

The number of sputum containers needed for diagnosis may be calculated as follows:

* number of new pulmonary sputum smear-positive cases previous quarter
* multiplied by 10 (because on average, 10 TB suspects have been investigated for each new pulmonary sputum smear-positive case detected).
* Multiplied by 3 (because 3 sputum samples are needed from each TB suspect

The number of sputum containers needed for follow up of treatment is calculated as follows:

* number of new sputum smear-positive cases detected in the previous quarter
* multiplied by 6 (3 follow-up examinations of sputum samples each time)
* number of retreatment cases enrolled in the previous quarter;
* multiplied by 6 (3 follow-up examinations of sputum samples each time)
* number of sputum smear negative cases enrolled in the previous quarter;
* multiplied by 2 (one follow-up examination of 2 sputum samples)

The total number of sputum containers to order is calculated as follows:

* number needed for diagnosis, plus
* number needed for follow-up examinations, plus
* 10% for additional investigations, plus
* 20% for reserve stock, minus
* the number of sputum containers in stock at the end of last quarter

The National Reference TB Laboratory is responsible for determining and advising on the specifications for laboratory equipment and supplies.

Suggested specifications for sputum containers are:

* The container mouth should measure at least 50mm to facilitate sputum collection
* The container should have a watertight screw cap permitting full hermetic closure to prevent leakage during transportation
* The container should be made of disposable material (plastic) that can be destroyed easily by burning.
* The container should be made of translucent material so that the level of sputum in the interior can be clearly seen.

## 3 Calculating number of Xpert catridges?



**Swaziland Childhood Tuberculosis Card**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ENROLMENT** | **NAME:**  Gender: Male/Female | **AGE:\_\_\_years\_\_\_\_months**  DOB:\_\_/\_\_/\_\_\_ | | | **TB Registration No:** | | **Other factors:**  Manutrition: Y/N  Nutrition Suppliment: Y/N | | **Identified possible source case**: Y/N  **Other children in contact source case:**  List ages and check if screened: Y/N | |
| **Primary Caregiver Name:**  Relationship to child | **TYPE OF TB(Circle all that apply)**  **PTB EPTB:**  **Smear-pos**  **Smear-neg**  **Smear not done** | | | Regimen (Circle)  **2RHZE 4RH**  **2RHZE 10RH**  Other: | | Rapid test reactive Y/N  CPT Y/N  ART Y/N | |  | |
| **FOLLOW-UP** | **Phase in treatment** | **Start of treatment** | **Month 1** | **Month 2** | **Month** | **Month** | **Month** | **Month** | **Final Review** | **Outcome (Circle)** |
| **VISIT DATE**  **(DD/MM/YY)** |  |  |  |  |  |  |  |  | **Cured**  (onlty relates to sputum-smear)  **Treatment Complete**  **Defaulted**  (treatment interrupted for 2 consecutive months or more  **Died**  (for any reason during the course of treatment)  **Transferred out**  (to another recording and reporting unit)  **Treatment Failure**  (only relates to sputum smear-positive cases) |
| **Weight (kg)** |  |  |  |  |  |  |  |  |
| **Intensive phase**  **List fixed dose combination**  **(eg RHZ 60:30:150 or RHZE (150/75/400/275**)**) with numbers or portions of tablets**  **OR**  **Individual TB drugs with numbers or portions of tablets** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Continuation phase**  **As above** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Any Adverse Effects (specify)** |  |  |  |  |  |  |  |  |
| **Any TB doses missed in past month (Y/N)** |  |  |  |  |  |  |  |  |

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Schaaf HS, Zumla A, (?????year)Tuberculosis: A comprehensive Clinical Reference, 1st edition,

World Health Organization. 2012.WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders. Geneva, WHO

1. Health Centres in general have between 20-60 beds and should have a Public Health Unit (PHU). It is unclear whether they should have a functional operating theatre. There are five HCs in the country (see map). [↑](#footnote-ref-1)
2. Clinic Type A does not have a without maternity unit, while Clinic Type B has a maternity unit. [↑](#footnote-ref-2)
3. WHO Geneva: Laboratory services in TB Control : Culture Part III 1998 [↑](#footnote-ref-3)
4. High lactate (hyperlactatemia) is a potentially serious side effect resulting from mitochondrial toxicity in patients who have been on NRTIs (especially d4T and ddI) for > 4 months. If hyperlactatemia is not recognized early, it will progress to lactic acidosis, which carries a significant risk of mortality. A point-of-care lactate machine should ideally be available in all sites where ART is being made available. Any patient developing symptoms of hyperlactatemia (weight loss, fatigue, nausea, vomiting, abdominal pain, and/or shortness of breath) should have a lactate level checked the same day, and be immediately managed by a trained clinician. [↑](#footnote-ref-4)
5. Report of the meeting of the WHO Global Task Force on XDR-TB, Geneva 9-10 October 2006 [↑](#footnote-ref-5)
6. Tuberculosis Handbook WHO. 1998 [↑](#footnote-ref-6)
7. Community Contribution to TB Care: Practice and Policy. WHO. 2003. [↑](#footnote-ref-7)
8. Carol Yu Centre for Infection; http://www.hku.hk/hkucoi [↑](#footnote-ref-8)
9. Pathology Laboratory of Arkansas [↑](#footnote-ref-9)
10. Francis J. Curry National Tuberculosis Center [↑](#footnote-ref-10)
11. Botswana-Baylor Children’s Clinical Centre of Excellence [↑](#footnote-ref-11)