BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS IN ETHIOPIA

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Dedication

This work is dedicated to all the teachers who nurtured our minds and enlightened us.

Student number: 62121901

D E C L A R A T I O N

I declare that **BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS** is my own work and that all the sources used or quoted have been indicated and duly acknowledged by means of complete references and that this work has not been submitted before for any other degree at any other institution.

Ahmed Reshid Tusho — 11 November 2022

Signature — **Date**

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ABSTRACT

Purpose: The purpose of this study was to develop best practice guidelines to address barriers to treatment completion of patients with drug-resistant tuberculosis (DR-TB) in Ethiopia.

Method: This study utilised a research design that is exploratory, descriptive, and contextual in nature, guided by the convergent concurrent mixed method design. Quantitative data were collected using a pre-tested questionnaire from 487 randomly selected DR-TB patient charts at Hospitals A, B, and C, Ethiopia. Quantitative data were analysed using SPSS version 24 for Windows. The associations between treatment completion and independent variables were assessed by logistic regression.

In-depth interviews with fifteen experienced healthcare providers (HCPs) who have been working with the patients on programmatic management of DR-TB were conducted. Moreover, six focus group discussions (FGDs) were conducted with 42 purposively selected DR-TB patients with a previous history of unsuccessful treatment outcomes and currently on retreatment regimens in Hospitals A, B, C, and D. A group of seven patients comprised each focus group session. A conventional content analysis approach was used, focusing on both the manifest and latent content of the narratives. ATLAS.ti 8 software was used in data coding and sorting.

Findings: Among the 487 study patients included in the quantitative strand, 354 (72.69%) had successful treatment completion. On the other hand, 133 (27.31%) had not completed treatment. Age, registration group, comorbidity, drug susceptibility testing (DST) results, psychotic symptoms, drug-induced hepatitis, renal toxicity,

electrolyte disturbance, and arthritis were factors which had statistically significant association with treatment completion. From the in-depth interviews, three themes and fourteen categories emerged, which captured the views of healthcare providers on DR-TB treatment completion. From the FGDs, five themes and twenty categories emerged on the lived experiences of previously treated DR-TB patients on completion of treatment. This study established a number of barriers to treatment completion for patients with DR-TB in Ethiopia related to clinical Issues, drug-related factors, patient factors, the health system, socio-economic factors, programmatic factors, and provider-related factors. Findings from this study and a systematic review of existing evidence informed the development of best practice guidelines addressing barriers to treatment completion for patients with DR-TB in Ethiopia.

Conclusion: The findings established a wide range of barriers to treatment completion for patients with DR-TB in Ethiopia. Derivied from the findings of the study and informed by a systematic review of existing evidence, best practice guidelines on barriers to treatment completion for patients with DR-TB in Ethiopia were developed.

Key words: barriers, best practice guidelines, clinical issues, drug-resistant tuberculosis, healthcare providers, health system, lived experience, patient factors, socio-economic factors, treatment completion.

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TABLE OF CONTENTS

Page

LIST OF TABLES

LIST OF FIGURES

Abbreviations and Acronyms

ADRs	Adverse drug reactions
AEs	Adverse events
AFB	Acid-fast bacilli
AGREE	Appraisal of Guidelines for Research & Evaluation
AHRI	Armauer Hansen Research Institute
ALERT	All Africa Leprosy, TB and Rehabilitation Training Centre
ART	Antiretroviral therapy
BMI	Body mass index
CDC	US Centres for Disease Control and Prevention
CNS	Central nervous system
CSF	Cerebrospinal fluid
CMI	Cell-mediated immunity
CT	Computerised tomography
DDIs	Drug-drug interactions
DIH	Drug-induced hepatotoxicity
DNA	Deoxyribonucleic acid
DTH	Delayed-type hypersensitivity
DOT	Directly-observed therapy
DR-TB	Drug-resistant tuberculosis
DST	Drug susceptibility testing
ECDC	European Centre for Disease Prevention and Control
ECG	Electrocardiogram
EPTB	Extra-Pulmonary TB
ESAT-6	Mycobacteria protein early secretory antigen-6
FGD	Focus group discussion
GABA	Gamma-aminobutyric acid
GFR	Glomerular filtration rate
GI	Gastrointestinal
GLC	Green Light Committee
HBM	Health Belief Model
HBV	Hepatitis B virus
HCPs	Health care providers

HCV	Hepatitis C virus
HEWs	Health Extension Workers
ICU	Intensive Care Unit
IEC	Information education communication
IFN- γ	Interferon gamma
IHRERC	Institutional Health Research Ethics Review Committee
IL-12	Interluekin-12
iNOS	Inducible nitric oxide synthase
IPD	Inpatient department
IPLS	Integrated Pharmaceutical Logistics System
KCL	Potassium Chloride
LED	Light-emitting diode
LPA	Line probe assay
LTFU	Lost-to-follow-up
MDR-TB	Multidrug-resistant tuberculosis
MODS	Microscopy observed drug susceptibility
MMP9	Matrix metalloproteinase 9
MRI	Magnetic Resonance Imaging
MSF	Médecins Sans Frontières
MTB	Mycobacterium tuberculosis
NAATs	New nucleic acid amplification tests
NADH	Nicotinamide adenine dinucleotide
NGO	Non-governmental organization
NHMRC	National Health and Medical Research Council
NICU	Neonatal Intensive Care Unit
NIAID	The National Institute of Allergy and Infectious Diseases
NRA	Nitrate reductase assay
NTCP	National TB Control Programme
OI	Opportunistic infections
OPD	Outpatient department
PCR	Polymerase chain reaction
pDST	Phenotypic DST
PLHIV	People Living with HIV

PMDT	Programmatic management of drug-resistant TB
POA	Pyrazinoic acid
PrEP	Pre-exposure prophylaxis
RNAs	Ribonucleic acids
RR-TB	Rifampicin-resistant TB
SCC	Short-course chemotherapy
SCD	Sickle cell disease
SDGs	Sustainable Development Goals
SLDs	Second-line drugs
SLI	Second-line injectable
SNPTB	Smear Negative Pulmonary TB
SPSS	Statistical Package for the Social Sciences
TB	Tuberculosis
TDM	Therapeutic drug monitoring
TFC	Treatment follow-up centre
TIC	Treatment initiating centre
TFT	Thyroid function test
TLA	Thin layer agar
T2DM	Type two diabetes mellitus
TNF-α	Tumour necrosis factor-α
TSH	Thyroid-stimulating hormone
UNISA	University of South Africa
WGS	Whole-genome sequencing
WHO	World Health Organisation
WRD	WHO-recommended rapid diagnostic
XDR-TB	Extensively drug resistant tuberculosis

CHAPTER ONE

INTRODUCTION AND BACKGROUND TO THE RESEARCH PROBLEM

1.1 INTRODUCTION

Tuberculosis (TB) has existed for millennia and remains a major global public health problem (WHO 2021b:31). The disease is caused by bacteria of the mycobacterium tuberculosis (MTB) complex and usually affects the lungs, although other organs are equally affected in up to one-third of cases. MTB is an intracellular pathogen that readily survives and replicates in human macrophages (Byng-Maddick & Noursadeghi 2016:1; Jameson, Fauci, Kasper, Hauser, Longo & Loscalzo 2018:1236).

TB has killed more people than any other infectious disease in history. It has claimed over a billion lives in the past two centuries (Paulson 2013:S2). It causes ill-health in millions of people each year and is one of the top ten causes of death worldwide, ranking above HIV/AIDS as an infectious disease (WHO 2018:27; WHO 2021b:1; Sah, Craig & Mandelbaum 2021:12; Masuku, Berhanu, Van Rensburg, Ndjeka, Rosen, Long, Evans & Nichols 2020:3).

The emergence of multidrug-resistant tuberculosis (MDR-TB) has made tuberculosis management more complicated than before. MDR-TB is a variant of TB caused by mycobacterium tuberculosis strain resistant to Rifampicin and Isoniazid (WHO 2021b:10). Drugs used to treat drug resistant tuberculosis (DR-TB) are more expensive, more toxic, and less effective than those used to routinely treat TB, making the treatment of DR-TB complex in a number of ways (Leveri, Lekule, Mollel, Lyamuya & Kilonzo 2019:2; Bhering, Sarubbi Junior, Kritski, Souza, FBA & Duarte 2020:62-63; McNally, de Wildt, Meza & Wiskin 2019:2; Baluku, Nakazibwe, Naloka, Nabwana, Mwanja, Mulwana, Sempiira, Nassozi, Babirye, Namugenyi, Ntambi, Namiiro, Bongomin, Katuramu, Andia-Biraro & Worodria 2021:1; Florman, Hudson & Loveday 2020:1).

Drug resistance is caused by mutations during bacterial proliferation that confer drug resistance with variable frequency even in the absence of anti-TB drugs. Exposure to a single drug or suboptimal drug concentrations provide a selective environment that

favours drug-resistant bacteria and the development of drug resistant tuberculosis (DR-TB). Likewise, failure to complete prescribed therapy contributes significantly in the development of DR-TB. Failure to comply with therapy or to metabolize drugs effectively could result in secondary resistance. Such resistance develops later in the course of treatment in a patient who initially has a sensitive strain (CDC 2021:19; Mesfin, Beyene, Tesfaye, Admasu, Addise, Amare, Dagne, Yaregal, Tesfaye & Tessema 2018:2).

1.2 BACKGROUND

Drug-resistant tuberculosis (DR-TB) is a major threat to the global efforts designed to control TB. According to the 2020 Global TB Report, in 2019, the World Health Organisation (WHO) estimated that 465,000 people developed rifampicin resistant TB (RR-TB) out of which 78% were MDR-TB (WHO 2020b:13). Likewise, according to the 2019 Global TB Report, in 2018, WHO estimated that there were approximately half a million new cases of rifampicin-resistant TB (of which 78% had multidrug-resistant TB) (WHO 2019b:27). Similarly in the 2018 Global TB Report, worldwide in 2017, there were 558 000 people who developed TB that was resistant to rifampicin and of these, 82% had MDR-TB (WHO 2018:27).

Patients on DR-TB treatment regimens need to be monitored for treatment response or failure and for their safety, using reasonable schedules of relevant clinical and laboratory testing. Response to treatment and toxicity is monitored through regular history taking, physical examination, chest radiography, special tests such as audiometry, visual acuity tests, electrocardiography and laboratory monitoring (WHO 2019a:34).

Ethiopia committed to the goal of ending the TB epidemic by 2030, primarily through its endorsement of End TB Strategy at the World Health Assembly in May 2014 and its adoption of the Sustainable Development Goals (SDGs) in September 2015. Specific targets for 2030 set in the End TB Strategy are a 90% reduction in the absolute number of TB deaths and an 80% reduction in TB incidence, compared to the levels in 2015. This is only feasible if all those with TB are promptly diagnosed and effectively treated and patient-centred care is in place, backed by a supportive health care system (WHO 2018:1;WHO 2016a:55; Sah et al 2021:12-13; WHO 2022b:3).

The first End TB Strategy milestones for reduction in TB disease burden were a 35% reduction in the total number of TB deaths and a 20% reduction in the TB incidence rate, compared with levels in 2015. In this regard, globally, milestones for reducing the TB disease burden have not yet been reached, although there are some success stories (WHO 2022b:16).

Globally, the reduction in the total number of TB deaths between 2015 and 2021 was 5.9%, about one sixth of the way to the milestone of 35%. The WHO African Region is now closest to reaching the first milestone, with a 26% reduction between 2015 and 2021. By 2021, six high TB burden countries had reached or passed the first milestone of a 35% reduction in TB deaths compared with 2015 (Bangladesh, Kenya, Mozambique, Uganda, the United Republic of Tanzania, and Zambia). A seventh high TB burden country, Ethiopia, was very close to doing so, with a reduction of 34%. (WHO 2022b:16–18).

Globally, the cumulative reduction in the TB incidence rate from 2015 to 2021 was 10%, exactly halfway to the first (2020) milestone of 20%. However, there is a success story in the WHO African Region in 2021, where the 2020 milestone of the End TB Strategy has been passed with a reduction of 22% since 2015 (WHO 2022b:18).

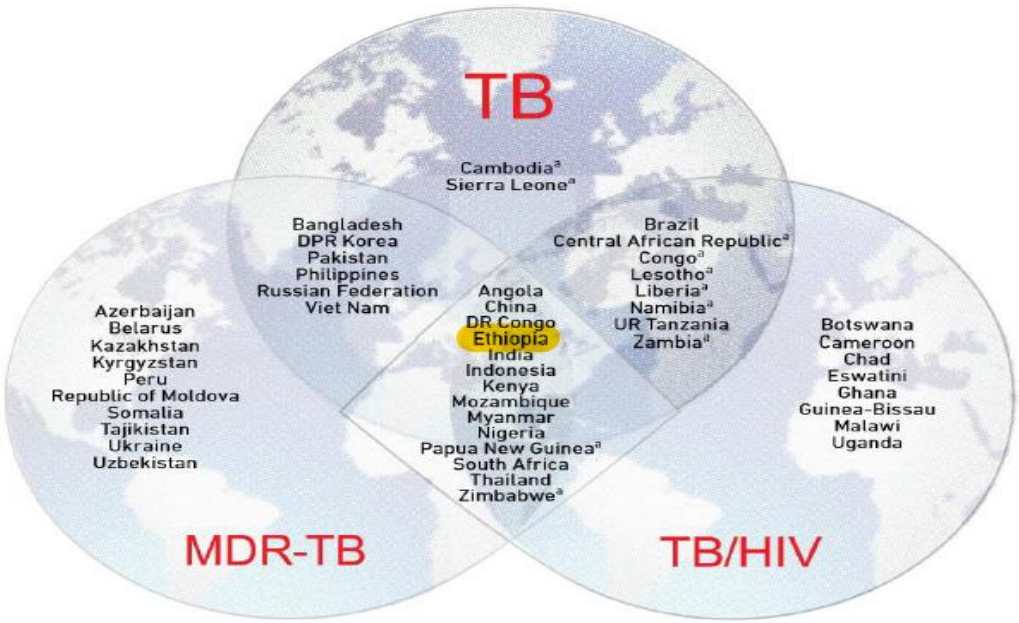


Figure 1.1 Countries in the three high-burden country lists for TB, TB/HIV and MDR-TB being used by WHO during the period 2016–2020, and their areas of overlap, (WHO 2018:24; WHO 2019b:3).

Ethiopia is one of the 14 countries overlapping in all three lists, until it transitioned out of the list of 30 high MDR/RR-TB burden countries in 2021 (WHO 2021b: 35).

1.3 STATEMENT OF THE RESEARCH PROBLEM

Treatment of DR-TB is substantially more complex, costlier, and less effective than standard therapy, typically requiring a higher number of drugs, including injectables and a longer treatment duration than that of drug-susceptible cases. DR-TB can be incapacitating and life threatening (WHO 2016c:1; Baluku et al 2021:1). Moreover, TB strains with drug resistance are more difficult to treat than drug-susceptible ones and such resistance threatens global progress towards the targets set by the END TB strategy of the WHO (WHO 2019a:8).

Drug-susceptible tuberculosis programmatic management can be executed with fairly simple health care infrastructure, but with the DR-TB, this course is more complex. In the first place, a high level of human resources is needed to diagnose and treat DR-TB patients. The accompanying longer duration of daily treatment and work should be extended. Moreover, the drugs are quite toxic and people develop intolerance quickly. Even in countries with a successful tradition of tuberculosis control programmes such as those in the WHO's Western Pacific Region, the fight against multi-drug resistant tuberculosis confronts vast challenges (Leveri, Lekule, Mollel, Lyamuya & Kilonzo 2019:2; Bhering, Sarubbi Junior, Kritski, Souza & Duarte 2020:62-63; McNally, de Wildt, Meza & Wiskin 2019:2).

The large number of pills, the side-effects of treatment, and the need for daily injections and routine long-term hospitalisation place great demands on patients and healthcare systems. As a result, there has been a record 20% of patients who consistently discontinue treatment early in many facilities, and up to 52% in some facilities (Cox, Furin, Mitnick, Daniels, Cox & Goemaere 2015:492; Jakasania, Shringarpure, Kapadia, Sharma, Mehta, Prajapati & Kathirvel 2020:2; Khachatryan, Grigoryan, Dadu, Kumar, Akopyan, Dumchev, Harutyunyan & Matteelli 2021:5). Furthermore, food insecurity, access to health care and stigma contribute to treatment non-adherence (Wingfield, Tovar, Huff, Boccia, Montoya, Ramos, Datta, Saunders, Lewis, Gilman & Evans 2017:275; Jakasania et al 2020:8).

According to the Global TB Report 2022, globally, the latest treatment outcome data show treatment success rates of 60% for MDR/TB (2019 cohort). Similarly, the 2022 Global TB Report shows the treatment success rate for MDR/RR-TB in Ethiopia was 68% in the 2019 cohort. To clarify, the proportion of MDR/RR-TB patients in the 2019 cohort who successfully completed treatment (that is, cured or treatment completed) was 68% in Ethiopia. Furthermore, according to the 2021 Global TB Report, the treatment success rate for MDR/RR-TB in Ethiopia was 70% in the 2018 cohort (WHO 2021b:19; WHO 2022b:44).

Adherence to TB treatment is an essential element in TB control programmes, and poor adherence is an extreme risk. Non-adherence to therapy can cause relapse, continued transmission and the increase of extensive drug resistance. Previous studies indicate that a number of variables may contribute to patient adherence, including awareness about TB and its management, socio-economic variables such as age, literacy, occupation, change of residential place; and behavioural factors including perceived barriers about TB treatment, beliefs about TB treatment, perceived stigma, perception about disease and its treatment, substance abuse and social support (Azizi, Karimy & Salahshour 2018:706-707; Tola, Garmaroudi, Shojaeizadeh, Tola, Yekaninejad, Ejeta, Kebede & Kassa 2017:448,455).

Further, when it comes to DR-TB, anecdotal evidence shows that treatment interruption and non-adherence to treatment makes patients more susceptible to TB. There is, therefore, a dire need for further exploration of the variables related to treatment completion. WHO (2019:34) indicates that treatment interruption contributes to decreased treatment success.

TB treatment success rate (for drug-susceptible and drug resistant TB combined) is one of top 10 indicators set for monitoring the implementation of the End TB Strategy at global and national levels, and this target level of $\geq$ 90% is for 2025. This study contends that it is critical time to embark on strategies to improve treatment completion of DR-TB treatment in general (WHO 2018:14).

A review of research on DR-TB treatment completion shows that despite the importance of treatment completion to the success of therapy in patients with DR-TB, little is known about barriers, enablers and factors related to treatment completion in Ethiopian patients. In this regard, a good understanding of the views and experiences

of previously treated patients and experts on barriers and enablers of treatment completion, including the identification of factors associated with treatment completion, are crucial to improving the treatment success of DR-TB.

In addition, despite programmatic management of DR-TB implementation in Ethiopia, there are gaps in achieving the objectives of treatment success. The treatment success rates in the country have shown little improvement over the years. For instance, according to the Global TB Reports, treatment success rates for MDR/RR-TB in Ethiopia were 72% in the 2016 cohort, 75% in the 2017 cohort, 70% in the 2018 cohort, and 68% in the 2019 cohort (WHO 2019b:105; WHO 2020b:104; WHO 2021b:19; WHO 2022b:44).

Barriers to DR-TB treatment completion seem to be unaddressed in the programmatic management of DR-TB, and not much is known about the experiences of previously treated DR-TB patients as well as the views of HCPs practising on DR-TB regarding barriers to treatment completion in Ethiopia. Furthermore, there appears to be no specific guideline that would be used to address barriers to treatment completion and improve treatment success in the country. Hence this study, via the Health Belief Model (HBM), strives to identify views and experiences of previously treated DR-TB patients and experts treating DR-TB to establish such barriers and enablers of DR-TB treatment completion. The study equally strives to determine factors associated with DR-TB treatment completion in Ethiopia.

1.4 RESEARCH AIM

The purpose of this study is to develop best practice guidelines for treatment completion of patients with drug resistant tuberculosis in Ethiopia.

1.5 RESEARCH OBJECTIVES

1.5.1 Qualitative strand

The objectives of this study are designed to:

- Describe the views of experts managing DR-TB patients on treatment completion.
- Describe the experiences of previously treated DR-TB patients on treatment completion.

1.5.2 Quantitative strand

The objective in this quantitative strand is designed to:

- Determine factors associated with treatment completion of patients on DR-TB treatment.

1.5.3 Mixed

In the mixed method strand, the objective is designed to:

- Explain factors associated with the treatment completion with findings from the qualitative strand.

1.5.4 Best practice guidelines

- Develop best practice guidelines aimed at addressing barriers to treatment completion for patients with DR-TB in Ethiopia.

1.6 RESEARCH QUESTIONS

1.6.1 Qualitative strand

- What are the views of experts treating DR-TB patients on treatment completion?
- What are the experiences of previously treated patients on treatment completion?

1.6.2 Quantitative strand

- What are the factors associated with DR-TB treatment completion?

1.6.2 Mixed

- In what ways do qualitative interviews with patients and experts serve to explain factors associated with treatment completion?

1.7 THEORETICAL FOUNDATIONS OF THE STUDY

1.7.1 Research paradigm

Babbie (2021:29) describes a paradigm as a frame of reference through which to observe and understand a phenomenon. Paradigms are neither true nor false; as ways of looking at a research conundrum, they are only more or less useful. Each paradigm offers a different way of looking at human and social life. Each makes its own assumptions about the nature of social reality. Each opens up new understandings, suggest different theories, and inspire different research strategies (Babbie 2021:30;

Leavy 2017:12). A paradigm is a general organising framework for theory and research that includes basic assumptions, models of quality research, and methods for seeking answers to the conundrum (Neuman 2014:85).

Paradigms guide all research activity. In the execution of the current study, pragmatism was utilised. Pragmatism arises from actions, situations, and consequences rather than from antecedent conditions (as in post-positivism). It is about applications - what works - and solutions to problems. Instead of focusing on methods, researchers emphasise the research problem and use all available approaches to understand the problem (Creswell 2014:39).

Likewise, a pragmatic approach allows the possibility of choosing the appropriate research methods from the wide range of qualitative and/or quantitative methods, and this pluralism is a strength of pragmatism that has several advantages for social justice research. It sets an inclusive framework of inquiry that supports interdisciplinary and cooperative research about social injustices (Kaushik & Walsh 2019:12).

The elements for each worldview differ, and they are reflected in different philosophical assumptions, such as ontology, epistemology, axiology, methodology, and rhetoric (Creswell & Plano Clark 2018:37).

Ontology deals with what is real and refers to the nature of reality when researchers conduct their inquiry (Creswell & Plano Clark 2018:37; Leavy 2017:12). Epistemology refers to how we gain knowledge of what we know (what is the relationship between the researcher and the researched?). Pragmatists aim at practicality (for example, researchers collect data by “what works” to address the research question). Researchers may focus on impartiality (for example, researchers objectively collect data through instruments) and focus on closeness (for example, researchers visit participants at their sites to collect data) (Creswell & Plano Clark 2018:38; Leavy 2017:12). In this study, the researcher collected data employing mixed methods which best address the research questions and used inductive and deductive reasoning. The quantitative data determined factors associated with treatment completion of patients on DR-TB treatment whereas the qualitative data described the views of experts and experiences of the previously treated DR-TB patients on treatment completion.

Axiology refers to the role of values in research. Pragmatists look at multiple stances (for example, researchers include both biased and unbiased perspectives according to Creswell & Plano Clark (2018:38).

Methodology refers to the processes of research. Pragmatists combine, for example, both quantitative and qualitative data (Creswell & Plano Clark 2018:38; Leavy 2017:16).

1.7.2 Theoretical framework

Polit and Beck (2017:119) note that a theoretical framework is the overall conceptual underpinning of a study based on a theory. The HBM model used in this study assumes that health-seeking behaviour is influenced by an individual's perception of the threat of a health problem and the value attached to actions aimed at reducing that specific threat. The major components of the HBM include perceived susceptibility, perceived severity, perceived benefits and costs, motivation, and enabling or modifying factors. Perceived susceptibility is a person's perception that a health problem is personally relevant or that a diagnosis is correct. Even when one recognises personal susceptibility, action does not occur unless the individual perceives the severity to be high enough to have grim implications. Perceived benefits are the patients' beliefs that a given treatment will cure the illness or help prevent it, and perceived barriers include the complexity, duration, and accessibility of the treatment (Polit & Beck 2017:124).

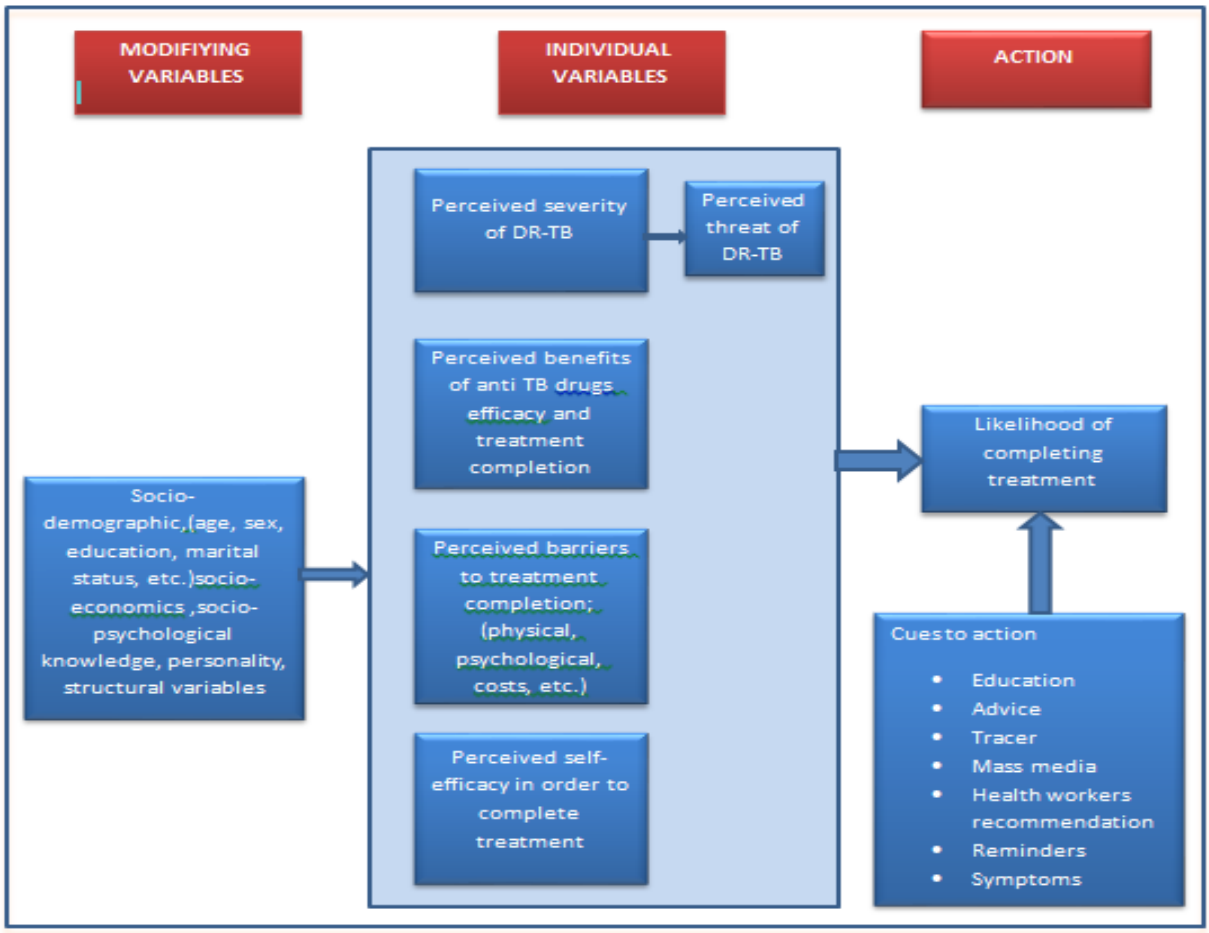


Figure 1.2 Theoretical framework, adapted from, Alemayehu (2015:10) and Glanz, Rimer and Lewis (2008:52).

1.8 SIGNIFICANCE OF THE STUDY

The knowledge generated from this study has potential applications for clinical practice and programmatic management of MDR-TB. It contributes to the provision of standard of care for patients. This study also benefits the DR-TB patients by proffering advice on the possible best practice guidelines in addressing barriers to treatment completion of drug resistant tuberculosis. Treatment completion contributes significantly to the alleviation of economic, social, psychological and physical suffering related to the disease.

The health care leadership and programme managers could focus on the contributions of this study to apply its recommendations in tangible practices that could reach every patient and consolidate the national programme by including practical problem-solving

decisions at the national level. Further, the findings of this study could serve as background research material and literature to other researchers in the field.

1.9 DEFINITION OF TERMS

Treatment completed: This is treatment completed according to national recommendation without evidence of failure but with no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

Cured is defined as treatment completed according to national recommendation without evidence of failure and three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

Treatment failed: Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of:

- lack of conversion by the end of the intensive phase, or
- bacteriological reversion in the continuation phase after conversion to negative after intensive phase, or
- evidence of additional acquired resistance to fluoroquinolones or second line injectable drugs, or
- Adverse drug reactions.

Lost-to-follow-up (LTFU): A patient who has been on treatment for at least four weeks and whose treatment was interrupted for eight or more consecutive weeks.

Died: A patient who dies from any reason during the course of TB treatment.

Not Evaluated: A TB patient for whom no treatment outcome is assigned.

MDR-TB is defined as resistance to at least isoniazid and rifampicin, the two most powerful first-line anti-TB medicines.

RR-TB is defined as TB resistant to rifampicin. WHO recommends an MDR-TB treatment regimen for patients with RR-TB.

Pre-XDR-TB is TB that is resistant to rifampicin and any fluoroquinolone.

XDR-TB is defined as TB that is resistant to rifampicin, plus any fluoroquinolone, plus at least one of the drugs bedaquiline and linezolid.

Best practice is a technique that, through experience and research, has proven to lead to a desired result. A commitment to using the best practices in any field is a commitment to using all the knowledge and technology at one's disposal to ensure success. The term is used frequently in the fields of healthcare, government administration, the education system, project management, hardware and software product development.

1.10 RESEARCH METHODS AND DESIGN

1.10.1 Research design

Nieswiadomy and Bailey (2018:63) state that a research design is a comprehensive plan for conducting an investigation that stretches from the initial research question through the methods of data analysis, interpretation, and reporting. Most narrowly, a design means a method of data collection, such as an interview, survey, or experiment.

1.10.1.1 Mixed methods research.

A methodological trend that has gained momentum is the planned integration of qualitative and quantitative data within single studies (Polit & Beck 2017:577). According to these researchers, many areas of inquiry are enriched through the judicious triangulation of qualitative and quantitative data (Polit & Beck 2017:578). The advantages of mixed methods include complementarity, practicality, incrementality and enhanced validity (Polit & Beck 2017:578). By using mixed methods, this study avoids the limitations of a single approach and, supported by complementary types of data, it is more confident about the validity of results (Polit & Beck 2017: 578).

This study used the convergent concurrent (parallel) design. As stated by Polit and Beck (2017:584), the purpose of the convergent design (sometimes called a triangulation design) is to obtain different, but complementary data about the central phenomenon under study - that is, to triangulate data sources. In this design, qualitative and quantitative data are collected simultaneously and with equal priority. The goal is to converge on "the truth" about a problem or phenomenon. The

researcher's job is to link the two data sets, often at the interpretation stage of the project.

1.10.2 Research Methods

Research Methods are the techniques researchers use to structure a study, gather and analyse information relevant to generating answers to the research question (Polit & Beck 2017:10).

1.10.2.1 Population of the study

One of the many definitions of population is that it is the entire aggregation of cases in which a researcher is interested (Nieswiadomy & Bailey 2018:137; Hissong, Lape & Bailey 2015:47). The population for a study is composed of two groups: the target population and the accessible population, or study population (Nieswiadomy & Bailey 2018:170).

The target population is the entire group of people or objects to which the researcher wishes to generalize the findings of a study. The target population consists of people that meet the designated set of criteria of interest to the researcher (Nieswiadomy & Bailey 2018:170). The target population for the quantitative strand was patients diagnosed with DR-TB and registered for treatment between July 2010 and September 2016 at treatment-initiating hospitals in Ethiopia. Moreover, the target population for the qualitative strand was previously treated DR-TB patients and healthcare providers working on the clinical and programmatic management of DR-TB in treatment initiating hospitals in Ethiopia.

The study population, or accessible population, is the portion to which researchers have reasonable access (Gray, Grove & Sutherland 2017:329). The study population is the aggregate of cases that conform to set criteria and that are accessible for a study (Polit & Beck 2017:249). The study population for the quantitative strand was patients diagnosed with DR-TB and registered for treatment between July 2010 and September 2016 at selected Hospitals A, B, and C. In turn, the study population for the qualitative strand were previously treated DR-TB patients and healthcare providers working on the clinical and programmatic management of DR-TB at selected treatment initiating Hospitals A, B, C, and D.

1.10.2.2 Setting of the study

Study setting is the physical location and context in which data collection takes place in a study (Polit & Beck 2017:744). The study settings were DR-TB treatment initiating hospitals in Ethiopia, hospitals A, B, C, and D.

1.10.2.3 Sample and sampling methods

1.10.2.3.1 Sampling

Sampling is the process of selecting cases to represent an entire population, to permit inferences about the population. A sample is a subset of population elements, which are the most basic units about which data are collected (Polit & Beck 2017:250). When a sample is chosen properly, the researcher is able to make claims about the population based on the data from the sample alone. The results of the sample are then used to estimate the characteristics of the entire population (Nieswiadomy & Bailey 2018:170).

Samples are chosen through two types of sampling procedures: probability and nonprobability. Probability sampling involves the use of a random selection process to obtain a sample from members of a population. The goal of probability sampling is to obtain representative elements of populations. There are four types of random sampling procedures: simple, stratified, multistage cluster, and systematic (Nieswiadomy & Bailey 2018:171; Polit & Beck 2017:251).

Samples are sometimes selected in multiple phases, in what is called multistage cluster sampling. In the first stage, large units or broad groups (clusters), such as hospitals, are selected. Then, in the next stage, within the selected sites, individuals are sampled. In staged sampling, it is possible to combine probability and nonprobability sampling. For example, the first stage can involve the deliberate (nonrandom) selection of study sites. Then, people within the selected sites can be selected through random procedures (Polit & Beck 2017:251).

In nonprobability samples, elements are selected by non-random methods. (Nieswiadomy & Bailey 2018:175; Polit & Beck 2017:251,252). Samples may be chosen from available groups of subjects by several different methods, including convenience, quota, and purposive (Nieswiadomy & Bailey 2018:175).

Purposive sampling uses researchers' knowledge about the population to make selections. Researchers might decide purposely to select people who are judged to be particularly knowledgeable about the issues under study. Researchers select participants based on personal judgment about which ones will be most informative (Polit & Beck 2017:251,252,741).

- **For quantitative strand:**

In the first stage of multistage sampling, Hospitals A, B, and C were selected based on their DR-TB treatment service duration and patient numbers. Treatment-initiating hospitals that started DR-TB treatment services in 2010 and had been giving the services at the time of the data collection period were selected.

In the second stage of multistage sampling, systematic sampling was employed to select samples randomly. At the time of data collection, a total of 1885 patients with DR-TB had been registered in the DR-TB registers between July 1, 2010 and September 30, 2016 at selected treatment initiating hospitals A, B, and C. Accordingly, a sampling frame was developed by using the list of patients from DR-TB registers.

Systematic sampling is the selection of every *k*th case from a list. By dividing the population size by the desired sample size, the researcher establishes the sampling interval, which is the standard distance between the selected elements (Polit & Beck 2017:722).

The first step was to obtain a list of the total population (N) which was 1885. Then, the sample size (n) was determined, which was 501 (see Table 1.1). Next, the sampling interval width (*k*) was determined by N/n. Hence, the sampling interval was:

k = 1885/501 = 3.8 (4, rounded to the nearest whole number). Thus, every fourth element of the population list was selected for the sample.

Within the first sampling interval, the random starting point, or the first sample, was generated by reading the table of random numbers. After selecting the first sample, a fixed interval of four was used to identify successive study elements to be included in the study.

- **For qualitative strand:**

Purposive sampling: This is a method in which the researcher selects participants based on personal judgment about which ones are the most informative (Polit & Beck 2017:251,741). Researchers draw on their experience, ingenuity, and/or previous research to intentionally obtain units of analysis so that the sample they obtain may be regarded as representative of the relevant population (Nieswiadomy & Bailey 2018:177). Purposive sampling was used to recruit DR-TB patients to take part in the focus group discussions and to select HCPs working in the clinical and programmatic management of DR-TB patients to participate in the in-depth interviews.

1.10.2.3.2 Eligibility criteria or inclusion criteria:

The criteria designating the specific attributes of the target population by which people are selected for inclusion in a study comprise the eligibility criteria (Polit & Beck 2017: 250,727).

- Patients who were diagnosed with DR-TB and registered for treatment between July, 2010 and Sep, 2016. All study hospitals had already started DR-TB treatment service by 2010 and patients registered in 2016 had finished treatment of 24 months by then (Chart review).
- Healthcare providers working in the clinical and programmatic management of DR-TB patients at least for two years (In-depth interview).
- Participants provided informed consent to engage in the study (FGD, In-depth interview)
- Participants were 18 years and above (FGD, In-depth interview).

1.10.2.3.3 Exclusion criteria:

The criteria specifying characteristics that a target sample does not have (Polit & Beck 2017:250,728). This study excluded all:

- Patients who discontinued treatment within one month of beginning therapy (Chart review).
- Patients who died within one month of beginning therapy (Chart review).

- Patients who commenced treatment for the purposes of this study rather than routine programmatic treatment (Chart review).
- Not willing to give informed consent to participate in the study (FGD, In-depth interview).
- Younger than 18 years (FGD, In-depth interview).
- HCPs working in the clinical and programmatic management of DR-TB for less than two years (In-depth interview).

1.10.2.4 Sample size determination for quantitative.

The sample size was determined based on the following formula:

Sample size (n) = $(z\ (\alpha/2)^2 * p(1-p)/d^2 * 1.5$

Where p is 68% Ethiopia treatment success rate for DR-TB cases who started on treatment in 2013 (WHO, 2016a:79), 0.05 error allowance (d), 1.96 two-sided critical value for 95% confidence level (z), 0.05 level of satisfaction significance (α) and 1.5 for design effect compensation.

Therefore, sample size (n) = $(z\ (\alpha/2)^2 * p(1-p)/d^2 * 1.5$

$$= (1.96)^2 * 0.68(0.32)/ (0.05)^2 * 1.5 = 501$$

Then this calculated sample size was allotted to the three selected hospitals using probability proportional to size based on the number of DR-TB patients on DR-TB treatment registers.

Table 1.1: Calculated sample size for each hospital

Hospitals	**Number of patients**	**Sample allocated**
Hospital A	1188	316
Hospital B	549	146
Hospital C	148	39
Total	**1885**	**501**

1.10.2.5 Data Collection Methods and Procedures

Yin (2016:55) defines data collection as a means of gathering required information in detail from different sources. Creswell (2014:269) explains the key idea with convergent parallel mixed method design is to collect both forms of data using the same or parallel variables, constructs, or concepts. Polit and Beck (2017:175) define data collection instrument as the formal written document used to collect and record information, such as a questionnaire when structured methods are used and when unstructured methods are used, there is typically no formal instrument, but there may be a list of the types of information needed.

For the quantitative strand, the quantitative data were collected using pre-tested questionnaire (Annexure G) from unit DR-TB registers and patient charts. For the qualitative strand, data collection tools were focus group discussions guide for patients (Annexure I) and interview guide for healthcare providers (Annexure J). In both focus groups and in-depth interviews, open ended probing questions were utilized to probe the discussions.

1.10.2.5.1 Focus-Group Interviews

Pioneered by Robert K. Merton and others in the 1940s, focused group interviews are especially appropriate when the topic under study deals with interaction in groups (Yin 2016:149; Vogt, Gardner & Haeffele 2012:41). As with other types of interviews, the format allows the researcher the flexibility to explore unanticipated issues as they arise in the discussion. The results have high “face validity”: because the method is readily understood, the findings appear believable. Furthermore, the cost of focus-group interviews is relatively low, they provide quick results, and they can increase the sample size of qualitative studies by permitting more people to be interviewed at one time (Polit & Beck 2017:512; Nieswiadomy & Bailey 2018:71).

Focus group interviews were conducted with 42 purposively selected DR-TB patients with failed previous treatment or treatment interruption or lost to follow up and currently on retreatment regimen in Hospitals A, B, C, and D. A group of seven patients was assembled for a discussion in each focus group session. A total of six FGD sessions were conducted. The FDGs were conducted at weekends for convenience of the participants.

1.10.2.5.2 In-Depth Interviewing

Leavy (2017:5) and Punch (2014:144) recommend interviewing as the leading data collection tool in qualitative research and as a good way of accessing people's perceptions, meanings, definitions of situations and constructions of reality. The researcher explores a few general topics to help identify and clarify the participant's views but otherwise respects the way the participant frames and structures the responses. This method, in fact, is based on an assumption fundamental to qualitative research: the participant's perspective on the phenomena of interest should unfold as the participant views it (the emic perspective), not as the researcher views it (the etic perspective) (Polit & Beck 2017:468; Yin 2016:143).

In-depth interviewing with health care providers in the above hospitals was conducted. The interviews took place in private offices at their respective institutions. A convenient time was selected by the participants to minimize interruption in their work responsibilities. Totally, fifteen experienced HCPs including senior internal medicine specialist physicians, general practitioner physicians, health officers, and nurses working in patient and programmatic management of DR-TB participated in the interview.

1.10.2.5.3 Chart Reviews

Studies with a retrospective design are those in which a phenomenon existing in the present is linked to a phenomenon that occurred in the past. The signature of a retrospective study is that the researcher begins with the dependent variable (the effect) and then examines whether it is correlated with one or more previously occurring independent variables (potential causes) (Polit & Beck 2017:205). A retrospective chart review was conducted at Hospitals A, B, and C.

The quantitative data were collected by three trained MSc graduates and experienced data collectors. Training was given to data collectors by this researcher for a day regarding ethical aspects of data collection, inclusion and exclusion criteria of the study units, and the questionnaire. In the meantime, a contract agreement was signed between the researcher and data collectors and card room staff who prepared selected patient charts and the runners who brought the charts to data collectors. In

addition to data available on DR-TB registers and TB treatment cards, medical record numbers were taken from the DR-TB register were used to retrieve patient charts (cards) from the card room.

1.10.2.6 Data Management and Analysis

1.10.2.6.1 Quantitative Strand

The data were coded, verified, cleaned for outliers and wild codes, and its internal consistency checked by the researcher. Any discrepancies were corrected against the hard copy of the questionnaires. To assure confidentiality of data, the collected hard copy data were kept in a lockable cabinet. The electronic data set was retained in the researcher's computer with passwords.

Quantitative analysis, as described by Polit and Beck (2017:741), is the process of manipulation of numeric data through statistical procedures for the purpose of describing phenomena or assessing the magnitude and reliability of relationships among them. Data entry and descriptive and inferential statistics analysis were applied using SPSS version 24.

1.10.2.6.2 Qualitative Strand

Data management in qualitative research is reductionist in nature: it involves converting masses of data into smaller, manageable segments. Qualitative data analysis is constructionist: it involves putting segments together into meaningful conceptual patterns. Qualitative analysis involves discovering pervasive ideas and searching for general concepts through an inductive process (Polit & Beck 2017:535).

As Polit and Beck (2017:530) indicate, the purpose of data analysis is to organise, provide structure to, and elicit meaning from data. In qualitative studies, data collection and data analysis often occur concurrently rather than after all data are collected. The search for important themes and concepts begins from the moment data collection gets underway (Polit & Beck 2017:530). In this study the analysis began concurrently with the data collection.

The analysis of qualitative materials typically begins with a search for broad categories and then themes. Themes emerge from the data. They often develop within categories of data but may also cut across them (Polit & Beck 2017:535).

Qualitative content analysis is the analysis of the content of narrative data to identify prominent themes and patterns among the themes. Thus, a central feature of content analysis is that it is a way of condensing a voluminous number of words of a text into smaller content categories (Polit & Beck 2017:537).

In qualitative content analysis, data is broken down into smaller units. The literature on content analysis often includes references to meaning units. A meaning unit is words, sentences or paragraphs containing aspects related to each other through their content and context. A meaning unit, essentially, is the smallest segment of a text that contains a recognizable piece of information (Polit & Beck 2017:537).

Content analysis often makes the distinction between manifest and latent content. Manifest content is what the text actually says – its visible components. In purely descriptive studies, qualitative researchers may decide to focus mainly on summarizing the manifest content communicated in the text. More often, however, content analysts also analyses what the text talks about, which involves interpretation of the meaning of its latent content. Interpretations vary in depth and level of abstraction and are usually the basis for themes (Polit & Beck 2017:538).

In this study the conventional content analysis approach was used, focusing on both manifest and latent content of the narratives. In conventional content analysis, the study starts with data and the codes emerge and are defined during data analysis (Polit & Beck 2017:538). Qualitative data were coded, sorted and analysed using ATLAS.ti 8 software.

1.10.2.7 Validity, Reliability and Trustworthiness

Quantitative researchers use several criteria to assess the rigour of a study, sometimes referred to as its scientific merit. Two especially important criteria are reliability and validity. *Reliability* refers to the accuracy and consistency of information obtained in a study. The term is commonly associated with methods of measuring

variables. *Validity* is a more complex concept that broadly concerns the soundness of the study's evidence - that is, whether the findings are unbiased and well grounded. Like reliability, validity is an important criterion for evaluating methods to measure variables. In this context, the validity question is whether the methods are really measuring the concepts that they purport to measure (Polit & Beck 2017:161).

1.10.2.7.1 Validity

This is a quality criterion that relates to the degree to which the inferences made in a study are accurate and well-founded; in measurement, the degree to which an instrument measures what it purports to measure (Polit & Beck 2017:747).

1.10.2.7.2 Reliability

This construct refers to the extent to which a measurement is free from measurement error; more broadly, the extent to which scores for people who have not changed are the same for repeated measurements; statistically, the proportion of total variance in a set of scores that is attributable to true differences among those being measured (Polit & Beck 2017:742).

1.10.2.7.3 Trustworthiness

The most often used framework of quality criteria is that of Lincoln and Guba, who identified five criteria for evaluating the trustworthiness of an inquiry: credibility, dependability, confirmability, transferability, and authenticity. Procedures to help ensure the rigour and usefulness of a qualitative study include triangulation, searching for disconfirming evidence, engaging in reflexivity, member checking, prolonged engagement in the field, collaboration, developing an audit trail and peer debriefing (Polit & Beck 2017:559-568).

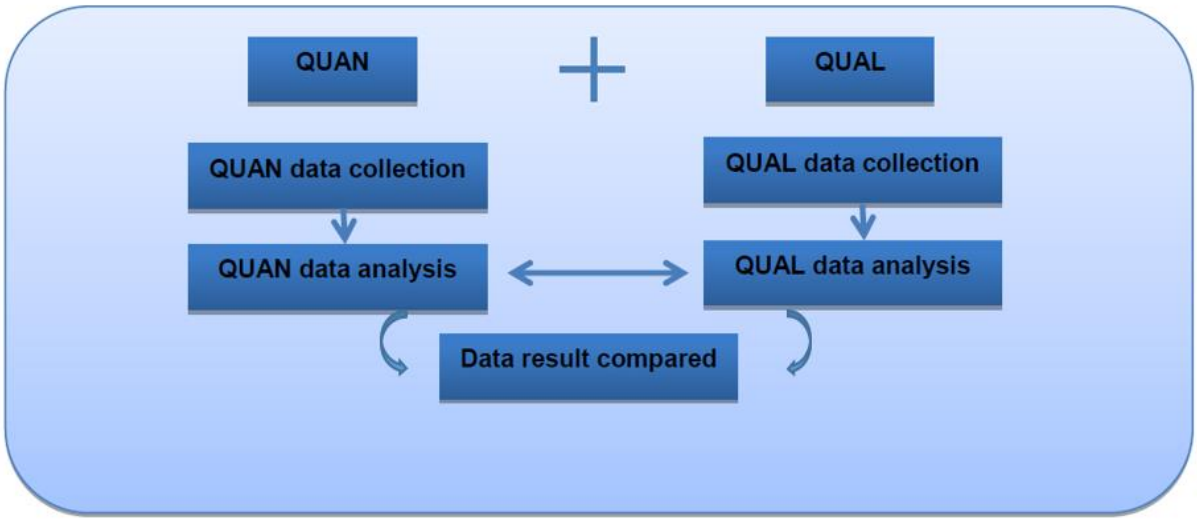


Figure 1.3 Visual Model of Concurrent Triangulation (Creswell 2003:214)

Data were compared and best practice guidelines were developed as envisaged in the model above.

1.11 ETHICAL CONSIDERATIONS

Ethics clearance was sought from the Ethics and Higher Degrees Committee of the Department of Health Studies in the College of Human Sciences at the University of South Africa (UNISA) (Annexure A). A letter of permission to conduct the study was obtained from the Federal Ministry of Public Health of Ethiopia (Annexure D) and permission from the management the hospitals was obtained. In addition an approval letter from Armauer Hansen Research Institute (AHRI)/ ALERT Hospital Ethics Review Committee (Annexure B) and from Saint Peter's Specialized Hospital Research and Evidence Generation Directorate, The Office of Institutional Health Research Ethics Review Committee (IHRERC) (Annexure C). Informed consent and respect for recruited participants were respected throughout the study.

1.12 SCOPE OF THE STUDY

This study was conducted at selected DR-TB treatment initiating hospitals in Ethiopia, namely, Hospital A, B, C, and D. The study utilised mixed method approach through which both quantitative and qualitative data were collected. In the quantitative strand factors associated with treatment completion of DR-TB patients were captured and in

the qualitative strand views of experts managing DR-TB patients and experiences of previously treated patients on treatment completion were described. The study investigated barriers for treatment completion of patients with DR-TB. At the end, the study developed best practice guidelines to address barriers for treatment completion of patients with DR-TB with the singular aim of contributing to the improvement of treatment outcomes of patients with DR-TB in Ethiopia.

In the quantitative strand, the study is limited by its retrospective design, as socio-demographic behavioural variables were abstracted from routine medical assessments conducted upon initiation of therapy and some information might be missed due to incomplete records. Likewise, in the qualitative strand, previously treated patients might have forgotten their past treatment experiences and may not share the entire information about such experiences retrospectively.

1.13 CONCLUSION

Chapter one presented a general overview of the study. The chapter covered the introduction, background, statement of the research problem, purpose and objectives of the study. It charted the theoretical foundation of the study, established the significance of the study, definition of terms, research methods and design, ethical considerations and scope of the study. The next chapter reviews relevant and recent literature pertinent to the study.

CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION

The first chapter presented an overview of the study which includes background and statement of the research problem, purpose and objectives of the research, theoretical frameworks and brief methodology followed. This chapter deals with the literature review, which entails thorough scrutiny of different scientific studies and material related to the problem in this study. Literature was searched using search terms like tuberculosis, drug-resistant tuberculosis, drug-resistant tuberculosis treatment, drug-resistant tuberculosis treatment outcomes, and health belief model on different databases such as MEDLINE (Medical Literature Online), CINHAL (Cumulative Index to Nursing and Allied Health Literature) Plus, Science Direct, Sage Journals Online, PubMed Central, Global Health, and Google Scholar. Bordens and Abbott (2011:66) describe literature review as the process of locating and evaluating the research literature in a specific area of interest. Nieswiadomy and Bailey (2018:63) also mention that literature review involves critically assessing accounts of what others have had to say on one's topic or on closely related topics, and, in particular, tracking down and establishing the points of convergence or divergence from the specific focus identified in one's study.

2.2 TUBERCULOSIS

Tuberculosis (TB) is one of the oldest diseases known to affect humans and is likely to have existed in prehominids. The earliest recorded human case of TB dates back 9000 years. Tuberculosis was known under various names such as "phthisis", "scrofula" and "consumption" in classical times, in the medieval ages and in the pre-industrial revolution. It was also known as the White Plague during the Industrial Revolution (Jameson, Fauci, Kasper, Hauser, Longo & Loscalzo 2018:1236; Sah, Craig & Mandelbaum 2021:12)

The disease is caused by bacteria of the mycobacterium tuberculosis (MTB) complex and usually affects the lungs, although other organs are affected also in up to one-third of TB cases. If properly treated, TB caused by drug-susceptible strains is curable

in virtually all cases. If untreated, the disease may be fatal within five years in 50-65% of cases. Transmission usually takes place through the airborne spread of droplet nuclei produced by patients with infectious pulmonary TB (Jameson, Fauci, Kasper, Hauser, Longo & Loscalzo 2018:1236).

TB continues to be one of the major infectious killer diseases globally and has decimated nearly a billion lives over the past two centuries. The emergence of multi-drug resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) make eradication and control strategies both complex and expensive, if at all successful. Drug-resistant TB (DR-TB) affects TB control programmes due to its large costs and complexity of treatment. In 2014, $US3.8 billion was spent on the diagnosis and treatment of drug-susceptible TB and $US1.8 billion on DR-TB (47% of the total spent on the drug-susceptible TB) despite the latter comprising <5% of the total case load. Furthermore, DR-TB poses a major threat to healthcare providers (HCPs) in TB endemic countries and is directly responsible for almost 25% of global TB mortality (Dheda, Cox, Esmail, Wasserman, Chang & Lange 2017:36)

In Ethiopia, TB has been recognised as one of the main public health challenges since the 1950s. The National TB Control Programme (NTCP) was established in 1976. In the early 1990s the country introduced the directly observed treatment short course (DOTS) strategy on a pilot basis in a few areas of the country with subsequent expansion that led the existing level of 95% and 100% health facilities and geographical coverage, respectively. At national level, there is one TB programme manager who oversees a team of eleven others responsible and working closely with the nine regional health bureaus and the two city administrations in Ethiopia. Community TB care initiatives have been in place since 2010. The programmatic management of DR-TB (PMDT) also resumed on pilot sites in the same year (EPHI 2014:10-11; Eshetie, Gizachew, Dagnew, Kumera, Woldie, Ambaw, Tessema & Moges 2017:2).

The country has responded to the emerging threat of DR-TB since 2010 through the launch of DR-TB treatment programme at St. Peter's TB Specialized Hospital on a pilot basis. The first cohort of 45 DR-TB patients has received second line drugs (SLDs) treatment after approval of the Green Light Committee (GLC). The treatment of DR-TB with SLDs has been scaled up to other regional treatment centres, based

on insights gleaned from the pilot programme and in line with expansion of TB culture and drug-susceptibility testing (DST) (EPHI 2014:14).

Table 2.1: Timeline of TB Control Activities in Ethiopia

1960s	First TB sanatorium established in Ethiopia
1976	National TB Control Programme (NTCP) begun
1992	First TB DOTS programme piloted
1994	Central office of NTCP combined TB and Leprosy
1997-2001	TB and Leprosy control programme is integrated into general health service
2003	Health Extension Worker Programme introduced
2003-2005	The first nationwide anti-TB drug resistance surveillance conducted
2004	Initial rollout of collaborative TB/HIV activities
2007	WHO Green Light Committee application submitted for approval and support for implementing DR-TB treatment
2008	Tuberculosis, Leprosy and TB/HIV Prevention and Control Programme Manual, 4th Edition
2008	Green Light Committee application approved for a pilot DR-TB treatment programme for 45 patients at St. Peters Hospital
2010	Introduction of the programmatic management of multidrug resistant tuberculosis
2011	National TB survey conducted
2011	Release of National TB and Leprosy Strategic Plan 2011-2015
2013	Guidelines for Clinical and Programmatic Management of TB, Leprosy and TB/HIV, 5th edition
2013	Revised National Tuberculosis and Leprosy Strategic Plan 2012-2020
2014	Guidelines on Programmatic management of drug resistant tuberculosis in Ethiopia. 2nd edition
2016	Clinical and programmatic guides for drug-resistant tuberculosis patients management with new and re-purposed TB drugs in Ethiopia
2016	Guidelines for Clinical and Programmatic Management of TB, Leprosy and TB/HIV. 6th edition

(Reves & Angelo 2016:3,7; EFMOH 2014:1; EFMOH 2016c:3; EPHI 2014:8)

2.2.1 Etiologic agent

Mycobacteria belong to the family Mycobacteriaceae and Actinomycetales. Of the pathogenic species belonging to the mycobacterium tuberculosis (MTB) complex, the most common agent of human disease is MTB. The complex incudes mycobacterium bovis, mycobacterium caprae, mycobacterium africanum, mycobacterium microti, mycobacterium pinnipedii, and mycobacterium canetti (Jameson et al 2018:1236; WHO 2021b:31; CDC 2021:5).

MTB is a rod-shaped, nonspore-forming, thin aerobic bacterium measuring 0.5 µm by 3 µm. Mycobacteria, including MTB, are often neutral on Gram's staining. Once stained, however, the bacilli cannot be decolorised with acid alcohol; this property justifies their classification as acid-fast bacilli (AFB). The acid resistance is mainly due to the bacilli's high content of mycolic acids, long chain cross-linked fatty acids and

other cell wall lipids. In the mycobacterial cell wall, lipids (for example mycolic acids) are linked to underlying arabinogalactan and peptidoglycan. This structure confers very low permeability of the cell wall, thus reducing the effectiveness of most antibiotics. Another molecule in the mycobacterial cell wall, lipoarabinomannan, is involved in the pathogen-host interaction and facilitates the survival of MTB within macrophages. The complete genome sequence of MTB comprises 4 043 genes encoding 3 993 proteins and 50 genes encoding ribonucleic acids (RNAs) (Jameson et al 2018:1236; CDC 2021:9).

2.2.2 Epidemiology

Worldwide TB is one of the top ten causes of death and the second leading cause from a single infectious agent, after COVID-19. Millions of people continue to fall sick with TB each year. Globally, the estimate is that 9.9 million people (range, 8.9 – 11 million) developed TB disease in 2020; adult male accounted for 56% while adult female and children accounted for 33% and 11% respectively. Similarly, the estimates of TB burden for Africa in 2020 is 2.5 million people (range, 2.2 -2.8 million). Furthermore, according to the WHO global TB report 2021, estimate of incidence of TB burden for Ethiopia in 2020 is 151, 000 which is 132 per 100, 000 population. In Ethiopia again, TB case notification for the same year is 108, 200 cases, which makes treatment coverage (notified/estimated incidence) 71% (WHO 2021b:1, 9, 37; CDC 2021:5).

It is estimated that over 84% of global TB deaths occur in developing countries. TB affects people mainly within the economically productive age group (15–54 years) and is associated with negative social consequences (see Figure 2.1). These adverse consequences include children leaving school because their parents would have contracted TB and women who would have been abandoned by their families because of their disease. Co-infection with the human immunodeficiency virus (HIV) has increased the risk of developing active TB, thereby making TB the leading cause of death among people with HIV. Furthermore, the emergence and spread of multidrug-resistant Mycobacterium tuberculosis have increased the seriousness of the TB problem (Leveri et al 2019:4; WHO 2021b:9).

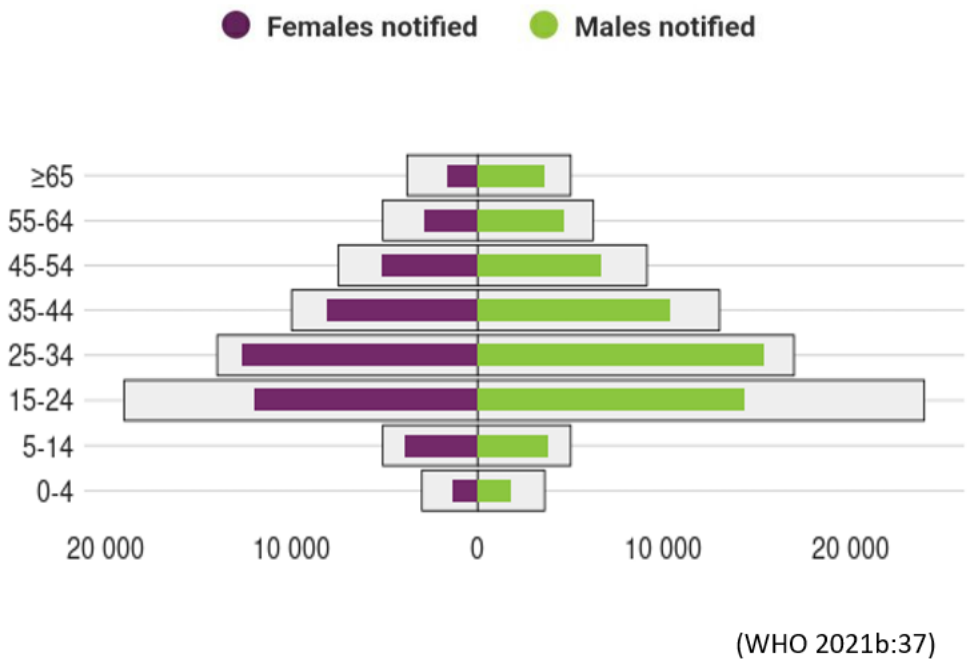


Figure 2.1 Notified TB cases by age group and sex, 2020, Ethiopia

2.2.3 Transmission

2.2.3.1 *From exposure to infection*

Tuberculosis is acquired through the inhalation of droplets containing live mycobacterium. The tiny droplets nuclei dry rapidly; the smallest (<5-10 µm in diameter) can remain airborne for several hours and reach the terminal airways when inhaled. There can be up to 3 000 infectious nuclei per cough. Other routes of transmission of tubercle bacilli (for example, through the skin or placenta) are uncommon and of no epidemiologic significance (Jameson et al 2018:1238).

TB patients whose sputum smear is positive by microscopy (i.e., whose sputum contains AFB visible by microscopy) are the most likely to transmit the infection. Patients with cavitary pulmonary TB are the most infectious and produce sputum containing as many as 10^5-10^7 AFB /mL. On the other hand, patients with smear negative and only culture-positive results are less infectious, although they have been responsible for up to 20% of transmission in some studies, and those with culture-negative pulmonary TB and extra-pulmonary TB (EPTB) are essentially non-infectious (Jameson et al 2018:1238).

2.2.3.2 *From infection to disease*.

Endogenous factors such as the individual's innate immunologic and non-immunologic defences and level of function of cell-mediated immunity (CMI) play an important role in prevention of the disease developing after infection takes place. Primary TB is an illness which occurs directly following infection and is common among children in the first few years of life and among immunocompromised individuals. This kind of TB can be severe and disseminated; however, it is less transmissible. Secondary (or post primary) TB is the result of the reactivation of a dormant bacilli contained by the immune system. This happens when TB infection is acquired later in life in the presence of mature immunity which can contain the infection. Post primary TB, because of frequent cavitation, is more infectious (Jameson et al 2018:1239).

2.2.4 Natural history of disease

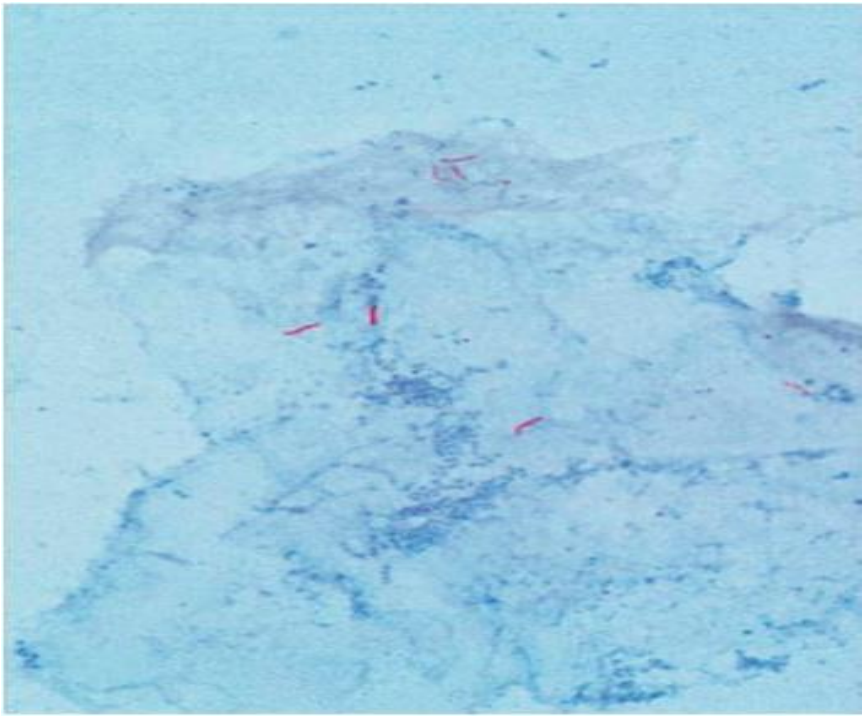
Studies in different countries before the era of anti-TB medicines confirm that untreated TB is often fatal. About one-third lost their lives in a period of one year after diagnosis and more than 50% died within five years. Among sputum smear positive cases, the mortality in five years was about 65%. In those who survived at five years, nearly 60% had undergone spontaneous remission while the rest were still excreting the bacteria. Proper treatment under good programmatic conditions results in high chances of getting cured. However, inadequate use of anti-TB drugs, while reducing death rates, could result in many chronic infectious cases often with drug-resistant strains (Jameson et al 2018:1239).

2.2.5 Pathogenesis and immunity

2.2.5.1 Infection and macrophage invasion.

The first contact of TB bacilli takes place when droplet nuclei containing MTB from infectious patients are inhaled. Ciliated mucosal cells in the upper air way trap the majority of them and expels these, with only a few <10% reaching the alveoli. There alveolar macrophages phagocytize the bacilli. Phagocytes have cell-surface molecules including complement receptors and type A scavenger receptors that make them bind to mycobacteria. The bacterial cell wall glycolipid lipoarabinomannan inhibits the intracellular increase of calcium ions which results in impaired phagosome-

lysosome fusion and helps the bacteria to survive within the phagosome (Jameson et al 2018:1239).



(Jameson et al 2018: 1236)

Figure 2.2 Acid-fast bacillus smear showing MTB bacilli.

2.2.5.2 The host response and granuloma formation

Early stage of interaction of host-bacilli is when MTB undergoes a period of extensive growth within naïve un-activated macrophages, and more naïve macrophages are recruited to the early granuloma. At this early phase MTB utilizes a specific virulence mechanism to subvert host cellular signalling and to elicit an early proinflammatory response that promotes granuloma expansion and bacterial growth. The mycobacteria protein early secretory antigen-6 (ESAT-6) induces secretion of matrix metalloproteinase 9 (MMP9) by nearby epithelial cells that are in contact with the infected macrophages. MMP9, in turn, stimulates recruitment of naïve macrophages, thus inducing granuloma maturation and bacterial growth (Jameson et al 2018:1240).

About 2-4 weeks after infection, two host responses to MTB develop: a macrophage-activating cell mediating immunity (CMI) response and a tissue-damaging response. The macrophage activating response is a T cell mediated phenomenon that leads to the activation of macrophages that are capable of killing and digesting tubercle bacilli.

The tissue damaging response is the result of a delayed-type hypersensitivity (DTH) reaction to various bacillary antigens; it destroys un-activated macrophages that contain multiplying bacilli but also causes caseous necrosis of the involved tissues (Jameson et al 2018:1240).

With the development of specific immunity and the accumulation of a large number of activated macrophages at the site of the primary lesion, granulomatous lesions are formed. These lesions consist of accumulations of lymphocytes and activated macrophages that develop into epithelioid and giant cell morphologies. Initially, the tissue damage response can limit growth of mycobacteria within macrophages. As mentioned above, this response, mediated by various bacterial products, not only kills macrophages but also produces early solid necrosis in the centre of the tubercle. Although mycobacterium tuberculosis can survive, its growth is inhibited within this necrotic environment by low oxygen tension and low pH. At this point, some lesions may heal by fibrosis, with subsequent calcification, whereas inflammation and necrosis occur in other lesions (Jameson et al 2018:1240).

Moreover, host cells have various mechanisms, such as the production of nitric oxide and inflammatory cytokines to control intracellular replication of MTB. Inducible nitric oxide synthase (iNOS) is transcriptionally under the control of Interferon gamma (IFN-γ) and tumour necrosis factor-α (TNF-α). Interluekin-12 (IL-12) provides a crucial link between activated mononuclear phagocytes and T cells by regulating the production of IFN-γ (Byng-Maddick & Noursadeghi 2016:1).

2.2.6 Diagnosis

Expedited and accurate diagnosis of TB, HIV-associated TB and drug-resistant TB, followed by provision of treatment in line with international standards, prevents mortality and reduces morbidity. Early diagnosis also prevents further transmission to others. Furthermore, the 2020 and 2025 milestones for reduction in TB incidence and TB deaths set in the End TB Strategy in Ethiopia require the case fatality ratio (the proportion of people with TB who die from the disease) to fall to 10% by 2020 and to 6.5% by 2025. To realise these milestones, prompt diagnosis and effective treatment are the core strategies (Migliori, Tiberi, Zumla, Petersen, Chakaya, Wejse, Torrico, Duarte, Alffenaar, Schaaf, Marais, Cirillo, Rendon, Pontali, Piubello, Figueroa,

Ferlazzom, Garcia-Basteiro, Centis, Visca, D'Ambrosio & Sotgiu 2020:S17; WHO 2017:64).

2.2.6.1 AFB microscopy

AFB microscopy is a presumptive diagnostic procedure that identifies acid fast bacilli from specimens, such as sputum or a lymph node biopsy, under a microscope examination. It is a cheap and widely used procedure in developing countries even though it has a low sensitivity (40-60%) of diagnostic capacity and is certainly time-consuming. Most modern laboratories processing large numbers of diagnostic samples use auramine-rhodamine staining and fluorescence microscopy instead of light microscopy of specimens stained with Ziehl-Neelsen basic fuchsin dyes. Less expensive light-emitting diode (LED) fluorescence microscopes are now available and widely in use currently (Jameson et al 2018:1247; WHO 2017:4; WHO 2018:6; WHO 2021b:31).

2.2.6.2 Mycobacterial culture

Definitive diagnosis depends on the isolation and identification of MTB from a clinical specimen or the identification of specific sequences of deoxyribonucleic acid (DNA) in a nucleic acid amplification test. Specimens may be inoculated onto egg- or agar-based medium (for example, Lowenstein-Jensen or Middlebrook 7H10) and incubated at 37^{o}C. Because most species of mycobacteria, including MTB, grow slowly, four up to eight weeks may be required before specific and significant growth is detected (Jameson et al 2018:1247; WHO 2017:4; WHO 2018:6).

2.2.6.3 Nucleic acid amplification

Several test systems based on amplification of mycobacterial nucleic acid are available. These systems permit the diagnosis of TB in as little as several hours, with high specificity and sensitivity approaching that of culture (Jameson et al 2018:1247).

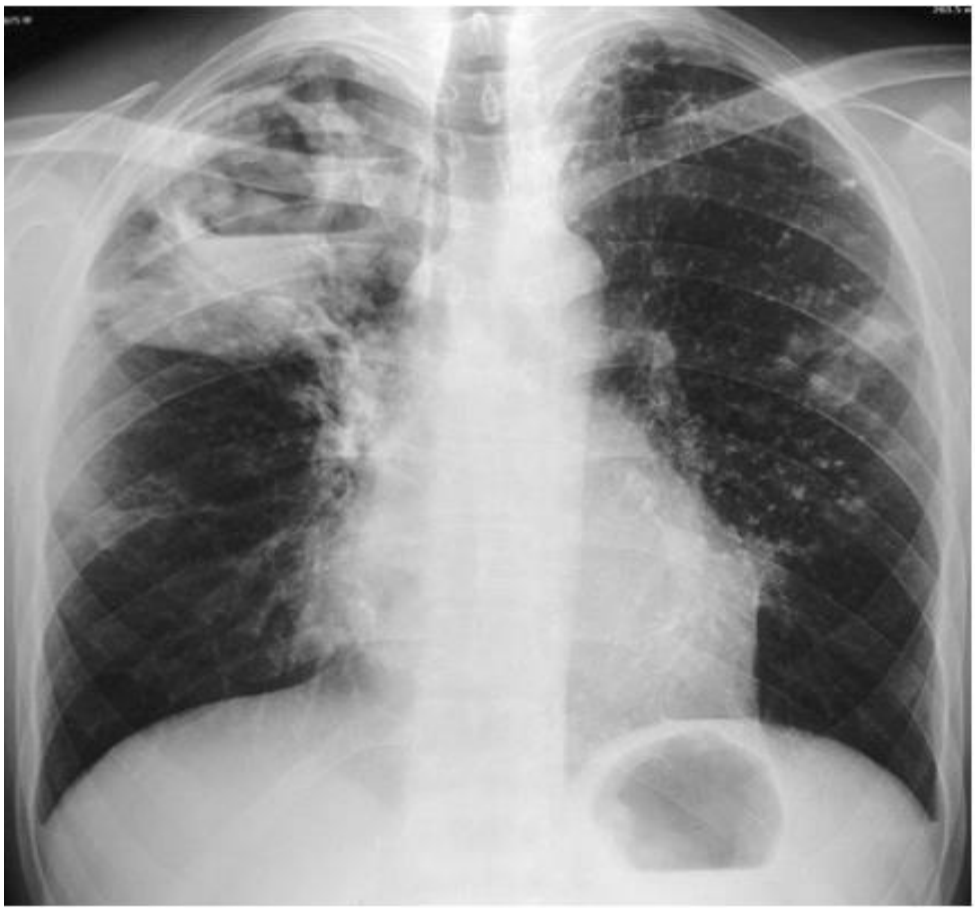
2.2.6.4 Drug susceptibility testing

Drug susceptibility testing (DST) for isoniazid and rifampicin should be performed on the initial isolate of TB bacteria to detect MDR-TB, if risk factors for drug resistance are present or the patient either fails to respond to first line treatment or has a relapse after the completion of treatment. And if DR-TB is diagnosed, on the top of that DST

for second-line anti-TB drugs, particularly for the fluoroquinolones and the injectable, are mandatory (Jameson et al 2018:1248; Migliori et al 2020:S17; WHO 2018:6; WHO 2020a:18).

2.2.6.5 Radiographic procedures

The classic picture seen in a chest radiograph is that of the upper-lobe disease with infiltrates and cavities (Fig 2.2), but virtually any radiographic pattern from a normal film or solitary pulmonary nodule to diffuse alveolar infiltrates may be seen. Computerised tomography (CT) may be useful in interpreting questionable findings on plain chest radiography and may be helpful in diagnosing some forms of EPTB. Magnetic resonance imaging (MRI) is equally useful in the diagnosis of intracranial TB (Jameson et al 2018:1248).



(Jameson et al 2018:1242)

Figure 2.3 Chest radiograph showing a right upper lobe infiltrate and a cavity with an air-fluid level in a patient with active tuberculosis

2.2.6.6 Additional diagnostic procedures

Sputum induction by ultrasonic nebulization of hypertonic saline, fibreoptic bronchoscopy with bronchial brushings and endobronchial biopsy of a lesion, and bronchoalveolar lavage are additional procedures that facilitate the diagnosis by producing specimens for AFB smear and mycobacterial culture. In children, induced sputum specimens and specimens from early morning gastric lavage may support diagnosis of TB. Invasive procedures, such as cerebrospinal fluid (CSF), pleural fluid and biopsy samples for pleural disease, biopsy and culture of bone marrow and liver tissue, can be performed for patients with suspected extrapulmonary TB and these have a good diagnostic yield (Dlodlo, Brigden, Heldal, Allwood, Chiang, Fujiwara, Graham, Guillerm, Harries, Koura, Kumar, Lin, Meghji, Mortimer, Piubello, Roth, Satyanarayana, Sekadde, Solovič, Tonsing & Van Deun 2019:113). In general, a diagnosis of TB in HIV positive patients is often challenging due to atypical clinical and radiological presentations, higher rates of smear negative pulmonary and extra pulmonary TB (Diendéré et al 2015:1250).

2.3 DRUG-RESISTANT TUBERCULOSIS

The burgeoning DR-TB epidemic is a public health problem and a threat to TB control. Although TB incidence and mortality has decreased in several parts of the world, the overall prevalence of DR-TB is increasing in many high burden countries, particularly in Africa (Khachatryan, Grigoryan, Dadu, Kumar, Akopyan, Dumchev, Harutyunyan & Matteelli 2021:1; Mitnick, Rodriguez, Hatton, Brigden, Cobelens & Grobusch 2016:2; WHO 2021b:9).

Three major categories of DR-TB are used for global surveillance and treatment. DR-TB is resistant to both rifampicin and isoniazid, the two most powerful anti-TB drugs. RR-TB is resistant to rifampicin. Pre-XDR-TB is defined as TB that is resistant to rifampicin and any fluoroquinolone. XDR-TB is resistant to rifampicin, plus any fluoroquinolone, plus at least one of the drugs bedaquiline and linezolid (WHO 2021b:19).

Drug resistance is caused by spontaneous mutations during bacterial multiplication that confer resistance to the drugs at different frequencies, even in the absence of anti-TB drugs. Strains of MTB resistant to individual drugs arise from spontaneous

point mutations in the bacterial genome that occur at low but predictable rates (10^{-7} – 10^{-10} for the key drugs). Because there is no cross-resistance among the commonly used drugs, the probability that a strain could be resistant to two drugs is the product of the probabilities of resistance to each drug and thus is low (Bang, Lillebaek, Thomsen & Andersen 2010:288; Jameson et al 2018:1253; Mesfin, Beyene, Tesfaye, Admasu, Addise, Amare, Dagne, Yaregal Tesfaye & Tessema 2018:2).

Exposure to a single drug or suboptimal drug concentrations provides a selective environment favouring drug-resistant bacteria and the development of DR-TB (Bang, Lillebaek, Thomsen & Andersen 2010:288; CDC 2021:114; Molie, Teklemariam, Klinkenberg, Dessie, Kumsa, Mohammed, Debebe, Assefa, Habte, Bedru, Fiseha & Seyoum 2019:2). On programmatic aspect, mono-therapy - that is the failure of the health care provider to prescribe at least two drugs to which tubercle bacilli are susceptible or failure of the patient to take properly prescribed therapy - ultimately gives rise to DR-TB (Jameson et al 2018:1253).

DR-TB may be either primary or acquired. Primary drug resistance develops in a strain infecting a patient who has not been treated previously. It occurs by primary transmission of drug-resistant MTB strains. Acquired resistance develops during treatment with an inappropriate regimen. For acquired resistance, MTB develops resistance by spontaneous chromosomal mutations. Given that frequencies of mycobacterium tuberculosis mutations that correlate with drug resistance occur infrequently and resistance mutations for different drugs are understood to be unlinked, additional drug resistance is unlikely when > 3 effective drugs are used in combination. For inadequate drug treatment caused by poor regimen selection, inadequate drug supply, non-adherence, or sub therapeutic drug concentrations, subpopulations of drug-resistant mycobacterium tuberculosis might be selected, amplified, and become the predominant strain (Jameson et al 2018:1253; Kemper, Kipiani, Mirtskhulava, Tukvadze, Magee & Blumberg 2015:993; Molie, Teklemariam, Klinkenberg, Dessie, Kumsa, Mohammed, Debebe, Assefa, Habte, Bedru, Fiseha & Seyoum 2019:2; CDC 2021:20).

Although its causes are microbial, clinical and programmatic, DR-TB is essentially a man-made phenomenon. From a microbiological point of view, resistance is caused by a genetic mutation that renders a drug ineffective against mutated bacilli. From a

clinical and programmatic perspective, it is an inadequate treatment regimen that allows a drug-resistant strain to become the dominant strain in a patient infected with TB. Table 2.2 summarises the common causes of inadequate treatment (Dlodlo et al 2019:113; Molie et al 2019:2; WHO 2008:3).

Table 2.2: Causes of inadequate TB treatment

Health care providers: Inadequate regimens	**Drugs: inadequate supply Or quality**	**Patients: inadequate drug intake**
Inappropriate guidelines Failure to follow guidelines Lack of guidelines Substandard training Absence of treatment monitoring Poorly organised or funded TB control programmes	Poor quality Unavailability of some drugs (stock-outs or delivery disruptions) Inappropriate storage conditions Wrong doses or combination	Poor adherence Lack of information Lack of money Lack of transportation Adverse effects Social barriers Malabsorption Substance dependence

(WHO 2008:3; Molie et al 2019:2)

The incidence of drug resistance has increased since the first drug treatment for TB was introduced in 1943. The emergence of DR-TB following the widespread use of rifampicin beginning in the 1970s led to use of second-line drugs. Improper use of these drugs has fuelled the generation and subsequent transmission of highly resistant strains of TB termed XDR-TB (Mesfin et al 2018:2; WHO 2008:4).

Treatment of DR-TB is substantially more complex, more costly, and less effective than standard therapy, typically requiring a higher number of drugs, including injectable agents and a longer treatment duration than that of drug-susceptible TB cases. MDR- and XDR-TB can be incapacitating and life-threatening. Furthermore, current treatment options can be disabling and lead to medical complications. The advent of novel antibiotics such as Bedaquiline and Delamanid is a vital step in the treatment of DR-TB (WHO 2016a:1; WHO 2016c:1; Baluku, Nakazibwe, Naloka, Nabwana, Mwanja, Mulwana, Sempiira, Nassozi, Babirye, Namugenyi, Ntambi, Namiiro, Bongomin, Katuramu, Andia-Biraro & Worodria 2021:1).

In developing countries where there are limited resources including finance, and skilled personnel to tackle DR-TB, the burden of the disease is significantly high making prevention and control activities problematic. Similarly, in Ethiopia, the low socioeconomic status of the population, poor treatment outcomes, longer treatment

time, higher treatment costs, and many more complications make DR-TB a more complex disease than TB (Eshetie et al 2017:2; Mesfin et al 2018:3; Safaev, Parpieva, Liverko, Yuldashev, Dumchev, Gadoev, Korotych & Harries 2021:1).

2.3.1 Epidemiology

2.3.1.1 Global Perspective

According to the latest 2021 global TB report, worldwide in 2020, there were 132 222 cases of MDR/RR-TB and 25 681 cases of pre-XDR-TB or XDR-TB detected, culminating in a combined total of 157 903 (WHO 2021b:19-20). Likewise, in 2019, globally, there were an estimated 465 000 incident cases of MDR/RR-TB, among which 206,030 were detected and notified and 177 099 actually enrolled on treatment (WHO 2020b:13, 71). Furthermore, globally, in 3-4% of new TB cases and 18-21% of previously treated cases had MDR/RR-TB (WHO 2021b:10).

Approximately three-quarters of all TB cases worldwide are concentrated in the economically productive age group, between the ages of 15 and 59 years (Leveri et al 2019:4; WHO 2021b:9). Similarly, younger TB patients are significantly more likely than older patients to have DR-TB. Most of the patients with established social risk factors (alcohol and drug abuse, incarceration and HIV infection) are in this younger age group. Failure to complete prescribed therapy is understood as contributing to the development of DR-TB, and occurs frequently in drug and alcohol abusers (Fisher-Hoch, Whitney, McCormick, Crespo, Smith, Rahbar & Restrepo 2008:891; Mesfin et al 2018:2).

DR-TB is a growing problem in resource-poor settings where adequate diagnosis and treatment are often unavailable. Sub-Saharan Africa is among the hardest hit by DR-TB (Matteelli, Centis, D'Ambrosio & Migliori 2012:78; Mesfin et al 2018:2).

2.3.1.2 Ethiopian and Sub-Saharan Perspective

The global tuberculosis report 2021 notes that from the global estimated 9.9 million people who developed TB disease in 2020, the WHO African Region contributes 25% to this figure (WHO 2021b: 9). Moreover, according to the global TB report 2020, in Ethiopia, 0.71% of new TB cases and 12% of previously treated cases had MDR/RR-TB in 2019 (see Tables 2.3 & 2.4) (WHO 2020b:23, 56).

Table 2.3: Estimated incidence of MDR/RR-TB in 2019, Ethiopia, Africa and Globally

	Estimated % of new cases with MDR/RR-TB	Estimated% previously treated cases with MDR/RR-TB	Number
Ethiopia	0.71	12	1,400
Africa	2.6	11	77,000
Global	3.3	18	465,000

(WHO 2020b:23, 56)

Table 2.4: Notifications of TB, MDR/RR-TB and Pre-XDR/XDT-TB cases in 2020, Ethiopia, Africa and Global

	Notified New TB Cases	MDR-TB	Pre-XDR/XDR-TB
Ethiopia	108,200	591	7
Africa	1,400,000	17,800	1200
Global	5,800,000	150,400	22,000

(WHO 2021b:37)

2.3.2 Diagnosis

According to Alene, Viney, McBryde, Tsegaye and Clements (2017:359) and Woldeyohannes, Assefa, Aman, Tekalegn and Hailemariam (2019:11), for effective PMDT, it is essential to detect the disease as early as possible and subsequently ensuring that those diagnosed complete their treatment and get cured. Moreover, early diagnosis and treatment of all individuals with any variation of tuberculosis is a critical and recommended scheme in the END TB Strategy (Migliori et al 2020:S17). This signifies the importance of early diagnosis in the big picture of programmatic prevention and control of tuberculosis including DR-TB.

To further clarify the issue of diagnosis, it is prudent to mention the results of some studies in this area. A study conducted in the Oromia region, Ethiopia, by Woldeyohannes et al (2019:11) to assess the predictors of time to unfavourable treatment outcomes among patients with DR-TB reported delayed diagnosis as one

of the factors leading to unfavourable treatment outcomes. Another study conducted in North-West Ethiopia, by Alene et al (2017:359) aimed to assess DR-TB treatment outcomes and determine predictors of poor treatment outcomes, asserted that late diagnosis of DR-TB might be responsible for unfavourable outcomes. Another study conducted in Tanzania by Mpagama, Ezekiel, Mbelele, Chongolo, Kibiki, de Guex and Heysell (2020:1-2) aimed to explore patients' viewpoints and experiences with personal and socio-behavioural obstacles from DR-TB diagnosis to treatment. This study showed a considerable delay in diagnosis of DR-TB in the country, signifying therefore the importance of early diagnosis for the successful outcome of drug resistance treatments. The results recommend early diagnosis as strategically significant for the successful outcome of drug resistance treatments.

One of the strategies to avoid missed opportunities in DR-TB diagnosis is to provide diagnostic opportunities for all TB patients. In this regard, the End TB Strategy calls for universal access to DST; that is, DST for at least rifampicin for all TB cases, plus DST for at least fluoroquinolones and second-line injectable agents among all TB cases with rifampicin resistance. DST methods include both phenotypic (conventional) and genotypic (molecular) testing methods (WHO 2017:73; Migliori et al 2020:S17; Lange et al 2019:646).

In 2019, there were 2.2 million (61%) of the 3.6 million new bacteriologically confirmed and previously treated TB cases notified globally that were tested for rifampicin resistance, with coverage of 59% for new TB patients and 80% for previously treated TB patients (WHO 2020b:91). This confirms that a large number of patients do not start their treatment early enough and this delay impinges upon the success in their treatment which is consequently very low.

2.3.2.1 Culture-based tests for DR-TB

Conventional culture-based drug susceptibility testing involves establishing and verifying the presence mycobacterium tuberculosis growth in the presence of specific anti-TB drugs. Solid agar methods are the diagnostic gold standard, while liquid culture methods have equivalent performance, and are WHO-endorsed. The main drawback of these culture-based methods is the long delay (usually several weeks) in obtaining DST results. Treatment regimens used during these delays may not be effective and

may culminate in additional drug resistance (Calligaro, Moodley, Symons & Dheda 2014:187; Safaev et al 2021:2).

Strategies of prevention and control of DR-TB should focus on improving access to DST and minimising the delays in diagnosis. In this aspect, new technologies in rapid growth and microscopy-based DST, such as the microscopy observed drug susceptibility (MODS) method and thin layer agar (TLA) technique have reduced the delay to less than two weeks. Recently, the direct nitrate reductase assay (NRA), a rapid and in-expensive phenotypic method based on the metabolic activity of MTB, which is usually performed on solid media, has been shown to accurately diagnose DR-TB after approximately 21 days when performed directly on smear-positive specimens (Migliori et al 2020:S17; Calligaro et al 2014:187).

2.3.2.2 Molecular DST

There are also tests for TB that is resistant to first-line and second-line anti-TB drugs. These include Xpert MTB/RIF, which simultaneously tests for TB and resistance to rifampicin; rapid line probe assays (LPAs) that test for resistance to rifampicin and isoniazid (referred to as first-line LPAs); a rapid LPA that tests for resistance to fluoroquinolones and an injectable anti-TB drugs (referred to as a second-line LPA); and sequencing technologies (Migliori et al 2020:S19; WHO 2018:6; WHO 2017:4; WHO 2022a:30).

New nucleic acid amplification tests (NAATs) have changed the diagnosis by reducing the time interval between sample collection and susceptibility results from weeks to hours, and are also easy to perform as automated in operation. These tests play a pivotal role in transforming TB and DR-TB control programmes as they provide rapid DST results at the time of TB diagnosis. In this way, they increase case detection and access to immediate anti-TB treatment regimen and finally reduce transmission at the community level (Calligaro et al 2014:187; Safaev et al 2021:2; WHO 2022a:18).

At present, one of the most widely used nucleic acid amplification assay is Xpert®MTB/RIF (Cepheid Sunnyvale, CA, USA,). It is a semi-nested quantitative real-time polymerase chain reaction (PCR) assay provides a simultaneous diagnosis of TB and rifampicin resistance in less than two hours. It is an automated cartridge-based system that can be performed in remote locations away from reference laboratories

and potentially at the point-of-care by personnel with minimal laboratory training. Apart from sputum samples, respiratory specimens and extrapulmonary samples can also be accurately used (Lange et al 2019:646; WHO 2018:6).

A line probe assay is a type of laboratory-based nucleic acid amplification assay in which the products are hybridized to a nitrocellulose strip. An example is the MTBDR-plus assay (Hain Lifesciences), which offers similar performance to Xpert MTB/RIF for TB and excellent performance for MDR/TB detection. It has the advantage of interrogating for resistance to both rifampicin and isoniazid. Recently, the MTBDRsl assay (second line) assay was introduced to test for drug-resistance to second line injectable drugs, fluoroquinolones and ethambutol (Lange et al 2019:646; Safaev et al 2021:2).

2.3.3 Drug-resistant TB treatment

DR-TB is a serious public health problem associated with higher mortality and failure rates, especially in HIV-infected patients. It is more expensive and complicated to treat compared to drug-susceptible TB, and is transmittable for long periods of time, even when treated (Leveri, Lekule, Mollel, Lyamuya & Kilonzo 2019:2; McNally, de Wildt, Meza & Wiskin 2019:2; Woldeyohannes et al 2019:2).

Globally, 153 119 cases of MDR/RR-TB were notified in 2016, and 129 689 were enrolled for treatment. The number of MDR/RR-TB cases commencing on treatment in 2016 was only 22% of the estimated incidence of MDR/RR-TB (WHO 2017:63, 84). Similarly, 160 684 cases of MDR/RR-TB globally were notified in 2017. Of these, a total of 139 114 people (87%) were enrolled on treatment with a second-line regimen, and this is still only 25% of the estimated 558 000 people who developed MDR/RR-TB in 2017 (WHO 2018:2, 3, 67).

Likewise, according to the global TB report 2019, a global total of 186 772 cases of MDR/RR-TB were notified in 2018, and 156 071 cases were enrolled for treatment (WHO 2019b:73). Also, the global TB report 2020 notified that a total of 206 030 people with MDR/RR-TB were detected and notified in 2019, while 177 099 enrolled on treatment (WHO 2020b:71). Furthermore, according to the latest global TB report 2021, there were 132 222 cases of MDR/RR-TB and 25 681 cases of pre-XDR-TB or

XDR-TB detected and notified, for a combined total of 157 903; and 150 359 were enrolled for treatment in 2020 (WHO 2021b:19-20).

In many countries, one of the barriers to adequate access to treatment of drug-resistant TB is that the network for the programmatic management of drug-resistant TB (PMDT) is too centralised and reliant on hospital-based models of care, making it unsuitable for the use of outpatient models of care (WHO 2017:85).

According to WHO (2021b:31), treatment for DR-TB is longer and requires more expensive and more toxic drugs than the conventional variant. Until early 2016, the treatment regimens recommended by WHO typically lasted for 20 months and cost about US$2000-5000 per person (WHO 2017:4). Currently, treatment for individuals diagnosed with DR-TB requires medicines that cost about US$1 000 per person (WHO 2021b:31).

Tuberculosis is a worldwide problem and the emergence of multidrug-resistant variants has made its management more complicated. Drugs used to treat DR-TB are more expensive, more toxic, and less effective than those used for routine TB treatment, making DR-TB difficult to treat (Kundu, Basu, Sarkar, Nath & Biswas 2021:392). When compared to drug-susceptible TB, Calligaro et al (2014:186) and Baluku et al (2021:1) further describe the treatment of patients with DR-TB as complex, and characterised by a longer duration of treatment, use of less effective but more toxic drugs, higher relapse rates, and a reduced chance of treatment success.

Therapeutic management of drug-resistant TB involves regimens with lower efficacy and greater toxicity than those used for drug-susceptible TB (Harris, Khan, Martin, Allen, Moore, Fielding & Grandjean 2016:2; Baluku et al 2021:1). According to the global TB report 2021, only 59% of MDR/RR-TB patients (2018 cohort) had a successful treatment outcome, compared to 86% for drug-susceptible TB (2019 cohort) (WHO 2021b:9, 20).

Despite the discovery of bedaquiline and delamanid, the first anti-TB drugs to get approval in over 40 years, with novel mechanisms of action and endorsed by WHO in drug-resistant tuberculosis regimen construction, the problem remains one of access and effectiveness that is also lower than that of drug-susceptible TB (Harris et al 2016:2).

Scholars Mitnick, Rodriguez, Hatton, Brigden, Cobelens and Grobusch (2016:2) state that effective management of DR-TB requires prevention, case detection, care and treatment, surveillance, drug management, and monitoring and evaluation of programme performance. These activities should be coordinated by national TB control programmes, and are referred to collectively as the "programmatic management of drug-resistant tuberculosis" (PMDT).

2.3.3.1 Shorter MDR/RR-TB regimen for adults and children (Previous regimen before 2020 WHO updates)

According to WHO guidelines, shorter MDR/RR-TB regimen of 9-12 months may be used in patients who are diagnosed with RR-TB or MDR-TB not previously treated for more than one month with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents was excluded or is considered highly unlikely (WHO 2016b:7,18; WHO 2019a:10,31,35).

The shorter MDR/RR-TB treatment regimen was standardised in content and duration and consists of two separate phases. The first is an intensive phase of four months (extended up to a maximum six months in case of lack of sputum smear conversion) and includes the following drugs: gatifloxacin (or moxifloxacin), kanamycin, prothionamide, clofazimine, high-dose isoniazid, pyrazinamide and ethambutol. The second is a continuation phase of five months with the following medicines: gatifloxacin (or moxifloxacin), clofazimine, pyrazinamide, and ethambutol. This second phase is injection free (WHO 2016b:18-19).

2.3.3.2 Shorter all-oral bedaquiline-containing regimen for MDR/RR-TB

Currently, according to the most recent WHO guidelines (2020a:12), a shorter all-oral bedaquiline-containing a regimen of 9–12 months' duration is recommended in eligible patients diagnosed with MDR/RR-TB who have not been exposed to treatment with second-line TB medicines used in this regimen for more than one month and in whom resistance to fluoroquinolones has been excluded (WHO 2020a:12). The shorter all-oral bedaquiline-containing regimen is composed of bedaquiline (used for six months), in combination with levofloxacin/moxifloxacin, ethionamide, ethambutol, isoniazid (high-dose), pyrazinamide and clofazimine for four months (with the possibility of extending to six months if the patient remains sputum smear positive at the end of the four months); followed by five months of treatment with levofloxacin/moxifloxacin,

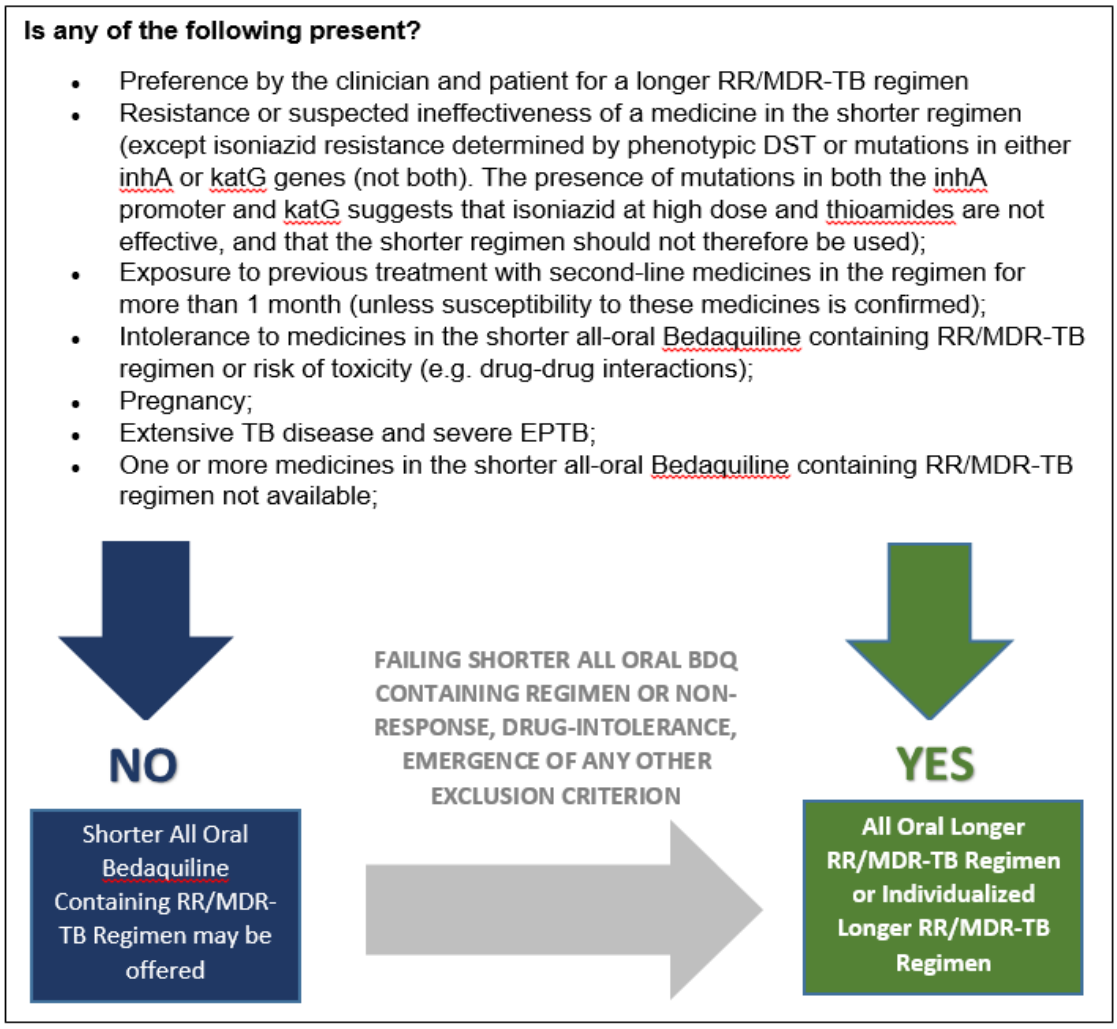
clofazimine, ethambutol and pyrazinamide (WHO 2020a:12; WHO 2022a:45). Before starting the shorter, all-oral, bedaquiline-containing regimen, access to WHO-recommended rapid DST is essential, especially for detecting resistance to rifampicin and fluoroquinolones (WHO 2020a:18).

In patients with bacteriologically confirmed MDR/RR-TB, the second-line LPA (MTBDRsl) may be used as the initial test, in preference to culture and phenotypic DST, to detect resistance to fluoroquinolones (WHO 2020a:18). Resistance mutations to fluoroquinolones detected using MTBDRsl should be considered a contraindication for the shorter regimen (WHO 2020a:19).

According to WHO (WHO 2020a:17), decisions to start newly diagnosed patients who do not have any of the following conditions on the shorter all-oral bedaquiline-containing regimen should be made according to patient preference and clinical judgment (see Figure 2.4).

- Without resistance or suspected ineffectiveness of a medicine in the shorter regimen (except isoniazid resistance).
- Without exposure to previous treatment with second-line medicines in the regimen for more than 1 month (unless susceptibility to these medicines is confirmed).
- With no extensive TB disease and with no severe EPTB.
- Not pregnant.

The all-oral bedaquiline-containing regimen consists of an intensive phase of four months that may be extended to six months, and a continuation phase of 5 months, giving a total duration of 9–11 months (WHO 2020a:19).



(WHO 2019a: 38; WHO 2020a:17; WHO 2022a:45)

Figure 2.4 Criteria in deciding when the shorter MDR-TB regimen may be offered

2.3.3.2 Longer MDR-TB regimens for adults and children (Previous regimen before 2019 WHO updates)

In patients with RR/MDR-TB, a regimen with at least five effective TB medicines is recommended during the intensive phase, including pyrazinamide and four core second-line TB medicines – one chosen from Group A, one from Group B, and at least two from Group C. If the minimum number of effective TB medicines cannot be composed as given above, an agent from Group D2 and other agents from Group D3 may be added to bring the total to five (WHO 2016b:7, 24).

According to WHO recommendations, duration of administration of the injectable agent, or the intensive phase, is guided by culture conversion. This injectable agent should be continued for at least eight months and four months after the patient first becomes culture negative - whichever is longer (EFMOH 2014:51,52). And the duration of treatment is guided by culture conversion and the therapy must be continued for a minimum of 20 and at least 18 months after culture conversion – whichever is longer. Extension of therapy to 24 months may be indicated in chronic cases with extensive pulmonary damage (EFMOH 2014:51, 52).

Table 2.5: Previous grouping of medicines recommended for the treatment of RR-TB and MDR-TB.

Group A. Fluoroquinolones		Levofloxacin	Lfx
		Moxifloxacin	Mfx
		Gatifloxacin	Gfx
Group B. Second-line injectable agents		Amikacin	Am
		Capreomycin	Cm
		Kanamycin	Km
		(Streptomycin)	(S)
Group C. Other core second-line agents		Ethionamide/ prothionamide	Eto/Pto
		Cycloserine/ terizidone	Cs/Trd
		Linezolid	Lzd
		Clofazimine	Cfz
Group D. Add-on agents	D1	Pyrazinamide	Z
		Ethambutol	E
		High-dose isoniazid	H^h
	D2	Bedaquiline	Bdq
		Delamanid	Dlm
	D3	*p*-aminosalicylic acid	PAS
		Imipenem-cilastatin	Ipm
		Meropenem	Mpm
		Amoxicillin-clavulanate	Amx-Clv
		(Thioacetazone)	(T)

(WHO 2016b:23)

2.3.3.3 The composition of longer MDR-TB regimens as of 2019.

The 2019 WHO global recommendations on the treatment of MDR-TB regrouped into three (A, B and C) the medicines endorsed for use in the longer MDR-TB regimen (LTR) based on recently available efficacy and safety data as depicted in Table 2.6 (EFMOH 2019:46). The new recommendations signal an important departure from previous approaches of treating MDR-TB. Fully oral regimens are the preferred option for most patients and injectable agents are no longer among the priority medicines considered when designing longer MDR-TB regimens (EFMOH 2019:47).

In MDR/RR-TB patients on longer regimens, all three Group A agents and at least one Group B agent should be included to ensure that treatment starts with at least four anti-TB agents likely to be effective, and that at least three agents are included for the rest of the treatment after bedaquiline has been discontinued. If only one or two agents from Group A are used, both agents from Group B are to be included. If the regimen cannot be composed of agents from Group A and B alone, Group C agents are added to complete the regimen. In the current guidelines, kanamycin and capreomycin are not to be included in the treatment of MDR/RR-TB patients on longer regimens (WHO 2019a:9; EFMOH 2019:49-50).

Starting with five agents is preferred in Ethiopia for the following reasons. First of all, reliable DST is not available for one or more of the agents, for example, quinolones. Secondly, two of the four agents are likely to be stopped before the end of treatment, for instance bedaquiline stopped at month six and linezolid might be stopped because of toxicity (EFMOH 2019:49).

Table 2.6: Current grouping of medicines recommended for use in longer MDR-TB regimens

Groups & steps	Medicine	
Group A:	Levofloxacin *or* Moxifloxacin	Lfx Mfx
	Bedaquiline	Bdq
	Linezolid	Lzd
Group B:	Clofazimine	Cfz
	Cycloserine *or* Terizidone	Cs Trd
Group C:	Ethambutol	E
	Delamanid	Dlm
	Pyrazinamide	Z
	Imipenem–cilastatin *or* Meropenem	Ipm–Cln Mpm
	Amikacin (*or* Streptomycin)	Am (S)
	Ethionamide *or* Prothionamide	Eto Pto
	p-aminosalicylic acid	PAS

(WHO 2019a:24; WHO 2020a:28)

2.3.3.4 The duration of longer MDR-TB regimens

In MDR/RR-TB patients on longer regimens, a total treatment duration of 18-20 months or 15-17 months after culture conversion is suggested for most patients; the duration may be modified according to the patient's response to therapy (WHO 2019a:10, 31). And in patients on longer regimens that contain amikacin or streptomycin, an intensive phase of 6-7 months is suggested; the duration may be modified according to the patient's response to therapy (WHO 2019a:10, 31).

Table 2.7: Suggested MDR/RR-TB regimen composition in Ethiopia

Regimen Type	Regimen composition	Remarks on use
All Oral bedaquiline containing Shorter MDR/RR-TB Regimen (STR), 9-12 months	4–6 $Bdq_{(6m)}$ -Lfx-Cfz-Z-E-Hh-Eto / 5 Lfx-Cfz-Z-E	Refer to the eligibility criteria for its use.
All Oral Longer MDR/RR-TB Treatment Regimen (LTR), 18-20 months	18 $Bdq_{(6m\ or\ longer)}$ - Lfx-Lzd-Cfz-Cs	Preferred regimen for MDR/RR-TB patients not eligible to be treated with all-oral Bdq containing Shorter regimen.
Individualised LTR, 18-20 months, but could be extended up to 24 months	Regimen composition depends on whether each of the medicines in the list could be used as an effective drug based on reliable DST result or likelihood of effectiveness as well as intolerance	Recommended when construction of standardized LTR with at least 3 group A and 2 group B drugs is not possible due to intolerance to the medicines, acquired additional resistance, etc.

(EFMOH 2019a:44; EFMOH 2021:120)

2.3.3.6 Surgical interventions in patients with DR-TB

Before the advent of chemotherapeutic agents, surgical procedures were part of the management of tuberculosis. Collapsing the lung by creating an artificial pneumothorax or by plombage was considered an effective intervention in dealing with lobes of affected, non-functioning lungs. With the advent of anti-TB drugs, however, interest in surgical approaches has decreased. In the current situation of burden of drug-resistant TB with decreasing effectiveness of medical treatments, there has been increasing interest in the use of surgery as a therapeutic option (Harris et al 2016:2).

WHO (2019a:46) also states that surgery has been employed in treating TB patients before the advent of chemotherapy. WHO further elaborates, in many countries, surgery remains one of the treatment options for TB. With the difficult prospect in many settings of insufficient regimens to treat MDR/XDR-TB, and the risk of serious

sequelae, the role of lung surgery is being re-evaluated to reduce the amount of lung tissue with intractable pathology, reduce the bacterial load and thus improve prognosis (WHO 2019a:46).

The main procedures currently employed are resection of segments, lobes or whole lung. These operations can minimize bulk of the disease, reduce bacillary load, and get rid of devitalised lung which is poorly penetrated by the drugs and serve as sanctuary site for the bacteria. Preoperative assessment in dealing with residual lung function and timing of surgery to save non affected part are determinants of a successful surgical outcome. And surgery is not recommended in patients with extensive bilateral disease and partial lung resection for patients with DR-TB is considered an option only under conditions of good surgical facilities, trained and experience surgeons, and with careful selection of candidates (Harris et al 2016:2; Kemper et al 2015:999; WHO 2016b:8; WHO 2019a:47).

2.3.3.7 Adjuvant Therapies

Adjuvant therapies in DR-TB treatment are indispensable and comprise nutritional support and corticosteroids. In addition to causing malnutrition, DR-TB can be exacerbated by poor nutritional status. Without nutritional support, patients already suffering from baseline hunger could become enmeshed in a vicious cycle of malnutrition and disease. The second-line anti-tuberculosis medications can also further decrease appetite, making adequate nutrition a massive challenge. The adjuvant use of corticosteroids has been shown to reduce mortality and can be beneficial in conditions such as severe respiratory insufficiency, central nervous system or pericardial involvement (Lin, Harries, Kumar, Critchley, van Crevel, Owiti, Dlodlo & Dejgaard 2019:63).

Table 2.8: Desirable and undesirable effects of Medicines to treat DR-TB

Drugs	Mechanism of action	Adverse events
Fluoroquinolones: Levofloxacin *OR* Moxifloxacin	fluoroquinolones inhibit mycobacterial DNA gyrase and topoisomerase preventing cell replication and protein synthesis, and are bactericidal The fluroquinolones are well absorbed orally, achieve high serum levels, and distribute well into body tissues and fluids. Adverse effects are relatively infrequent and include gastrointestinal intolerance, rashes, dizziness, and headache.	The potential to prolong the QTc interval leading to cardiac arrhythmias
Bedaquiline	Bedaquiline is a new diarylquinoline with a novel mechanism of action. Bedaquiline is bactericidal for drug-susceptible and MDR strains of MTB. Inhibition of the mycobacterial ATP synthetase proton pump.	Nausea, vomiting, abdominal pain, headache and slight prolongation of the QTc interval
Linezolid	Linezolid's mechanism of action is to disrupt protein synthesis by binding to the bacterial 50S ribosome Linezolid is an oxazolidinone used primarily for the treatment of drug-resistant gram-positive infections. However, this drug is active in vitro against MTB.	Adverse reactions of linezolid include lactic acidosis, thrombocytopenia, anaemia, peripheral neuropathy and optic neuropathy. One of the main adverse effects of
Clofazimine	Clofazimine probably contributes to the sterilising function of DR-TB regimens where pyrazinamide is not effective	clofazimine is skin discoloration or darkening. Clofazimine may prolong the QT interval
Cycloserine (or terizidone)	Cycloserine is an analog of the amino acid-alanine and prevents cell wall synthesis. It inhibits the action of enzymes, including alanine racemase, that are involved in the production of peptidoglycans.	Cycloserine and terizidone has well-established association with neuropsychiatric adverse reactions.
Ethambutol	Ethambutol is a bacteriostatic antimycobacterial agent first synthesized in 1961. Ethambutol is bacteriostatic against MTB. Its primary mechanism of action is the inhibition of the arabinosyltransferases involved in cell wall synthesis, which probably inhibits the formation of arabinogalactan and lipoarabinomannan.	Ocular toxicity, which can be difficult to diagnose in young children.
Delamanid	Delamanid is a nitro imidazole agent. Works by inhibiting mycobacterial cell wall synthesis	Moderate QTc prolongation
Pyrazinamide	The exact mechanism of action of pyrazinoic acid (POA) is unclear, but fatty acid synthetase may be the primary target in MTB. It is more active against slowly replicating bacteria than against actively replicating ones. Pyrazinamide is a pro drug that is converted by the mycobacterial pyrimidase to the active form, POA. This agent is active only in acidic environments, as are found within phagocytes or granulomas.	Hyperuricemia, hepatotoxicity
Imipenem-cilastatin, meropenem, clavulanate and Thioacetazon	Carbapenems (imipenem-cilastin or meropenem) appear to be hydrolysed more slowly by M. tuberculosis when combined with clavulanic acid. Related to the penicillin/cephalosporin family but classified as belonging the carbapenem.	Diarrheal, nausea, vomiting and seizure
Second-line injectable agents: Amikacin, Kanamycin, capreomycin and streptomycin	Amikacin and kanamycin are aminoglycosides that exert mycobactericidal activity by binding to the 16S ribosomal subunit. The mechanism of capreomycin's action is not well understood but involves interference with the mycobacterial ribosome and inhibition of protein synthesis	Ototoxicity, vestibular toxicity, nephrotoxicity, and neurotoxicity (Am. Km) hypokalaemia and hypomagnesaemia (Cm) Pain at injection site

Ethionamide (or prothionamide)	A derivative of isonicotinic acid. Its mechanism of action is through inhibition of the inhA gene product enoyl-acyl carrier protein (acp) reductase, which is involved in mycolic acid synthesis. Ethionamide is a bacteriostatic against metabolically active bacteria.	Gastrointestinal disturbance, Hypothyroidism may occur, especially in combination with PAS
Para-aminosalicylic acid (PAS)	Para-aminosalicylic acid is an oral agent used in the treatment of MDR- and XDR-TB. Its bacteriostatic activity is due to inhibition of folate synthesis and of iron uptake. PAS has relatively little activity as an anti-tuberculous	High level nausea, vomiting, and diarrhoea
High-dose isoniazid	Isoniazid has excellent bactericidal activity against both intracellular and extracellular, actively dividing MTB. This drug is bacteriostatic against slowly dividing organisms. Isoniazid is a prodrug activated by the mycobacterial KatG catalase/peroxidase; isoniazid is coupled with reduced nicotinamide adenine dinucleotide (NADH). The resulting isonicotinic acyl-NADH complex blocks the mycobacterial ketoenoylreductase known as InhA, binding to its substrate and inhibiting fatty acid synthase and ultimately mycolic acid synthesis	Drug induced liver injury and peripheral neuropathy. Rash, fever, anaemia, acne, arthritic symptoms, a systemic lupus erythematosus-like syndrome, optic atrophy, seizures, and psychiatric symptoms.

(WHO 2016b:26; PIH 2013:36-44; EFMOH 2016a:11; Jameson et al 2018:1276-1278)

2.3.4 Drug-resistant TB treatment outcomes

Many scholars assert that the aims of TB treatment are to cure the patient, prevent death and relapse of the disease, curb transmission of infection and prevent the development of acquired drug resistance. These aims of TB treatment can be affected by unfavourable factors which may result in poor treatment outcomes (Alene, Viney, McBryde, Tsegaye & Clements 2017:357; Abuaku, Tan, Li, Chen & Huang 2010:281-282; Baluku et al 2021:2; Baye, Sarhie & Endalew 2018:1; Lin et al 2019:61).

Different studies indicate that DR-TB is associated with much poorer treatment outcomes compared to the drug-susceptible TB. These poor outcomes are linked to longer periods of infectivity, which result in enhanced transmission of DR-TB strains in the community at large (Bhering, Sarubbi Junior, Kritski, Souza & Duarte 2020:62-63; Leveri, Lekule, Mollel, Lyamuya & Kilonzo 2019:2; McNally, de Wildt, Meza & Wiskin 2019:2).

According to Ahmad, Javaid, Syed Sulaiman, Afridi, Zainab and Khan (2018:1) and Kemper et al (2015:993) the main factor for poor treatment success for DR-TB treatment is the use of SLDs, which are expensive, poorly tolerated, and less effective and need a prolonged duration for treatment.

Khachatryan et al (2021:5) indicated that presence of resistance to anti-TB drugs is a significant challenge for achieving successful treatment outcomes in DR-TB patients. Furthermore, unfavourable outcomes in DR-TB patients, such as treatment failure and death, is highly linked to prior TB treatment with either first-line or second-line agents (Leveri, Lekule, Mollel, Lyamuya & Kilonzo 2019:2; Safaev et al 2021:8).

The 2017 WHO global TB report shows that treatment success rate of 54% for 2014 cohort of MDR/RR-TB patients and the remaining 46% did not complete their treatment: in 8% the treatment failed, 16% died, 15% were lost to follow-up and 7% had no outcome information. Similarly, the report indicates treatment success rate of 30% for the 2014 cohort of XDR-TB patients and the remaining 28% died, 21% treatment failed, and 20% were lost to follow-up or their treatment outcome was not evaluated (WHO 2017:63,89,90).

Likewise, the 2018 WHO global TB report treatment outcome data shows treatment success rates of 55% and 34% for the 2015 cohort MDR/RR-TB and XDR-TB patients respectively (WHO 2018:67). From the remaining 2015 MDR/RR-TB cohorts, in 8% the treatment failed, 15% died, 14% were lost to follow-up and for 7% there was no outcome information. From the remaining 2015 XDR-TB cohorts, 26% died, treatment failed for 19%, and 21% were lost to follow-up or their treatment outcome was not evaluated (WHO 2018:96).

In the same way, the 2019 WHO global TB report treatment outcome data confirms treatment success rates of 56% and 39% for 2016 cohort MDR/RR-TB and XDR-TB patients respectively. From the remaining 2016 MDR/RR-TB cohorts in 8% the treatment failed, 15% died, 15% were lost to follow-up and for 6% there was no outcome information, while from the remaining 2016 XDR-TB cohorts, 26% died, treatment failed for 18%, and 18% were lost to follow-up or their treatment outcome was not evaluated (WHO 2019b:102-103).

According to WHO global TB report of 2020, for the cohort of MDR/RR-TB in 2017, the proportion of patients who successfully completed treatment was 57%. In the same cohort, 7% had failed treatment, 15% died, 16% were lost-to-follow-up and 5% had no outcome information. In the same report, for the cohort of Pre-XDR-TB in 2017, it was reported that 47% successfully completed treatment, while 24% died, 11% had failed treatment, 18% had no outcome information (WHO 2020b:106).

Moreover, according to the 2021 WHO global TB report, the treatment outcome data showed a treatment success rate of 59% for the 2018 cohort of MDR/RR-TB patients (the latest MDR/RR-TB patient cohort for whom data are available), as shown in Figure 2.5 (WHO 2021b:20).

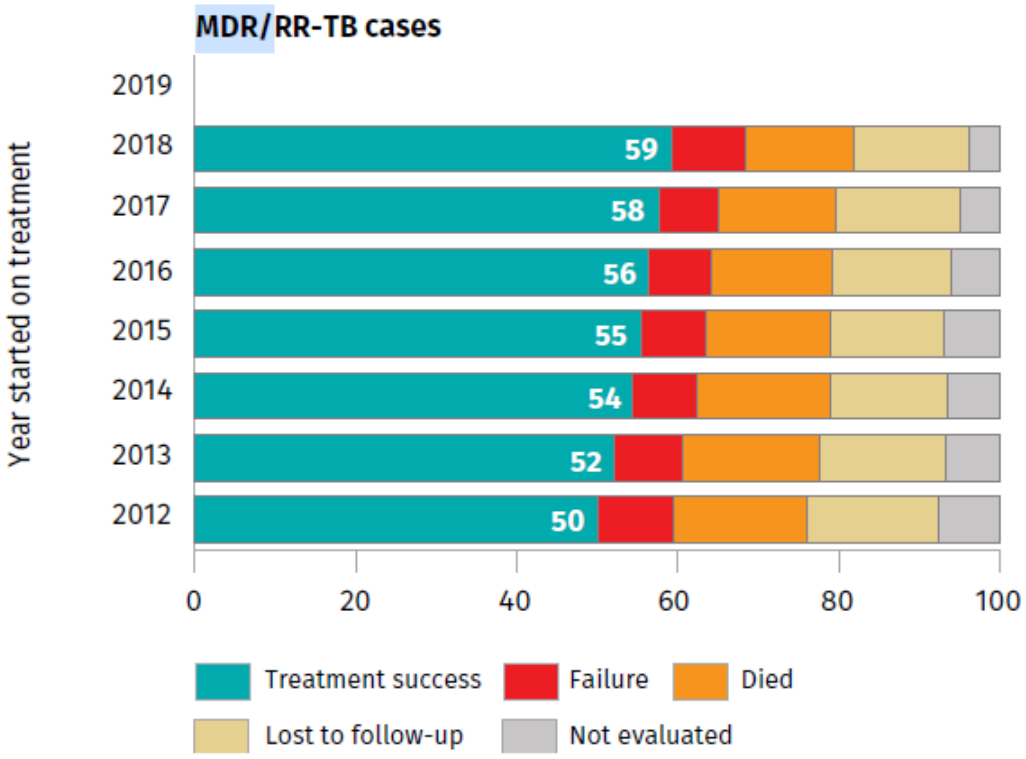


Figure 2.5 Treatment outcomes for MDR/RR-TB cases, 2012-2018 globally (WHO 2021:19).

In their study in Georgia, Kemper et al (2015:996) identified that risk factors associated with unfavourable treatment outcomes were acquired resistance, high baseline drug resistance, and sputum smear or culture positivity at four and six months. Kemper et al (2015:997), in the same study, indicated an alarmingly high rate of acquired drug resistance during SLD treatment (13.5%), including development of XDR-TB (9.9%) and strong association between acquired resistance and poor treatment outcomes. In addition, the result of the study show baseline cavitary disease, high grade smear positivity, increased drug resistance and persistent smear positivity at follow up sputum examinations associated with acquired resistance.

The cavitary lesion is an ideal setting for acquired resistance, given the high bacterial loads, active mycobacterial replications, reduced exposure to host defences, and potentially low penetration by drugs. The fibrotic wall of the cavity and the variable

vascularisation could reduce the penetration of the SLD drug, resulting in drug-selection pressure, and emergence of acquired resistance (Kemper et al 2015:999).

Magee, Kempker, Kipiani, Tukvadze and Howards (2014:4) in their study in Georgia corroborate factors significantly associated with lower conversion rates and ultimately with poor DR-TB treatment outcomes to include current smoking, cavitary disease, disseminated TB and low body mass index (BMI). Similarly, Magee et al (2014:6) in another study in Georgia demonstrate that higher baseline AFB smear grade is a predictor of poor DR-TB treatment outcomes.

Abuaku et al (2010:285) shows that, in a study conducted in Hunan, China, gender also plays a significant role in developing TB disease and completing the course of treatment. Male TB patients were identified to have higher risk of treatment default and higher burden of the disease than their female counterparts. The underlying reason is that males bear a higher burden of smoking and substance abuse compared to females, globally, which are a predisposing factor for TB and negative TB treatment outcomes.

Abuaku et al (2010:285) and Safaev et al (2021:8), similarly assert that age also affects treatment outcomes of TB patients. As the age of the patient increases, the risk of treatment interruption increases and chances of death also rise. The researchers mention that these negative treatment outcomes are associated with old age in several studies. The explanation could be increasing comorbidities as well as the general physiological deterioration associated with old age.

Researchers Woldeyohannes et al (2019:11) are convinced that delay in diagnosis and embarking on appropriate treatment comprise some of the challenges culminating in poor treatment outcomes. Another study conducted in Tanzania by Mpagama et al (2020:1-2) showed a considerable delay in diagnosis of DR-TB in the country. This means that in resource-poor settings, for most patients, multiple opportunities for an DR-TB diagnosis were missed prior to referral.

Early diagnosis and starting of treatment is crucial for the effective treatment of DR-TB and the possibilities of successful outcomes. Delay in the diagnosis of DR-TB results in patients presenting with chronic disease, progressive parenchymal destruction, higher bacillary loads and continuing transmission (Mookherji & Algria-

Flores 2018:8). As the WHO global TB report shows (2018:67), there are large gaps in detection and treatment of DR-TB universally. In 2017, the number of MDR/RR-TB cases started on treatment was only 25% of the estimated incidence of 558 000 cases (WHO 2018:67).

In resource-limited settings, poor treatment outcomes may be a result of unavailability of laboratory tests required for monitoring of toxic effects of SLDs. These laboratory tests need trained human resources and equipped laboratory capacity in tandem with the availability of reagents to run the necessary tests. As DR-TB treatment takes up to two years and the toxic nature of the drugs further complicates the medical trajectory, adverse events may result in poor patient adherence to prescribed treatment. Ultimately, the situation may culminate in treatment interruption or other unfavourable outcomes (Reves & Angelo 2016:10).

According to WHO reports, one of the challenges for the prevention, diagnosis and treatment of DR-TB are co-morbidities like HIV infection and diabetes mellitus. Reports have shown high mortality rates among HIV-infected patients with DR-TB (WHO 2008:90). Diabetic patients with DR-TB are at risk of poor DR-TB treatment outcomes; because the presence of diabetes mellitus may potentially generate the adverse effects of anti-tuberculosis drugs, especially renal dysfunction and peripheral neuropathy (Baluku et al 2021:2; Dlodlo et al 2019:11; WHO 2008:83).

The diagnosis of TB (including DR-TB) in HIV-infected people is more difficult and may be confused with other pulmonary or systemic infections. The presentation is more likely to be extrapulmonary or sputum smear-negative than in HIV-uninfected TB patients, especially as immunosuppression advances. This can result in misdiagnosis or delays in diagnosis, and in turn, higher morbidity and mortality which are both unfavourable outcomes (WHO 2008:94; Woldeyohannes et al 2019:7).

Barriers to good treatment outcomes for HIV infected people with DR-TB are enormous. Drug-drug interaction among medicines for both ailments is common. The multiple medicines involved in DR-TB with recognised high toxicity risks, often combined with ART, results in a high incidence of adverse effects. Adverse events consequently affect adherence and may lead to unfavourable outcomes (Girum, Tariku & Dessu 2017:335; WHO 2008:94)

According to the WHO studies, the major bottlenecks in achieving success in tuberculosis treatment are associated with poverty and low socioeconomic status (WHO 2015:79). Dr. Mario Raviglione, former Director of the World Health Organisation's Global TB Programme, stated the following:

> It was apparent, however, that while enhancing access to diagnosis and treatment remarkably improved outcomes in terms of reducing suffering and death, it had very little effect on achieving the desired impact in terms of declining the incidence rates and driving down the TB epidemic. This is not entirely surprising: TB is not only a biomedical and a public health problem but also a disease associated with poverty. TB will continue thriving as long as poverty persists. The End TB Strategy, whose aim is to end the TB epidemic, therefore combines a holistic mix of health and social interventions (WHO 2015: [sp]).

In their study investigating the factors contributing to the treatment interruption of tuberculosis patients in Tembisa, South Africa, Human, Smith and Tshabalala (2010:48,55) elucidated that socio-economic, TB policy related and health care related issues including unemployment, lack of permanent addresses and socioeconomic factors were complicating pressures in this regard.

A study conducted in Tomsk, (Russian Federation) to identify barriers to successful treatment of tuberculosis shows co-morbid conditions do significantly contribute to poor treatment outcomes and substance abuse is strongly associated with non-adherence and default. In this study, comorbid conditions such as alcoholism and cardiovascular disease and late presentation contribute substantially to mortality (Gelmanova, Keshavjee, Golubchikova, Berezina, Strelis, Yanova, Atwood & Murray 2007:703). Similarly, WHO also states alcohol use is a strong risk factor for TB disease and poorer treatment outcomes at the individual level (WHO 2017:14).

In a Georgian study, researchers Gegia, Magee, Kempker, Kalandadze, Chakhaia, Golub and Blumberg (2015:393) found that the risk of a poor tuberculosis treatment outcome was 70% greater in current smokers compared to never smokers. Patients being treated for MDR tuberculosis had a three-fold greater risk of a poor outcome compared to patients being treated for other forms of tuberculosis. They also found that patients who had recently stopped smoking had a lower risk of a poor tuberculosis

outcome than current smokers. In addition, other studies have shown that smoking is associated with increased risk of tuberculosis mortality, tuberculosis treatment failure, and relapse after treatment completion (Gegia et al 2015:396).

In another study in Georgia, smoking was identified as a barrier to tuberculosis treatment success. Existing evidence strongly suggests that smoking is a high risk factor for developing active TB and is associated with TB treatment failure. And among patients with DR-TB, current smoking was verified as a risk factor for lower rates of sputum culture conversion (Magee et al 2014:6; Leveri et al 2019:2).

Adherence is a major problem in the treatment of DR-TB because of the long duration of treatment and adverse effects of second line drugs (Molie et al 2019:2). Non-adherence to TB treatment has serious negative consequences, resulting in high defaulter rate, further resistance and treatment failure (Girum et al 2017:331).

Some of the reasons for poor adherence and loss-to-follow up involve the competing priorities faced by poor populations: the need to earn money on a daily basis, duties and responsibilities towards family members and substance misuse as a coping strategy against poverty. Combinations of several factors resulting from the difficult social and economic conditions are likely to contribute to this problem (Tola et al 2017:448).

Among many negative influences on the adherence of patients to their treatment success is a reaction of the health care providers towards them (Jakasania, Shringarpure, Kapadia, Sharma, Mehta, Prajapati & Kathirvel 2020:5). In a study undertaken in Pakistan, Khan, Walley, Witter, Shah and Javeed (2005:363) reported that health care providers negatively posed strong barriers to patients' adherence to TB treatment. In another study conducted in Ghana, unfriendly and indifferent health providers were identified as influencing patients on TB treatment to default (Norgbe et al 2011:68). Similarly, Reves and Angelo (2016:10) explains some health care staff feel unprepared because of limited training on how to manage patients and sometimes avoid patients.

In general, treatment of DR-TB is a serious and tough undertaking for many reasons. The large number of pills, the side effects of treatment and the need for daily injections, and the long duration of treatment place great demands strain on patients and

healthcare systems. As a result, consistently over 20% of patients discontinue treatment early in many facilities, and up to 52% in some facilities (Cox, Furin, Mitnick, Daniels, Cox & Goemaere 2015:492).

Table 2.9: Reasons for non-adherence to TB treatment

Healthcare factors	Treatment factors	Patient factors
Inaccessible service; travelling distances and lack of transport and/or money Expenses incurred by attending hospitals/clinics Long waiting times Unfriendly staff members Inadequate confidentiality Seeing different health workers at each visit to the clinic Poor communication style Lack of interpreters or culturally appropriate staff Other personal and social Healthcare providers characteristics	Long treatment duration Large pills, or large number of pills Side-effects Disruption of daily routines Errors during prescribing or dispensing Cost	Life stressors (lack of resources, unemployment, life events) Low education level or illiteracy Health beliefs Community stigma Poor understanding of TB and treatment rationale Substance abuse, such as alcohol Patients might not believe that they need TB treatment; or they might not feel sick

(McLean 2003:7)

2.4 CONCLUSION

In this chapter, a wide-ranging and comprehensive literature review on tuberculosis especially on DR-TB, was presented. The literature illustrates etiology, epidemiology, diagnosis, treatment and treatment outcomes of DR-TB in detail. The next articulates the research design and methodology followed in this study.

CHAPTER 3

RESEARCH DESIGN AND METHODOLOGY

3.1 INTRODUCTION

Chapter two discussed the historical background of tuberculosis and emergence of drug resistant TB and its threat to control programmes worldwide. The chapter also described aetiology, transmission, diagnosis and treatment and treatment outcomes of tuberculosis and drug resistant tuberculosis. In addition, factors related to unfavourable treatment outcomes were further synthesised in the chapter.

This chapter presents the theoretical framework, the paradigm, research approaches, research design and methods used in this study to achieve the stated objectives. The research methods include sampling procedures, data collection, data analysis and ethical considerations.

3.2 HEALTH BELIEF MODEL

The health belief model (HBM) is perhaps the oldest and most widely used social cognition model in health psychology. HBM is a psychological model and conceptual framework that attempts to explain and predict health behaviours by focusing on the attitudes and beliefs of individuals. HBM is the most commonly used theory in health education and health promotion to explain change and maintenance of health-related behaviours and as a guiding framework for health behaviour interventions (LaMorte 2019:1; Tarkang & Zotor 2015:4; Tola, Garmaroudi, Shojaeizadeh, Tola, Yekaninejad, Ejeta, Kebede & Kassa 2017:448).

Godfrey Hochbaum, Irwin Rosenstock and Stephen Regels developed the HBM in the early 1950s in the United States to help answer low participation of the public in health screening programmes, for instance, a free TB screening (LaMorte 2019:1; FHI 2002:2; Tarkang & Zotor 2015:3).

According to the HBM, people will take action to prevent, screen for, or control their health conditions if they believe they are susceptible to disease (perceived susceptibility), if they believe the disease would have serious consequences (perceived severity), if they perceive that there are benefits to engaging in the behaviour (perceived benefits), and there are few barriers that prevent this behaviour

(perceived barriers). Thus, an individual will weigh perceived susceptibility and severity of the disease against the balance of benefits and barriers to making those changes (Glanz, Rimer & Viswanath 2015:100; LaMorte 2019:1; Riekert, Ockene & Bert 2014:122).

The HBM aims at assessing the health behaviour of individuals through the perceptions and attitudes a person may have towards disease or health condition and negative outcomes of certain actions. The HBM was conceptualised around the individual's beliefs and attitudes captured in four constructs representing the perceived threats and net benefits. These constructs are *perceived susceptibility* and *perceived severity,* which make up the *perceived threat,* and *perceived benefits* and *perceived barriers* which make up the net benefit (Mukumbang, Belle, Marchal & Wyk 2017:2).

3.2.1. Components of the HBM

According to LaMorte (2019:1) and Tarkang and Zotor (2015:34) the HBM has three major components:

- Individual perceptions of health.
- Modifying factors including demographic, sociopsychological, and structural variables.
- The benefits of taking the preventive measures.

3.2.1.1 *Individual Perceptions*

Individual perceptions are a person's beliefs about their own susceptibility to a disease, as well as the seriousness with which one views the perceived threat of the illness (Glanz et al 2015:102; Tarkang & Zotor 2015:4).

3.2.1.2 *Modifying Factors*

Modifying factors such as demographic, socio-psychological and structural variables can affect an individual's perception and thus indirectly influence health-related behaviours (Nwobodo & Ba-Break 2015:497; Tarkang & Zotor 2015:4).

3.2.1.3. *Variables Affecting the Likelihood of Initiating and Maintaining Action*

Perceived benefits minus the perceived barriers to take action (accessibility, affordability and acceptability); this equals the likelihood of taking actions to change behaviours (Tarkang & Zotor 2015:4).

3.2.2 Concepts of the HBM

The basic concept of the HBM is that health behaviour is dependent on personal beliefs or perceptions regarding a health condition or disease and interventions available to lower its occurrence. It comprises many primary constructs. Perceived susceptibility, perceived severity, perceived benefit, perceived barrier, and self-efficacy can predict why people engage in actions to prevent, screen, or control health related conditions, including illness (Diddana, Kelkay, Dola & Sadore 2018:2).

The concept of self-efficacy, the most recent addition to the HBM, was adapted directly from Bandura's work (1977:193), while cues to action was added to estimate events or experiences that fuel a person's direct need to take action (Alemayehu 2015:29).

3.2.2.1 *Perceived Susceptibility*

The first concept of HBM is *perceived susceptibility* defining an individual's beliefs about the chances of contracting a health condition. An individual's perception that a health problem is personally relevant helps to take the necessary action in avoiding the health problem. For this to happen, activities must take place that increase individual perceptions of their vulnerability to the health condition. People who think they are susceptible to HIV/AIDS are more likely to use condoms to protect against sexual transmission of the disease (LaMorte 2019:1; Li, Yang, Zhang, Fisher, Tian & Sun 2015:910).

3.2.2.2 *Perceived Severity*

Perceived severity refers to one's beliefs about how serious a condition and its consequences are. When one recognises one's susceptibility to a certain health problem or condition, it may not motivate one to take the necessary preventive actions unless one realises that getting that health problem would have serious physical and social implications. It is when one realises the magnitude of the negative consequences of a condition, that one takes the necessary actions to avoid these negative consequences (Tola et al 2017:450). For instance, people must perceive DR-TB as a serious and fatal disease that has severe consequences, before they can embark on long and toxic treatment regimens.

3.2.2.3 *Perceived Benefits*

Perceived benefits refer to one's beliefs in the efficacy of the recommended action in reducing the risk or seriousness of the impact. The person must believe that taking a specific action could help prevent a problem from occurring. It is this belief that gives a person the confidence to take action based on the expected outcomes. Similarly, DR-TB patients should have a belief in the efficacy of anti-TB drugs and that the medications could make them better from their disease.

3.2.2.4 *Perceived Barriers*

Perceived barriers refer to one's beliefs in the tangible and psychological costs of the recommended behaviours. There can be various barriers that influence people's decisions to take certain actions. Perceived barriers to health actions include phobic reactions, physical and psychological barriers, accessibility factors, personal characteristics, possible hindrances to engage in preventive behaviours, including such factors as cost, inconveniences and unpleasantness. Perceived barriers also include cost, duration, complexity of the deserved behaviours and access to services that would support taking and maintaining the necessary actions. Only when people realise that they are capable of dealing with these barriers, are they able to take the necessary actions (Alemayehu 2015:28). Similarly, perceived tangible and psychological barriers to DR-TB patients affecting their successful treatment completion were investigated.

3.2.2.5 *Cues to Action*

The HBM's *cues to action* are events or experiences, personal (physical symptoms of a health condition), interpersonal, or environmental (media publicity), that motivate a person to take action. It requires motivation on the part of the individual to have a desire to comply with the prescribed action or treatment, to have concerns about health matters, to be willing to seek and accept health care and to engage in positive health activities (Tola et al 2017:449). In this regard, the experience of previously treated DR-TB patients with regard to events, either interpersonal or environmental, that motivated and engaged them towards successful treatment adherence and completion was explored and described.

3.2.2.6 *Self-Efficacy*

The sixth concept of the HBM is *self-efficacy*. This is the strength of an individual's belief or confidence in one's own ability to respond to novel or difficult situations and to deal with any associated obstacles or setbacks. It is one's ability to successfully undertake action (Helelo 2018:35). In this study, the strength and determination of previously treated DR-TB patients by themselves to resist hindering factors throughout the treatment duration were explored as an important enabling factor to successful treatment completion.

LaMorte (2019:1) and Tola et al (2017:449) describe the HBM as using two aspects of individuals' representations of health behaviour in response to threat of illness: *perceptions of illness threat* and *evaluation of behaviours to counter this threat*. Threat perceptions depend upon two beliefs: the perceived susceptibility to the illness and perceived severity of the consequences of the illness. Together, these two variables determine the likelihood of the individual following a health-related action, although their effect is modified by individual differences in demographic variables, social pressure and personality. The particular action taken is determined by the evaluation of the available alternatives, focusing on the benefits or efficacy of the health behaviour and the perceived costs or barriers to performing the self-same behaviour. So, individuals are likely to follow a particular health action if they believe themselves to be susceptible to a particular condition which they also consider to be serious, and believe that the benefits of the action taken to counteract the health threat outweigh the cost (LaMorte 2019:1;Tola et al 2017:449).

In their opinions, Neeraj and Eke (2016:37) and Bakan and Erci (2018:211-222) consider that the HBM views a change in health behaviour as based on a rational assessment of the balance between the obstacles and the benefits of action. According to the model, the perceived seriousness, and susceptibility to a disease influence the individual's perceived threat of a disease. Similarly, perceived benefits and perceived barriers influence perceptions of the effectiveness of health behaviour. In turn, demographic and socio-psychological variables influence both perceived susceptibility and perceived seriousness, and the perceived benefits and perceived barriers to action. Perceived threat is influenced by cues to action, which can be

internal (for example, symptom perception) or external (for example, health communication).

According to Bakan and Erci (2018:214) HBM explains the relationship between a person's beliefs and behaviours and the effects of individual motivation on health behaviours at decision-making level. In HBM, which is a cognitive approach in the main, the individual is expected to demonstrate preventive health behaviours when he or she perceives a threat against their health or expect the benefit of some interventions that prevent the perceived health threat.

The HBM affirms that increases in perceived threats and perceived benefits will end up with lower barriers to action and encourage an individual to exercise the recommended behaviours (Enwereji & Eke 2016:37).

Mukumbang et al (2017:2) mention that the HBM usefully describes demographic and psychological factors that influence health motivation, and more interestingly identifies the factors that perpetuate actual adherence behaviour. However, it also fails to operationalise a realist causal explanation. That is, it fails to identify what mechanisms are triggered under what context of action to bring the expected results.

Lynch and Jackson (2019:68) state that in using the HBM, the likelihood of involvement in protective behaviour is affected by the perceived risk of the health problem, the benefits of involvement in the protective behaviour, and the sheer barriers to involvement in the protective behaviour.

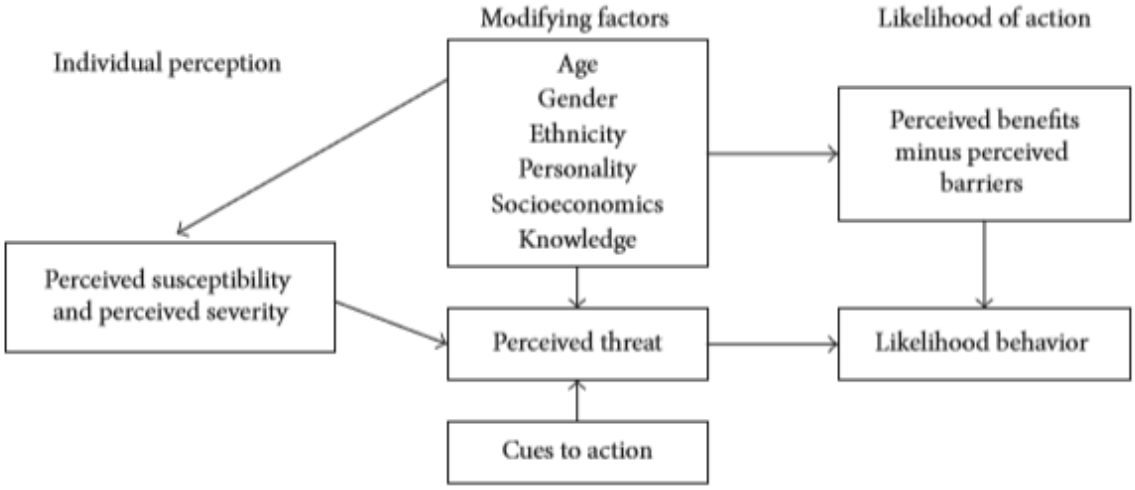
Azizi, Karimy and Salahshour (2018:707) in their study describing the determinants of adherence to TB treatment in Iranian patients via HBM, allude to influences such as knowledge, attitudes, beliefs and perceptions that affect the individual behaviour of patients, such as adherence to TB treatment. HBM is suggested as a valuable model for describing these behaviours and treatment adherence to guide planning for control programmes.

A good understanding of the process of TB treatment adherence and identifying the factors that determine it are the cornerstones of treatment success. Their study provides support for the idea that HBM constructs might contribute to predicting therapeutic adherence in TB patients. HBM is a useful model in explaining healthy behaviours, including treatment adherence (Azizi, Karimy & Salahshour 2018:709).

The researchers Cronin, Hankins, Byrd, Pernell and Kassim (2018:683) in their study on modifying factors of the health belief model associated with missed clinic appointments among patients with sickle cell disease (SCD), demonstrate that modifying components of the HBM, including age, financial security, health literacy, spirituality, and lacking cues to action such as reminders, are important in missed appointments. In this study, modifying factors, including demographic characteristics, clinical characteristics, lifestyle and physical characteristics, health system-related factors, personality, and socio-economics, of HBM associated with treatment completion of DR-TB treatment were explored and described.

3.2.3 Limitations of HBM

As a psychological model HBM does not take into consideration other factors, such as environmental, economic and social factors, that may influence health behaviours. As a theory, it does not show the relationships between the variables or provide clear frameworks on how to combine the variables for a better result during the intervention (Enwereji & Eke 2016:37).



(Diddana, Kelkay, Dola & Sadore 2018:2)

Figure 3.1 Health Belief Model

In this study, the HBM provided the theoretical framework used to explore treatment completion of patients with drug resistant tuberculosis. Constructs from HBM were used to guide development of interview guides for the study. Accordingly, barriers and

facilitators of treatment completion of patients with drug resistant tuberculosis were deeply and extensively explored.

3.3 RESEARCH PARADIGM

Guba (1990:17) defines worldviews as “a basic set of beliefs that guide action.” Creswell and Creswell (2018:5) submit that others have called them paradigms while Babbie (2021:29) describes a paradigm as a model or frame of reference through which to observe and understand a specific research conundrum.

Paradigms are neither true nor false; as ways of looking, they are only more or less useful. Each of the paradigms offers a different way of looking at human social life. Each paradigm makes its own assumptions about the nature of social reality. Each can open up new understandings, suggest different kinds of theories, and inspire different kinds of research (Babbie 2021:30). A paradigm therefore is understood as a general organising framework for theory and research that includes basic assumptions, key issues, models of quality research, and methods for seeking answers (Neuman 2014:85).

Creswell and Creswell (2018:5) see worldviews as a general philosophical orientation about the world and the nature of research that a researcher brings to a study. Worldviews are beliefs and values that researchers bring to a study, and they may be drawn from at least one or more perspectives, such as post-positivism, constructivism, participatory worldviews, and pragmatism (Creswell & Plano Clark 2018:35).

The research paradigm used in this study is pragmatism, which arises out of actions, situations, and consequences rather than antecedent conditions (as in post-positivism). There is a concern with applications - what works - and solutions to problems. Instead of focusing on methods, researchers emphasise the research problem and use all approaches available to understand the problem (Creswell & Creswell 2018:10).

As a philosophical underpinning for mixed methods studies, Morgan (2007:70) and Tashakkori and Teddlie (2010:95-97) convey its importance in bringing attention to the research problem in social science studies and then using pluralistic approaches to

get insight into the problem. Pragmatism derives from the work of Charles Sanders Pierce, William James, George Herbert Mead, and John Dewey (Creswell & Creswell 2018:10; Kaushik & Walsh 2019:2).

Pragmatism is typically associated with mixed methods research, where the focus is on the consequences of research, on the primary importance of the question asked rather than the methods, and the use of multiple methods of data collection to inform the problems under study. Thus, it is pluralistic and oriented toward “what works” in practice (Creswell & Plano Clark 2018:35-36; Gray, Grove & Sutherland 2017:311). Furthermore, a pragmatic approach allows the possibility of choosing the appropriate research methods from the wide range of qualitative and/or quantitative methods, and this pluralism is a strength of pragmatism that has several advantages for social justice research. It sets an inclusive framework of inquiry that supports interdisciplinary and cooperative research about social injustices (Kaushik & Walsh 2019:12).

According to Creswell and Creswell (2018:10-11), pragmatism provides a philosophical basis for research:

- Pragmatism is not devoted to any one system of philosophy and reality. This works for mixed methods research in that inquirers draw liberally from both quantitative and qualitative assumptions when they engage in their research.
- Individual researchers have freedom of choice. In this respect, researchers are free to choose the methods, techniques and procedures of research that best meet their needs and purposes.
- Pragmatist researchers do not see the world as an absolute unity. Similarly, mixed methods researchers look at many approaches to collecting and analysing data rather than subscribing to only one (for example, quantitative or qualitative).
- Truth is what works at the time. It has no basis in a duality between reality independent of the mind or within the mind. Therefore, in mixed methods research, researchers use both quantitative qualitative data because they work to provide the best understanding of the research problem.

- The pragmatic researchers look to the problem and how to research the conundrum based on the intended consequences ─ where they want to go with it. Researchers who use this method need to establish a purpose for their mixing, a rationale for why quantitative and qualitative data should be mixed in the first place.
- Proponents of pragmatism agree that research always occurs in social, historical, political, and other contexts. Thereby, mixed method studies may include a postmodern turn, a theoretical lens that is reflective of social justice and political aims.
- Proponents of pragmatism believe in an external world independent of the mind as well as that lodged in the mind. But the same researchers believe that we need to stop asking questions about reality and the laws of nature. They would simply like to change the subject.
- Thus, for investigators employing mixed methods, pragmatism paves the door to multiple methods, different world views, and different assumptions, as well as different forms of data collection and analysis (Creswell & Creswell 2018:10-11).

There are several elements for each worldview that differ, and they are reflected in different philosophical assumptions, such as ontology, epistemology, axiology, methodology, and rhetoric (Creswell & Plano Clark 2018:37).

Ontology deals with what is real and refers to the nature of reality when researchers conduct their inquiries. Pragmatists view reality as both singular (for example, there may be a theory that operates to explain the phenomenon of study) as well as multiple (for example, it is important to assess varied individual input into the nature of the phenomenon as well) (Creswell & Plano Clark 2018:37).

Epistemology refers to how we gain knowledge of what we know (what is the relationship between the researcher and that being researched?). Pragmatists aim at practicality (for example, researchers collect data by "what works" to address a research question). Researchers may focus on distance and impartiality (for example, researchers objectively collect data on instruments) and focus on closeness (for example, researchers visit participants at their sites to collect data) (Creswell & Plano Clark 2018:38).

Axiology refers to the role of values in research. Pragmatists look at multiple stances (for example, researchers include both biased and unbiased perspectives) (Creswell & Plano Clark 2018:38).

Methodology refers to the process of research. Pragmatists combine processes (for example, researchers collect both quantitative and qualitative data and mix them) (Creswell & Plano Clark 2018:38).

Rhetoric refers to the language of research. Pragmatists use formal or informal rhetoric (for example, researchers can employ both formal and informal styles of writing) (Creswell & Plano Clark 2018:38).

3.4 PURPOSE OF THE STUDY

Neuman (2014:38) states that the purposes of social research can be divided into three groups, depending on what the researcher is trying to achieve: to explore a new topic, describe a social phenomenon, or explain why something happens.

The purpose of this study was to describe the views of experts around why they believe that Ethiopia does not have 100% DR-TB treatment completion and to describe the lived experiences of previously treated DR-TB patients to ascertain why some complete treatment and others do not. And finally, the study strives to develop best practice guidelines to address barriers to successful treatment completion for patients with drug-resistant tuberculosis in Ethiopia.

3.5 STUDY OBJECTIVES

The objectives of this study were:

For the qualitative strand, the specific objectives were designed to:

- Describe the views of experts managing DR-TB patients on treatment completion
- Describe the experiences of previously treated DR-TB patients on treatment completion.

For the quantitative strand, these were designed to:

- Determine factors associated with treatment completion of patients on DR-TB treatment.

For the mixed methods, the objective strives to:

- Explain factors associated with treatment completion utilising findings from qualitative strand.

For best practice guideline, the objective was designed to:

- Develop best practice guidelines aimed at addressing barriers to treatment completion for patients with DR-TB in Ethiopia.

Therefore, the study sought to answer the following questions:

- What are the views of experts treating DR-TB patients on treatment completion?
- What are the experiences of previously treated patients on treatment completion?
- What are the factors associated with DR-TB treatment completion?
- In what ways do qualitative interviews with patients and experts serve to explain factors associated with treatment completion.

3.6 RESEARCH DESIGN

Nieswiadomy and Bailey (2018:63) indicate that a research design is a comprehensive plan for conducting an investigation that stretches from the initial research question through the methods of data collection, analysis, interpretation, and reporting. Creswell and Plano Clark (2018:51) concur and describe research design as the overall process of research starting from conceptualising a problem to listing research questions, and on to data collection, analysis, interpretation, and report writing.

Research designs are types or strateges of inquiry within qualitative, quantitative, and mixed methods approaches that provide specific direction for procedures in a study. Research designs are procedures for collecting, analysing, interpreting, and reporting data in research studies (Creswell & Creswell 2018:12). Leavy (2017:8) therefore

describes research design in succinct terms as the process of building a structure, or plan for a research project.

3.6.1 Research Design Types

As explicated below, this study utilised a research design that is exploratory, descriptive and contextual in nature.

3.6.1.1 Exploratory

Exploratory research allows the researcher to investigate the full nature of the phenomenon, the manner in which it is manifested, and other factors which are related to it. The questions asked are: What is the nature of the phenomenon? What is the process by which the phenomenon evolves or is experienced (Polit & Beck 2017:40). In addition, exploratory research enables the researcher to analyse topics where there is insufficient information on the phenomenon under investigation (Creswell and Creswell 2018:162). Furthermore, exploratory research empowers the researcher to study a subject that has not been described in detail and to understand the phenomenon under investigation from the viewpoints of the study participants (Babbie 2021:91).

Exploratory research offered this researcher an opportunity to gain insight into the experiences of previously treated DR-TB patients and views of healthcare providers on treatment completion and multiple meanings were discovered.

3.6.1.2 Descriptive research

Descriptive research is the exploration and description of phenomena in real-life situations – a natural setting. It provides an accurate account of the characteristics of particular individuals, situations, and groups (Gray, Grove & Sutherland 2017:28, 32). A descriptive study allows a researcher to observe, describe, and clarify concepts. It amplifies the dimensions, variations, and importance of the phenomenon. This process involves identifying and understanding the nature of phenomena and the relationship among them. Descriptive research provides information about the scope of a problem, its key characteristics, and conditions under which it is most likely to occur (Leavy 2017:24; Polit & Beck 2017:304).

Gray, Grove and Sutherland (2017:12-13) identify four advantages of descriptive studies. First, descriptive studies enable a researcher to describe what exists under the study situation. Secondly, descriptive studies assist a researcher with the discovery of new information and meanings. Third, descriptive studies promote an understanding of the situations by a researcher. And finally, descriptive studies enable a researcher to classify information for use.

Descriptive design assisted this researcher in identification of experiences of patients and views of healthcare providers on treatment completion and in discovering and describing new information on barriers and enablers to treatment completion of patients with DR-TB.

3.6.1.3 Contextual research

Context pertains to something and is dependent on the milieu (Collins English Dictionary 2022) in which it occurs. Contextual research focuses on developing a deeper understanding of the problem and identifying unexpected issues. This is done within the time, space, and value context in which the study is conducted. It involves the researcher going into the participants' environment to observe and receive first-hand information and understand the meanings ascribed to a conundrum. What makes the research contextual are situations, instances, and life events or lived experiences with a particular meaning that is known to people in their specific environment (Creswell & Creswell 2018:7-8). This study was conducted in a natural setting or real-life situation of the previously treated DR-TB patients and healthcare providers, where DR-TB treatment and care occurs.

3.6.2 Mixed method research design

"A new star in the social science sky" (Mayring 2007:1).

A methodological trend that has gained momentum is the planned integration of qualitative and quantitative data within single studies (Polit & Beck 2017:577; Yin 2016:304). Creswell and Plano Clark (2018:5) define mixed method research as a philosophical assumption and methods of inquiry that guide the direction of the collection and analysis and the mixture of qualitative and quantitative data within a single study.

Creswell and Creswell (2018:41) explain mixed method research involves collection of both quantitative and qualitative data, integration of the two forms of data, and use of unique designs that may involve diverse philosophical assumptions and theoretical frameworks. The basic assumption of this kind of inquiry is that the combination of both approaches provides a more complete understanding of a research problem than either approach alone.

The researcher bases the inquiry on the assumption that the collection of different types of data would lead to a more complete understanding of a research problem than either quantitative or qualitative data alone (Creswell & Creswell 2018:11).

According to Polit and Beck (2017:578), many areas of inquiry can be enriched through the judicious triangulation of qualitative and quantitative data. The advantages of mixed methods include complementarity, practicality, incrementality and enhanced validity. By using mixed methods this study avoids the limitations of a single approach and it is supported by complementary types of data. In this regard, it is more confident about the validity of results (Leavy 2017:263; Polit & Beck 2017:578).

The concept and field of mixed methods research is relatively new with major work in developing it traceable from the middle to late 1980s. Its origins, however, go back further (Creswell & Creswell 2018:12). Early thoughts about the value of mixed multiple methods ─ called mixed methods ─ resided in the idea that all methods have bias and weaknesses, and the collection of both quantitative and qualitative data neutralises the weaknesses of each form of data (Creswell & Creswell 2018:12).

3.6.2.1 Advantages of using mixed methods

Creswell and Plano Clark (2018:12-14) explain the advantages of using mixed methods as it:

- Provides strengths that balance the weaknesses of both quantitative and qualitative research
- Extends an opportunity for studying a research problem to produce more evidence than either quantitative or qualitative research alone.
- Enables researchers to use all of the tools of data collection available rather than being restricted to the types of data collection typically associated with quantitative research or qualitative research.

- Helps researchers answer questions that cannot be answered by quantitative or qualitative approaches alone.
- Mixed method research encourages the use of multiple worldviews, or paradigms (for example, beliefs and values), rather than the typical association of certain paradigms with quantitative research and others for qualitative research. It also encourages us to think about a paradigm that might encompass all of quantitative and qualitative research, such as pragmatism.
- Mixed method research is “practical” in the sense that the researcher is free to use all methods possible to address a research problem.

In this study the researcher got an in-depth understanding of experience of the patients using focus group discussions and views of HCPs through in-depth interview regarding barriers to treatment completion which are not possible to get by only document reviews. Further, the researcher comprehensively understood factors related to sabotaging treatment completion of patients taking drug resistant TB.

3.6.3 The convergent design

This study used the convergent concurrent (parallel) mixed method design. As stated by Polit and Beck (2017:584), the purpose of the convergent design (sometimes called a triangulation design) is to obtain different, but complementary data about the central phenomenon under study - that is, to triangulate data sources. In this design, qualitative and quantitative data are collected simultaneously and with equal priority. The goal of this design is to converge on “the truth” about a problem or phenomenon. The researcher’s job is to link the two data sets, often at the interpretation stage of the project.

In this approach, the researcher collects both quantitative and qualitative data, analyses them separately, and then compares the results to see if the findings confirm or disconfirm each other (Creswell & Creswell 2018:12; Leavy 2017:263).

According to Creswell and Plano Clark (2011:70-71), the convergent parallel design occurs when the researcher uses concurrent timing to implement the quantitative and qualitative strands during the same phase of the research process, prioritises the

methods equally, and keeps the strands independent during analysis and then mixes the results during the overall interpretations.

Convergent design is the most well-known approach among the mixed methods. The inception of this design by scholars goes back as early as the 1970s. The convergent design was initially conceptualised as a “triangulation” design where the two different methods were used to obtain triangulated results about a single topic, but it often becomes confused with the use of triangulation in qualitative research, and researchers often use this design for purposes other than to produce triangulated findings. Since the 1970s, this design has gone by many names, including simultaneous triangulation, parallel study, convergence model, and concurrent triangulation. Regardless of the name, convergent design occurs when the researcher collects and analyses both quantitative and qualitative data at the same phase of the research process and then merges the two sets of results into an overall interpretation (Creswell & Plano Clark 2018:68).

The purpose of the convergent design is to obtain different but complementary data on the same topic to best understand the research problem. The aim in deploying convergent design is to benefit from bringing together the differing strengths and non-overlapping weaknesses of quantitative methods (large sample size, trends, generalization) with those of qualitative methods (small sample, details, in depth). This design also gives the researcher an opportunity to triangulate the methods by directly comparing and contrasting quantitative statistical results with qualitative findings for the purpose of corroboration and validation. Other purposes for this design include illustrating quantitative results with qualitative findings, synthesising complementary quantitative and qualitative results to develop a more complete understanding of a phenomenon, and comparing multiple levels within a system (Creswell & Plano Clark 2018:68).

3.6.3.1 The convergent design procedures

There are four major steps in the convergent design. In the first step, the researcher collects both quantitative and qualitative data about the topic of interest. These two types of data collection are concurrent but separate ─ that is, one does not depend on the results of the other and have equal importance for addressing the study’s research

questions. Second, the researcher analyses the two data sets separately and independently from each other using typical quantitative and qualitative analytic procedures (Creswell & Plano Clark 2018:69).

Once the two sets of initial results are in hand, the researcher reaches the point of interface and works to merge the results of the two data sets in the third step. This step involves directly comparing the separate results or transforming results to facilitate relating the two data types during additional analysis. In the final step, the researcher interprets to what extent and in what ways the two sets of results converge, diverge from each other, relate to each other, and/or combine to create a better understanding in response to the study's overall purpose (Creswell & Plano Clark 2018:69).

3.6.3.1.1 Data collection in the convergent design

The key idea with this design is to collect both forms of data using the same or parallel variables, constructs, or concepts (Creswell & Creswell 2018:219).

This study used a convergent concurrent mixed method design to get an in-depth understanding of the lived experiences of patients using focus group discussions and the views of healthcare providers through an in-depth interview regarding barriers to treatment completion. Further, the researcher had a comprehensive understanding of factors associated with treatment completion in patients taking DR-TB treatment, garnered from a review of the DR-TB registers and patient charts.

In this study, six focus group discussions with previously treated DR-TB patients, in-depth interviews with 15 HCPs working in the DR-TB programme, and document reviews of the medical records of 487 DR-TB patients were conducted simultaneously and with equal emphasis.

For the quantitative strand, the quantitative data were collected using pre-tested questionnaire from DR-TB registers and patient charts. On the other hand for the qualitative strand, data collection tools were focus group discussions guide for FGDs and interview guide for in-depth interviews.

Quantitative data were collected on socio-demographic and lifestyle characteristics, such as history of alcohol consumption and history of non-prescription drugs and on clinical characteristics, including body mass index and presence of comorbidities such as diabetes, chronic liver disease, chronic renal failure, hypertension, CNS disorders, and HIV.

The quantitative data were also collected on the registration group at the start of treatment, classification of TB types, resistance type, bacteriology result, prior TB drug use, outcome of most recent TB treatment, HIV testing and test result, and linkage to HIV chronic care.

Likewise, quantitative data were collected on DST testing results and DST techniques, chest X-ray findings, and the availability and results of monthly monitoring laboratory and clinical tests. In this respect, weight measurement, complete blood count, serum electrolyte, liver function test, urea/creatinine, thyroid function, and audiometry were assessed. Furthermore, adverse events encountered during treatment, the presence of treatment supporters, and final treatment outcomes were also included in the quantitative data collection.

In the FGDs, data were collected on the lived experiences of previously treated DR-TB patients regarding perceived barriers to treatment completion. The focus areas of the collected data were on patients' experience of daily DOT and adherence, time spent at the facility while seeking DR-TB treatment services and availability of different types of DR-TB treatment services. Moreover, data were also collected on their experience on the availability of laboratory and follow-up services and adequacy the staff at the facility is to provide DR-TB treatment services, and satisfaction with the way the DR-TB treatment services are being offered.

During FGDs, data were collected on the main adverse events experienced during the treatment, the main challenges faced while on DR-TB treatment, and the reasons for interrupting the previous DR-TB treatment. In addition, data were collected on the support obtained and challenges faced at home, work, or other places during treatment. Furthermore, the perceived severity of the disease, the perceived benefit of treatment adherence and completion, and suggestions for improvement of the programme were also included in the data collection.

In the in-depth interview, data were collected on the views of HCPs regarding factors contributing to low treatment outcomes and barriers to completion of treatment in general. Similarly, data were collected on the views of HCPs on reasons why patients default from treatment, the main challenges to patient follow-up, and the challenges to the provision of DR-TB treatment services. On the other side, availability of ancillary drugs and allocation of enough staff to DR-TB treatment services, including competency to deliver services effectively, were also among the collected data.

In the in-depth interview, data were also collected regarding the types of services offered, satisfaction with the services being provided, and suggestions for improvement of the DR-TB treatment services and successful treatment outcomes.

3.6.3.1.2 Data analysis in the convergent design

The two databases are analysed separately and then brought together. There are several ways to merge the two databases. The first approach is called a side-by-side comparison. These comparisons can be viewed in the discussion sections of mixed method studies. The researcher first reports the quantitative statistical results and then discusses the qualitative findings (for example, themes) that either confirm or disconfirm the statistical results. Alternatively, the researcher could start with the qualitative findings and then compare them to the quantitative results. Mixed methods researchers call this a side-by-side approach because the researcher makes the comparison within a discussion, presenting first one set of findings and then the other (Creswell & Creswell 2018: 221).

3.6.3.1.3 Interpretation in the convergent design

The interpretation in the convergent approach is typically written into a discussion section of the study. In contrast, the results section report on the findings from the analysis of both the quantitative and qualitative databases, the discussion section includes a report comparing the results from the two databases and notes whether there is convergence or divergence between the two sources of information. Typically the comparison does not yield a clean convergent or divergent situation, and the differences exist on a few concepts, themes, or scales (Creswell & Creswell 2018: 220).

A mixed methods design is useful when the quantitative or qualitative approach, singly, is inadequate to best understand a research problem and the strengths of both quantitative and qualitative research (and its data) can provide the best understanding (Creswell & Creswell 2018:12).

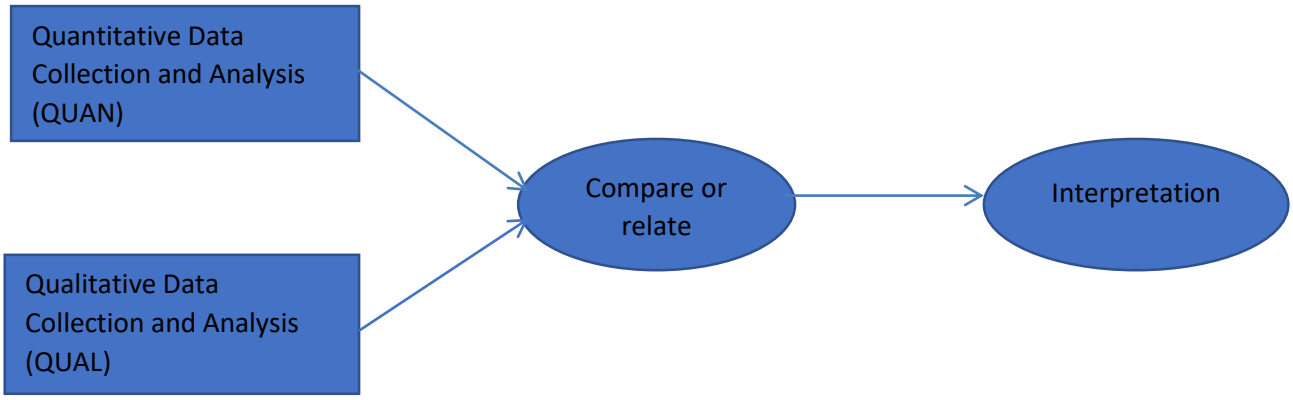


Fig 3.2 Convergent Parallel Mixed Methods Design (Creswell & Creswell 2018:219)

Creswell and Plano Clark (2018:69) describe the convergent parallel design as one in which both quantitative and qualitative data are collected simultaneously but separately and have equal importance in addressing the study questions. Vogt, Gardner and Haeffele (2012:107) and Creswell and Plano Clark (2018:118) elucidate when to combine research designs. First when you want to elaborate, clarify, or build on findings from other methods and second when you want to "tell the full story" in an area of inquiry. In this study focus groups with previously treated DR-TB patients, in-depth interviews with HCPs working in the DR-TB programme and document reviews of treatment charts, registers and cards were undergone simultaneously and with equal emphasis.

3.7 RESEARCH METHODS

Research methods are the techniques researchers use to structure a study and to gather and analyse information relevant to the research question (Polit & Beck 2017:10). Likewise, Creswell and Creswell (2018:16) state research methods involve the forms of data collection, analysis, and interpretation that researchers propose for their studies. Moreover, Leavy (2017:93) emphasises that research methods should be selected on the basis of their ability to best address the purpose of the research

and to answer research questions, in fact, considering pragmatic issues like resources and time.

3.7.1 Setting of the study

Study setting is the physical location and conditions in which data collection takes place in a study (Polit & Beck 2017:744). The study settings were four DR-TB treatment initiating hospitals in Ethiopia. Hospitals A, B, C, and D were included in the study.

Hospital A is one of the hospitals under the Federal Ministry of Health and was established in 1961 and has been serving the country for more than a half century mainly on TB. It was the first hospital in the country to begin DR-TB therapy in 2009. Currently the hospital has 259 beds including 44 beds for DR inpatient service. The past three years were times of change and adaptation to the new system and environment, and development of new services with multidisciplinary approach.

The hospital provides various services, especially in tuberculosis diagnosis and treatment, and has a vision to be the best client-oriented medical service provider, academic institution in the country and to become Centre of Excellence for diagnosis and treatment of TB in East Africa (Damtew, Ali & Meressa 2014:390).

Hospital B is a tertiary level referral hospital on the edge of Addis Ababa, specialising in Hansen's disease, also known as leprosy. It was originally the All-Africa Leprosy Rehabilitation and Training Centre (hence the acronym), but tuberculosis is now added to the official name: All Africa Leprosy, Tuberculosis, and Rehabilitation Training Centre (ALERT 2018:1).

Hospital B's activities focus on its rehabilitation of leprosy patients, training programmes for leprosy workers around the world and leprosy control. From the beginning, Hospital B provided leprosy training to medical students at the University of Addis Ababa. There is currently a 240-bed teaching hospital, which includes dermatology, ophthalmology, and surgery departments, also an orthopaedic workshop, and a rehabilitation program. It also gives treatment for DR-TB patients since March 2011 (ALERT 2018:1).

Hospital C: Established in 1938, it was the first missionary hospital in Ethiopia. In 2008, the College of Health Science Education was officially inaugurated. The hospital and

medical college serve a catchment area of more than five million in the Oromia region and educate medical students and residents. It has more than 300 beds and nine beds are for in patient drug resistant TB services. It started its DR/TB treatment services in May 2013 (CIHRT 2018:1).

Hospital D: Established in 1947 and located in Oromia region 47 kilometres from the capital city, it serves catchment area population of more than 1.2 million. It has more than 102 beds and twelve are designated for inpatient drug resistant TB services. Major services in the hospital are out patient (OPD), paediatrics, Emergency, Obstetrics and gynaecology, inpatient department (IPD), ICU, Neonatal ICU, Dentistry, Ophthalmology, psychiatry, physiotherapy, dermatology, laboratory imaging services, pharmacy, TB/HIV and MDR/TB services (Bishoftu Hospital 2019:2).

3.7.2 Population of the study

One of the many definitions of population is that it is the entire aggregation of cases in which a researcher is interested (Nieswiadomy & Bailey 2018:137; Hissong, Lape & Bailey 2015:47). In other words, a population is a complete set of persons or objects that possess some common characteristic of interest to the researcher (Nieswiadomy & Bailey 2018:170). Moreover, a population is the theoretically specified aggregation of study elements that we are interested in generalizing about (Babbie 2021:199).

The population for a study is composed of two groups: the target population and the accessible population (Nieswiadomy & Bailey 2018:170).

3.7.2.1 The target population

The target population is the entire group of people to which the researcher wishes to generalize the findings of a study. The target population consists of people or things that meet the designated set of criteria of interest to the researcher (Nieswiadomy & Bailey 2018:170). Furthermore, the target population is the entire set of individuals or elements (objects, events, or substances) that meet the sampling criteria for inclusion in a study and to which the study findings are generalized (Gray, Grove & Sutherland 2017:329).

3.7.2.1.1 The target population for this study

- **For quantitative phase:**

The target population for the quantitative phase of this study was medical records of patients who were diagnosed with DR-TB and registered for treatment between July 2010 and September 2016 at all treatment initiating hospitals in Ethiopia.

- **For qualitative phase:**

The target population for the qualitative phase of this study was previously treated DR-TB patients and healthcare providers working on the clinical and programmatic management of DR-TB at all treatment initiating hospitals in Ethiopia.

3.7.2.2 The accessible population or study population

In cases where the likelihood of being able to obtain a list of the target population is low, the researcher usually samples from an available group called the accessible population or study population (Nieswiadomy & Bailey 2018:170). An accessible population is the portion of the target population to which researchers have reasonable access (Gray, Grove & Sutherland 2017:329). Likewise, the accessible population is the aggregate of cases that conform to designated criteria and that are accessible for a study (Polit & Beck 2017:249). To summarize, a study population is the group of elements (individuals or objects) from which the sample is actually selected (Babbie 2021:200; Leavy 2017:12).

3.7.2.2.1 The study population for this study

- **For quantitative phase:**

The study population for the quantitative phase of this study was medical records of patients who were diagnosed with DR-TB and registered for treatment between July 2010 and September 2016 at selected treatment initiating hospitals A, B, and C.

- **For qualitative phase:**

The study population for the qualitative phase of this study was previously treated DR-TB patients and healthcare providers working on the clinical and programmatic management of DR-TB at selected treatment initiating hospitals A, B, C, and D.

3.7.3 Sample and sampling methods

Collecting data from all members of the population is probably not possible. In addition, the accuracy gained when the whole population is included is often not worth the time and money involved, and it might not be possible to gain access to the whole population. Rather than selecting every element in the population, a sample or subset of the population is selected to represent the population. When a sample is chosen properly, the researcher is able to make claims about the population based on the data from the sample alone. The results of the sample are then used to estimate the characteristics of the entire population (Nieswiadomy & Bailey 2018:170).

Sampling entails selecting cases to represent an entire population, to permit inferences about the population. A sample is a subset of population elements, which are the most basic units about which data are collected (Polit & Beck 2017:250).

Samples are chosen through two procedures: probability and nonprobability sampling. Probability sampling involves the use of a random selection process to obtain a sample from members of a population. The goal of probability sampling is to obtain representative elements of populations. In probability sampling, researchers can specify the probability that an element of the population will be included in the sample. Greater confidence can be placed in the representativeness of probability samples. There are four types of random sampling procedures: simple, stratified, multistage cluster, and systematic (Nieswiadomy & Bailey 2018:171; Polit & Beck 2017:251).

Samples are sometimes selected in multiple phases, in what is called multistage cluster sampling. In the first stage, large units or broad groups (clusters), such as hospitals, are selected. Then, in the next stage, within the selected sites, individuals are sampled. In staged sampling, it is possible to combine probability and nonprobability sampling. For example, the first stage can involve the deliberate (non-random) selection of study sites. Then, people within the selected sites can be selected through random procedures (Polit & Beck 2017:251). In the quantitative strand of this study, multistage cluster sampling was used to select DR-TB patients' medical records from selected DR-TB treatment-initiating hospitals.

In nonprobability samples, elements are selected by non-random methods. There is no way to estimate the probability that each element has of being included in a nonprobability sample, and every element usually does not have a chance for

inclusion. Nonprobability sampling is less likely than probability sampling to produce representative samples. This restricts the generalizations that can be made about the study findings. Despite this fact, most studies in health disciplines rely on nonprobability samples (Nieswiadomy & Bailey 2018:175; Polit & Beck 2017:251,252).

Samples may be chosen from available groups of subjects by several different methods, including convenience, quota, and purposive (Nieswiadomy & Bailey 2018:175). Purposive sampling uses researchers' knowledge about the population to make selections. Researchers might decide purposely to select people who are judged to be particularly knowledgeable about the issues under study. Researchers select participants based on personal judgment about which ones will be most informative (Polit & Beck 2017:251,252,741). Furthermore, researchers can use their previous experiences and research findings to obtain units of analysis which can be regarded as representative of the relevant population (Nieswiadomy & Bailey 2018:177).

In the qualitative strand of this study, purposive sampling was used to recruit DR-TB patients who took part in the focus group discussions and to select HCPs working in the clinical and programmatic management of DR-TB patients who participated in the in-depth interviews.

3.7.3.1 Quantitative Phase sampling

In the first stage of multistage sampling, Hospitals A, B, and C were selected based on their DR-TB treatment service duration and patient numbers. Treatment-initiating hospitals that started DR-TB treatment services in 2010 and had been giving the services at the time of the data collection period were selected.

In the second stage of multistage sampling, systematic sampling was employed to select samples. At the time of data collection, a total of 1885 patients with DR-TB had been registered in the DR-TB registers between July 1, 2010 and September 30, 2016 at selected treatment initiating hospitals A, B, and C. Accordingly, a sampling frame was developed by using the list of patients from DR-TB registers.

Systematic sampling is the selection of every *k*th case from a list. By dividing the population size by the desired sample size, the researcher establishes the sampling

interval, which is the standard distance between the selected elements (Polit & Beck 2017:722).

The desired sample size is established at some number (n). The size of the population must be known or estimated (N). By dividing N by n, a sampling interval (*k*) is established. The sampling interval is the standard distance between sampled elements (Polit & Beck 2017:257).

The first step was to obtain a list of the total population (N) which was 1885. Then, the sample size (n) was determined, which was 501 (see Table 3.1). Next, the sampling interval width (*k*) was determined by N/n. Hence, the sampling interval was:

k = 1885/501 = 3.8 (4, rounded to the nearest whole number). Thus, every fourth element of the population list was selected for the sample.

As a criterion for considering systematic sampling as a type of probability sampling is that a random starting point must be chosen. A procedure to obtain this starting point is to select the first element randomly from within the first sampling interval. Hence, the sampling interval width was 4, a number between 1 and 4 could be selected as the random starting point (Nieswiadomy & Bailey 2018:175).

The random starting point, or the first sample, was generated by reading the table of random numbers. After selecting the first sample, a fixed interval of four was used to identify successive study elements to be included in the study.

Sample size determination for quantitative

The sample size was determined based on the following formula:

Sample size (n) = $(z\ (\alpha/2)^2 * p(1-p)/d^2 * 1.5$

where p is 68% Ethiopia treatment success rate for MDR-TB cases started on treatment in 2013 (WHO 2016a:79), 0.05 error allowance (d), 1.96 two-sided critical value for 95% confidence level (z), 0.05 level of satisfaction significance (α) and 1.5 for design effect compensation.

Therefore, sample size (n) = $(z\ (\alpha/2)^2 * p(1-p)/d^2 * 1.5$

$= (1.96)^2 * 0.68(0.32)/ (0.05)^2 * 1.5 = 501$

Then this calculated sample size was allotted to selected three hospitals using probability proportional to size based on number of DR-TB patients on DR-TB treatment registers.

Table 3.1: Calculated sample size for each hospital

Hospitals	Number of patients	Sample allocated
Hospital A	1188	316
Hospital B	549	146
Hospital C	148	39
Total	1885	501

3.7.3.2 Qualitative Phase sampling

Purposive Sampling: A nonprobability sampling method in which the researcher selects participants based on personal judgment about which ones will be most informative (Polit & Beck 2017:251,741). Researchers can use their previous experiences and research findings to obtain units of analysis which can be regarded as representative of the relevant population (Nieswiadomy & Bailey 2018:177). Researchers can use their previous experiences and research findings to obtain units of analysis which can be regarded as being representative of the relevant population.

Purposive sampling was used to recruit DR-TB patients who take part in the focus group discussions and to select HCPs working in the clinical and programmatic management of DR-TB patients who participate in the in-depth interviews.

3.7.4 Eligibility criteria

Polit and Beck (2017:250,727) describes eligibility criteria as the norms designating the specific attributes of the target population by which people are selected for inclusion in a study. Study participants who were found to be compatible with the following criteria were included for the data collection.

3.7.5 Exclusion criteria

The criteria specifying characteristics that a target population does not have (Polit & Beck 2017:250,728). Those study participants who fall in the following category were excluded in the data collection process.

Table 3.2: Inclusion and Exclusion criteria

Criteria	Qualitative (FGD)	Qualitative (In-depth interview)	Quantitative (Chart review)
Inclusion	• Provide informed consent to participate in the study • 18 years and above	• Provide informed consent to participate in the study • 18 years and above • HCPs working in the clinical and programmatic management of DR-TB at least for two years	• Patients who were diagnosed with DR-TB and registered for treatment between July, 2010 and Sep, 2016
Exclusion	• Not willing to give informed consent to participate in the study • Younger than 18 years	• Not willing to give informed consent to participate in the study • HCPs working in the clinical and programmatic management of DR-TB for less than two years • Younger than 18 years	• Patient who discontinued treatment within one month of beginning therapy • Patients who died within one month of beginning therapy • Patients who were started treatment for purpose of study rather than routine programmatic treatment

3.7.6 Data collection methods and procedures

Yin (2016:55) defines data collection as a means of gathering required information in detail from different sources. Creswell (2014:269) explains the key idea with convergent parallel mixed method design is to collect both forms of data using the same or parallel variables, constructs, or concepts. For the quantitative strand, the quantitative data were collected using pre-tested questionnaire (Annexure G) from unit DR-TB registers and patient charts.

For the qualitative strand, data collection tools were focus group discussions guide for patients (Annexure I) and interview guide for healthcare providers (Annexure J). In

both focus groups and in-depth interviews, open ended probing questions were utilized to probe the discussions.

3.7.7 Data Collection Instruments

Polit and Beck (2017:175) define data collection instrument as the formal written document used to collect and record information, such as a questionnaire when structured methods are used and when unstructured methods are used, there is typically no formal instrument, but there may be a list of the types of information needed.

3.7.7.1 Quantitative Strand:

For the quantitative strand of the study, the researcher developed a structured questionnaire based on conceptual framework of the study and extensive literature review (Annexure G). Data-set available on DR-TB registers and DR-TB patient treatment cards were also considered. During the overall process of questionnaire development a statistician was consulted and engaged.

3.7.7.2 Qualitative Strand:

For the qualitative strand of the study, the researcher prepared a written topic guide, which is a list of areas or questions to be covered with each participant (Polit & Beck 2017:511) for the in-depth interview (Annexure J), and interview guides for the focus groups (Annexure I). Polit and Beck (2017:512) describe questioning route, that is, the series of questions used to guide the interview, is key to an effective focus group session.

3.7.7.2.1 Focus-Group Interviews

Pioneered by Robert K. Merton and others in the 1940s, focused group interviews are especially appropriate when the topic under study deals with interaction in groups (Yin 2016:149; Vogt, Gardner & Haeffele 2012:41). As with other types of interviews, the format allows the facilitator the flexibility to explore unanticipated issues as they arise in the discussion. The results have high “face validity”: because the method is readily understood, the findings appear believable. Furthermore, the cost of focus-group interviews is relatively low, they provide quick results, and they can increase the sample size of qualitative studies by permitting more people to be interviewed at one

time (Marshall & Rossman 2011:149; Nieswiadomy & Bailey 2018:71). Polit and Beck (2017:510) explain focus group sessions are carefully planned discussions that take advantage of group dynamics for accessing rich information in an economical manner and the optimal group size is 6 to 12 people.

Focus group interviews were conducted with 42 purposively selected DR-TB patients with failed previous treatment or treatment interruption or lost to follow up and currently on retreatment regimen in Hospitals A, B, C, and D. A group of seven patients was assembled for a discussion in each focus group session. A total of six FGD sessions were conducted. The FDGs were conducted at weekends for the convenience of the participants and in private rooms made available by the hospitals.

The researcher started each discussion sessions through short introduction of the topic, purpose and ethical aspects of the study. In addition, the researcher explained the need to record the discussions on audiotape to ensure that the researcher captures what they state accurately. Informed consent form (Annexure E&F) provided and permission sought from the participants. As a means of stimulating the sessions, the participants introduced themselves.

The research assistant (the moderator) guides the discussion according to a written set of questions in the interview guide. The discussions were tape recorded and notes were taken during the discussion by the research assistant. On average the discussion sessions took around 1 hour and 30 minutes.

3.7.7.2.2 In-depth Interviewing

Leavy (2017:5) and Punch (2014:144) recommend interviewing as the leading data collection tool in qualitative research and as a good way of accessing people's perceptions, meanings, definitions of situations and constructions of reality. This method enables the researcher to explore and describe the participant's views through the help of a few general topics but otherwise respects the way the participants frame and structure their responses. Interviewing is based on an assumption fundamental to qualitative research: the participants perspective of the phenomena of interest should unfold as the participant views it (the emic perspective), not as the researcher views it (the etic perspective) (Polit & Beck 2017:468; Yin 2016:143). In-depth interviewing with healthcare providers who have been working on the patient and programmatic management of DR-TB were conducted.

The interviews took place in private offices at their respective institutions. A convenient time was selected by the participants to minimize interruption in their work responsibilities. The researcher started each discussion session through a short introduction of the topic, purpose and ethical aspects of the study. In addition, the researcher explained the need to audio-record the discussions to ensure that the researcher captured what stated accurately. An informed consent form (Annexure E&F) was provided and permission was sought from the participants. During the interview after the icebreaker and grand tour question, lists of probing follow up questions were used to guide the interview. Notes of key points were taken by the researcher during the interview session.

Polit and Beck (2017:497) noted a guiding principle to determine sample size in qualitative research is data saturation, which implies sampling to the point at which no new information is obtained and information redundancy is achieved. Interviews were conducted until the researcher believed the data were saturated and interviews lasted on average around 50 minutes to 1 hour. Totally, fifteen experienced HCPs including senior internal medicine specialist physicians, general practitioner physicians, health officers, and nurses working in patient and programmatic management of DR-TB participated in the interview.

3.7.7.2.3 Chart review

Studies with a retrospective design are ones in which a phenomenon existing in the present is linked to phenomenon that occurred in the past. The signature of a retrospective study is that the researcher begins with the dependent variable (the effect) and then examines whether it is correlated with one or more previously occurring independent variables (potential causes) (Polit & Beck 2017:205). Retrospective data from DR-TB registers and patient charts at Hospitals A, B, and C were collected.

The quantitative data were collected by three trained MSc graduates and experienced data collectors. Training was given to data collectors by this researcher for a day regarding ethical aspects of data collection, inclusion and exclusion criteria of the study units, and the questionnaire. In the meantime, a contract agreement was signed between the researcher and data collectors and card room staff who prepared selected patient charts and the runners who brought the charts to data collectors. In

addition to data available on DR-TB register and TB treatment cards, medical record numbers were taken from the DR-TB register were used to retrieve patient charts (cards) from the card room.

In the agreement, signed between the researcher and the data collectors, the roles and responsibilities of data collectors, runners, card room staff, and remuneration and termination of the agreement were included. In addition, the data collectors collected pilot data from 25 randomly selected DR-TB patient charts at Bishoftu hospital, a site which was not selected for the quantitative data collection. Based on the pilot test outcomes, minor amendments of the questionnaire were made (incomplete data items from the register in most cases were removed from the questionnaire). Data collectors were updated about the minor amendments before the actual data collection was resumed.

The researcher created good rapport with authorities of the selected hospitals and presented ethical clearance certificate and permission letters from federal ministry of health. The overall data collection process was supervised and managed by the researcher. Likewise the researcher frequently visited and paid close observation of the data collection process. Random checks of the completed questionnaires were done to monitor completeness and consistency of data collection activities. Immediate feedback was given in case of needful corrections.

3.7.8 Data management and Analysis

3.7.8.1 Quantitative Strand

The data were coded, verified, cleaned for outliers and its internal consistency checked by the researcher. Any discrepancies were corrected against the hard copy of the questionnaires. To assure confidentiality of data, the collected hard copy data were kept in a lockable cabinet. The electronic data set was retained in the researcher's computer with passwords.

Quantitative analysis, as described by Polit and Beck (2017:741), is the process of manipulation of numeric data through statistical procedures for the purpose of describing phenomena or assessing the magnitude and reliability of relationships

among them. Quantitative data were analysed using SPSS version 24 for windows. To validate the findings, a professional statistician was engaged in the process.

3.7.8.2 Qualitative Strand

Data management in qualitative research is reductionist in nature: it involves converting masses of data into smaller, manageable segments. Qualitative data analysis is constructionist: it involves putting segments together into meaningful conceptual patterns. Qualitative analysis involves discovering pervasive ideas and searching for general concepts through an inductive process (Polit & Beck 2017:535).

As Polit and Beck (2017:530) indicate, the purpose of data analysis is to organise, provide structure to, and elicit meaning from data. In qualitative studies, data collection and analysis often occur concurrently rather than after all data are collected. The search for important themes and concepts begins from the moment data collection gets underway (Polit & Beck 2017:530). In this study the analysis began concurrently with the data collection.

Qualitative analysis encompasses the organization and interpretation of narrative data for the purpose of discovering important underlying themes, categories, and patterns of relationships (Polit & Beck 2017:741).

The analysis of qualitative materials typically begins with a search for broad categories and then themes. Themes emerge from the data. They often develop within categories of data but may also cut across them (Polit & Beck 2017:535). Polit and Beck (2017:535) borrowed the definition of theme offered by DeSantis and Ugarriza (2000:362) “a theme is an abstract entity that gives meaning and identity to a current experience and its variant manifestations. As such, a theme captures and unifies the nature or basis of the experience into a meaningful whole.”

3.7.8.2.1 Qualitative content analysis

Qualitative content analysis is the analysis of the content of narrative data to identify prominent themes and patterns among the themes (Polit & Beck 2017:537). Patton (2002:453) defined qualitative content analysis as “any qualitative data reduction and sense-making effort that takes a volume of qualitative material and attempts to identify

core consistencies and meaning". Thus, a central feature of content analysis is that it is a way of condensing a voluminous number of words of a text into smaller content categories (Polit & Beck 2017:537).

In qualitative content analysis, data is broken down into smaller units. The literature on content analysis often includes references to meaning units. A meaning unit is words, sentences or paragraphs containing aspects related to each other through their content and context. A meaning unit, essentially, is the smallest segment of a text that contains a recognizable piece of information (Polit & Beck 2017:537).

The labels attached to meaning units are the codes (Polit & Beck 2017:537). Codes are heuristic devices; labelling a condensed meaning unit with a code allows the data to be thought about in new and different ways. The success of a content analysis is highly dependent on the integrity of the coding process. Codes are, in turn, the basis for developing categories. In what is sometimes referred to as "secondary coding," the creation of categories involves gathering meaning units together that capture the substance of a topic – that is, that fit into a cluster (Polit & Beck 2017:538).

Content analysis often makes the distinction between manifest and latent content. Manifest content is what the text actually says – its visible components. In purely descriptive studies, qualitative researchers may decide to focus mainly on summarizing the manifest content communicated in the text. More often, however, content analysts also analyses what the text talks about, which involves interpretation of the meaning of its latent content. Interpretations vary in depth and level of abstraction and are usually the basis for themes (Polit & Beck 2017:538).

In this study the conventional content analysis approach was used, focusing on both manifest and latent content of the narratives. In conventional content analysis (often referred to as inductive content analysis), the study starts with data and the codes emerge and are defined during data analysis (Polit & Beck 2017:538). ATLAS.ti 8 software was used in data coding and sorting. To verify the findings of the qualitative data set, a professional qualitative expert was utilised as a co-coder in the process.

3.7.9 Rigour

3.7.9.1 Quantitative Strand: Reliability and validity

Quantitative researchers use several criteria to assess the rigor of a study, sometimes referred to as its scientific merit. Two especially important criteria are reliability and validity. Reliability is related to the accuracy and consistency of information obtained in a study. The term is most often associated with the methods used to measure variables. Validity is a more complex concept that generally refers to the soundness of study's evidence, whether the results are unbiased and well-founded. Validity, like reliability, is an important criterion for evaluating methods used to measure variables. In this context, the validity question is whether the methods are really measuring the concepts that they purport to measure (Polit & Beck 2017:161).

3.7.9.1.1 Validity

Polit and Beck (2017:747) reiterate that validity is a quality criterion referring to the degree to which inferences made in a study are accurate and well-founded; in measurement, the degree to which an instrument measures what it is intending to measure. Similarly, Babbie (2021:151) defines validity as a term describing a measure that accurately reflects the concept it is intended to measure. Validity refers to the extent to which an empirical measure adequately reflects the real meaning of the concept under consideration (Babbie 2021:151). Neuman (2014:218) has the notion that validity suggests truthfulness.

3.7.9.1.2 Face validity

That quality of an indicator that makes it seem a reasonable measure of some variable (Babbie 2021:151). Neuman (2014:216) explained face validity is a judgement by the scientific community that the indicator really measures the construct. The pre-test was conducted, and results were analysed using SPSS version 24 for Windows, showing alignment with the objective.

3.7.9.1.3 Criterion-related validity

Criterion-related validity refers to the degree to which a measure relates to some external criterion (Babbie 2021:152; Neuman 2014:217).

3.7.9.1.4 Construct validity

Construct validity refers to the degree to which a measure relates to other variables as expected within a system of theoretical relationships (Babbie 2021:152; Neuman 2014:217). The researcher ensured construct validity by carrying out correlation or exploratory factor analysis in the pilot study for each section of the instrument.

3.7.9.1.5 Content validity:

Content validity refers to the degree to which a measure covers the range of meanings included within a concept (Babbie 2021:153; Neuman 2014:216).

The questionnaire was developed by the researcher and some additional measures were taken to enhance validity of the tool. To ensure its content validity, the items were developed based on the title, design, objectives and concepts of the selected model. At the same time, two senior expert physicians in the DR-TB programme were involved in the review of the questionnaire. A pre-test was also conducted to ascertain relevance of the questionnaire.

3.7.9.1.6 Reliability

Polit and Beck (2017:742) describe reliability as the extent to which a measurement is free from measurement error; more broadly, the extent to which values of individuals who have not changed are the same on repeated measurements; statistically, the proportion of total variance in a set of scores that is attributable to true differences among those being measured (Polit & Beck 2017:742).

Reliability is a matter of whether a particular technique, applied repeatedly to the same object, yields the same result each time (Babbie 2021:149). According to Neuman (2014:218) reliability means dependability or consistency and measurement reliability means that the numerical results an indicator produces do not vary because of characteristics of the measurement process or measurement instrument itself.

Stability reliability is reliability across time. Using the test-retest method can verify an indicator's degree of stability reliability. Verification requires retesting or re-administering the indicator to the same group of people (Babbie 2021:150; Neuman 2014:212).

Representative reliability is reliability across subpopulations (for example, different classes, races, sexes, age groups) or different types of cases. A subpopulation analysis verifies whether an indicator has this type of reliability (Neuman 2014:212-213).

Equivalence reliability applies when a researchers use multiple indicators – that is, when a construct is measured with multiple specific measures (for example, several items in a questionnaire all measure the same construct). Special statistical measures (for example, Cronbach's alpha) also can determine this type of reliability (Neuman 2014:213). The normal range of values of Cronbach's alpha, or coefficient alpha, is between.00 and +1.00, and higher values reflect better internal consistency. The Cronbach alpha value close to +1 indicates that the instrument is consistently measuring what it is supposed to measure (Polit & Beck 2017:308).

To enhance the reliability of this study some measures were taken. Before actual data collection the questionnaire was piloted. Internal reliability of the items in the data collection instrument was ensured by calculating Cronbach's alpha coefficients by SPSS software, and it was found to be 0.78, indicating a good level of internal consistency of the instrument with the sample used.

In addition, the data collectors were healthcare providers who have proximity with the DR-TB programme and research. On the top of that the data collectors were trained on how to extract and record information from the register and patient charts on the questionnaire. Further, the entire process of data extraction was closely monitored and strict supervision was provided during the data collection as well.

3.7.9.2 Qualitative Strand: Trustworthiness

Nieswiadomy and Bailey (2018:63) state in a nut shell that the most often used framework of quality criteria is that of Lincoln and Guba, who identified five criteria for evaluating the trustworthiness of the inquiry: credibility, dependability, confirmability, transferability, and authenticity.

3.7.9.2.1 Credibility

Credibility is described by Polit and Beck (2017:559) as confidence in the truth value of the data and interpretations of them. The researcher endeavoured to establish

confidence in the truth of the findings in the study. Prolonged engagement and sufficient time during data collection was invested to ensure an in-depth understanding of the experiences and viewpoints of participants. The researcher recorded the participants' demeanour and behaviours during discussions and thoroughly described the interview context.

3.7.9.2.2 Dependability

Dependability, according to Polit and Beck (2017:559), refers to the stability (reliability) of data over time and over conditions. Likewise, it refers to evidence that is consistent and stable (Polit and Beck 2012:175). The researcher prepared a written topic guide, which is a list of areas or questions to be covered with each participant for the in-depth interview, and interview guides for the focus groups. Mock interviews were conducted prior to the actual interview. The researcher communicated with some of the participants for verification of their responses. Brand new audio recorder of an excellent quality was used for recordings and the interviews were transcribed verbatim to enable accurate capturing of the interviews. Description of the advantages and challenges of the methods used in the study was also indicated.

3.7.9.2.3 Confirmability

Confirmability explained by Polit and Beck (2017:559-560) as criterion which refers to objectivity, that is the potential for agreement between two or more independent people about the accuracy, relevance, or meaning of the data. The researcher thoroughly took notes throughout the interviews sessions. In addition, the researcher gave participants feedback about emerging interpretations in order to give them an opportunity to assess and validate whether the researchers' interpretations are good representations of their realities and to ensure that the results accurately depicted their experiences and views. Member checking refers to asking study participants to review and react to study data and emerging interpretations (Polit & Beck 2017:564).

3.7.9.2.4 Transferability

Transferability is the extent to which qualitative findings can be transferred to or have applicability in other settings or groups (Polit & Beck 2017:560). The researcher gave detailed and vivid descriptions of the study participants and the research context in

which the data were collected and the experiences and processes observed the inquiry

3.7.9.2.5 Authenticity

Authenticity is the degree to which researchers faithfully show a range of different realities and deliver the feeling of lives as they are lived (Polit & Beck 2017:560). The researcher gave lucid and textured descriptions, with judicious inclusion of verbatim quotes from study participants in order to contribute to the authenticity of the study.

Procedures to help ensure the rigor and usefulness of a qualitative study: Triangulation, searching for disconfirming evidence, engaging in reflexivity, member checking, prolonged engagement in the field, collaboration, developing an audit trail and peer debriefing (Creswell & Creswell 2018:199-201; Marshall & Rossman 2011:40).

Triangulation refers to using multiple referents to draw conclusions about what constitutes truth. Data triangulation involves the use of multiple data sources for the purpose of validating conclusions (Polit & Beck 2017:563). In this study to involve person and space triangulation, data were collected in four hospitals and were gathered through focus groups with patients and individual interviews with service providers.

Member checking refers to asking study participants to review and react to study data and emerging interpretations (Polit & Beck 2017:564). In this study, member checking was carried out during data collection through deliberate probing to ensure that the researcher had properly interpreted the participants' meanings. The thematic analysis was reviewed by two healthcare providers and three patients.

Peer debriefing is conducting sessions with peers to review and explore aspects of the inquiry. An independent colleague researcher reviewed the data collection transcripts and the themes that emerged and the interpretations given by the researcher.

3.7.10 Mixing qualitative and quantitative data sets

Creswell (2017:222) explains that in convergent parallel mixed method designs, the two data bases are analysed separately and then brought together. Likewise in this

study, the quantitative data and qualitative data sets were analysed separately and then brought together at interpretation.

The interpretation in the convergent approach is typically written into a discussion section of the study. Whereas the results section report on the findings from the analysis of both the quantitative and qualitative databases, the discussion section includes a report comparing the results from the two databases and notes whether there is convergence or divergence between the two sources of information (Creswell 2017:222).

The two data bases are analysed separately and then brought together. There are several ways to merge the two databases. The first approach is called a side-by-side comparison. These comparisons can be viewed in the discussion sections of the mixed methods studies. In this study the quantitative statistical results first reported and discussed and then the qualitative findings reported and discussed that either confirm or disconfirm the statistical results; see Figure 3:2. Mixed methods authors call this approach a side-by-side because the researcher makes the comparison within a discussion, presenting first one set of findings and then the other (Creswell 2017: 222).

3.7.11 Best practice guideline development

Based on the findings of the study and informed by a systematic review of existing evidence in the literature, the researcher developed best practice guidelines addressing barriers to treatment completion for patients with DR-TB in Ethiopia. In addition, clinicians, programme managers, healthcare providers, public health experts, and stakeholders were selected purposively based on their programmatic, clinical, and practical experience in the area of DR-TB management to validate the adequacy of the document.

3.8 ETHICAL CONSIDERATIONS

Polit and Beck (2017:727) define ethics as “a system of moral values that are concerned with the degree to which research procedures adhere to professional, legal and social obligations to the study participants”. According to Polit and Beck

(2017:139-142) ethical principles for protecting study participants include beneficence, respect for human dignity and justice. Beneficence deals with the duty to minimize harm and maximize benefits. Respect for human dignity concerns the right to self-determination and the right to full disclosure. Justice is about participants' right to fair treatment and their right to privacy.

Likewise, according to scholars Emanuel, Wendler, Killen and Grady (2004:931) ethical principles in developing countries include collaborative partnership, social value, scientific validity, fair selection of study population, favourable risk-benefit ratio, independent review, informed consent, and respect for recruited participants and study communities.

In this study, procedures that were followed were to adhere to ethical principles risk/benefit assessment, informed consent, confidentiality procedures, and external reviews by institutional review boards. Regarding risk/benefit the researcher fully disclosed aspects of the study including the likely risks and benefits to the participants. For example, the information they give may help others with similar problems and increased knowledge about their condition from the discussions. Similarly, it was also explained about the risks, such as loss of time during the interview, transport costs (taxi or bus fare), and physical discomfort during the interview.

Informed consent is an important procedure for safeguarding participants. Adequate information about the study and explanation regarding their free choice to consent or decline participation voluntarily. The researcher documented a consent form (Annexure E&F) which was signed before the interviews were commenced. It had information about the study purpose, how much time would be required to do the interview and the voluntary nature of participation.

Confidentiality was protected through appropriate procedure implementation. Identification numbers or codes were substituted for participants' names on records and files. All data were kept in a lockable cupboard during the study period, and only accessible to the researcher. Questionnaires and audio recordings were kept securely, to be disposed of five years after the completion of the study.

Ethics clearance was sought from the Ethics and Higher Degrees Committee of the Department of Health Studies in the College of Human Sciences at the University of South Africa (UNISA) (Annexure A). A permission letter to conduct the study was also

obtained from the Ethiopian Federal Ministry of Public Health (Annexure D), and permission from hospital management was obtained. In addition, approval letter from Armauer Hansen Research Institute (AHRI) ethics review committee (Annexure B) and from the Hospital-A Research and Evidence Generation Directorate, The Office of Institutional Health Research Ethics Review Committee (IHRERC) (Annexure C).

3.9 CONCLUSION

This chapter dwelt on elaborating the research approach, method and design, study setting and population, sampling and ethical issues related to data collection and study participants. This study employed a questionnaire, and interview guides to collect the respective data sets. In addition, this chapter explicated the data management and analysis procedures, as well as how data validity and reliability and trustworthiness of the study were maintained. Furthermore, the chapter specifies the measures taken to adhere to universal ethics principles. The subsequent chapter dwells on the presentation and analysis of the data.

CHAPTER FOUR

PRESENTATION AND ANALYSIS OF FINDINGS: QUANTITATIVE STRAND

4.1 INTRODUCTION

Chapter three discussed the theoretical framework, paradigm, research approaches, research design and methods used in this study to achieve the stated objectives, as well as the data analysis plan. Chapter four presents findings of the quantitative data analysis in the form of text, tables and graphs.

The chapter presents quantitative data analysis, baseline and clinical characteristics of DR-TB patients and factors associated with treatment completion of patients on DR-TB treatment. Chapter five dwells later on qualitative data presentation and analysis of barriers, challenges and facilitators of treatment completion of DR-TB treatment from the views of experts and the lived experiences of previously treated patients. In this study, the analysis was conducted to achieve the following objectives set for the research, designed to:

- Determine factors associated with treatment completion of patients on DR- TB treatment.
- Describe the views of experts managing DR-TB patients on treatment completion.
- Describe experiences of previously treated DR-TB patients on treatment completion.
- Explain factors associated with treatment completion with findings from qualitative strand.
- Develop best practice guidelines aimed at addressing barriers to treatment completion for patients with DR-TB in Ethiopia.

4.2 QUANTITATIVE FINDINGS

Quantitative analysis is the process of manipulation of numeric data through statistical procedures for the purposes of describing phenomena or assessing the magnitude and reliability of relationships among them (Polit and Beck 2017:741). Quantitative data were analysed using the Statistical Package for the Social Sciences (SPSS) version 24 for windows. A professional statistician was engaged in an independent

analysis to verify the findings. A sample size of four hundred and eighty-seven (487) patients out of the planned five hundred and one (501) were included in the study, configuring a response rate of 97.2%. Fourteen (14) patients were excluded because of discontinuation of therapy and death within the first month of therapy, having incomplete medical records and starting treatment for the purpose of this study.

4.2.1 Socio-demographic characteristics of the patients

4.2.1.1 Age

The ages of the patients ranged from 18 years to 71 years. The mean age was 31.4 years (95% CI: 30.4 – 32.3) and the standard deviation was 10.8. The median age was 29.5 years and the median class was 25 - 34. The mode was 27.8 years and the modal class was the same as that of the median group. The majority of the patients (73.3%) were less than 35 years old. A similar result was reported in a study conducted by Mesfin, Beyene, Tesfaye, Admasu, Addise, Amare, Dagne, Yaregal Tesfaye and Tessema (2018:2) in Ethiopia on determining drug resistance patterns of MTB among DR-TB suspected cases and associated risk factors. Table 4.1 provides the details of the age distribution of the patients.

Table 4.1: Age distribution of the study patients

Age categories	Frequency	%
18 -24	152	31.21
25 – 34	205	42.09
35- 44	71	14.57
45 -54	35	7.18
55 – 64	17	3.49
≥65	7	1.43

4.2.1.2 Gender

Two hundred and forty-five (245 (50.3%) of the patients were males and 242 (49.7%) were females. Figure 4.1 depicts information of the gender of the patients included in the study.

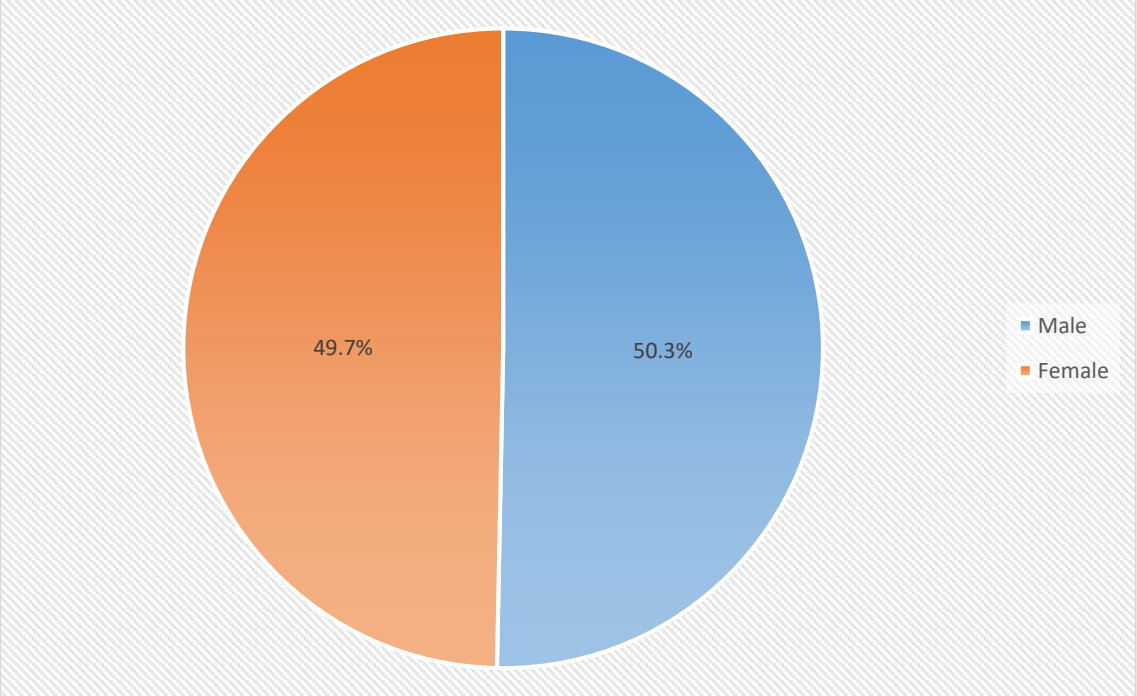


Figure 4.1 Gender of patients

4.2.1.3 Residence

The majority of the patients, 364 (74.7%), were from urban areas as identified by their residential addresses, while 123 (25.3%) were from rural areas (see Figure 4.2). This finding was consistent with a study done by Woldeyohannes, Assefa, Aman, Tekalegn and Hailemariam (2019:5) on predictors of time to unfavourable treatment outcomes among patients with multidrug resistant tuberculosis in Oromia region, Ethiopia.

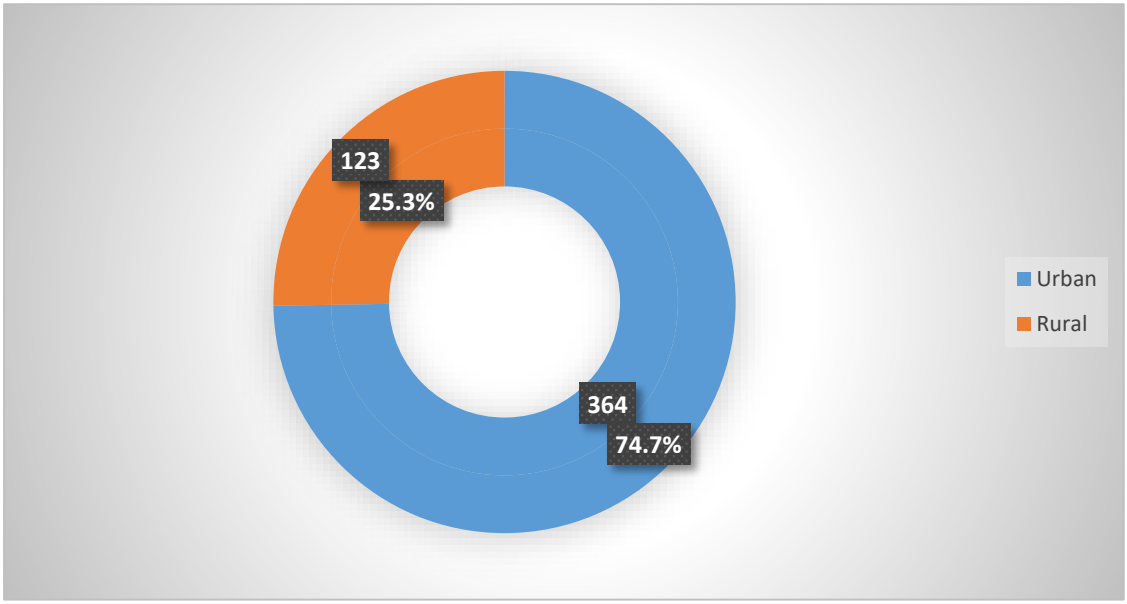


Figure 4.2 Residence of the patients

4.2.1.3 Marital status

Information on the marital status of the patients is presented in the figure below. Married and single patients constituted about 210 (43.1%) and 242 (49.7%) respectively. Divorced and widowed patients comprised 22 (4.5%) and 13 (2.7%) respectively as shown in Figure 4.3.

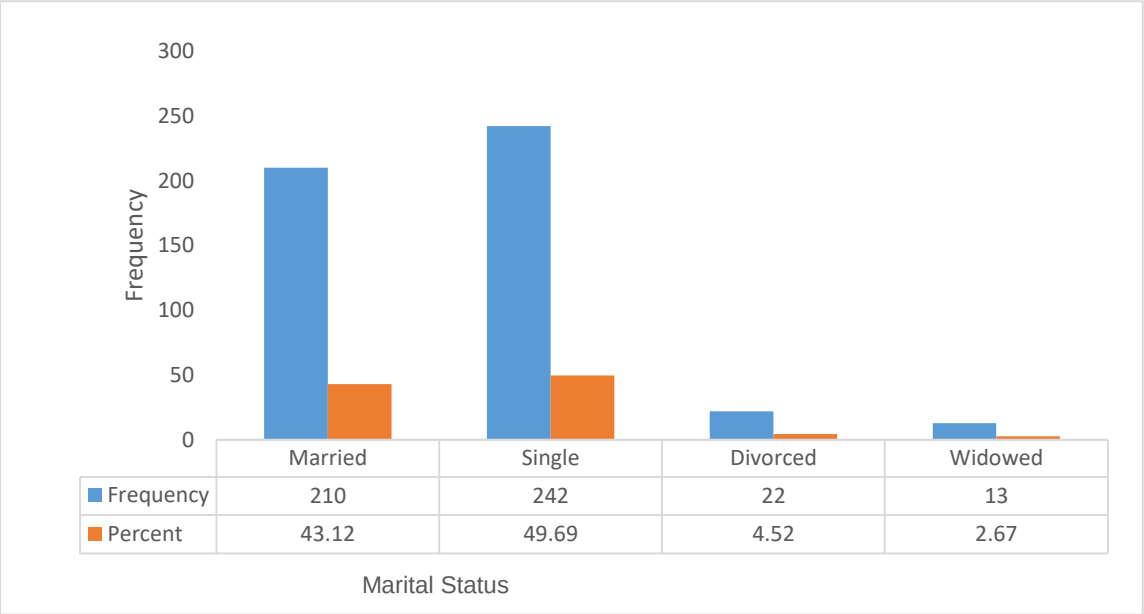


Figure 4.3 Marital status of the patients

4.2.1.4 Employment

One hundred and eighty-three (183) patients (37.58%) were employed and 165 (33.88%) were not employed at the beginning of their therapy. Students constituted 86 (17.66%), while seven (1.44%) were not working during initiation of their treatment. Other category constituted 46 (9.44%) of the patients (see Figure 4.4).

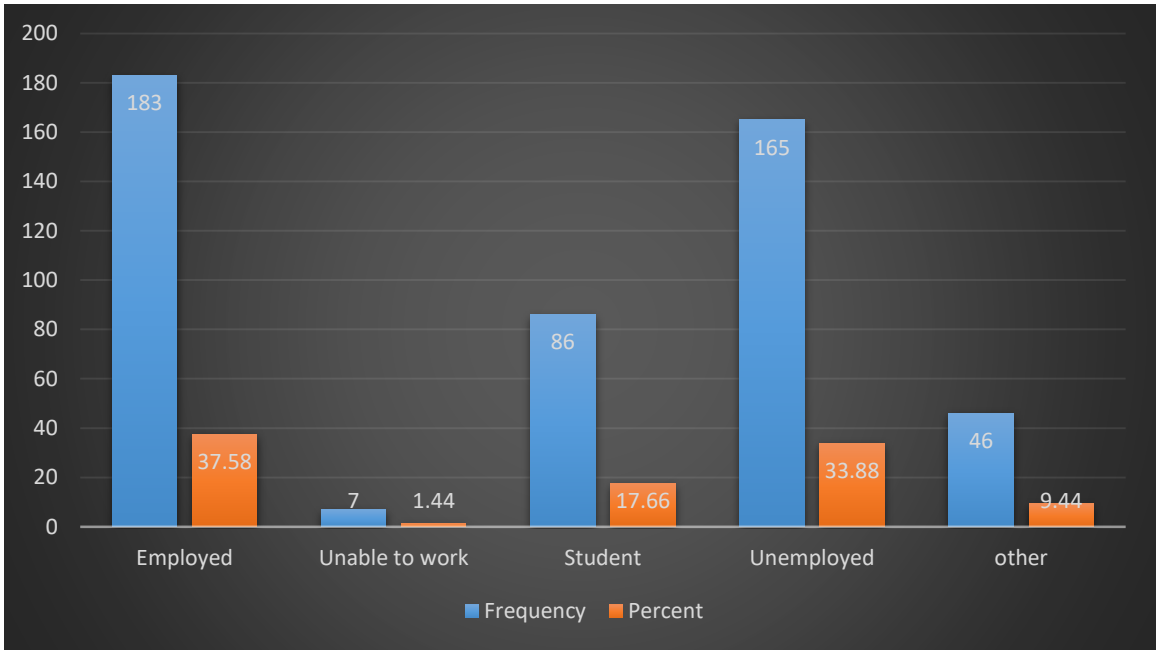


Figure 4.4 Employment of the patients

4.2.2 Lifestyle and physical characteristics

4.2.2.1 History of alcohol consumption

Ninety-eight (20.12%) of the study patients had a history of alcohol consumption, while 389 (79.88%) had no history of alcohol consumption at the beginning of their treatment (see Figure 4.5).

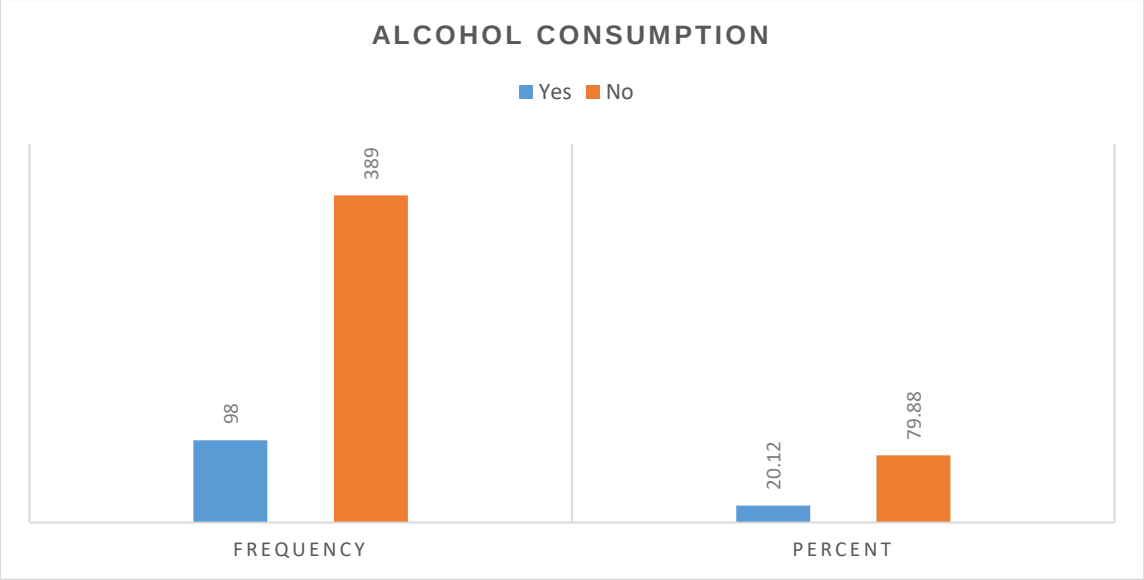


Figure 4.5 History of alcohol consumption of the patients

4.2.2.2 History of non-prescription drugs

Fifty-five (11.29%) of the study patients had a history of using non-prescription drugs, including substances like khat and cannabis, while 432 (88.71%) had no history of substance use at the beginning of their treatment (see Figure 4.6).

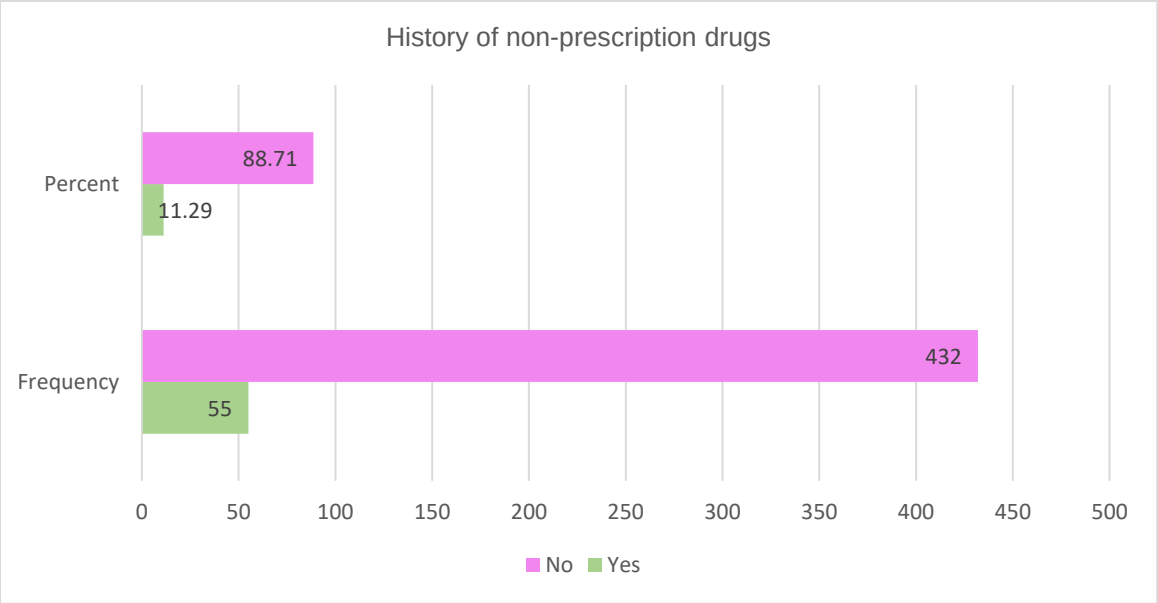


Figure 4.6 History of using non-prescription drugs

4.2.2.3 Treatment supporter

Four hundred and thirty-five (89.32%) of the study patients have had a treatment supporter at the initiation of their treatment, while 52 (10.67%) of them did not have any as shown in Figure 4.7.

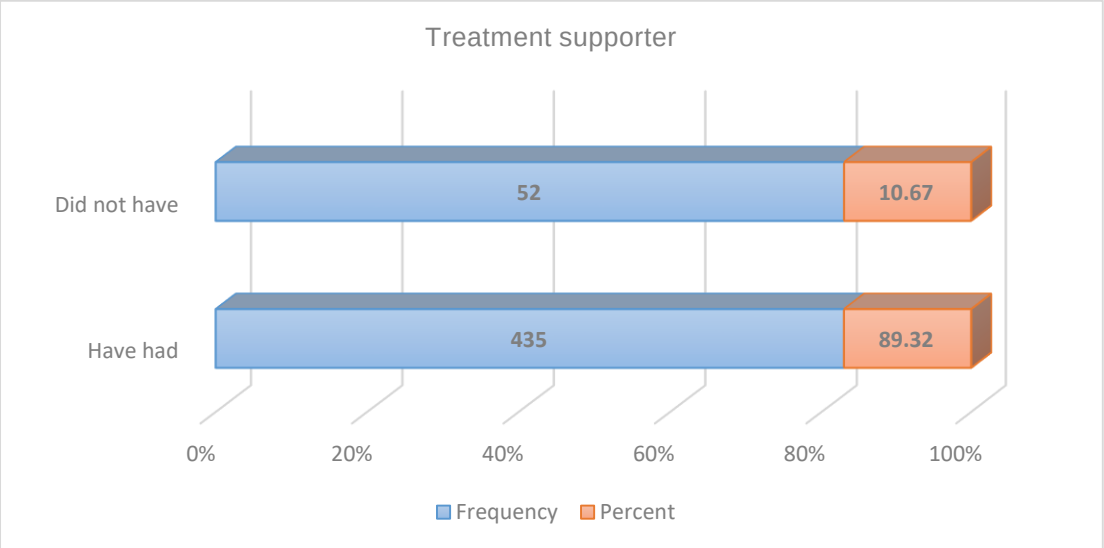


Figure 4.7 Treatment supporter

4.2.3 Clinical characteristics of patients

4.2.3.1 Body mass index (BMI) of the patients

Body mass index (BMI) is a person's weight in kilograms divided by the square of height in metres. Three hundred and fifteen (315 (64.68%) of the study patients had BMI of less than 18.5 (underweight), while 156 (32.03%) and 16 (3.28%) had BMI of 18.5-25 (normal) and greater than 25 (over weight) respectively. Figure 4.8 depicts BMI of patients.

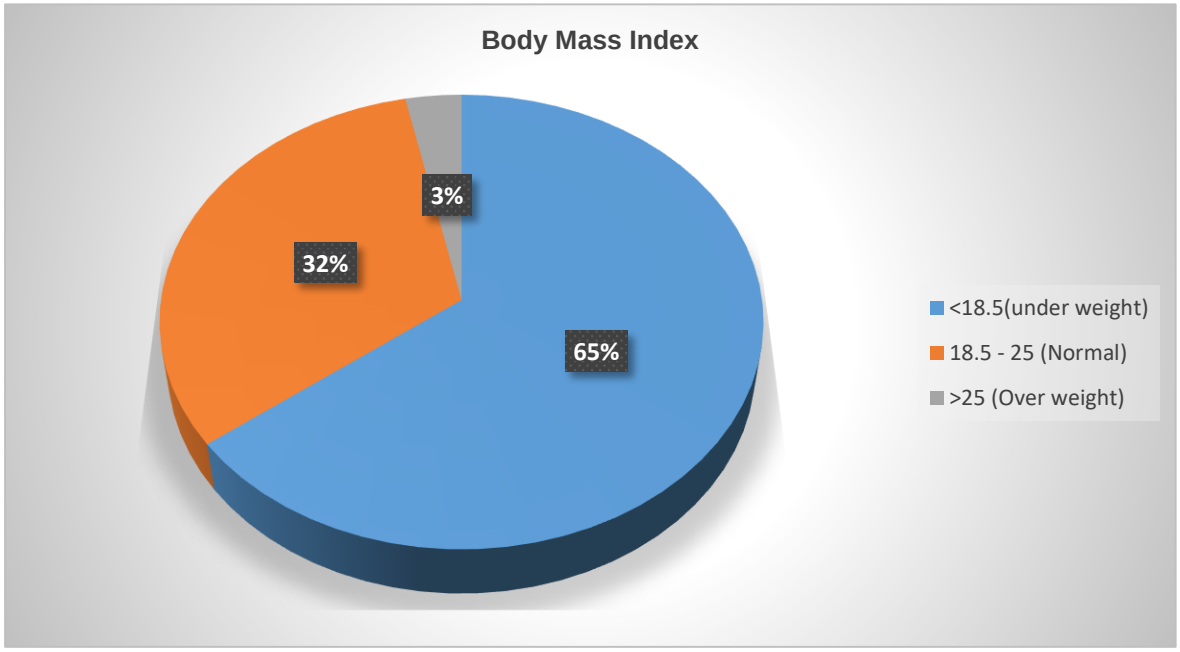


Figure 4.8 Body Mass Index of the study patients

4.2.3.2 Comorbidities of the study patients

HIV and diabetes constitute major comorbidities of the study patients. One hundred and seventeen (117 (68.02%) of the patients have had HIV, while 39 (22.67%) have had diabetes as a comorbid condition at the beginning of their therapy. CNS disorder and chronic renal failure were 1 (0.58%) and 1 (0.58%) respectively (see Figure 4.9).

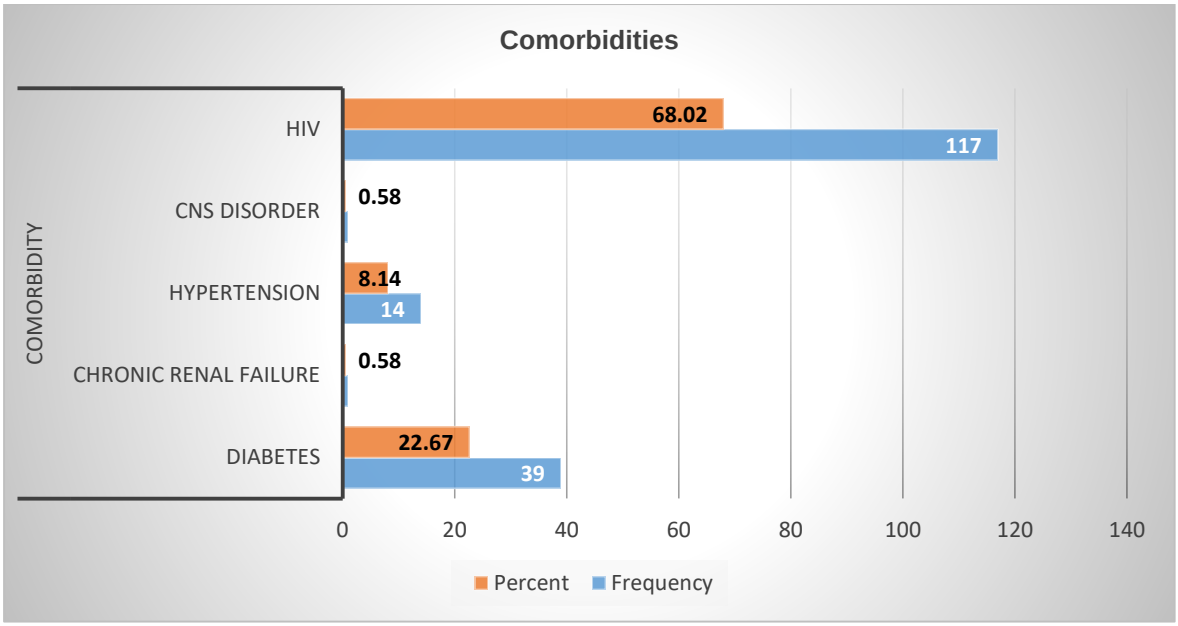


Figure 4.9 Comorbidities of patients at start of therapy

4.2.3.3 Registration group at start of treatment

The majority of the registration group 267 (54.82%) had history of failure with first line drugs retreatment regimen, followed by relapse 76 (15.60%) and failure 71 (14.91%) of first line drugs new treatment regimen respectively. There were 48 (9.85%) new patients, 6 lost-to-follow-up (1.23%), and transfer-in amounted to 5 (1.03%), of the registration groups, as shown in Figure 4.10.

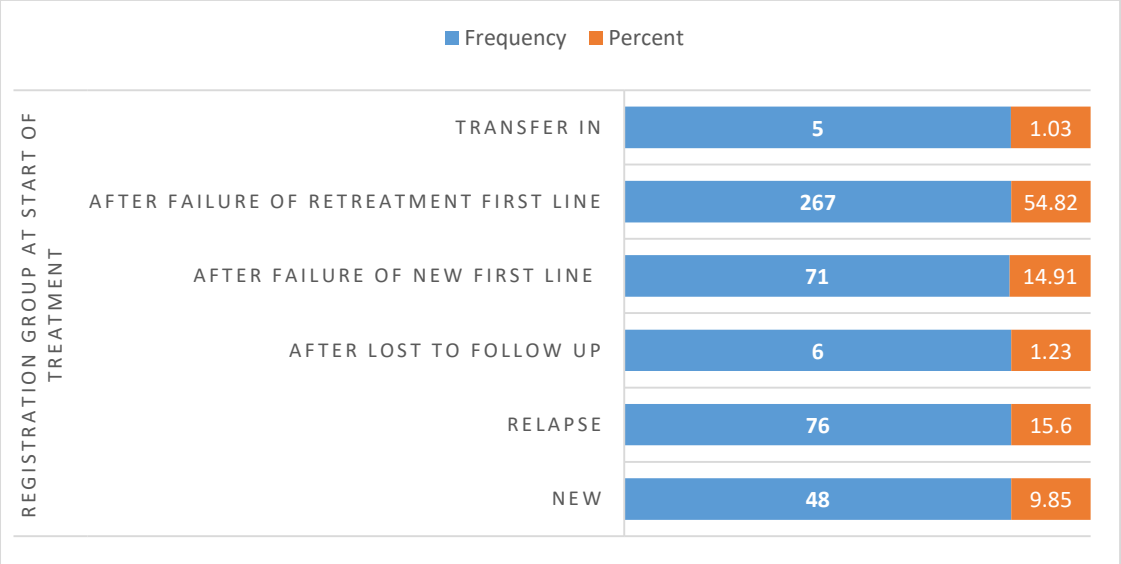


Figure 4.10 Registration group at start of treatment.

4.2.3.4 Type of TB

Pulmonary TB 465 (95.48%) constitutes the biggest classification type. Extra-pulmonary TB (EPTB) is only 22 (4.52%) of the cases. Figure 4.11 shows types of classification. This result resonates with the studies reported by Baye et al (2018: 2) and Alene, Viney, McBryde, Tsegaye and Clements (2017:354).

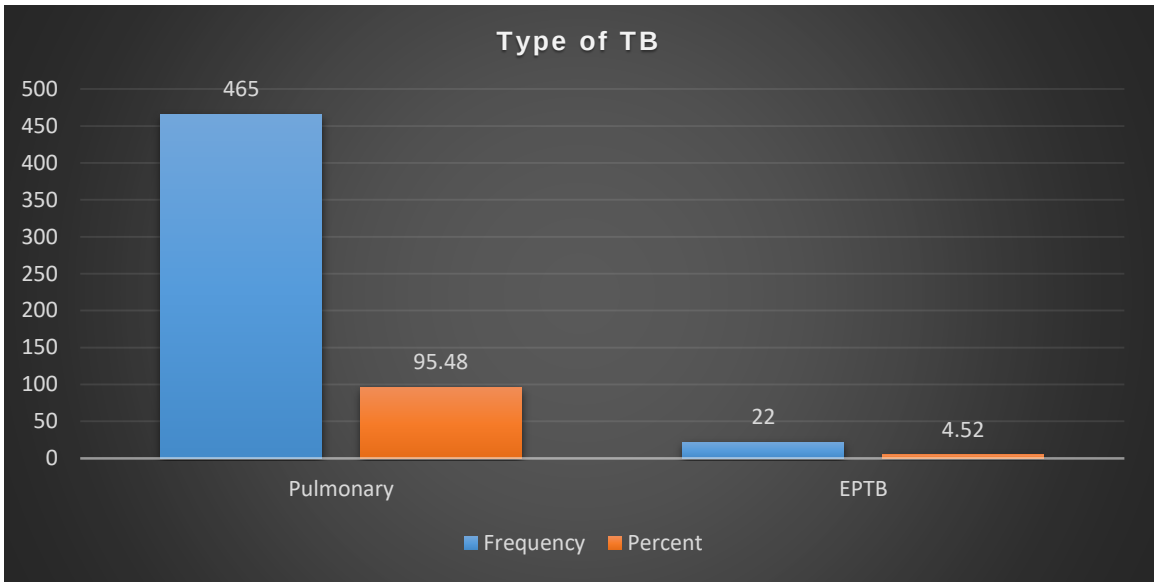


Figure 4.11 Classification of TB types

4.2.3.5 Resistance Type

The majority of the patients 484 (99.0%) were diagnosed with MDR/RR-TB, while Pre-XDR-TB diagnosis were 3 (1.0%). There was no diagnosis of XDR-TB in the study patients as shown in Figure 4.12.

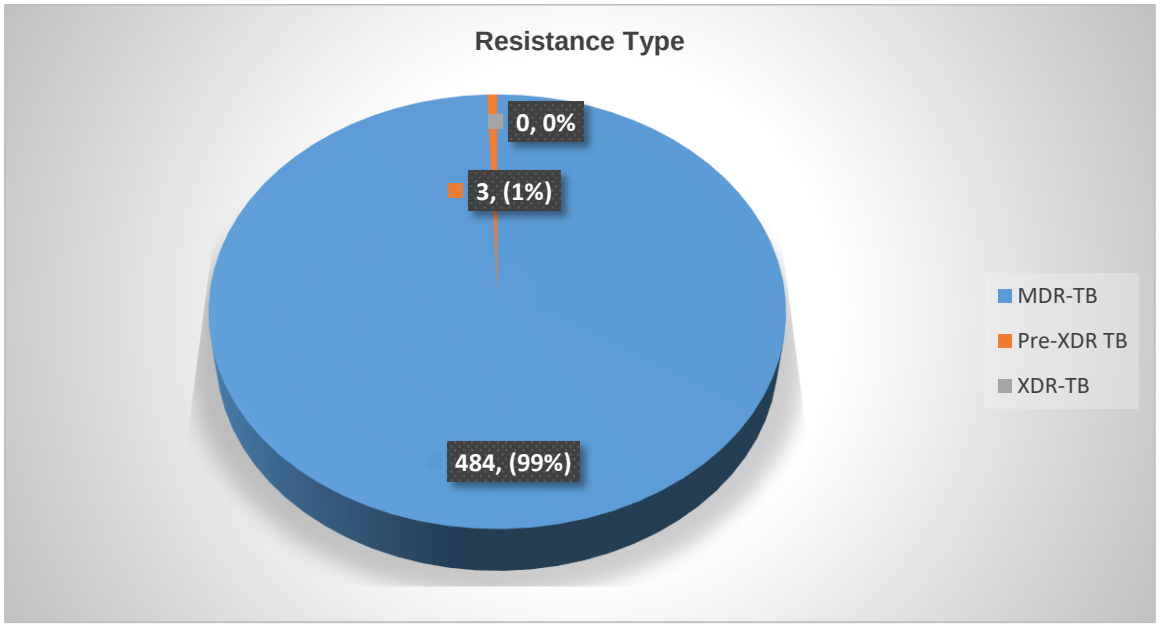


Figure 4.12 TB resistance type of patients

4.2.3.6 Bacteriology result

Four hundred and eighty-four (99%) study patients had bacteriologically confirmed diagnosis with either phenotypic or genotypic diagnostic methods. On the other hand, only three (1%) of the study patients were diagnosed clinically and had no bacteriologic results (see Figure 4.13).

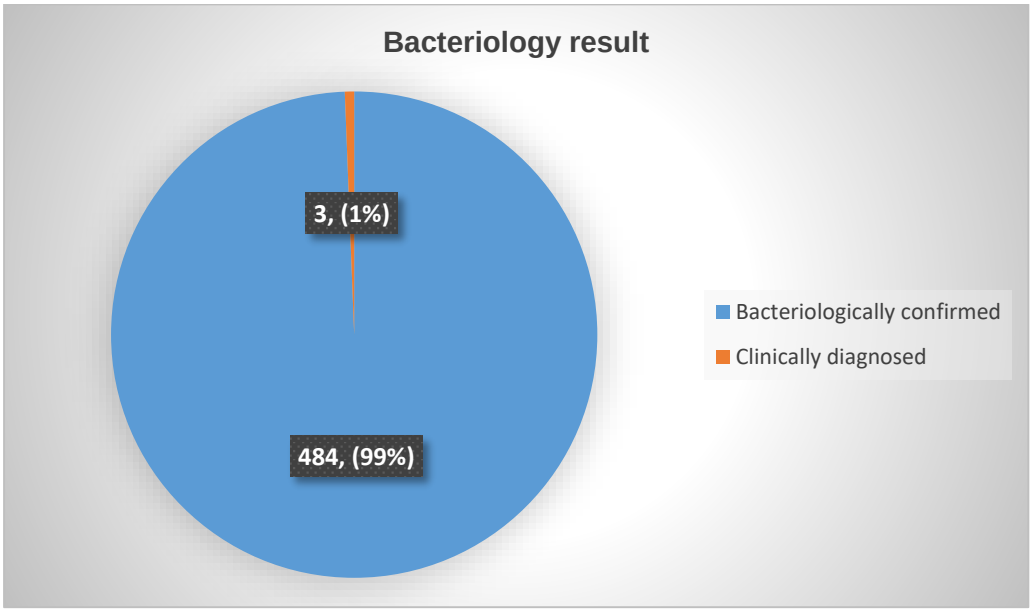


Figure 4.13 Bacteriology result of the patients

4.2.3.7 Prior TB drug use

Forty-eight (48) patients were new and had no TB treatment history (see Figure 4.10). All 439 (100%) patients with treatment history of TB, aslo had a history of taking only first line anti-TB drugs (anti-TB drugs used for treating drug susceptible TB, rifampicin, isoniazid, pyrazinamide and ethambutol). There was no patient with a history of taking second line anti-TB drugs (anti-TB drugs used for treating drug resistant TB, (see Table 2.6) as shown in Figure 4.14.

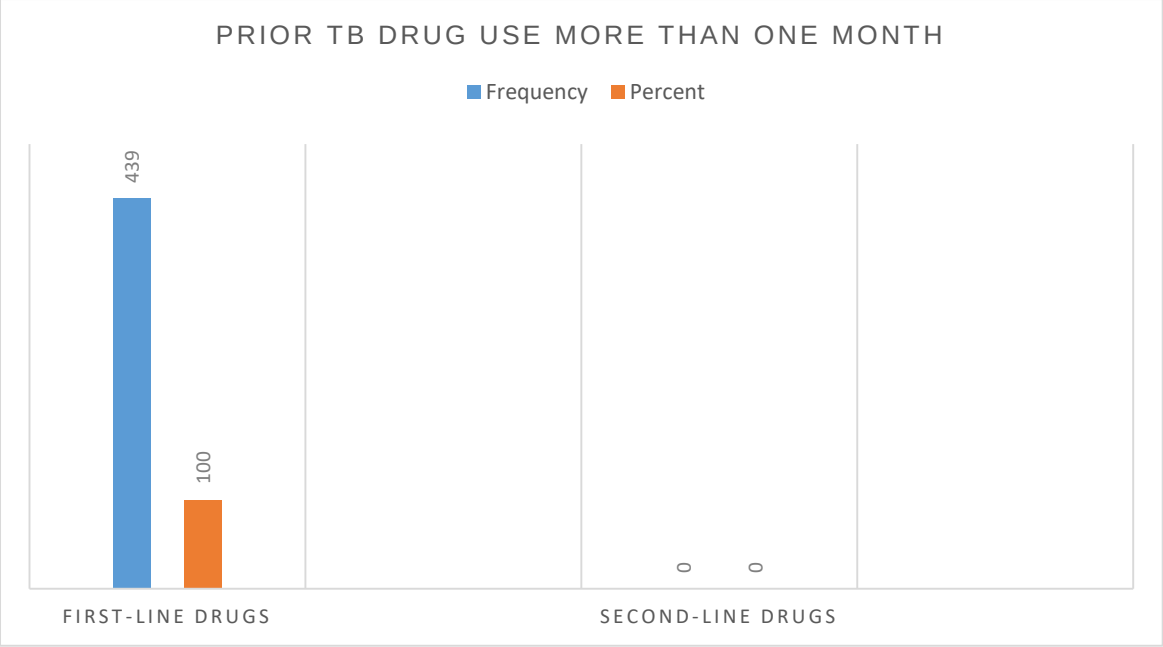


Figure 4.14 Prior TB drug use for more than one month of patients

4.2.3.8 Outcome of most recent TB treatment

Figure 4.15 depicts treatment outcomes of all 439 patients with prior history of TB treatment. Ten (2.28%) patients had cured and 69 (15.72%) had completed favourable treatment outcomes. However, the majority of the patients had unfavourable treatment outcomes, failed 336 (76.54%), lost-to-follow-up 9 (2.05%) and not evaluated 15 (3.42%) respectively.

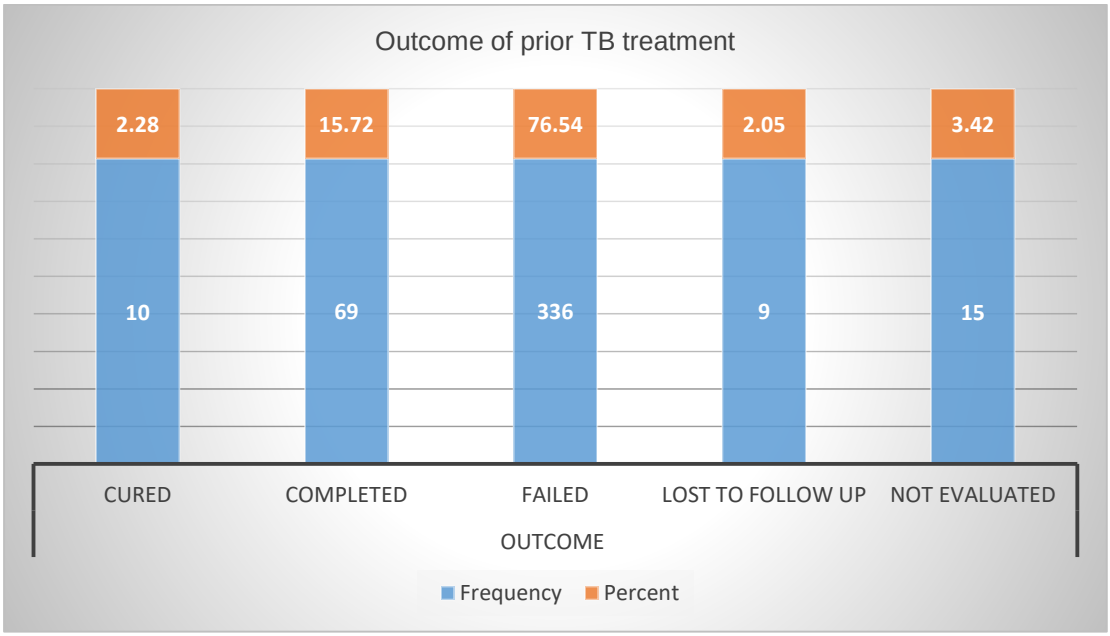


Figure 4.15 Outcome of most recent TB treatment of patients

4.2.3.9 HIV testing and status of patients

There was documented information of the HIV testing and status for most of the patients. In this regard, 467 (95.89%) had been tested for HIV and 4 (0.82%) had not, while the information of 16 (3.28%) patients was not known. From those clients tested 116 (24.84%) were reactive (positive) for HIV. And 351 (75.16%) were found to be negative (see Figure 4.16).

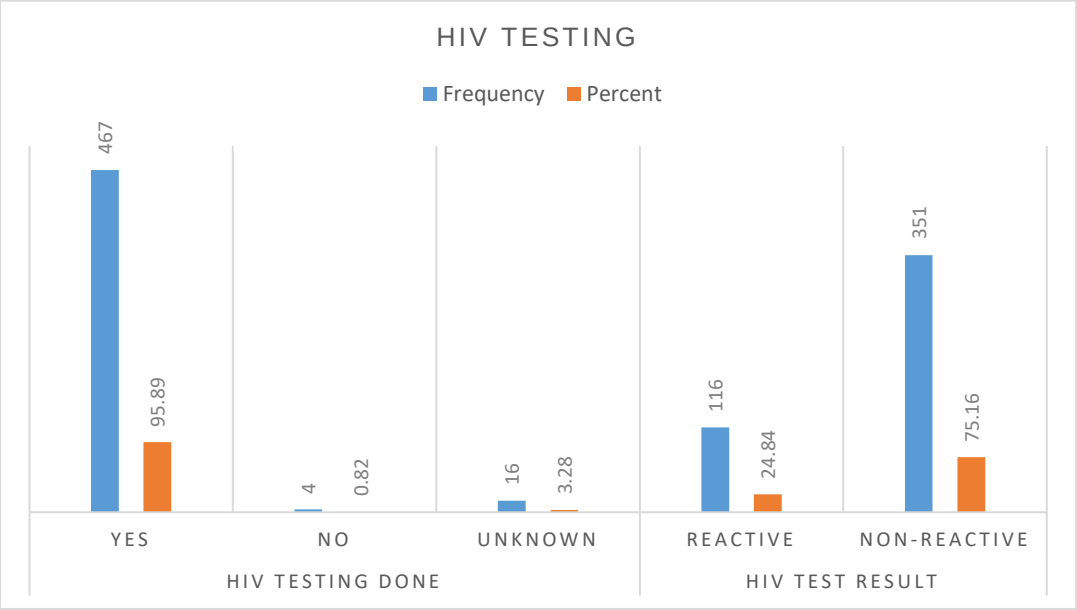


Figure 4.16 HIV testing and status of patients

4.2.3.10 Linkage to ART and CPT

From 116 clients reactive for HIV, 102 (87.93%) and 109 (93.96%) were linked to chronic care services and started CPT and ART, respectively (see Figure 4.17).

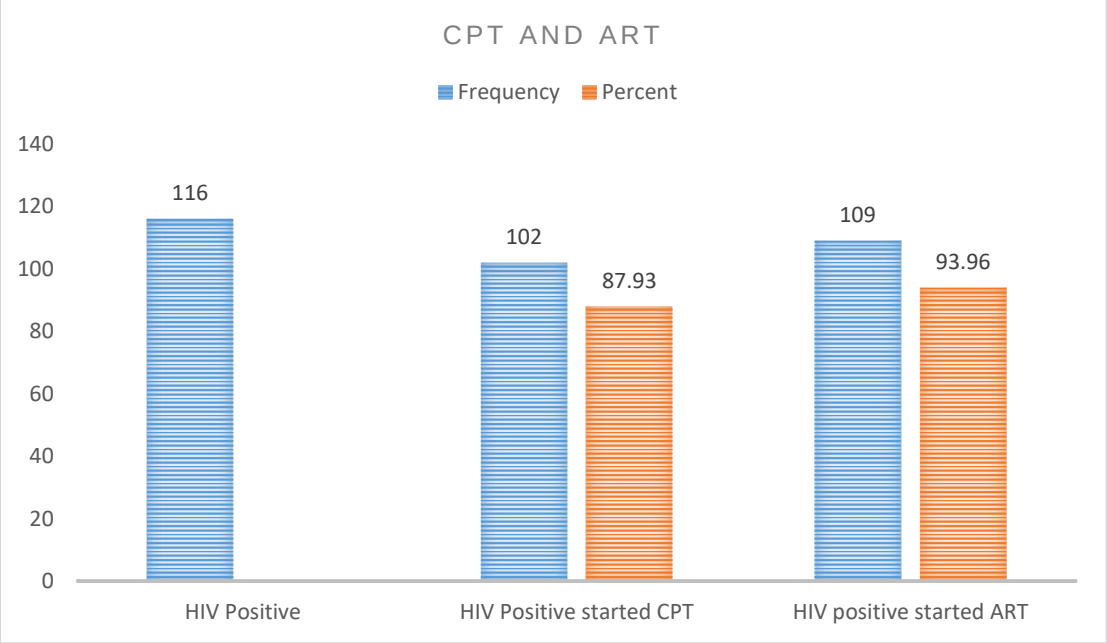


Figure 4.17 Linkage to ART and CPT

4.2.3.11 Baseline audiometry of the patients

Baseline audiometry was not done for 480 (98.56%), the majority of the patients. Baseline audiometry was done only for seven (1.44%) of the study patients at the beginning of therapy, as shown in Figure 4.18.

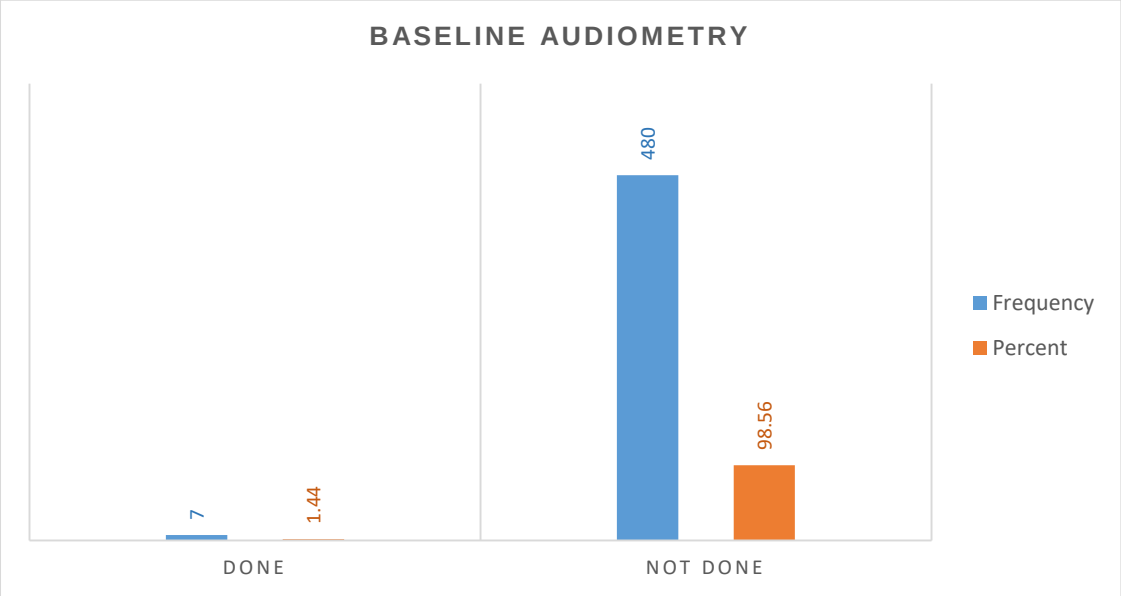
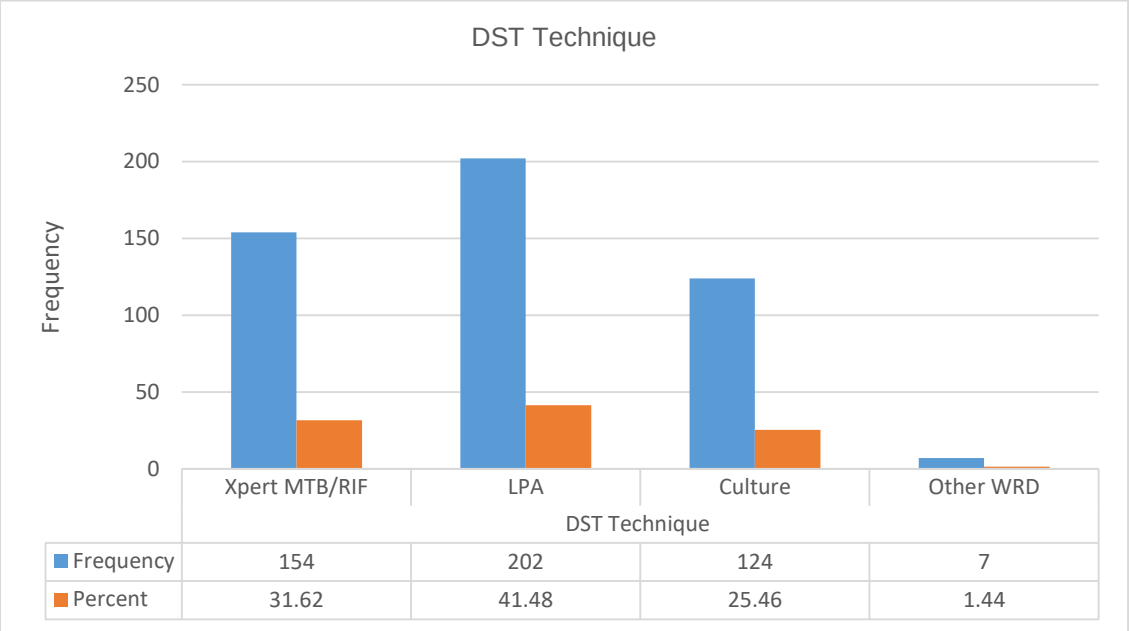


Figure 4.18 Baseline audiometry of the patients

4.2.3.12 Drug susceptibility testing technique

A majority of the study patients, i.e., 154 (31.62%), 202 (41.48%) diagnosis was made by Xpert MTB/RIF and line probe assay (LPA) respectively. Furthermore, 124

(25.46%) and 7 (1.44%) of the patients were diagnosed by culture and WHO-recommended rapid diagnostic (WRD) respectively (see Figure 4.19).



	Xpert MTB/RIF	LPA	Culture	Other WRD
Frequency	154	202	124	7
Percent	31.62	41.48	25.46	1.44

Figure 4.19 Drug susceptibility technique for diagnosis

4.2.3.13 Delay of second-line drug treatment of patients

From the time of diagnosis to initiation of treatment, 217 (44.56%) study patients had delay in the treatment initiation of less than 30 days. On the other hand, 46 (9.45%) of the patients had delays of second-line anti-TB treatment initiation of 30-60 days. Likewise, 51 (10.47%) study patients had to wait for 61-120 days to start second-line treatment, and 173 (35.52%) had to wait for more than 120 days for the commencement of second-line treatment (see Figure 4.20).

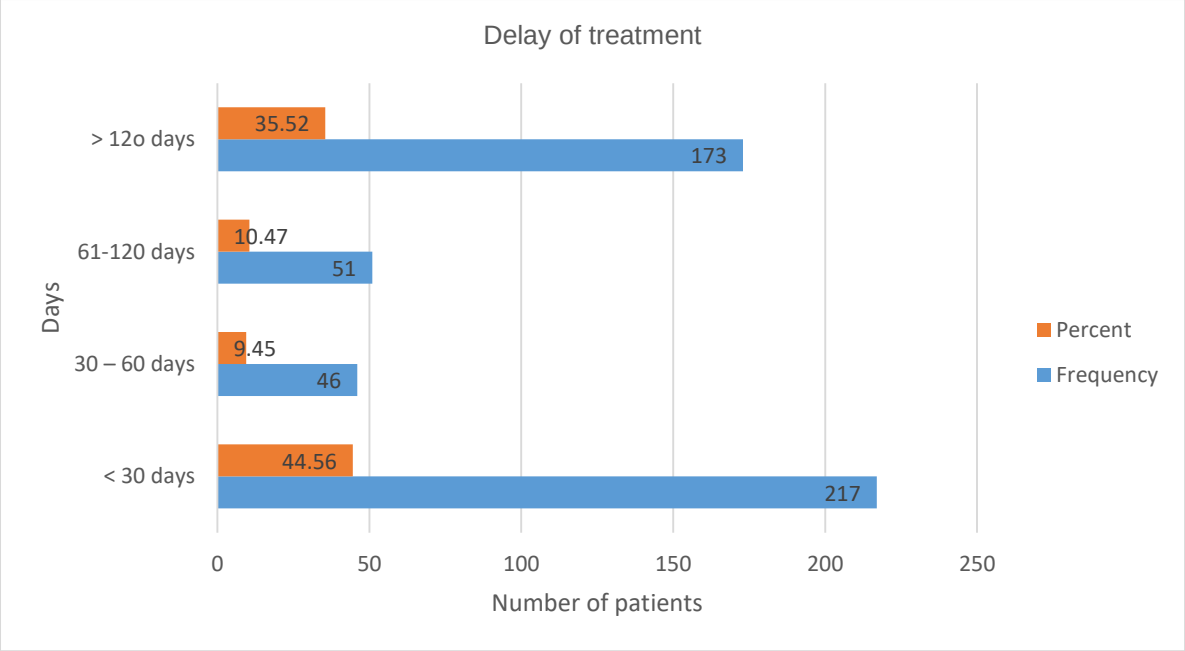


Figure 4.20 Delay of second-line drug treatment

4.2.3.14 Chest x-ray findings of patients

A total of 242 patients had x-ray examinations. Thirty-three patients (13.64%) had x-ray findings of bilateral disease with cavities, while 199 (82.23%) and 10 (4.13%) patients had fibrosis and normal findings respectively. Figure 4.21 shows x-ray findings of the patients.

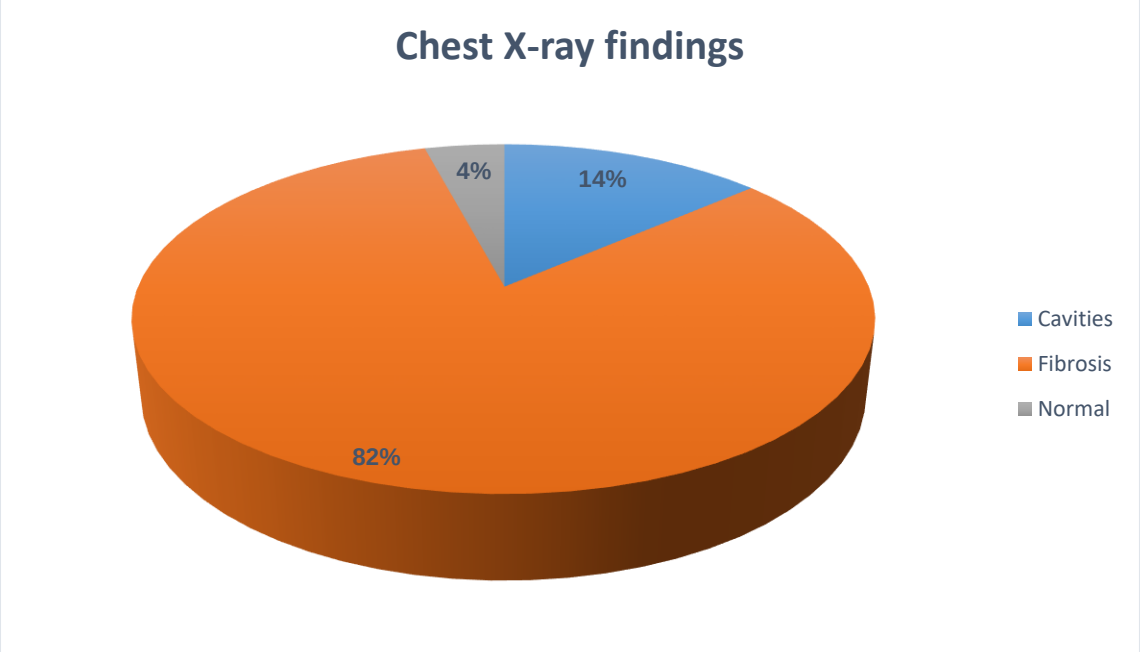


Figure 4.21 Chest x-ray findings of the patients

4.2.3.15 Scheduled monitoring laboratory investigations of the patients

Scheduled monitoring laboratory investigations were performed monthly as shown in Table 4.2 during the course of treatment duration and as the need arose except for thyroid-stimulating hormone (TSH) tests which should be done quarterly. In this regard, all investigations were routinely performed most of the time on schedule for the patients, except audiometry which was only performed regularly for 12 (2.46%) patients.

Table 4.2: Scheduled monitoring laboratory investigations

Investigations	Yes		No	
	Number	%	Number	%
Weight	467	95.89	20	4.11
CBC	466	95.88	20	4.12
Serum electrolyte	454	93.22	33	6.78
Liver function tests	463	95.07	24	4.93
Urea/creatinine	467	95.89	20	4.11
TSH	437	89.73	50	10.27
Audiometry	12	2.46	475	97.54

4.2.3.16 Adverse events encountered during treatment

The majority of the patients 360 (73.92%) had developed gastritis and 289 (59.34%) had experienced nausea and vomiting while on treatment. Arthralgia, electrolyte disturbance and depression anxiety had affected 146 (29.98%), 136 (27.93%) and 51 (10.47%) of the study patients respectively during the treatment. Figure 4.23 shows details of the adverse experiences of the study patients while on treatment.

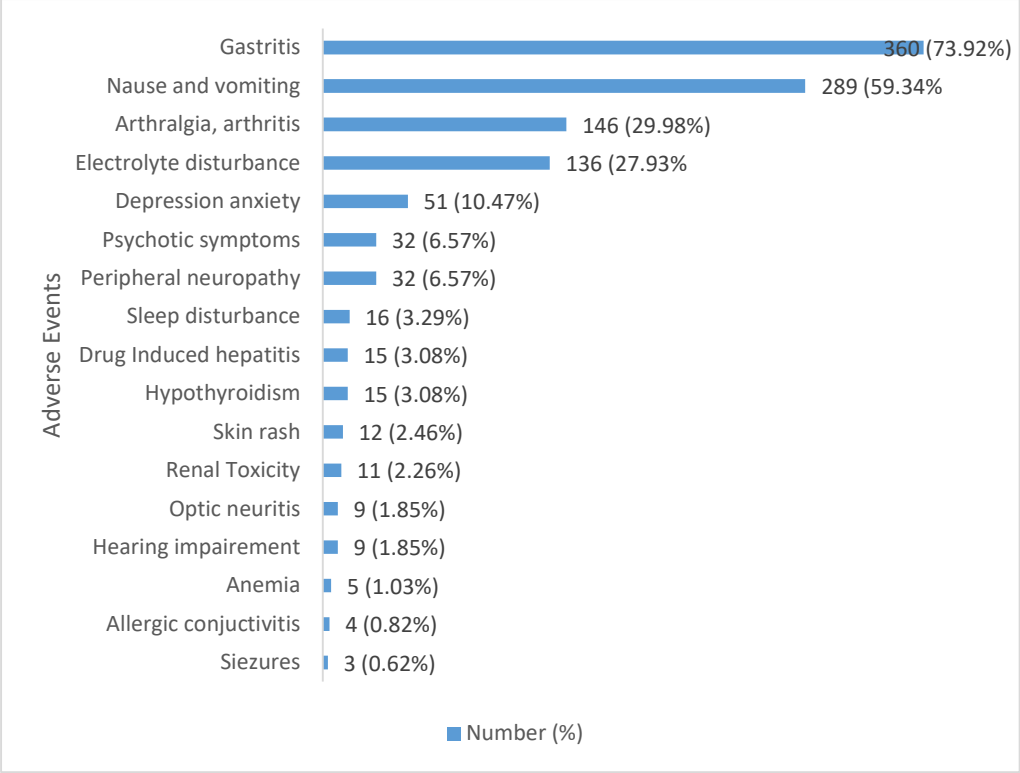


Figure 4.22 Adverse events occured

4.2.3.17 Final treatment outcome of study patients

Ninety-six (19.71%) and 258 (52.98%) of the study patients had favourable treatment outcomes as cured and completed respectively, making successful treatment completion of 354 (72.69%). On the other hand, 72 (14.88%) had died while on treatment and 6 (1.24%) had outcome of treatment failure. A significant number of 47 (9.71%) of the patients had been lost-to-follow-up and eight (1.65%) of them had not been evaluated.

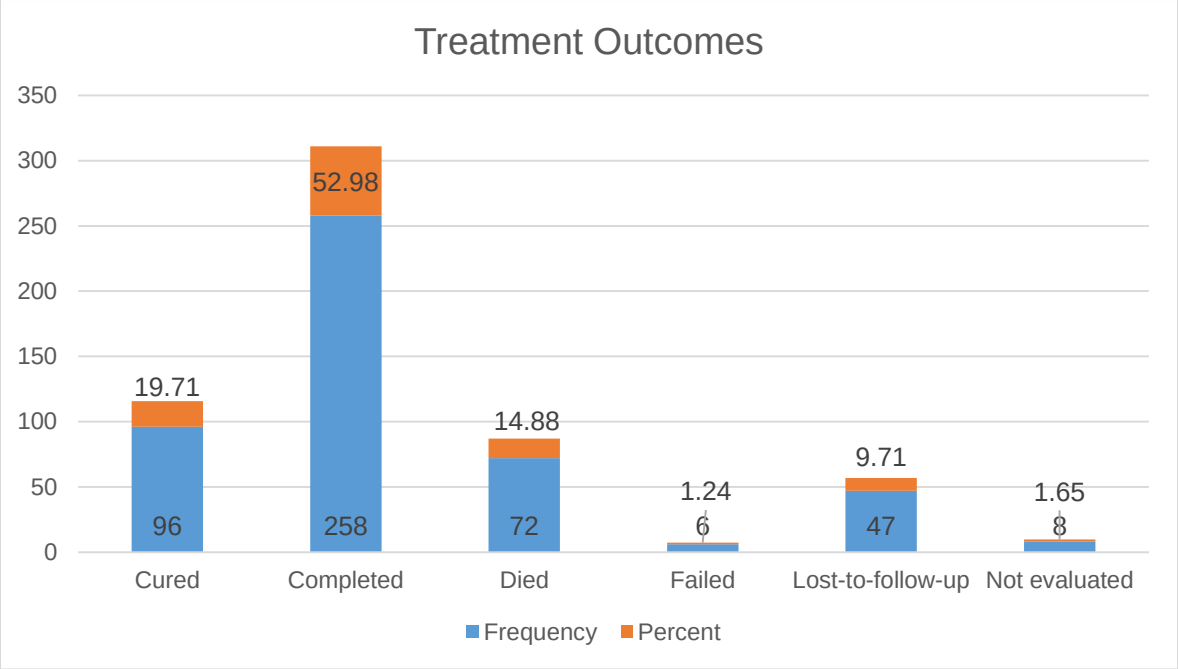


Figure 4.23 Final treatment outcomes of the patients

4.2.4 Factors associated with treatment completion of patients on DR-TB treatment

In this section, analysis of factors associated with treatment completion of patients on DR-TB treatment is presented. The analysis aims to identify the presence and strength of the association between dependent and independent variables. The dependent variable, treatment completion, was categorised based on the treatment outcomes of patients on DR-TB treatment. Those patients who had favourable treatment outcomes of cured and completed were regarded as treatment completed. On the other hand, those patients with unfavourable treatment outcomes died, failure, lost-to-follow-up and not evaluated were regarded as not treatment completed.

The association between dependent and independent variables was assessed by logistic regression. To determine the association X2, p-values, crude and adjusted Odds Ratios with 95% confidence intervals were calculated.

Age, employment, history of alcohol consumption, BMI, comorbidity, registration group at start of treatment, HIV test results, comorbidity, DST technique, psychotic symptoms, drug induced hepatitis, renal toxicity, electrolyte disturbance and arthritis were factors which had statistically significant associations with treatment completion before adjusting the confounder (see Table 4.3, Table 4.4, Table 4.5). However, after adjusting for confounders in multiple logistic regression with model fitness, Hosmer

and Lemeshow test x2=10.780, df=8, and p=0.215; age, registration group, comorbidity, DST result, psychotic symptoms, drug-induced hepatitis, renal toxicity, electrolyte disturbance, and arthritis were found to have a statistically significant association with treatment completion.

The analysis shows that patients in the age group of 55 – 64 years were less likely to successfully complete treatment (AOR=0.16, 95%CI: 0.04 - 0.59) compared to other age groups. Likewise, patients in the registration group after lost-to-follow-up at the start of treatment were less likely to successfully complete treatment (AOR= 0.05, 95%CI: 0.004-0.54).

Again, in this study, not having comorbidity (AOR=2.06, 95%CI: 1.06-4.00), not having adverse events; psychotic symptoms (AOR= 2.79, 95% CI: 1.14 - 6.82), drug induced hepatitis (AOR=12.00, 95%CI: 2.43 - 59), renal toxicity (AOR= 8.31, 95% CI 1.51-45.6) and electrolyte disturbance (AOR=1.75, 95%CI: 1.03 - 2.95) were significantly associated with treatment completion. Patients with comorbidity and the above adverse events were less likely to complete treatment compared to those who did not have comorbidity and these adverse events, respectively. On the other hand, arthritis had statistically significant association with treatment completion (AOR= 2.17, 95% CI: 1.20-3.93), patients with arthritis were more likely to complete treatment compared to those who did not have arthritis. Also, among drug susceptibility testing (DST) techniques, line probe assay (LPA) was another factor associated with treatment completion (AOR=2.11, 95%CI: 1.11 - 4.01). Patients diagnosed with LPA were more likely to complete treatment compared to the other DST techniques. The detailed logistic regression analysis is illustrated in Table 4.6.

Table 4.3: Socio-demographic and clinical characteristics of patients by treatment completion

Characteristics	Subcategories	Treatment completion		P value
		Completed	Not Completed	
Age	18 -24	127 (83.55)	25 (16.45)	0.001
	25 – 34	139 (67.80)	66 (32.20)	
	35- 44	53 (74.65)	18 (25.35)	
	45 -54	24 (68.57)	11 (31.43)	
	55 - 64	8 (47.06)	9 (52.94)	

	≥65	3 (42.86)	4 (57.14)	
Gender	Male	178 (72.65)	67 (27.35)	0.985
	Female	176 (72.73)	66 (27.27)	
Address	Urban	262 (71.98)	102 (28.02)	0.544
	Rural	92 (74.80)	31 (25.20)	
Marital status	Married	143 (68.10)	67 (31.90)	0.219
	Single	186 (76.86)	56 (23.14)	
	Divorced	16 (72.73)	6 (27.27)	
	Widowed	9 (69.23)	4 (30.77)	
Employment	Employed	134 (73.22)	49 (26.78)	0.022
	Unable to work	6 (85.71)	1 (14.29)	
	Student	73 (84.88)	13 (15.12)	
	Unemployed	108 (65.45)	57 (34.55)	
	Other	33 (71.74)	13 (28.26)	
History of Alcohol Consumption	Yes	63 (64.29)	35 (35.71)	0.037
	No	291 (74.81)	98 (25.19)	
History of non-prescription drugs	Yes	37 (67.27)	18 (32.73)	0.338
	No	317 (73.38)	115 (26.62)	
Treatment supporter	Yes	313 (72.62)	118 (27.48)	0.887
	No	38 (71.70)	15 (28.30)	
BMI	<18.5	213 (67.62)	102 (32.38)	0.002
	18.5 - 25	126 (80.77)	30 (19.23)	
	>25	15 (93.75)	1 (6.25)	
Comorbidity	Yes	119 (60.41)	78 (39.59)	0.000
	No	235 (81.03)	55 (18.97)	
Diabetes	Yes	24 (58.54)	17 (41.46)	0.034
	No	330 (73.99)	116 (26.01)	
Hypertension	Yes	9 (60.0)	6 (40.0)	
	No	345 (73.09)	127 (26.91)	0.263
	New	31 (64.58)	17 (35.42)	
	Relapse	47 (61.84)	29 (38.16)	
	After lost-to-follow-up	2 (33.33)	4 (66.67)	

Registration group at start of treatment	After failure of new first line drug regimen	45 (63.38)	26 (36.62)	0.001
	After failure of retreatment first line drug regimen	213 (79.78)	54 (20.22)	
	Transfer in	4 (80.00)	1 (20.00)	
	Other	12 (85.71)	2 (14.29)	
Type of TB	Pulmonary	335 (72.04)	130 (27.96)	0.141
	EPTB	19 (86.36)	3 (13.64)	
Resistance Type	MDR-TB	352 (72.73)	132 (27.27)	0.814
	Pre-XDR TB	2 (66.67)	1 (33.33)	
Bacteriology result	Bacteriologically confirmed	353 (72.93)	131 (27.07)	0.125
	Clinically diagnosed	1 (33.33)	2 (66.67)	
Prior TB drug use more than one month	First-line drugs	325 (74.03)	114 (25.97)	0.110
	Second-line drugs	1 (33.33)	2 (66.67)	
HIV test result	Reactive	72 (62.07)	44 (37.93)	0.003
	Non-reactive	267 (76.07)	84 (23.93)	
HIV Positive started CPT	Yes	63 (61.76)	39 (38.24)	0.855
	No	9 (64.29)	5 (35.71)	
HIV positive started ART	Yes	68 (62.39)	41 (37.61)	0.782
	No	4 (57.14)	3 (42.86)	
Baseline audiometry	Done	5 (71.43)	2 (28.57)	0.940
	Not done	349 (72.71)	131 (27.29)	
DST Technique	Xpert MTB/RIF	92 (59.74)	62 (40.26)	0.000
	LPA	158 (78.22)	44 (21.78)	
	Culture	99 (79.84)	25 (20.16)	
	Other WRD	5 (71.43)	2 (28.57)	
Chest x-ray	Cavities	18 (54.55)	15 (45.45)	0.001
	Fibrosis	159 (79.90)	40 (20.10)	
	Normal	5 (50.00)	5 (50.00)	

Table 4.4: Scheduled monitoring of laboratory investigations by treatment completion

Variables	Subcategories	Treatment completion		P value
		Completed	Not completed	
Weight	Yes	341 (73.02)	126 (26.98)	0.431
	No	13 (65.00)	7 (35.00)	
Complete blood count	Yes	340 (72.96)	126 (27.04)	0.434
	No	13 (65.00)	7 (35.00)	
Serum Electrolyte	Yes	331 (72.91)	123 (27.09)	0.689
	No	23 (69.70)	10 (30.30)	
Liver function tests	Yes	337 (72.79)	126 (27.21)	0.834
	No	17 (70.83)	7 (29.17)	
Urea/creatinine	Yes	340 (72.81)	127 (27.19)	0.783
	No	14 (70.00)	6 (30.00)	
TSH	Yes	318 (72.00)	119 (27.79)	0.135
	No	36 (75.86)	14 (28.00)	
Audiometry	Yes	11 (91.67)	1 (8.33)	0.112
	No	343 (72.21)	132 (29.41)	

Table 4.5: Adverse events identified by treatment completion

Variables	Subcategories	Treatment completion		P value
		Completed	Not completed	
Nausea and vomiting	Yes	202 (69.90)	87 (30.10)	0.095
	No	152 (76.77)	46 (23.23)	
Gastritis	Yes	263 (73.06)	97 (26.94)	0.760
	No	91 (71.65)	36 (28.35)	
Peripheral neuropathy	Yes	26 (81.25)	6 (18.75)	0.261
	No	328 (72.09)	127 (27.91)	
Seizures	Yes	1 (33.33)	2 (66.67)	0.125
	No	353 (72.93)	131 (27.07)	
Hearing impairment	Yes	6 (66.67)	3 (33.33)	

	No	348 (72.80)	130 (27.20)	0.682
Depression anxiety	Yes	37 (72.55)	14 (27.45)	
	No	317 (72.71)	119 (27.29)	0.981
Psychotic symptoms	Yes	17 (53.13)	15 (46.88)	
	No	337 (74.07)	118 (25.93)	0.010
Hypothyroidism	Yes	10 (66.67)	5 (33.33)	
	No	344 (72.88)	128 (27.12)	0.595
Drug induced hepatitis	Yes	2 (13.33)	13 (86.67)	
	No	352 (74.58)	120 (25.42)	0.000
Renal toxicity	Yes	2 (18.18)	9 (81.82)	
	No	352 (73.95)	124 (26.05)	0.000
Electrolyte disturbance	Yes	84 (61.76)	52 (38.24)	
	No	270 (76.92)	81 (23.08)	0.001
Optic neuritis	Yes	5 (55.56)	4 (44.44)	
	No	349 (73.01)	129 (26.99)	0.244
Arthralgia, arthritis	Yes	123 (84.25)	23 (15.75)	
	No	231 (67.74)	110 (32.26)	0.000

Table 4.6: Logistic regression analysis of variables with treatment completion

Variables	**Category**	**Treatment completion**		**COR (95%CI)**	**P – value**	**AOR (95% CI)**	**P-value**
		Completed	**Not completed**				
Age in years	18 -24	127 (83.55)	25 (16.45)	1.00			
	25 -34	139 (67.80)	66 (32.20)	0.41 (0.24-0.69)	0.001	0.56 (0.27-1.16)	0.125
	35- 44	53 (74.65)	18 (25.35)	0.58 (0.29-1.15)	0.119	0.90 (0.34-2.35)	0.830
	45 -54	24 (68.57)	11 (31.43)	0.43 (0.18-0.98)	0.047	0.48 (0.16-1.40)	0.183
	55 -64	8 (47.06)	9 (52.94)	0.17 (0.06-0.49)	0.001	0.16 (0.04-0.59)	0.006
	≥65	3 (42.86)	4 (57.14)	0.15 (0.03-0.70)	0.016	0.35 (0.04-2.92)	0.334
History of alcohol consumption	Yes	63 (64.29)	35 (35.71)	1.65 (1.03-2.64)	0.038	0.92 (0.49-1.73)	0.807
	No	291 (74.81)	98 (25.19)	1.00			

BMI	<18.5	213 (67.62)	102 (32.38)	1.00			
	18.5 - 25	126 (80.77)	30 (19.23)	2.01 (1.26-3.19)	0.003	1.70 (0.98-2.94)	0.055
	>25	15 (93.75)	1 (6.25)	7.18 (0.93-55.12)	0.058	6.98 (0.85-57.1)	0.070
Registration group at start of treatment	New	31 (64.58)	17 (35.42)	1.00			
	Relapse	47 (61.84)	29 (38.16)	0.88 (0.42-1.88)	0.758	0.56 (0.22-1.46)	0.240
	After lost-to-follow-up	2 (33.33)	4 (66.67)	0.27 (0.04-1.65)	0.158	0.05 (.004-0.54)	0.014
	After failure of new first line drug regimen	45 (63.38)	26 (36.62)	0.94 (0.44-2.03)	0.893	0.48 (0.17-1.30)	0.153
	After failure of retreatment first line drug regimen	213 (79.78)	54 (20.22)	2.16 (1.11-4.19)	0.022	1.00 (0.39-2.59)	0.984
	Transfer in	4 (80.00)	1 (20.00)	2.19 (0.22-21.22)	0.498	3.42 (0.48-24.2)	0.217
	Other	12 (85.71)	2 (14.29)	3.29 (0.65-16.45)	0.147	2.63(0.36-18.97)	0.336
HIV test result	Reactive	72 (62.07)	44 (37.93)	1.00			
	Non-reactive	267 (76.07)	84 (23.93)	1.94 (1.24-3.04)	0.004	1.50 (0.84-2.69)	0.166
Comorbidity	Yes	119 (60.41)	78 (39.59)	1.00			
	No	235 (81.03)	55 (18.97)	2.80 (1.85-4.21)	0.000	2.06 (1.06-4.00)	0.033
DST Technique	Xpert MTB/RIF	92 (59.74)	62 (40.26)	1.00			
	LPA	158 (78.22)	44 (21.78)	2.41 (1.52-3.84)	0.000	2.11 (1.11-4.01)	0.021
	Culture	99 (79.84)	25 (20.16)	2.66 (1.54 - 4.59)	0.000	1.78 (0.83-3.83)	0.137
	Other WRD	5 (71.43)	2 (28.57)	1.68 (0.31 - 8.96)	0.541	1.30 (0.21-8.09)	0.773
Psychotic symptoms	Yes	17 (53.13)	15 (46.88)	1.00			
	No	337 (74.07)	118 (25.93)	2.51 (1.22 -5.20)	0.013	2.79 (1.14-6.82)	0.024
Drug induced hepatitis	Yes	2 (13.33)	13 (86.67)	1.00			
	No	352 (74.58)	120 (25.42)	19.06(4.24-85.71)	0.000	12.00 (2.43-59)	0.002
Renal toxicity	Yes	2 (18.18)	9 (81.82)	1.00			
	No	352 (73.95)	124 (26.05)	12.77(2.72-59.93)	0.001	8.31 (1.51-45.6)	0.015
Electrolyte disturbance	Yes	84 (61.76)	52 (38.24)	1.00			
	No	270 (76.92)	81 (23.08)	2.06 (1.34-3.15)	0.001	1.75 (1.03-2.95)	0.035
Arthralgia, arthritis	Yes	123 (84.25)	23 (15.75)	2.54 (1.54-4.19)	0.000	2.17 (1.20-3.93)	0.010
	No	231 (67.74)	110 (32.26)	1.00			

1.00: reference category; COR: Crude Odds Ratio; AOR: Adjusted Odds Ratio; CI: confidence interval.

4.3 CONCLUSION

The chapter presented quantitative data analysis of socio-demographic and clinical characteristics of DR-TB patients and factors associated with treatment completion of patients on DR-TB treatment. The next chapter dwells on qualitative data analysis and presentation of findings that include barriers, challenges and facilitators of treatment completion of DR-TB treatment from the views of experts and the lived experiences of previously treated patients.

CHAPTER FIVE

ANALYSIS AND PRESENTATION OF FINDINGS: QUALITATIVE STRAND

5.1 INTRODUCTION

This section presents the study findings on the in-depth interviews conducted with healthcare providers who have been working in the patient and programmatic management of DR-TB as well as FGDs with DR-TB patients who have a previous history of unsuccessful treatment outcomes and who are currently on a retreatment regimen on their views and experiences, respectively. The biographical data of the participants and discussants are presented first, followed by the themes and categories that emerged. The literature control on key findings as well as conclusions, are presented later in Chapter six.

In this study, a conventional content analysis approach was employed to describe the experiences and views of HCPs and DR-TB patients on the treatment completion of DR-TB treatment. Both in-depth interviews and focus group discussions were conducted in Amharic, the official language of Ethiopia. The in-depth and focus group interviews were then transcribed verbatim by the researcher and the transcriptions were audited by an experienced public health expert while listening to the original audio content. Subsequently, transcripts in the Amharic version were translated into English with the consultation of an experienced English translator. In addition, the English transcription was back translated to Amharic to ensure accuracy. All aspects of data management and analysis were performed by using Atlas. ti version 8 software application. To verify the findings of the qualitative data set, a professional qualitative research expert was employed as a co-coder in the process.

5.1.1 Demographic characteristics of the participants

The demographic profile of HCPs and patients who participated in the in-depth interviews and focus group discussions are described below, respectively.

5.1.1.1 Demographic characteristics of healthcare providers

Fifteen (15) HCPs working in DR-TB treatment and management including senior physicians and nurses participated in the in-depth interviews. The demographic characteristics of the participants including age, sex, profession and work experience

in DR-TB are illustrated in Table 5.1 below. The mean age of the participants was 38.3 years, ranging from 28 to 50 years. Among the 15 interviewed HCPs 11 (73.3%) were male and four were female. DR-TB related work experience ranges from 2 – 9 years, with an average of 5.9 years. The majority of the participants 10 (66.7%) were medical doctors (physicians) including specialists, while four were nurses and one was a health officer.

Table 5.1: characteristics of healthcare providers participated in the in-depth interview

Participant Code	Age	Sex	Profession	Service year in DR-TB
P1	28	F	Medical doctor	2
P2	28	M	BSc Nurse	3
P3	34	M	Health Officer	9
P4	50	M	BSc Nurse	5
P5	38	M	Medical doctor (Internist)	6
P6	28	M	Medical doctor	4
P7	36	F	Medical doctor (Internist)	8
P8	42	F	BSc Nurse	7
P9	45	M	Medical doctor (Internist)	5
P10	31	M	BSc Nurse	3
P11	45	M	Medical doctor (Internist)	7
P12	50	M	Medical doctor (Internist)	9
P13	29	F	Medical doctor	3
P14	45	M	Medical doctor	8
P15	46	M	Medical doctor (Internist & Pulmonologist)	9

5.1.1.2 Demographic characteristics of FGDs participants

The mean age of the FGD participants was 31 years, ranging from the youngest aged 19 to the oldest 56 years. The majority of the participants 15 (35.7%) were in the 25 – 34 age group. Thirty 30 (71.4%) of the participants were males. The majority of the participants, 33 (78.6%) were from urban areas determined by residential address. The majority of the participants were single 26 (61.9%) and unemployed 34 (81.0%). Table 5.2 depicts information of the participants included in the focus groups.

Table 5.2: Demographic detail of participants of the focus groups (N=42)

Variables	Category	Frequency	%
Age Categories	18 – 24	12	28.6
	25 – 34	15	35.7
	35 – 44	10	23.8
	45 – 54	4	9.5
	55 – 65	1	2.4
Gender	Male	30	71.4
	Female	12	28.6
Address	Urban	33	78.6
	Rural	9	21.4

Marital Status	Married	12	28.6
	Single	26	61.9
	Divorced	3	7.1
	Widowed	1	2.4
Employment	Employed	8	19.0
	Unemployed	34	81.0

5.1.2 Themes identified in the in-depth interviews

From the in-depth interviews with HCPs three themes emerged, comprising (1) Barriers to treatment completion; (2) Challenges for patient follow-up; and (3) Cross cutting issues influencing treatment completion.

5.1.2.1 Theme 1: Barriers to treatment completion

This theme was identified from in-depth interviews with health workers. They shared views regarding barriers to treatment completion of patients with DR-TB. The theme comprises six categories and numerous subcategories as illustrated in Table 5. 3.

Table 5.3: Theme 1: Barriers to treatment completion – categories and sub-categories

Theme 1	Categories	Sub-categories
Barriers to treatment completion	Clinical Issues	Delay in management of side-effects Comorbidity Complicated treatment Long illness before treatment Prognosis Delay in diagnosis Badly affected lung Come with advanced conditions Surgical management Extensive resistance
	Drug-related factors	Side-effects Long treatment duration High pill burden Fed up with injection Effectiveness
	Patient factors	False sense of cure Addiction Lack of awareness Changing address Inconvenience Frustration Preference
	Health system related	Accessibility Facility setup Community-based DR-TB service

	Socio-economic factors	Economy Stigma Social problems Nutrition Employer non-cooperation
	Programmatic and provider related	Manner of handling patients Monitoring and follow-up Counselling

5.1.2.1.1 Clinical issues

- **Delay in management of side-effects**

This study identified that delay in the management of side-effects of the anti-TB drugs was one of the barriers to treatment completion, where quick management of side-effects was not in place, patients could quit the drugs and discontinued their treatment before completion. The following views were submitted by the HCPs who participated in the in-depth interviews regarding the delay of management of side-effects on treatment outcomes:

> *HP11: "Serious side-effects occur. They may be contributing. But in my opinion, beyond the side-effects, it is about how quickly and properly we can deal with the side-effects. So, if patients cannot get a solution to those problems quickly, they can discontinue the treatment".*
>
> *HP9: "Further, with regard to patients who sustain drug side-effects while on treatment, it is sad to see them suffering due to a shortage of ancillary drugs to treat those side-effects".*
>
> *HP10: "In order to avoid interruption of treatment, sufficient patient follow-up should be in place by health providers. Early treatment of side-effects means that patients will not quit drugs".*

- **Comorbidity**

Most of the study participant HCPs mentioned that comorbidities like HIV, diabetes, malnutrition, and chronic illnesses such as renal disease and lung disease complicate treatment. They also highlighted frustration due to the high pill burden and increased occurrence of adverse events as significantly reducing the success of treatment completion. The following are direct verbatim statements of the HCPs:

HP15: "If there are comorbidities like HIV, diabetes, and others, the treatment becomes complicated. The drugs have interactions. There is also a pill burden. When an HIV positive person get an MDR-TB, the medication he takes will be extremely high. If he takes another drug for an OI [opportunistic infection], and again if he takes ancillary drugs for adverse events, that will bring frustration and the patient may stop the drugs. This is one of the major barriers to interrupting the treatment".

HP7: "The other thing is that, in association with HIV, co-infected TB patients have high mortality, especially when they develop side-effects, it is higher. Similarly, the presence of co-morbidities like diabetes and malnutrition also contributes".

HP6: "Similarly, due to comorbid conditions, the chances of the occurrence of adverse events due to anti-TB drugs will increase. Therefore, when these adverse events appear from time to time, the patients will be fed up and exhausted and may interrupt the treatment".

- **Complicated treatment**

From the in-depth interviews, it became clear that one of the barriers to the successful treatment completion of DR-TB was that treatment of DR-TB is a complicated process compared to that of drug-susceptible TB. The participants mentioned that the treatment is given over a long time and is not as effective as the first-line drugs and poses the greater possibility of failure. The following are verbatim statements of the participants:

HP14: "When we compare with drug-susceptible TB, treatment of DR-TB is complicated and given for a long time".

HP6: "[By] the time a patient with drug resistance fails one phase of a regimen and enters into the next phase, the treatment becomes complicated. In such cases, you are obliged to use any choice you have at hand. The drugs are not as effective as first-phase drugs. So the subsequent courses have a greater possibility of failure. The drugs have limited effectiveness".

- **Long illness before treatment**

The participants informed the researcher that many patients with DR-TB come after long-term illnesses and their bodies are physically compromised and impaired, to

resist any adverse events due to the drugs. There is a high likelihood of discontinuing and quitting the drugs. The participants explained presenting with a long illness prior to DR-TB treatment as a barrier to treatment completion as follows:

HP14: "And it is only after a long illness, DR-TB patients come to treatment. From that perspective, it is known that the outcome is still low compared to the others".

HP15: "Um, and because many of them come after long-term illnesses, their bodies are physically impaired and they are unable to resist the side-effects of the drugs. During that time, there are overlapping problems and things like discontinuing and stopping of the medication will happen".

HP9: "Then again, the patients may be very tired and hurt when they come. When we see this situation, treating and curing patients can be very difficult. So it will not be like susceptible TB".

- **Prognosis**

Most of the study participants considered the prognosis of DR-TB more fatal than susceptible TB. The following statements were made by most of the health providers who participated in the study:

HP5: "Drug resistant TB prognosis is not as susceptible TB, where some patients survive and some die; it is highly fatal".

HP6: "The terribleness of the problem is more than ordinary drug resistance and difficult cure. There is a probability of death".

HP14: "Furthermore, patients may die early in treatment. Then there are those who die as soon as they start; and there are those who die after making a positive change".

HP14: "Beyond that, due to the severe adverse events, patients may lose their lives".

In addition, as DR-TB patients are not usually diagnosed on time and come after multiple first-line treatment courses. This creates a suitable lodging environment for the bacteria and cavities, which can make the treatment difficult. Further, repeated attacks of the lung result in fibrosis [scarring], which makes it difficult for the drugs to

penetrate the scar tissue and this makes a cure difficult. As a result, these could make the prognosis bad. The participants further explained the prognosis as:

HP9: "[Many] patients who require treatment for DR-TB, are rarely diagnosed timeously. They are repeatedly treated with first-line drugs for susceptible TB. Their lungs and bodies are also hurt. This in turn creates a suitable lodging environment for the bacteria and makes it difficult to cure the disease. For example, a cavity in the upper part of the lung is created and it can make it difficult to get rid of the germs there as quickly as possible. And again, after repeatedly being attacked by TB, it will result in scarring, which we call fibrosis, where the drugs cannot have their effect. For these reasons, DR-TB cannot be healed as quickly as drug-susceptible TB".

- **Delay in diagnosis**

This study identified that delay in diagnosis of DR-TB is a barrier to successful treatment completion. As time passes without getting diagnosed, the disease worsens with severe damage to the lung parenchyma and culminates in serious illness. Consequently, this results in poor outcomes.

HP11: "It takes a lot of time for most patients to be diagnosed with MDR-TB. So when patients come for treatment, they come with a serious illness, so the mortality rate will increase".

HP5: "In the rural areas, they don't have MDR-TB diagnostic facilities. If MDR-TB is not diagnosed early and the patient is treated for susceptible TB while having MDR-TB, the disease gets worse, and by the time MDR-TB is diagnosed the patient has severe damage to the lungs. This ends up in a poor outcome".

- **Badly affected lungs (advanced disease)**

This sub-category refers to participant HCPs describing patients with DR-TB who generally come with badly affected and deteriorating lungs with advanced and extensive lesions. This makes treatment and curing difficult, becoming a barrier to successful treatment completion. The participants elaborated as follows:

HP15: "In addition, generally these patients have significant or very severe lung problems. The lungs are badly affected and easily exposed to a variety of lung

problems. As a result they can easily die. The likelihood that the patients will die of a different condition than the TB is greater".

HP6: "Most patients who come here are coming after three or four phases of treatment. In the process, both their lungs have been deteriorating. Both of the lungs are harmed. It is difficult to cure them. The damage is advanced and extensive".

HP2: "Among factors which compromise treatment outcome, patients who come to this facility come with advanced conditions. They go beyond MDR-TB. They are in the final stage".

HP5: "In addition, they may come with an advanced disease which might not be cured and there might be a chance of death".

- **Surgical management**

This sub-category, surgical management, was recognised as one of the barriers to successful treatment completion of patients on DR-TB treatment. The service of surgical management of DR-TB was generally weak in Ethiopia and patients were not getting the surgical procedures timeously. In addition, there was no intensive care unit (ICU) service, which is a lifesaving service for DR-TB patients. The participants explained surgical management as follows:

HP4: "There is surgical management, yes, of course, but in Ethiopia I still think the surgical management is not very strong. In fact, DR-TB patients are suffering. Um, they are not being operated. If they were operated on early, a better outcome would have come. That thing is not being done. It must be strengthened. In addition, if we link surgical management and palliative care with chronic care, we can improve the current treatment outcome".

HP1: "We have a surgical department and yet we have a problem utilizing surgery service. There is a requirement to have a smear and culture conversion, and we do not have an intensive care unit (ICU) service for DR patients. DR-TB patients in need of surgery and ICU care are not receiving life-saving services".

- **Extensive resistance**

The study participants elaborated that the nature of DR-TB disease is quite different from drug-susceptible TB in that the characteristic of the bacterium is resistance to

first-line drugs, sometimes with extensive resistance. Hence, the disease results from an aggressive type of bacteria, and treatment is also difficult with available medicines. As a result, unfavourable treatment outcomes may occur eventually (Leveri, Lekule, Mollel, Lyamuya & Kilonzo 2019:2; Baluku et al 2021:2; Khachatryan et al 2021:5).

HP6: "Therefore, since patients coming to this facility are XDR, Pre-XDR, and not ordinary MDR patients, their treatment is also very difficult. They harbour aggressive TB bacteria which are difficult to treat with available drugs. In such a case, death is imminent and patients may die".

HP15: "The problem with the outcome is that what you are treating is already a resistant strain. It is not a susceptible strain. As you know, the drugs we use, except new drugs, for treating resistant strains have long been tried and are not effective. So, we are trying to treat resistant bacteria".

HP13: "Therefore, Mycobacterium tuberculosis mutates and becomes resistant. It becomes resistant to very effective first-line anti-TB drugs".

HP9: "In addition, a resistant TB bacilli, characteristically, passes through many challenges and is resistant to many anti-TB drugs. It is not eradicated with first-line drugs easily… All of these factors, I believe, contribute to a lower likelihood of success".

5.1.2.1.2 Drug-related factors

- **Side-effects**

In contrast to the sub-category above (delay in management of side-effects), which was about how quickly healthcare professionals are able to deal with the side-effects, this sub-category focuses purely on the existence of side-effects that are caused by DR-TB medication. The study participants noted that second-line anti-TB drugs cause significant adverse events, which affect adherence to the treatment, causing reluctance on the patient and even disappearance from follow-ups. Likewise, if the side-effects exist for a long time, patients prefer to quit their regimen.

HP14: "Most of the patients will develop at least one adverse event during treatment duration".

HP6: "Since patients on MDR-TB treatment are taking a large number of drugs, there are also a number of side-effects that may come into the picture. This reduces their quality of life. They can have headaches, daily gastrointestinal upset, joint pain, and others. This causes reluctance and initiate the patients to think that the drugs are causing them harm. The occurrence of adverse events every time can be considered as a barrier [to treatment completion]".

HP12: "Likewise, when there are repeated side-effects after many follow-ups, they may not show up on the next appointment day for fear of the continuation of treatment".

HP3: "The other vital thing I observed is the side-effects of the drugs. We try to manage the side-effects with different medications, but if the side-effects persist, they prefer to stop the treatment. If the side-effect is the one that should be treated as an inpatient, they do not want hospitalization. They argue that rather than being admitted to a hospital, it is preferable to discontinue treatment".

In addition, it was established that serious side-effects compel patients to interrupt their medication, disappear from follow-up, and default treatment (Jakasania, Shringarpure, Kapadia, Sharma, Mehta, Prajapati & Kathirvel, 2020:2; Dela, Tank, Singh & Piparva 2017:524-525; Bogale, Tsegaye, Abdulkadir & Akalu 2021:1344). In this study, the following vignettes crystallise the impressions of the participants:

HP15: "[M]any medications have their own serious side-effects. So, when these side-effects begin to appear, the frustration of people comes. So, they say that I can just go home and die, and I don't want to be treated…This is one of the reasons why many patients interrupt treatment".

HP15: "As I observed, most of the time, patients default due to side-effects. Everyone wants to be treated and cured at the beginning. They cry and push you to start their treatment. They are okay with the information that the drugs have side-effects. But after two or three months of starting treatment, arguments come up saying I will not take it and I better die. The major thing I observed to default and disappear is the drug's side-effects".

HP1: "There are lots of side-effects. The second-line anti-TB drugs have more side-effects. Side-effects are one of the factors patients stop their treatment".

HP4: "First, there are side-effects that are caused by the drugs, like vomiting, a burning sensation, and joint pain. These things make treatment completion difficult".

HP11: "The drugs are difficult. They have a lot of side-effects and there is a discontinuation associated with that".

- **Long treatment duration**

This sub-category, long treatment duration, which emerged from the interviews, was one of the factors that are barriers to treatment completion. Patients on second-line anti-TB regimens may get tired and bored over the extended time for treatment and may interrupt the medication. As time passes, since most of the patients quit their jobs to take the drugs, time and the anxiety of waiting exert stress on their lives and they may also interrupt their treatment to find work to support their lives (Eshetie, Gizachew, Alebel & van Soolingen 2018a:2-3; Molie, Teklemariam, Klinkenberg, Dessie, Kumsa, Mohammed, Debebe, Assefa, Habte, Bedru, Fiseha & Seyoum 2019:2; Baye, Sarhie & Endalew 2018:1).

HP15: "[T]he treatment itself takes a long time, and many people may not be able to complete the treatment. Patients may interrupt".

HP3: "What I think of as a barrier is when the duration of treatment is two years, as the time elongates, the patients become bored with the treatment".

HP4: "The treatment is taken for a long duration. So they discontinue or interrupt their jobs to take the treatment. So this poses stress for living and may be one reason from a living perspective [as a barrier to treatment completion]".

HP9: "[T]he drug must be given long enough to completely eliminate the disease. Because it is not curable in six months like susceptible TB, there is a need for up to two years of treatment. … . It may be difficult to finish the treatment course in that time".

- **High pill burden**

High pill burden was considered the primary barrier to treatment completion. According to the participating healthcare professionals, it is the primary reason patients attribute to their treatment interruption. Below are explanations provided by healthcare professionals regarding how the high pill burden affects the treatment process:

HP6: "The first barrier is pill burden. When we ask patients who return after lost-to-follow-up, why they interrupt, the reason they give us primarily is pill burden. The patient barely has a handfuls of breakfast to eat, but we give him [her] couple of handful pills to swallow. Hence, he [she] is apparently swallowing on an empty stomach. So, they cannot tolerate the pill burden".

HP13: "When we come to second-line drugs, there is no fixed dose combination. This means a patient may take at least five drugs a day. Five drugs means it is a type of drug not a tablet. A patient may take three to four tablets of each drug type. Therefore, they take lots of tablets. That means high pill burden".

HP2: "The other thing I told you is about pill burden. One patient may take eight to sixteen pills based on body weight. When they take this medication, different kinds of side-effects may appear".

- **Fed up with injection**

Similarly, being tired of being injected was also considered a significant barrier to treatment completion in the view of study participant health workers. Painful injection sites and higher chances of adverse events associated with injectable anti-TB medication cause fatigue and frustration in patients, resulting in interruption of therapy.

HP4: "The other reason is the long duration of injections for eight months, which has a big impact on the patients. They complain, 'Am I going to be injected for the whole eight months? ... Can I really do it?' On top of that, from my experience, the pain of the injection site will get more and more intense with time, and this makes the patients get fatigued from injections and forces them to interrupt their treatment".

HP6: "There are patients who interrupt therapy only because of not needing to take the injectable. When you look at the adherence of patients who take injectable and injectable-free regimens, those patients taking injectable-free regimens have a better capacity to complete treatment duration. In addition, adverse event episodes or frequencies are higher with injectables".

- **Effectiveness**

Effectiveness of second-line anti-TB drugs is recognised by participant HCPs as that of first-line anti-TB drugs. Second-line drugs are considered less potent and

suboptimal. Consequently, successful treatment completion may not be realised at the end (Buziashvili, Mirtskhulava, Kipiani, Blumberg, Baliashvili, Magee, Furin, Tukvadze & Kempker 2019:1005; Safaev, Parpieva, Liverko, Yuldashev, Dumchev, Gadoev, Korotych & Harries 2021:1).

HP13: "Effectiveness wise, first-line drugs are effective and second-line anti-TB drugs are less effective".

HP15: "Obliged to treat these patients with drugs that are suboptimal and previously been shown to be ineffective. A potent anti-TB medicine like rifampicin has not yet been developed. So, we are treating rifampicin-resistant strains with drugs less effective than rifampicin. Therefore, generally, more effective drugs are not developed. We are treating with less potent drugs a strain that is resistant to more potent drugs. One of the basic things is this".

5.1.2.1.3 Patient factors

- **False sense of cure**

At the beginning of treatment, patients were quite sick. But after they are put on treatment for a few months and the bacteria load decreases, they feel symptomatic resolution and think they are cured. When this happens, they may interrupt the treatment, despite recommendations that treatment should continue for the prescribed duration. The following are study participants' verbatim descriptions regarding the false sense of cure of patients who spent a couple of months on treatment:

HP12: "As mentioned earlier, the treatment is long-term. Many patients come very sick and weak when they come. It means that they are attacked by the disease harder. Um, when they take the treatment for several months, the bacteria load will decrease, and even patients who came with the stretcher and who were on oxygen will feel better in four to five to six months. The treatment, however, should continue for up to two years. But those patients who feel well may think that they are cured and may interrupt the treatment".

HP6: "First, the treatment of MDR-TB is given for a long time. When we see the treatment cycle, there are symptoms that respond to treatment immediately after the start of therapy. There are symptoms which respond in the middle of therapy. We give treatment till the end to eradicate the bacteria completely. Otherwise, the

difficult symptoms subside in the early course of treatment within the first 4 to 5 months. Patients feel completely healthy, and when they reach this phase, most of them consider themselves cured. So, they tend to avoid the drugs. Taking medication has its pain. They avoid pain associated with side-effects when they stop taking".

HP9: "On the other hand, when their weight increases, cough stops, and appetite improves, they think that they are recovered, and as much as possible, they want to stop the drugs. They tend to stop the treatment because no one likes to take drugs for a long time. Therefore, it is quite important to give them proper advice according to their age and behaviour regarding the importance of finishing and the danger of discontinuing the regimen. …. As they recover, they think they are cured completely because they still have a living issue. But this is one of the accounts of TB disease. Since the number of bacteria decreases as they begin treatment, many people recover and think they are better. At this point, those who had endured all of the side-effects reach a wrong decision. 'What would happen if I stopped the drug now? I am better and recovered now".

- **Addiction**

In this study, it was established that addiction was a barrier to treatment completion in patients on DR-TB therapy. They indicated that substance abuse affects treatment adherence and causes treatment interruption. Furthermore, patients suffering from addiction tend to relapse and practice their addiction soon after improvement of symptoms and do not abide by the treatment supervision by health providers. The HCP explained the impacts of addiction on patients receiving treatment as follows:

HP14: "… There are patients with different kinds of addiction. Those who take alcohol, smokers, and khat chewers. It is very hard for patients with substance abuse problems to keep track of their treatment. I think they also discontinued it because of such problems".

HP15: "Some patients may have, uh, problems with addiction. Substance abusers, alcoholics, if there are any of these things, most will not take the medicine unless we address that part".

HP3: "There is a patient factor. For example, if a patient has an addiction problem, he does not like to stay under supervised treatment. It can be alcohol. It can be

khat. If he has any other addiction, he wants to end treatment sooner. If patients feel better, they want to get back to their peer group and practice that addictive behaviour".

HP4: "… those addicted individuals, most of the time, they will return to their previous habits. For instance, people who have an addiction to khat and an addiction to alcohol think of the solid two years of treatment duration at the start and they feel to lose hope".

- **Lack of awareness**

In the interview, lack of awareness about the importance of treatment adherence for the full duration was singled out as a barrier to successful treatment completion. It was mentioned that there was a lack of awareness of the importance of completing the treatment to prevent a relapse of the disease. In addition, there is low knowledge about the severity of the disease and how much of it is fatal. Lack of awareness contributes to treatment non-completion as perceived by the health workers and they described the phenomenon as follows:

HP15: "There is a lack of awareness and understanding of the disease reflected in some areas. And what is the disease? How is it transmitted? How can society prevent it? How long does the treatment take? What are the consequences if you don't take it? Um…misunderstandings can also result in the drug being discontinued in some areas".

HP1: "The other can be related to knowledge. After patients take medication for some time, they think that it gives them some relief from the disease. They have a lack of awareness of the importance of completing the treatment otherwise the disease will relapse again".

HP3: "The other point is that knowledge of the severity of the disease in our population is very low. Our community does not have knowledge regarding how serious and how fatal the disease is. So, I think one factor is a lack of awareness".

HP6: "Lack of awareness is also a barrier. In the first place, most patients are not convinced of getting treatment. If they have enough awareness, they understand the necessity of treatment. If a patient starts treatment and interrupts, he thinks

that he will survive. When he interrupts, it reflects that he has a lack of awareness. He is unaware that the treatment is a must".

- **Changing address**

A permanent residential address allows for tracing patients on treatment in case any problem occurs in the treatment process and to reinstate their follow-up in case there is treatment interruption. However, some patients change their addresses and turn off their cell phones, thus making it difficult for them to complete their treatment. The following were submitted by study participants regarding the changing of address by patients:

HP3: "When patients default, they switch off their cell phones and change their home addresses. Bringing such patients back is a major challenge for us. If he resides in Addis Ababa, he can go to the suburbs, for example, Sululuta, and rent a house there, and you will not find him. We cannot find him if his phone is not working and his family does not have any information".

HP9: "In addition, after being discharged from the hospital for monthly follow-up, they may change their addresses and discontinue treatment".

- **Inconvenience**

This study also identified inconveniences during treatment time that disrupt treatment adherence and completion. It was indicated by the participants that conditions likely to cause inconvenience were daily travel and visits to health facilities for directly observed treatments; lack of money for daily transport; renting a room near to the clinic to continue treatment; and being admitted to a hospital. The health provider study participants mentioned the points as follows:

HP14: "Because patients need to go to the treatment facilities on a daily basis to take some of the drugs. This also has its own problems".

HP5: "If the patient does not have money and cannot get support, he may face transportation problems to come to the clinic daily".

HP6: "TFC also may not be located in their county. So, he needs to travel daily to the centre or rent a room there to continue treatment".

HP3: "When it is a hospital, they perceive that they are seriously ill and do not want admission. Most patients like to be treated as outpatients. Likewise, clients who have responsibility for family, for example, looking after children, do not like hospitalization, even passing a single night there. Some side-effects management, for example, electrolyte disturbance, mandates hospitalisation. Patient admission is required until the patient stabilises".

- **Frustration**

During the treatment journey, patients end up frustrated in many ways. One thing is, if their social problems are not addressed properly and there is no solution to these, patients become frustrated. In addition, long treatment duration with a large pill burden and the worrisome adverse events affecting already exhausted patients after months of first-line treatment. Frustration and thus treatment interruption are very likely. The following were mentioned by the HCPs who participated in the study as triggers of frustration by the patients on DR-TB treatment:

HP15: "There is despair".

HP11: "The support for addressing social problems is not enough. There is no transportation support in our hospital, for example. Food support is not continually available. This is what makes patients so frustrated".

HP15: "The patient is very happy at the start of treatment. He is happy to start the medicine. He wants to be saved. After starting, however, many medications have their own serious side-effects. So, when these side-effects begin to appear, the frustration of people comes".

HP4: "The treatment duration is lengthy, which causes stress to the patients. In the first place, they come for MDR-TB treatment after months of TB treatment with first-line drugs and are already bored. When they come, they come to try and are not sure whether to get cured, thinking they don't have any other options".

HP8: "It is boring that the treatment is long-term. The number of drugs is boring. The side-effects are tiring. Therefore, they will become aware of that and get bored".

HP9: "The drugs themselves have many side-effects. They take lots of drugs. Each drug has its own untoward effects. Side-effects may occur repeatedly. One adverse

event may come after treatment of the other. All these may create fatigue for patients".

- **Preference**

The study also established that one of the barriers to DR-TB treatment completion was patients' personal preferences for traditional medicines and religious activities like holy water and spiritual persuasions. The following were verbatim submissions by study participants regarding patients' personal preferences as a cause for treatment discontinuation:

HP15: "Um… what we observe in some individuals is that, without any reason, there is a tendency to interrupt treatment and preferring traditional medicine, going to holy water, and spiritual things. While on treatment, if the patient's lung is severely hurt and has structural problems, even if you clear the bacteria and the MDR is getting resolved, the patient may feel pain due to the wound on the inflamed parts. At that time, the patients think that they are not improving and sometimes, probably influenced by the family, may interrupt treatment and go to holy water sites and do spiritual things".

HP3: "The other gap I observed regarding defaulting is confusion related to religion. 'If I get holy water or if supplication is made for me, tuberculosis will vanish.' I remember a lady from Adama town stopped medication because she believed that after prayer, TB was gone through vomiting. I think this is a big gap. Taking medication and religion are different things. They can do both things together".

HP4: "Religion has its own impact. People believe holy water and prayers will cure their TB disease and discontinue their treatment regimens in between. The thing is, when patients come to start treatment, they come with baseline TB diagnostic positive results. But after a month or two, follow-up results turn out to be negative and their symptoms will somewhat improve. In that case, patients consider the holy water and prayers to have brought them such improvements and may quit therapy. This is from a lack of awareness that the disease will relapse".

HP6: "Sometimes, newly emerging barriers, which are related to religion, for instance, saying 'when I go to the holly water God will heal me', and consequently the patient will stop taking pills or quit treatment. In some religious denominations, prophets preach that God is the saviour and tell the individual to not take

medicines. On such occasions, the patients completely abandon scientific medicine and tend to follow the spiritual way".

5.1.2.1.4 Health system related

- **Accessibility**

This study verified that most health facilities which give DR-TB service are located in cities and district towns, making accessibility to patients located in the countryside difficult. These accessibility problems were underlying reasons for treatment interruption.

HP14: "With the current MDR-TB treatment service, the policy we have, and the accessibility of the health centres, there is a huge gap. The health centres are found in the cities and district towns. Therefore, most of the patients who discontinue treatment are those who come from the countryside or those with very low economic living conditions".

HP9: "There is also a place where some patients are located outside of the transportation service, which makes it very difficult for transportation."

HP4: "Distance between home and health facility and difficulty of daily ambulation all pave the way to treatment interruption. The thing is, from the start, they were poor economically. They don't have the capacity to pay for taxi fees. So, they take their drugs intermittently".

HP10: "One reason may be a lack of access to the service anywhere nearby".

In addition, most inpatient admissions are centralised, and patients would be displaced for a long time from their homes, creating psychosocial pressure on them. Patients may not resist such psychosocial pressure and may discontinue their treatment for good.

HP6: "The other is not getting the service where they want to get it. They travel and separate from their family to move to where the service is placed. First, they come to a treatment initiating centre (TIC). To reach TIC, patients travel up to 60km, 100km, even up to 700km. After completing TIC, they will be linked to a treatment follow-up centre (TFC). TFC may also not be located in their district. So, he needs to travel daily to the centre or rent a room there to continue treatment".

HP15: "Another barrier I think is that most MDR-TB treatments are centralized. People have to be displaced. They must be admitted. And these things bring a lot of pressure. As I said, a social crisis separates them from their family. This creates high psychological pressure on the patient. So, the patient may go away and never come back to complete the treatment."

- **Facility setup**

Infrastructure related problems like unavailability of sanitary facilities like showers and clean latrines for personal hygiene at in-patient wards could affect the smooth treatment process and patients could interrupt their treatment. The following statements were forwarded by study participants:

HP1: "Some problems are related to infrastructure. After isolating patients due to MDR-TB, there are problems with providing necessary things. Sanitation-related facilities like showers and clean latrines are not fulfilled in our ward and can even affect the treatment outcome".

HP12: "Patients also complain about the absence of a shower for personal hygiene. And they frequently ask for permission to go out and take a shower, which is difficult to give permission and to say do not a take bath. All These things can be reasons for patients to interrupt treatment and disappear".

HP2: "The infrastructure is very bad. There should be shower rooms, toilets should be clean, and there should be a recreation area and a garden. In the MDR ward, patients stay longer than in other wards. They may stay for up to one year. They need recreational and refreshment areas".

- **Community-based DR-TB service**

The study found that community-based DR-TB care has not been established in the country and patients cannot follow their treatment from home. The rural patients are the hardest hit in that there is no structure to follow their condition.

HP14: "And maybe the principle of community-based DR-TB care in our country is not in place. For drug-susceptible TB, the patient can follow treatment from home".

HP6: "Especially in the remote and rural areas, there is no structure that can listen to them and solve their problems, follow their condition and gives necessary support".

Moreover, the study participants mentioned the necessity of extending community-based care in a decentralized fashion particularly for drug-susceptible TB care to the lowest structural levels.

HP14: "The treatment needs to be more decentralized. Decentralizing in a sense, community-based service for most patients is feasible. As a result, health centre, health post, and health extension workers can participate".

HP14: "Now it is better to decentralize to the community-based service from hospital to health centre, from health centre to home, and if we find the option to follow them at home".

5.1.2.1.5 Socio-economic factors

- **Economic problems**

As TB is a disease of poverty and the underprivileged, patients with DR-TB are by far the most economically disadvantaged. Most of the patients live on minimal daily wages. Economic problems mean that it is hard to cover the daily transportation costs, the basic food, and rent in cases where the treatment facility is far away. In general, patients cannot afford the extra costs incurred during the treatment process. The HCPs described economic problems as an obstacle to successful treatment completion in the following submissions:

HP13: "So, patients need to go to the health facility on a daily basis for DOT and also need to eat nutritious food. Um, if their home is not near to the health centre, they have to rent a house".

HP4: "We had two patients previously who gave us hard times by repeatedly defaulting. The big reason is lack of economic capacity. Most of the patients are daily labourers. They live on daily work. At the same time, they should come daily to the clinic to take their daily drugs. So, they miss some days".

HP6: "These TB patients are from economically deprived families and communities. As a result, they cannot afford it on their own. They are dependent. They take them if the ancillary drugs are available. If not, they sit and wait".

HP12: "Most do not have relatives to accept them; they have no money. So, to continue treatment follow-up, they need at least money to cover room rent and food".

HP2: "Sometimes when there is a lack of reagents, tests are required to be done outside the hospital. The patients are reimbursed when they bring their receipts. The problem is, if the patient does not have money to pay, he cannot have the tests. Because first he has to pay, get the tests, and bring the receipts for reimbursement".

- **Low socioeconomic status**

In addition, Ethiopia is a developing country with low socioeconomic conditions. Most of the patients developing DR-TB are not economically independent. On top of that, the treatment takes long and patients need economic support for transportation and food while on treatment. Most of the time, it could be a family breadwinner who is sick. In such cases, a serious social crisis ensues, and the person could either drop out of therapy or stop it in the middle. Furthermore, these problems are not addressed sufficiently, making patients feel hopeless and quitting their treatment.

HP12: "The treatment is of long duration and patients need economic support. Similarly, they also need transportation and food support while on treatment. So, I think there is minimal economic support in this regard. So, if a patient could not work and eat well, he would probably have trouble quitting the treatment…They often ask for support. Because even if we say that MDR-TB or TB affects all segments of the population, it usually affects those who are economically weaker".

HP15: "Most of the time, it could be a mother or a father who is sick. It could be another family member who is the breadwinner for the family. When that person comes for treatment, the family is left without support and is in trouble. After a while, he/she starts thinking about his/her family. And it causes a serious social crisis. So, a family can be torn apart. If he is a farmer, he may leave the farm. He has nothing to eat next year. That could mean that he could either drop out of therapy or leave it in the middle".

HP15: "The other main challenge is the socio-economic problems of patients. So, when it is combined with the disease, they often run into challenges. They may not

have anything to eat at home. The sick person may be the family breadwinner. So, when he gets sick, that thing stops. And that concerns him. That is a big challenge".

HP1: "Patient socioeconomic factors play a significant role in people who interrupt treatment. Most of the time, since this part is not covered, at any time when they feel hopeless, they will interrupt or stop the treatment".

HP2: "The other major reason I think they discontinue treatment is that, since most of the patients have low socio-economic status, they should resume their work for a living and they cannot immediately work after taking medication. The work does not give them comfort in such a situation and may interrupt their follow-ups".

HP6: "In the first place, TB is the disease of the poor. TB patients come from economically deprived places and families. As we all know, the treatment is for a long time and is complicated. This low economic situation makes it difficult to support themselves. Without a balanced diet, they are forced to swallow large amounts of pills. They don't have the capacity to resist the drugs. They easily get fed up and become exhausted".

HP7: "Most of them come from low socioeconomic status. In order not to lose their income, they want to go to their work. In fact, they say they feel tired when they take their anti-TB medication. No one is there to support them".

- **Vulnerable population**

Besides the low socioeconomic background, one of the factors exposing patients to early treatment interruption is that they are vulnerable populations in society. They are marginalised and psychologically affected individuals in the community.

HP2: "There are some factors I consider [as exposing] patients to treatment interruption, for defaulting from treatment, and being lost-to-follow-up. In the first place, the social and economic problems of the patients are the major ones. When we take their history, most of the patients who come for treatment are those who do not have families, those who live and come from places that expose them to communicable diseases, daily labourers, those who come from congregate settings, and those who are very poor economically".

HP9: "Further, I think, what is very basic is their socioeconomic situation. They are the most vulnerable people in poverty. They are people who are marginalized by

the local community, including their family, because of their illness, and their psychology is affected. On top of this, they need sufficient time to recover".

- **Stigma**

In the study, stigma was mentioned by the study participants to be one of the causes of treatment interruption. Whenever and wherever there was stigma in the community towards DR-TB patients, patients tended to quit their treatment early.

HP10: "When the patients are stigmatized in the community, they may discontinue".

HP8: "There is a stigma. If there is MDR-TB, there is a stigma. They want to avoid being called MDR. They want to get out of their treatment in a short time".

- **Social problems**

While patients are on inpatient treatment for months, their families could experience problems, especially if the patient is a breadwinner. He/she cannot stay on treatment for long. He/she should feed his/her children and manage the family. In such situations, there is a tendency to interrupt the medication and return to work or find other employment. The following were verbatim statements of the study participants:

HP14: "For example, there was a patient who is a mother of children under our follow-up. She was sick and started treatment after a diagnosis of MDR-TB. She was admitted and treated in hospital for some months. As a result, after months of follow-up, her children and her family were in trouble. Then her relatives and family advised her that she had improved and recovered and needed to return to her home. And she returned to her children and discontinued treatment".

HP15: "The high state of this psychosocial problem in the country is because the population of Ethiopia is often below the poverty line and many of them are vulnerable to this disease because they are poor, and when these people are ill, they are concerned about their families and their problems are so high that if they do not address them, they are much more likely to quit".

Besides, there is a lack of family support, at least while the patient is in treatment. The presence of any economic and social support for the family could at least give some relief to the patients and enable them to focus on their treatment.

> *HP14: "There are patients who start and discontinue treatment because of a lack of family support. After starting treatment, spending some months in the hospital, and showing some improvements, the patient returns back to where he came from. By the time he returns, there are challenges he may face. His family may be in trouble. Therefore, there are patients forced to discontinue treatment in such conditions".*

In addition, not many DR-TB patients had a place to go to continue their treatment after discharge. They might have lost their jobs due to the illness. They might not have had any income or a place to live. They did not have adequate social support. These all make it difficult for them to complete their treatment regimens properly, and often they discontinue in the middle.

> *HP7: "HP7: "We are faced with too many patients who do not have social support. Sometimes we are worried about what we do. There are now two patients that we cannot send anywhere. When they come, they may be from the street. For instance, a patient came from a region far from the capital; his relatives left him here, and we don't have anywhere to send him back. If you just send him back, he will interrupt the drugs. He is almost in his sixth month and doing well".*

> *HP12: "… by the time patients are discharged from the hospital, they do not have a place to go".*

> *HP7: "Another challenge is that… they lose their job when they get sick. They do not have an income. Then if you made them discharged, what would they live on? First, they have no place to live. Second, they have no means to survive. There is no monthly salary".*

> *HP12: "By the time patients are discharged from the hospital, they do not have a place to go. Most do not have relatives to accept them".*

- **Malnutrition**

The study confirmed that most of the patients at the beginning of DR-TB treatment had malnutrition. Consequently, these malnourished patients' successful treatment

outcomes were negatively affected. Malnourished patients have reduced protein in the blood, which is important for some anti-TB drugs to enter the circulation, resulting in lower therapeutic efficacy of the medicines. Symptoms may reappear, and patients may lose trust in the medication and resort to stopping the treatment.

HP14: "Most of the patients at the start of treatment are malnourished. There are many patients with severe malnutrition…At least more than 60% of the patients have moderate malnutrition or enter into severe malnutrition at the beginning of treatment. They need nutritional rehabilitation. They need nutritional and therapeutic feeding".

HP15: "Nutritionally, the patients are so affected that it has a major impact on the treatment outcome".

HP5: "In late stages, not taking food well reduces protein in the blood. Some drugs enter blood circulation with the help of proteins, including drugs. In this case, the patient is taking the drugs but has no therapeutic value in the end. And this can also cause mistrust. The patient says I am taking the drugs but I feel the same symptoms. So, he may question why he would take the medicine and may interrupt taking".

- **Employer non-cooperation**

The study also found that employers were not cooperative with patients [their workers] on DR-TB treatment for a long time. They refused to grant DR-TB patients sick leave. This could push patients to discontinue the treatment until completion.

HP3: "Someone starts treatment after quitting his job because he was critically ill at that time, but after he knows that he is surviving, he wants to resume his job to continue his life. He could be a private firm employee. He could be a driver. I remember there were patients who worked on trucks. For example, one employer told his worker that he would not take any sick leaves afterwards and that he would be fired if he took a sick leave again. If he loses that job, he may not find similar jobs. So, it is customary that you find patients who say to you, I am now feeling good and healthy; and let me continue my job".

HP4: "Some of the patients who work at factories do not get permission".

HP8: "If they are also government employees, they will face something very difficult after three months. For instance, in fact, a city bus worker told me that she had been fired and she had argued in court for her job and was back at work. We assume that private employees will face more problems".

5.1.2.1.6 Programmatic and provider related

- **Manner of handling patients**

The study participants reiterated that if patients on treatment are not handled in a manner that is ethical and dignified, it becomes discouraging to continue their treatment.

HP15: "Moreover, handling is one thing. What I see in some places is that if we do not treat patients in a manner that is ethical and with dignity, that will be very discouraging to them and they may leave the treatment".

HP15: "Um… when we come to the patient side, the way we welcome patients has problems. If the health worker in charge doesn't welcome patients ethically, this is one challenge. The patient can lose interest and may not return".

In addition, a positive patient-physician relationship with a friendly approach and empathic concerns is necessary to develop trust and good relations. Otherwise, patients will retreat from the treatment.

HP3: "The other thing that matters for treatment completion is the patient-provider relationship. If I treat someone with a friendly approach, discussing problems, sharing his concerns, responding to his demands, and reassuring the future, the patient will develop trust in me and will continue to finish his medication. If I handle patients without empathy and tell them whether they should take or not take their medication, it is up to you, then the patients will absolutely retreat from the treatment. On the part of the provider, we have to develop good relationships".

- **Monitoring and follow-up**

The study participant HCPs indicated that proper and close monitoring and follow-up of patients on second-line anti-TB treatment was lacking. In addition to monthly follow-up tests, there should be routine and close monitoring for any adverse events and treatment response. However, the programme is not that robust in monitoring and follow-up of patients, which, in fact, is vital for successful treatment completion.

HP11: "Patients require close monitoring from health centres and hospitals".

HP14: "Rather than doing monthly weight measurements, sputum examinations, and certain blood samples, detailed follow-up for each patient to monitor changes and adverse events is not performed…When our physicians … provide treatment services, there are problems with the provision of regular medical follow-up tests and necessary support for each patient".

HP6: "[T]he TB programme in the country is not that strong especially in patient follow-up and monitoring. Patients may start treatment, but how many of them are being followed until they finish? How many of them are under directly observed treatment? How many of them are getting support? These are major questions to me".

HP14: "It requires proper monitoring by hospitals in order to make the treatment outcome successful. The monitoring should include clinical as well as laboratory tests. And if problems are identified, ancillary drug supply is needed to offset that".

- **Counselling**

This study identified inadequate pre-treatment counselling as one of the barriers to treatment completion. If counselling is not given about the importance of completing the whole treatment duration to prevent relapse and realise a relapse-free cure, patients tend to discontinue treatment upon symptom disappearance and clinical improvements.

HP14: "When a person [patient] starts treatment, he comes very sick, and after some months, he feels better and symptoms start to subside. Therefore, if the awareness given to him is not enough, neglecting events and ignoring things may occur to discontinue treatment. Therefore, perhaps, when a patient starts treatment, for how long it is necessary, in which month what changes are seen or expected, for how long do we continue? Regarding all these, there is a gap in giving sufficient awareness during pre-treatment counselling".

HP13: "… not having a clear discussion when starting from the very beginning. It can be about the things they experience; the presence or absence of side-effects; plus being able to get treatment if they experience side-effects; and what problems can happen when they discontinue the medication. … When we initiate treatment,

it is better to provide detailed information at the beginning. If the patient is not aware of what is happening, it can be a bottleneck for the treatment".

HP9: "… on the side of the health care provider, it may be that the lack of convincing and counselling work supported by psychologists".

5.1.2.2 Theme 2: Challenges for patient follow-up

Theme 2, challenges for patients during treatment follow-up, had four categories: support, supply, individual factors and, service delivery, as shown in Table 5.4.

Table 5.4: Theme 2: Challenges for follow-up – categories and sub-categories

Theme 2	Categories	Sub-categories
Challenges for patient follow-up	Weak support	Social support Programme support
	Supply shortage	Stock-out of ancillary drug supply Investigations
	Individual factors	Absenteeism Turnover Responsibility
	Service delivery	Delay of culture results Performance gaps Competency Quality

5.1.2.2.1 Weak support

- **Social support**

From the in-depth interviews, one of the challenges for patient follow-up identified was weak social support during treatment times. The participants indicated the psychosocial support during treatment was not properly addressed. Moreover, most of the patients were from low socioeconomic backgrounds, and on top of that, the treatment duration was long. However, the amount of support rendered to patients during treatment follow-up has been meagre, making follow-ups difficult for patients and indirectly affecting treatment completion. The following are verbatim descriptions by interviewees:

HP11: "The main challenge is still social support. The support for addressing social problems is not enough… psychosocial support is not well strengthened…in other

countries, this is highly supported. So, I consider the absence of it as a barrier on the patient side. Another aspect I care about is the social component. MDR psychosocial support remains unaddressed. If that part is not addressed, we will not make changes to the MDR. Psychosocial support should be very strong in order to improve treatment".

HP4: "Monthly support of 250 Birr (5$) for transport and food items like oats, oil, pasta … are given monthly, which amounts to 750 Birr (15$)".

HP7: "… in the first-place patients need social support, because the treatment is given for long periods and has side-effects. In addition, those who come for treatment are from low economic status and need support".

- **Programme support**

The weak programme support starting from the national to the facility level with regard to human resource capacity to properly give basic mentorship support to DR-TB treatment follow-up centres was identified as a complicating factor by the study participants. This could result in low clinical monitoring and affect successful treatment outcomes. The study participants pointed out programme support gaps as follows:

HP14: "The third challenge is the capacity of our health facilities. Specifically, providing the input required at the human resource level and preparing the healthcare providers to serve for a while, and maintaining basic mentorship services which is conducted from the hospital to the health centre".

HP14: "In general, there is a programme support gap at national, regional, and health facility level to focus and realize improvement of clinical monitoring quality as per the protocol".

5.1.2.2.2 Supply shortage

- **Stock-out of ancillary drug supply**

The study identified that there has been a chronic shortage of life-saving ancillary drugs used to treat adverse events of anti-TB drugs. In addition, there has been severe interruption of supply of ancillary drugs in the system and they are not available in hospitals most of the time. This makes management of adverse events secondary to anti-TB drugs difficult and eventually affects the treatment outcome.

HP14: "When we see in our hospitals and health facilities, let alone sufficient quantity, even those considered lifesaving, for instance, KCL [Potassium Chloride], due to its absence, many patients die suddenly. The supply was very difficult. This problem exists in most of our hospitals. Furthermore, drugs such as magnesium sulphate, which we use to manage electrolyte imbalance in critically ill patients, are in short supply".

HP2: "We cannot say ancillary drugs are available all in all. They are not available in the hospital most of the time. There are times when we do not find".

HP14: "… there is no adequate supply of ancillary drugs by the government system. Most of the time, patients are required to purchase it from outside".

"… Without a doubt, there is a disruption in the supply of ancillary drugs. There is no interruption of first-line and second-line drugs at present. But there is a problem regarding ancillary drugs in some places".

In addition, during treatment, if adverse events due to anti-TB drugs are not managed timeously because of a lack of ancillary drugs, the patient may die and/or interrupt the treatment.

HP6: "The adverse events come following TB treatment and they are treated by ancillary drugs. If the adverse events are not treated timeously and the patient suffers for a long time, the patient blames the anti-TB drugs for causing him another problem, and the patient may disappear from treatment. So, the unavailability of ancillary drugs is a big barrier and factor".

HP4: "Sometimes when ancillary drugs are ordered for adverse events, and if they are not available in the hospital pharmacy and patients are told to buy them from a private pharmacy, it is a challenge. He says, I don't have any money. Where do I get it?".

HP6: "In most MDR-TB treatment centres, these ancillary drugs are not available. This puts management of adverse events secondary to anti-TB drugs difficult. This will decrease the treatment outcome. Hence, if a patient sustains vomiting and you do not stop it, the patient may die. To stop the vomiting, ancillary drugs are needed. Therefore, what kills patients is not the TB disease; TB gives time, gives years".

HP9: "This is a problem we always raise. Ancillary drugs are inadequate. You even reminded me that one of the things that makes patients feel bored is that we cannot

treat their side-effects quickly. So, these drugs, which are given in conjunction with TB drugs, are in short supply, and we do not get them".

- **Investigations**

Investigations used to monitor treatment progress and the occurrence of adverse events were found to be inadequate during follow-ups. There was a lack of equipment, an interruption of laboratory service, and shortages in the laboratory supply system. Trained human resources to interpret results were equally unavailable. As a result, patient monitoring and care are compromised and could result in unsuccessful treatment completion.

HP11: "The major problems with follow-up from the system side are the lack of equipment necessary for follow-up like audiometry and ECG".

HP8: "Lack of resources for follow-up. Especially now with ECG paper. In some places, the machine itself does not exist. In some places, no one has been trained to interpret. The same thing with audiometry. That is another challenge. There is a shortage of necessary things required for follow-up at the system level".

HP14: "There is a problem of back up in the laboratory supply system. When a physician orders the necessary laboratory investigations, perhaps those tests may not be available in the hospital. So, patients go without getting it".

Furthermore, some investigations, which are necessary for the follow-up, were not available. This lack of follow-up tests has an impact. It is difficult to identify side-effects early and to follow patients' conditions in their absence.

HP13: "There are investigations which are necessary for the follow-up. For example, there are investigations that are considered necessary for those in the intensive phases. These investigations are even required in the continuation phase after the intensive phase is over. But the problem is that these investigations are not available at the hospitals. They are almost not available all the time. Therefore, we do not do them. It is not done for most of the patients".

HP6: "Most of the laboratories in the different facilities are not functional. There is a low chance of getting the laboratory tests we requested by the time we need them. The reagent may be over. The machine can be damaged. Therefore, you continue giving the drugs in the absence of laboratory services. But you cannot

follow the drugs' untoward effects. If you could not follow timeously, you would end up with a bad outcome. If you follow timeously, you will pick up and manage problems early and avoid factors which can lead to bad treatment outcomes".

HP1: "We do not have a system to follow everything. For instance, we do not have a thyroid function test (TFT). We have to send it to other institutions outside our hospital. It is a very expensive test, and our patients are in low socioeconomic status. For this reason, most of the time, TFT is not done. We have gaps in the laboratory. We cannot say all tests are available. We have chemistry, haematology and electrolytes".

HP4: "But the laboratory service is not completely available. Electrolyte tests are not always available. This lack of follow-up tests has an impact. It is difficult to identify side-effects early if these tests are not available. … Besides, some diagnostic tests like CT and Doppler, which are not present in the hospital, may be ordered, which the patient can't afford the fees. The physicians face a challenge following the patient's condition in such cases".

5.1.2.2.3 Individual factors

This category refers to individual factors affecting smooth treatment follow-up process.

- **Absenteeism**

The study also identified that patients may disappear from the treatment for various reasons. Patients could also miss their follow-up and clinic days. Moreover, during such circumstances, they also change their residential addresses, and health providers go to their neighbourhood to find them to continue their follow-up. This could affect the treatment course and the successful completion of the treatment.

HP13: "Patients may not come. Very few patients, actually. Most patients come".

HP10: "There is a possibility that patients on DOT may interrupt treatment and disappear. In such cases, there are times when we go and search for them at their homes".

HP8: "They do not come for follow-up. We try to call them, but the name they say is not their real name and no one knows them by that name in their neighbourhood.

For instance, one patient's name he gave us during registration was Tedros, but his real name in his neighbourhood is Daniel. They also turn off the phone".

- **Turnover**

  The study has indicated that there has been high trained staff turnover in the system. Those professionals with vast experience and training expertise have been leaving the government, creating a continuous training demand. This presents a challenge for proper patient follow-up and successful treatment completion at large.

  HP15: "Well, regarding healthcare providers, it is a bit difficult for me to say whether the allocation is enough or not. However, at the country level, a lot has been invested in training and capacity building. International, national, regional, and local training have been extensively undertaken. But the dynamics are very high. Since the movement of professionals from place to place, both inside and outside the country, is very high, keeping the dynamics is very challenging. You don't get a trained person in the same place after some time. At present, if continuous training is not given, big problems are being created".

  HP1: "… There is a high turnover of physicians".

  HP14: "In general, we are moving with what we say is the minimum. In particular, physicians will go for specialisation training after a few years' stay. So, it is important to train and prepare a physician every year. There are gaps in this regard".

  HP15:"High-level individuals are leaving government work. Those who took high-level training and have vast work experience are not staying in the system. So, if continuous training is not taking place, it has dangers".

- **Responsibility**

  The study participants reflected that health providers working on DR-TB care and treatment tend to avoid the responsibility and ignore assignments because of fear of risk. This definitely challenges treatment outcomes. The following are verbatim descriptions of the participants:

HP13: "What I am seeing right now from the health provider side is, uh, something being ignored, and …avoiding responsibility".

HP13: "Plus, avoiding assignments because of fear of risks. Therefore, I am just realizing that the MDR-TB treatment service in Ethiopia is going the wrong way".

HP13: "Further when it comes to healthcare providers, DR-TB is a risk, as we know. So, they think that, when the health provider works among patients, it will have a risk".

5.1.2.2.4 Service delivery

- **Delay of culture results**

Delay of culture and second-line DST results were mentioned to be one of the challenges during treatment follow-ups. Not getting the culture and DST results affected the clinical decision. Challenges with the delay of culture results were described by study participants as follows:

HP12: "The other big challenge is regarding culture. AFB is done in our hospital and we do not have any problems concerning it. But culture is done at EPHI. We do not get culture results timeously. So, we have a hard time deciding".

HP14: "The result of sputum culture does not come on time. So, giving a decision is based on a mere guess. Culture results are delayed to stop injectables or some other drug [duration and termination of treatment is guided by culture conversion]. In between, serious conditions may happen".

HP2: "The problematic part is the culture one. The culture results do not arrive timeously. Patient follow-up is done on a monthly basis. Culture follow-up is also done monthly. The culture results should also be available monthly on the follow-up dates to assess patient status. Does the patient convert? Is he resistant or not? When the second-line line-probe assay (LPA) is sent, the results should be known monthly with the culture results. Every result should be known every month. But results are coming at least once every three months".

HP2: "The culture issue is always on the agenda for discussion among the clinical team and culture results are always delayed".

- **Performance gaps**

The in-depth interview participants reported that there were performance gaps by health workers caring for and treating DR-TB patients. Health workers showed gaps in doing everything necessary during each follow-up for the patients. The study participants reflected the performance gaps as follows:

HP12: "I also think that there are performance gaps".

HP14: "On the side of our healthcare providers, there is a big gap of performance as per their training regarding what they should do during treatment follow-up, what should be done each month, and what should be looked up during each follow-up session".

HP14: "However, there is also a wide gap in working with strict discipline. For example, if eye examination is necessary monthly, failure to do that despite the presence of materials needed to do that. Rather than doing monthly weight measurements, sputum examinations, and certain blood samples, detailed follow-up for each patient to monitor changes and adverse events is not performed".

- **Competency**

The study participants indicated that treating and caring for DR-TB patients requires knowledge and skills from different medical disciplines. They mentioned the presence of a wide gap between all the disciplines, since the side-effects of the drugs affect all the human systems.

HP14: "There is a big gap in competency. Because it needs a skill in the first place. Applying all medical disciplines is needed in treating DR-TB. Because the side-effects affect all systems, it is not just about treating tuberculosis. Psychological support needs psychiatry, the same with ophthalmology, dermatology, etcetera. Therefore, it requires all the disciplines. When a patient comes, he should be observed and evaluated, with necessary tests done and treated immediately after. If drugs need to be changed or added, it should be done early. There is a huge gap to carry out all of these".

HP5: "The responsible body, whether government or non-government, should act together and provide training to healthcare providers regarding MDR/XDR-TB. So, I don't think the competency is enough".

- **Quality**

The minimum quality of treatment service in place following the decentralization of DR-TB treatment service was mentioned by the study participants. Hence, there has been a gap in delivering comprehensive quality medical care to all patients at all levels.

HP14: "It is hard to say that we were satisfied and did enough work. Because there is a gap in treatment service quality. …One challenge is the decentralization of treatment services and maintaining quality, at least what we call minimum quality".

HP6: "The majority of the centres where the majority of patients are getting services provide services below standard. Therefore, nationwide, the service is not backed by sufficient health providers and patients are not getting what is needed".

HP14: "I also recognize that there are gaps in the delivery of comprehensive quality medical care to all patients at all levels of care".

5.1.2.3 Theme 3: Cross cutting issues influencing treatment completion

Theme three refers to views of HCP study participants regarding cross-cutting issues influencing treatment completion of DR-TB. As shown in Table 5.5, the theme was divided into four categories: resources; government attention; donor dependency; and incentives.

Table 5.5: Theme 3: Cross cutting issues influencing treatment completion – categories and sub-categories

Theme 3	Categories	Sub-categories
Cross cutting issues influencing treatment completion	Resources	Trained human resources Budget Space
	Government attention	
	Donor dependency	
	Incentives	

5.1.2.3.1 Resources

This category refers to the views of health professional study participants regarding the limitation of resources affecting programmatic activities and treatment processes

and eventually affecting the successful completion of DR-TB treatment. The category comprises three subcategories: trained human resources, budget, and space.

- **Trained human resources**

The shortage of trained human resources and the lack of backup of trained staff were mentioned to be one of the cross-cutting issues affecting successful treatment processes and outcomes.

> *HP14: "The view is the same in some facilities with many patients. A facility that treats ten patients and a facility that treats a hundred will have at least one physician and one nurse. This has a fundamental problem. Because facilities with hundreds of patients may need two or three physicians and several nurses".*

> *HP6: "The other is minor support in some cases, for instance, rehabilitating nutritionally, and supporting psychologically. Many activities are performed by one health worker. Administration of medicine, giving psychotherapy, and managing adverse events are carried out by a single health worker".*

> *HP6: "The national programme training focuses on facilities that do not have any trained health providers on programmatic management of DR-TB. In most cases, it does not reach the level of giving training to extra staff and possessing back-up staff. This is a major deficiency. If you train many health workers, the service will not be interrupted in case someone is absent".*

> *HP8: "However, there may be a shortage of staff. For a variety of reasons, for instance, during maternity leave, there may be shortagee."*

In addition, the study participants also noted that there is no trained counsellor and/or social worker practicing the DR-TB programme helping patients needing their services.

> *HP13: "Currently, we have physicians, nurses but not social workers or counsellors."*

- **Budget**

The budget was also mentioned to be one of the decisive factors affecting across the programme activities like inpatient patient menu, nutritional support, home-based

follow-ups and other administrative costs. The following were reflections of the participants regarding budget shortages:

HP12: "Previously milk was provided to patients. Milk is a very decisive. It has now been six to seven months since it was stopped. Because the government budget was not enough to buy food year-round due to inflation in the market".

HP2: "This year the hospital complains of a shortage of budget. Since it is shared among all wards, the shortage happened".

HP6: "Previously, the number of patients was limited and you could frequently visit them at home. Currently, the number of patients is large and you use the same budget. Since you should go and visit many patients, the fortnightly and monthly visits are now changed to three to four monthly visits. Because it demands a cost, for instance, per diem, fuel, and the likes. You go to rural areas to patient homes and TFCs. The budget assigned for these activities is very limited and exacerbates the existing problems."

- **Space**

This study identified that a shortage of space for the DR-TB service complicates the programme in the health facilities. There was abundant evidence of this from a shortage of beds and rooms to the absence of an ICU to manage DR-TB cases, whether stable or complicated. This is supported by the following excerpts:

HP10: "There is a shortage of beds and rooms to separately admit MDR and XDR patients".

HP11: "There is a shortage of space. For starting new drugs like Bedaquiline, there are necessary examinations, for instance, ECG. So, to do such things, a separate room is needed. There is a shortage of that. Accidentally, if patients come on an emergency basis, there are no rooms for resuscitation".

HP7: "The other challenge is patients with complications. For example, a patient who develops severe pulmonary hypertension and is in need of continuous oxygen, what do we give them?"

5.1.2.3.2 Government attention

This study found that government attention to the programmatic management of drug resistant TB needs paramount attention. Infrastructure and programmatic activities and budget allocation wise, the government is expected to fully endorse the task and take full responsibility for activities supported by partners. The following excerpts support this:

> *HP13: "In addition, the government should also be paying attention. I don't think it was given a place on the government side. So, if given the space, they can force it. Infrastructure-wise, they can do what they think is important".*
>
> *HP2: "What I think is that communicable diseases like MDR-TB at a national level should need special attention".*
>
> *HP6: "Strong programmes, which can stand on their own, need to be designed by the government".*
>
> *HP9: "The federal ministry of health should take full responsibility for the activities supported by partners by allocating budget and assigning healthcare providers".*

Furthermore, the study found that the health system has not fully taken over the DR-TB programme as its own.

> *HP6: "The major problem is that MDR-TB service is considered a supplementary service. It is not taken as a major service. It is given to physicians who are assigned to other wards or departments as a major duty. They come when needed and go back to their department duties. It should not be like that. The patients in the MDR ward need appropriate care and strict follow-up. They require full-time nurses and physicians to work in the MDR unit."*
>
> *HP9: "I do not believe that adequate staff has been assigned. Because the treatment is very challenging. It is going to be a full-time job. Occasionally, we are getting help, but I do not think there are enough professionals around this."*

5.1.2.3.3 Donor dependency

The study participants indicated that the main challenge of the programme is that it is highly dependent on donors. This directly affects patient follow-up and monitoring. The following views were given by study participants regarding donor dependency:

"In some places, what I saw is that considering the DR-TB programme more of a partners' responsibility. There are lots of improvements, and externalisation has decreased a bit. But still now, there is a tendency to depend on the donor and wait for the donor".

HP9: "What I think of as a challenge is that it is the partner organizations that have made this service successful, primarily supporting it. I do not believe that the health system has fully taken over as its own and has acted well as its own".

HP13: "The biggest thing I think DR management is missing is that government involvement is still small. It is highly dependent on donors. It should not continue like this. So, the government has to get its hands on it from now on. A budget should be allocated. At the very least, there must be a government contribution. Ok, the government is working on health expansion and buying equipment. OK facilities are built. I understand that. That is cool. It is really good. But on top of that, DR management directly requires investment. Then I don't think about the donor thing anymore. Some fatigue is coming. We're seeing donors come out. One of the things that must happen in the future is that the government should adopt this TB programme as its own agenda, budgeting the programme and running it by the government".

HP6: "Currently, the challenges we face are that programmes like TB, HIV and malaria are donor dependent. When donors are good, the programmes become good. When the donors are not on board, the programme is also distracted. This trend was observed in the HIV programme and now it is being repeated in the TB programme. The government did not develop a sustainable TB programme. A programme which is independent of whether someone comes or goes, is not designed. Therefore, it is donor dependent. When a strong NGO comes, the programme faddishly good; there will be good patient follow-up, enrolment, and monitoring. When that NGO phases out, the intensity of programme activities slows down again. So personally, I believe a major gap is that our programme is donor

dependent. Even though the ownership is in the hands of the government, in most of the facilities, a feeling of ownership is not observed. Monitoring and addressing gaps and correcting errors is not seen on the side of the government".

5.1.2.3.4 Incentives

The HCPs who participated in the study emphasised the absence of risk allowance despite repeated demand by health workers. This could result in discouragement and inefficiency on the human side, affecting programme outcomes.

HP13: "When you work in the government sector, the pay is very small. It is not encouraging. Most of the healthcare providers are not encouraged to work in the MDR, since they don't have any payments".

HP13: "And the healthcare providers have been demanding risk allowances repeatedly. They say, 'That is not going to save our lives, but at least we should get paid since we risked our lives.' So, they are not happy in this case".

5.1.3 Themes identified in the focus group discussions

From the focus group discussion with previously treated DR-TB patients, five themes emerged, which comprise: (1) Perceived barriers to treatment completion; (2) Challenges for patient follow-up while on the treatment; (3) Facilitators and enablers for completing treatment; (4) Perceived benefits towards treatment completion; and (5) Perceived severity of the problem. For purposes of this write-up and to avoid confusing the reader, these themes are referred to as Theme 4 – Theme 8.

5.1.3.1 Theme 4: Perceived barriers to treatment completion

This theme refers to the experiences of previously treated DR-TB patients regarding perceived barriers to treatment completion. The theme comprises nine categories and numerous subcategories, as illustrated in Table 5. 6.

Table 5.6: Theme 4: Perceived barriers to treatment completion- categories and sub-categories

Theme 4	Categories	Sub-categories
Perceived barriers to treatment completion	Drug-related	Discomfort due to the drugs Adverse events Pill burden Treatment duration
	Clinical issues	Consulting after long illness Delay in diagnosis Sub-optimal dose
	Stigma and discrimination	Community stigma Healthcare provider stigma
	Economic challenge	Financial strain Loss of a job
	Patient support	Transport support Material support Treatment supporter
	Laboratory service related	Interruption of monitoring tests Unavailability of laboratory services
	Patient factors	False sense of recovery Returning to habits already quitted Personal Beliefs Fear of side-effects
	Provider-related factors	Responsiveness Poor communication
	Psychological challenges	

5.1.3.1.1 Second-line anti-TB drugs

- **Discomfort due to the drugs**

The FGDs participants described how the discomfort of the second-line anti-TB medicines has been one of the perceived barriers to treatment completion. They have experienced pain, vomiting, and discomfort while taking the drugs. In order to not feel the pain, the patient could quit the medication. The following statements were given by the FGD participants about their own experiences of discomfort due to the drugs:

F-FGD3: "First, it is because the drug is very hard. Once taken, it does not give you peace… I take 14 pills. It is very hard."

M-FGD3: "It makes you vomit every time you take the medicine, which is very painful, so you may feel like quitting the drug in order to prevent that pain coming".

M-FGD1: "… let alone two years, I did not think I would swallow for four months. When you swallow the pill, it stinks. The discomfort begins here from your throat".

F-FGD5: "The medicine is so boring and I was vomiting all the time… ".

- **Adverse events**

The focus group discussants explained that the second-line anti-TB drugs cause untoward adverse events that affect patients' smooth treatment adherence and completion. The following experiences were mentioned by the FGD participants:

M-FGD6: "The first time I came here, the drug was so heavy and I lost appetite. I did not eat for 3 days. It needs a lot of care, milk and food".

M-FGD6: "It crushes my body. I get tired after taking medicine. I couldn't do anything after that. It makes me sleepy. I will be better after I eat some food and drink some milk. Otherwise, the symptoms may last for 7 to 8 to 10 hours".

F-FGD6: "The drug is heavy. Sometimes there is a headache. Most of the time, it makes me vomit".

M-FGD4: "You feel dizzy, irritable, and it makes you quarrel with other people. It does not give you peace. I took the drug for one year and nine months. All in all, the drug is very hard".

- **Pill burden**

This sub-category refers to previously treated DR-TB patients' experiences of the high pill burden of second-line anti-TB drugs as their perceived barrier of treatment completion during their previous treatments. One of the FGD participants stated the following:

M-FGD1: "Fifteen to sixteen pills are taken at a time. People may become frustrated and quit treatment".

Another participant reiterated.

M-FGD4: "You know now you are struggling when you swallow sixteen to twenty pills. It has features of nausea and vomiting".

Another participant reiterated that too much pill burden could cause loss of hope and result in quitting the therapy.

F-FGD5: "The medicine is too much, because of that you lose hope".

- **Treatment duration**

The treatment duration of DR-TB with a second-line anti-TB treatment regimen takes longer time, and it was mentioned in the discussion that the long treatment duration was one of the factors for discontinuing the treatment. During the discussion, the long duration was boring and could cause loss of hope in patients. The following statements were mentioned by the FGD participants during the discussion:

M-FGD4: "The other thing is that the duration of the treatment is long and boring".

M-FGD2: "There are patients who interrupt treatment due to the economy or some other factor. It can be due to the long treatment duration".

M-FGD3: "First it was horrific when it was explained that the treatment is to be taken for 2 years, of which 8 months is with injection".

The same discussant reiterated:

M-FGD3: "The drug is taken for a long time, so that as time passes you lose hope in everything. And there are people who run their own businesses before they become sick. So when you are taking the drugs, everything stops. You know that you will not create or get that business again, so you lose hope. Therefore, when a person loses hope, he/she will not have an interest in taking the medicine and getting cured again".

The other discussant emphasized:

M-FGD4: "The primary reason people discontinue is because it is taken for a long duration of 20 months".

5.1.3.1.2 Clinical issues

- **Consulting after long illness**

The discussants explained that consulting after a long illness when the disease becomes serious, causing harm to their lungs, might hinder successful treatment completion and cure. The following were verbatim statements given by the focus group discussants:

M-FGD3: "They come for treatment after a long time without laboratory investigation and after the disease has become serious and has already caused harm to their body".

M-FGD3: "My first TB was fluid in my lungs [pulmonary effusion], and fluid was removed from my lungs two times. My lung accumulated fluid for the third time. After that, I started MDR treatment, but till now … I have not felt good".

F-FGD5: "… I had so much cough and a feeling of loss of energy. Then I went to holy water treatment. While on treatment there, I was feeling cold and did shiver. The sun bath did not help me a little. After that, I went to a health centre. They ordered for me a sputum examination and the result turned out to be MDR TB".

- **Delay in diagnosis**

This sub-category refers to FGD participants' experience of their delay in diagnosis of DR-TB, resulting in delayed clinical decisions in their treatment journey, complicating their successful treatment completion.

One participant stated:

M-FGD1: "At the health centre, they treated me for more than two months without diagnosing my real problem. They said typhoid or typhus. There is a delay in diagnosis. They give you painkillers. The pain may stop, but inside the disease continues to hurt you".

Another participant explained her experience of the long delay in her DR-TB diagnosis before she was actually diagnosed after more than a year of trial.

F-FGD1: "I was living in Wollega province and got sick there. My family did not take it seriously and took me to a nearby health facility. There, they ordered me tablets and injections. But my illness did not resolve; rather it was getting worse. Then they took me to Ambo and I had an x-ray examination. I was ordered six months of treatment for intestinal TB. On the tenth day of starting treatment, my belly swelled

like a pregnant woman. It prevented me from any movement. I couldn't stand up from my bed. I was unable to eat or drink. Really, I was near death.

My family took me here to Addis Ababa, and again I was x-rayed. They said that I have fluid in my abdomen and need an operation. I was operated on at a hospital in Addis Ababa. I finished six months of treatment but nothing improved. They checked me and said that the disease hurt me and that I should take a two-year treatment. Then I started MDR-TB treatment here at this hospital. I also had two more operations, and I am now feeling better".

- **Sub-optimal dose**

One of the most common side-effects of anti-TB drugs is vomiting. Not replacing the vomited dose of the medication results in a suboptimal dose. This prevents the successfulness of the treatment and results in unfavourable treatment outcomes. The FGDs participants stated their experience as follows:

M-FGD1: "The drugs come out immediately after swallowing. When it comes out, it should be swallowed after a while. But some patients leave it without replacing the vomited dose. This will harm the treatment and the disease will get worse".

M-FGD1: "The drug is very hard to take. I vomited frequently for the first six months. I was admitted here for three months. When I take a drug, the immediate side-effect is vomiting. While I was admitted here, if I vomited the drug, it was replaced and I took it after 30 minutes. But after discharge, the drug was given to me from the health centre, and there is no replacement. Because my home and the health centre were far away, there was nothing to be replaced."

5.1.3.1.3 Stigma and discrimination

- **Community stigma**

FGD participants explained their experiences of stigma and discrimination they encountered from the community while on their DR-TB treatment. The stigma and discrimination they faced were so bad that they were forced to discontinue their treatments. The focus group participants explained the stigma and discrimination associated with the treatment of DR-TB as follows:

F-FGD2: "Primarily, the reason I stopped the drug was because of discrimination. For example, when we wear a mask and enter the gate, starting from a healthcare provider, they keep a distance from you of around eight meters. When we walk down the road, everybody changes their ways on opposite sides of you. When everybody referred to us as MDR".

F-FGD3: "People do not want to eat with you and discriminate against you. So there are people who want to stop and die rather than live stigmatized. I think that also makes me lose hope".

M-FGD3: "The stigma and discrimination is so hard that I lost my friends with whom we grew up together and many people because of this disease. I'll tell you frankly, I prefer HIV to this disease".

- **Healthcare provider stigma**

In addition, denial of service by HCPs due to stigma was mentioned by participants of the focus groups. The following were verbatim statements by the study participants:

M-FGD5: "The service is hard for TB patients. You cannot get the service like other patients directly. You have to wait until 10 minutes before 6 o'clock to get the laboratory service. [This is to give space for other patients to leave the area]. And sometimes you do not get them and get the service from outside [private labs]. The laboratory and X-ray services are not comfortable for TB patients".

M-FGD4: "I am from the Oromia region, Mogol Encheni. The doctors over there discriminated against me and were not interested in treating me. I was diagnosed here, got my drug, and went back there, but I could not get anyone to receive and treat me. So I came back here, and they rented me a room, and now people are helping me for living".

5.1.3.1.4 Economic challenge

This category refers to the experiences of study participants in the focus groups about economic burdens and financial strains they faced while on treatment, forcing them to the extent of discontinuing their treatment.

- **Financial strain**

One of the participants explained.

> *M-FGD1: "Taking the drugs outside the hospital, being discharged from inpatient, is impossible for many patients. Everyone has no income. Most of us don't have a home. At that time, a patient can stop the treatment. Here in the hospital, the treatment is good. But after six or seven months when you are discharged, it is very difficult for most of us. While in the hospital, I have seen many patients return back to the hospital after interruption of treatment. When I heard their reasons, I was shocked. First, they have nothing to eat once discharged and go out of the hospital. Second, they don't have a residence or home".*

Another participant described how life was not convenient and affordable after discharge, making vulnerable patients quit their treatment.

> *M-FGD1: "Life is convenient here for four to five months, but when you are discharged, everything becomes new to you. Life is also not convenient [after discharge]. You can't afford to rent a house. So, you are vulnerable to quitting the treatment. You are worried about what you drink or eat; about what you do and then swallow the drugs".*

- **Loss of a job**

Furthermore, patients on the DR-TB treatment lose their jobs because of their illness and side-effects of the drugs and do not have any source of income to buy at least some of the nutritious food available locally, and they also cannot support their dependents at home. These economic challenges make continuing the treatment difficult for them. Participants noted economic challenges and consequences during treatment as follows:

> *M-FGD4: "The main problem is the economic problem. The drugs need nutritious food, otherwise they cause gastric pain and the like. It's difficult to take one year and nine months with this condition. It is difficult to continue using drugs if there is no work or other source of income".*

> *M-FGD1: "Challenges, there are many challenges. The main challenge for people to interrupt treatment is the economic challenge. Once you are admitted, you lose your job. You don't have any source of income".*

M-FGD6: "The first reason is the status of living. If they are poor and do not get enough food, it is difficult to continue the drug".

F-FGD2: "At the beginning, I was a waitress. Now I couldn't do that".

F-FGD2: "Not only that, I lost my job and many other things. Due to the side-effects of the drug, I still can't work. I was dismissed from my waitress job. I mean, I can't listen to people in a noisy environment. It screams inside my ears and head. Had it been resolved while I was admitted, it would not have reached this level. Wait till the injectable stops, wait for the medication to be over, only reassurance, and that is why I came to this level".

F-FGD2: "I dropped out of school after I got sick. I'm not working. I used to do crafting before".

5.1.3.1.5 Patient support

- **Transport support**

One of the challenges for patients during treatment follow-up was the problem of transportation. The treatment requires daily observation at follow-up centres and monthly follow-ups at treatment initiating centres. Therefore, transportation is the backbone of social support that should be in place during the whole course of the treatment regimens. However, transportation support was mentioned to be one of the challenges for patients affecting their successful treatment completion. The following statements were verbatim explanations of the study participants:

F-FGD2: "I did not get any transport fee".

M-FGD2: "… to come and collect the drug, there is no money for transport. … I remember, one day, I had no money to come here to collect … I came from my home to Merkato on foot, then asked a stranger on the street for some money for the taxi and came here".

M-FGD2: "…when I came here, there was a problem with transport".

M-FGD3: "… most of the people who suffer from this disease are economically weak. So, they do not have transport means. To come to the centre the whole two years is very tiresome".

M-FGD3: "You know, there is a problem with transportation. I have difficulty coming here from my home most of the time. So, I used to come intermittently".

- **Material support**

In the treatment process, patients need regular material support, for instance in the form of adequate monthly food baskets, covering house rents and subsistence for the dependent family members, including children, since patients lose jobs or cannot work while on treatment. This can oblige patients to look for work or daily labour for the purposes of their livelihoods, and then discontinue their treatment. Participants described challenges during treatment as emanating from the lack of material support they faced, as follows:

M-FGD6: "The other is related to life. For example, I rent a house and I learn. So I have to pay for both. In the meantime, I have no one to support me. So, there are many things that stress you and make you want to discontinue the drug".

F-FGD6: "Most of the patients discontinued the drug when no one supported them in their lives." It is difficult to swallow the drug without food, and to get food you must work, otherwise it is difficult to get enough food to swallow the drug and cover other expenses like house rent".

M-FGD1: "I don't have anyone to support me. I myself live on daily labour. It is worrisome to think about where to go if I am discharged".

F-FGD3: "When there is nobody to support you, You might decide to stop the medicine and go to work in order to live and make something that you think of".

- **Treatment supporter**

Furthermore, a treatment supporter is necessary to ensure that all doses are administered properly, to support patient adherence, and to encourage both family and patients. Lack of treatment supporter negatively affects the course of successful treatment completion.

M-FGD3: "Not having a treatment supporter who is beside you and encourages you".

M-FGD1: "I don't have anyone to support me".

5.1.3.1.6 Laboratory service related

- **Unavailability of laboratory services**

This sub-category refers to previously treated patients describing how unavailability of laboratory services and/or tests affected clinical decisions and, consequently, medical conditions getting worse for them. Eventually, an unfavourable treatment outcome may follow.

> *M-FGD1: "It is also good if laboratory tests, which are sent outside and done in private labs, are performed here in the hospital. Because we get an immediate solution if it is done here. If a patient does not have money at hand at that time, it takes time till he gets that money and clinical decisions are not made on time. So, things get worse for the patient".*
>
> *M-FGD1: "There are tests not available at the hospital but available at private labs and sent to be done there".*
>
> *M-FGD3: "…there is a laboratory problem. If you don't have enough money to pay for a test [that is not available in the hospital], you might not get it".*
>
> *F-FGD5: "I got a blood test and an ultrasound from outside. They gave me the address. I go and have the tests and bring the results here. But x-ray and sputum are done here".*
>
> *M-FGD6: "I did not get service here. I have got the service from outside, at private laboratories. They do not have the service here".*

- **Interruption of laboratory service**

In addition, there were interruptions of laboratory monitoring tests during treatment follow-up periods, making timeous monitoring and management of drug adverse reactions impossible in case one occurred. If adverse events are not managed timeously, patients may get frustrated and discontinue their treatment. On top of that, adverse events can also lead to bad treatment outcomes to the extent of taking life.

> *M-FGD6: "Previously they did blood investigations, but currently it is not done".*
>
> *M-FGD6: "For me currently, they have stopped sputum and blood examinations".*
>
> *M-FGD6: "Up to 8 months ago we were giving blood for investigation. Currently it is only a sputum investigation".*

5.1.3.1.7 Patient factors

- **False sense of recovery**

As we noted in the in-depth interview, when patients take medication for a couple of months and their bacteria load decreases and symptoms start to subside, patients could develop a false sense of cure and quit their therapy, in spite of the recommendation that they should continue medication for the prescribed duration.

> *M-FGD2: "I completed the first TB treatment. However, I did not have the final check-up. Just because I was recovered at the time, I just went out and left. Then it came back again…."*

> *M-FGD3: "And when you feel good and feel recovered and think you brought change; you might think that it is enough to take the medicine".*

- **Returning to habits already quitted**

This sub-category refers to previously treated patients' experiences of returning to their old habits and addictions. Consequently, this affects treatment adherence and eventually causes treatment interruption and unsuccessful outcomes.

> *M-FGD1: "Of course, you know, sometimes the drugs make you emotional and patients may start the habits they have already quit, like smoking and drinking alcohol. This exacerbates their health problems".*

> *M-FGD6: "On the other hand, I know patients who felt improvement and returned to their addiction. The drug brings harm when you start to use it for addictive things before completion of treatment".*

- **Personal Beliefs**

As we have seen in the in-depth interviews of healthcare professionals, the previously treated patients' experiences also indicated that personal beliefs were barriers to treatment completion. One of the study participants explained:

> *M-FGD5: "The others connect it with their belief. I have one friend that discontinued because he believes that he is going to be fine by only praying and returning back to treatment after a long time".*

- **Fear of side-effects**

This sub-category refers to FGD participants describing their fear of side-effects of second-line anti-TB drugs causing them to interrupt their treatment courses. The FGD participants described their fear of side-effects as follows:

> *M-FGD3: "I just have a fear that one day it [the skin lesion] will make me sick. Otherwise, even when I put some lotion on, it gets good".*
>
> *M-FGD3: "…because of the side-effects of the drugs, sometimes patients lose hearing capacity and are also unable to walk. So, when you see this happening to other patients, you may think to stop taking the drug".*
>
> *M-FGD3: "…There are lots of occasions that we consider stopping the drugs for fear of getting side-effects that we saw on other patients not affected us. For instance, there were many experiences of mine that I thought of quitting the medicine before my ears stopped hearing"*.

5.1.3.1.8 Provider-related factors

- **Responsiveness**

Most of the study participants stated that responsiveness was not in place at inpatient wards during their stay in the hospitals, especially during emergency situations. The response of the ward team was not fast enough to reverse situations. Most of the patients stated the following:

> *M-FGD3: [I]f they follow us on time… If I say I am feeling sick, they say drink milk, apply this ointment, or drink water. They even did not give us the time you gave to me now. No one talked to us; so, what is the meaning of our stay in the hospital? This is the problem…."*
>
> *M-FGD3: "Here in... there are not enough professionals and when we get sick, feel dizzy or suffer convulsions, they only say it is okay to drink water or something. There is no one who is responsible for giving us appropriate treatment. I have seen patients in distress and affected when they waste time trying to call doctors in an emergency".*

M-FGD3: "…To tell the truth, after I started taking the medicine, I felt pain in my waist, and here there was chest pain. I told them so many times but there is no one who will help me and I am still feeling the pain...".

- **Poor communication**

This sub-category involves study participants who were previously treated patients describing an experience where there was poor communication from health providers in telling them the seriousness of their problems and explaining their results. While some spoke, the others nodded in agreement, and the following were some of their verbatim vignettes:

M-FGD3: "…I am not good psychologically because I am not aware of the extent of my problems. No one tells us the level of our condition…".

M-FGD6: "… No one explains your results to you".

M-FGD1: "Actually, blood is taken monthly but we do not know our results".

F-FGD2: "Then after my body started to get rigid and rigid. No one communicates to us properly".

M-FGD3: "They did not tell us the result and it affects our psychology. We lose hope and if they tell us nothing about the result, we think that they do not have hope for us and that there is something worse".

Adequate information was crucial and should be part of the counselling process so that patients would have sufficient awareness to deal with their medication and treatment. Not giving adequate information was mentioned as being one of the challenges during the treatment process by the participants. The following points were mentioned during the discussion by the study participants:

M-FGD4: "No one gives adequate information on how to take medicine. There are 14 tablets given to all patients, and no one tells you that this drug is for this symptom or for that".

M-FGD5: "The problem is that they only give you the medicine and did not tell us how to take it".

M-FGD5: "As to me, it is not enough. Because, at least, no one is telling you how to take your drugs. For example, if the drug has to be taken within 30 to 40 minutes, patients take it the whole day because they do not know how to take".

M-FGD5: "We knew how to take it by our effort. No one told or advised us how to take".

5.1.3.1.9 Psychological challenges

This category refers to study participants describing their experiences regarding psychological challenges they sustained. They stated that emotional trauma, feelings of loneliness, and at times, loss of hope were making their treatment process painful. The following were psychological challenges expressed by FGD participants:

F-FGD2: "At the beginning, I was a waitress. Now I couldn't do that. When my own father knew I was sick with TB, he went so far as to deny it to me, saying that he did not know me. There is no family besides mine. No family near me. Except for God, there is no one around me".

M-FGD2: "I lost a lot of things when I started treatment. First of all, I was breastfeeding when my family took my baby from me. She was just five months old. I had to get treatment".

M-FGD2: "My reason for interruption was as follows… When I was diagnosed with TB, the doctor prevented me from working until I finished the drugs. But I know that I have to work since I don't have anyone to support me. I worked as a taxi assistant. I was working and taking my medication. And in the middle, my doctor came and told my friends that I didn't have to work there. He said, 'He is a TB patient and it is contagious. So he should not join you.' So I was isolated. Everyone just avoided me. All those who knew me in my neighbourhood ignored me, even to the point of spending the entire day alone in the forest. I got to the point of committing suicide. Many things happened to me. It is even to the point of eating out of a restaurant's trash".

5.1.3.2 Theme 5: Challenges for patient follow-up while on the treatment

Theme 5, which refers to experiences of previously treated DR-TB patients regarding their challenges during follow-up while on treatment, comprises four categories and corresponding subcategories as shown in Table 5.7. These challenges during treatment follow-up have an impact on successful treatment completion, though indirectly.

Table 5.7: Theme 5: Challenges for patient follow-up while on treatment - categories and sub-categories

Theme 5	Categories	Sub-categories
Challenges for patient follow-up while on the treatment	Weak patient follow-up	DOT laxness Follow-up every three months Adverse event monitoring
	Service delivery	Interruption of services Quality of food service
	Health system related	Accessibility Trained human resource
	Support and care after discharge	

5.1.3.2.1 Weak patient follow-up

- **DOT laxness**

As the acronym DOT indicates, DOT is a directly observed treatment. The treatment should be given under daily observation by the health provider or trained treatment supporter. The study participants' experiences indicated that during their treatment DOT was not strictly followed and health providers were not following whether they had taken the medicine or not. This affects proper adherence and could bring under treatment. Moreover, any adverse events, including life-threatening ones, may get complicated unnoticed.

> *M-FGD1: "They distribute the medication at 6 AM. I will keep it and swallow it at around 8 AM".*
>
> *F-FGD5: "It is good if they check who is taking the medicine or not. A nurse brings and gives the drugs and goes. It is good if they check".*
>
> *F-FGD5: "No, they did not check. Some patients took it, and others did not. They did not follow us…"*

M-FGD6: "The doctors do not check us whether we take it or not. They only give us "and go".

Other participants further reiterated that they were given weekly, biweekly, and monthly doses from the health centres.

F-FGD2: "When I was here, I used to take it daily. I was discharged from here. I was taken weekly from the health centre".

F-FGD5: "I come here once a month and I go to health centres every 15 days".

F-FGD5: "I was taking the medicine monthly from the health centre".

- **Follow-up every three months**

Treatment follow-up at TICs is usually conducted every month, and monitoring of adverse events and treatment responses is systematically followed and recorded. FGD participants' experiences indicated that treatment follow-ups were done every three months in some TICs. As a result, any patients' concerns, both clinical and social, could not be addressed timeously and patients may interrupt their treatment in such conditions.

F-FGD5: "I used to give blood tests every 3 months".

F-FGD5: "I had a check-up every 3 months, but I was taking the medicine monthly".

- **Adverse event monitoring**

This sub-category refers to previously treated patients expressing their experiences of developing drug side-effects due to a lack of proper monitoring of the occurrence of adverse events. One discussant explained.

M-FGD25: "…when I was treated here I only had tests for blood and sputum. There was no examination other than this".

Another participant reiterated that laboratory monitoring tests were not available at their TICs during follow-ups.

M-FGD6: "I get from outside [laboratory monitoring tests]. They send you to… So it is good if necessary laboratory tests are done here. As we know, the drugs have so many side-effects and they affect the kidneys, eyes, ears, and liver. If they do check-ups every month or at least every 3 months, I think it is good".

M-FGD6: "The other thing is why is the laboratory not doing liver and kidney tests? That is the main problem, because the medicines are hard".

Another participant mentioned that no laboratory monitoring tests were performed after baseline.

M-FGD5: "We got an examination at the beginning when we came here. They had tests for HIV, kidneys, and liver. After that, we did not get any kind of examination for 2 years".

5.1.3.2.2 Service delivery

- **Interruption of services**

Another challenge during treatment follow-up periods mentioned by study participants was the interruption of services. Due to a threadbare budget, many services like food provision, including milk and supplements, were interrupted. The following statements were noted by the study participants regarding interruption of complementary services:

M-FGD1: "Sometimes what is the hospital's own problem is, many times they raise it, there is no budget, and we don't have a budget. Of course, there may not be a budget. Um…we have no knowledge of it. They used to give us milk, plump nuts. We used to use them. Something that built up our bodies. That has just stopped. It is completely stopped…"

M-FGD1: "The treatment is good… Our problem is regarding the supplements. This drug needs milk. It really burns. In the past, they used to give us milk. That moment was a little better. When that milk stopped, our stomachs started to burn even worse. It makes the stomach sick. It hurts. You cannot eat food. Otherwise, in terms of treatment service, it is quite good".

- **Quality of food service**

In the discussion, the poor quality of food provided for patients treated as inpatients was mentioned as a challenge by study participants. The importance of the improvement in the quality of food was also mentioned in the discussion. This was thought to contribute to frustration, and it was explained by participants as follows:

M-FGD1: "…Previously, the food was doing well. Now it is of poor quality".

M-FGD5: "The food provided for patients should be improved".

F-FGD5: "I was admitted here for 5 months, and for 5 months I did not eat their food. It's not good for patients. The bread, the egg, and the meat were not freshly prepared and had changed in taste and texture. It has to be improved".

M-FGD1: "As they said before, if there is enough food and care, it will not hurt. Now most of the time, they complain and stop treatment due to that".

5.1.3.2.3 Health system-related

- **Accessibility**

As explained by the FGD participants, many health facility locations were far from their home town or districts. They were forced to rent a house and sustain the high cost of transportation to continue their follow-ups. The FGD participants stated accessibility issues as follows:

M-FGD3: "Many problems are encountered due to this disease. There is no health centre in my home town, and I should stay there to follow my treatment. I had to rent a house. I had to prepare my own food. There is a transport cost. Those are problems I faced. As it is known, the rent of the house is very expensive. On top of that, I do not have a job".

M-FGD6: "…if their living areas are far from the treatment site, there will be a transport problem and they may discontinue the drug".

M-FGD6: "The second reason is distance from home to treatment site, which can also make a patient quit. I struggled to come here while on follow-up because it is [the health centre] far from my home".

- **Trained human resources**

In addition, another discussant explained that even if there were health facilities nearby, the absence of trained health providers on programmatic management of DR-TB posed problems and obliged them to stay away from their home town where they got the treatment and follow-up services. One FGD participant stated that:

F-FGD6: "I asked them to transfer me to my neighbourhood because I had a job and rented a house there… but they said, we do not have a trained doctor over there to transfer you".

Moreover, it was also stated in the discussion that lack of training on the part of health providers affected proper follow-up and monitoring of patients. The following were mentioned regarding problems of a lack of trained human resources at treatment follow-up centres:

M-FGD6: "At the health centre, different people give me the drugs. I personally take them. They don't know the drugs. When the focal person goes on vacation, they do not know about the drugs. Last time, a female nurse gave me an incomplete dose of drugs. I told her it was not complete and she called the nurse on vacation and she told her that I knew the drugs. She was surprised by the number of the pills and asked how I could take this many pills. I explained to her that It was an MDR treatment, not a six-month TB treatment".

M-FGD6: "I take it from the health centre. There are a lot of problems there. There are people who don't know the drug we take. So we take it by ourselves. And there is no constant person to do that. They need to be trained".

5.1.3.2.4 Support and care after discharge

The FGD participants explained that one of their challenges during follow-up after discharge was the inadequacy of support and care necessary to continue with their therapy. The FGD participants described their challenges after discharge from hospitals as follows:

M-FGD6: "The other reason is the economic problem. For example, when we are here, they give us different types of food and milk timeously. Once we are discharged from here, it is difficult to get such types of food. By that time, the drug is very hard to take. It causes gastric burning, stress, and other symptoms. Likewise, if your home is far from the facility, it is difficult to pay rent and take medicine. Due to that, they may discontinue the treatment".

M-FGD1: "As my friend said here, some of the patients have relatives, and some have no relatives. There are those who do manual labour. As you all know, with this illness, it is impossible to take the drugs while doing daily labour. It needs many things. It needs care. You need something to drink and eat, but we don't have that. Therefore, when we are discharged from here, we are obliged to mix with the community to do daily labour. So, we prefer to stay here to get our treatment and care as much as possible".

M-FGD2: "It is better when we stay here. They serve food to us. Whether it is tasty or not, you eat it and take your medicine. You eat for the sake of your medicine. The doctor does not know our problem we face outside when we are discharged from here to continue the treatment. You need a home, but have no money to rent the house. 'Staying in the streets and taking medicine is very hard".

5.1.3.3 Theme 6: Enablers for treatment completion

Theme 6, enablers for treatment completion, refers to FGD participants who previously treated DR-TB patients regarding their experience of facilitators of the treatment process, including environmental, social, economic, organizational, and personal assets, which were believed by patients to have enabled them towards treatment completion. Theme 6, which comprises three categories and corresponding subcategories, is illustrated in Table 5.8.

Table 5.8: Theme 6: Enablers for treatment completion - categories and sub-categories

Theme 6	Categories	Sub-categories
Enablers for treatment completion	Cues to action	Caring for each other Community support Family support Compassionate care Counselling
	Programme related	Good linkage between TIC and TFC Having treatment supporter Monthly social support Quick service Reimbursement
	Self-efficacy	Determination

5.1.3.3.1 Cues to action

This category refers to the experience of previously treated patients with regard to events, either interpersonal or environmental, that motivated them towards the prescribed treatment process and engaged them in treatment adherence and completion.

- **Caring for each other**

From the FGD, one of the enablers for patients towards treatment adherence and completion during treatment was that they used to have a quality of care for each other. As mentioned by the study participants, caring for each other motivated them in the long treatment process to stick to the orders of the health providers and programme protocols. The FGD participants stated that caring for one another helped them stay in therapy because:

> *M-FGD2: "…When I was here, whatever food and drink we got we shared among ourselves".*
>
> *M-FGD3: "Because we were talking to each other and advising each other, we took it properly; I see the benefits of the treatments".*

- **Community support**

The community support for patients during the long DR-TB treatment was explained to be a great enabler to continue with their treatment, especially for those who did not have family and social support. Study participants explained the input of community support in their treatment process as:

> *F-FGD2: "I got support from the Mother Teresa organisation. The organisation assigned one care giver for me… Then the sister sent me fruits, food like bread once a week, and she also sent me clothes".*
>
> *F-FGD5: "I had no one. I was living on what they gave us from here, and sometimes the woman that rented the house for me also used to buy me teff [flour] once every two or three months. We have no relationship; she simply assisted me for the sake of God"*.

- **Family support**

Previously treated DR-TB Patients mentioned that family support was overwhelming in keeping them on their medication for such long periods. The role of family support as an enabler in their efforts towards treatment completion was reflected by FGD participants as:

> *F-FGD2: "Had it not been that we live with our family, otherwise it would have been difficult to survive. The food that is served in the hospital is not that good or enough".*

> *F-FGD2: "When I had a problem with transportation money, my father worked as a guard and tried to cover my transportation costs to help me continue my medication. They give us one can of powdered milk and two kilos of oats, which is not enough for a month"*.

> *M-FGD3: "There was no one to support me except my wife. I am here because of her".*

Another participant further reiterated that family support extends to advice and motivation to adhere to medication.

> *M-FGD3: "My family and friends call me and give me advice on how to take the medicine".*

- **Compassionate care**

This sub-category refers to healthcare professionals' sensitivity to their patients' suffering and their good wishes and commitment to relieving that suffering. The FGD participants described how compassionate care by the health providers enabled cooperation between them and providers in the treatment process. It was described that compassionate care could improve motivation and the physician-patient relationship. The following were verbatim statements of the study participant regarding compassionate care:

> *F-FGD2: "But when we came here, the first day I felt treated as a citizen. This is because, starting from the emergency room to the MDR ward, physicians were close to me and treated and took care of me until I was admitted to MDR. Three healthcare providers were with me making my bed, and by that time I was*

assuming they were making a film. By that time, I was asking myself why this type of service is not given to patients in other places".

M-FGD4: "…The professionals at the health centre are good. They treated us nicely".

F-FGD2: "…The reason I am able to take the XDR treatment so well now is that, because of the doctors' care, I get food properly. I have also been able to rent a house and live there freely. They paid my house rent… ".

- **Counselling**

The FGD participants reported that professional counselling was one of the enabling factors to stay on the treatment despite the occurrence of problems while on the treatment. The following sentences were noted by the FGD participants:

M-FGD5: "I became ill with gastric disease. There is an economic problem and you lose hope. When I was here, one guidance woman who gave us counselling gave me hope, besides the nurses. She helped me a lot to be here now".

M-FGD6: "… It is good they give us advice".

5.1.3.3.2 Programme related

- **Good linkage between TIC and TFC**

The study participants mentioned that the presence of good linkage between TICs and TFC benefited them in following their treatment without any interruption of any drug supply.

F-FGD2: "… the drugs are being sent to the health centre from the hospital properly… ".

- **Having treatment supporter**

It was also mentioned by the study participants that having a treatment supporter during treatment was one of the facilitators for smooth treatment completion.

F-FGD5: "I used to take either the injection or medicine at home. There was one nurse who brought the medicine to me at my home. I only came here for the check-up".

- **Monthly social support**

Most of the FGD participants claimed that monthly social support [food basket and pocket money] was available while on treatment. And like that of the community support, programme-based monthly social support was crucial as one of the enablers towards continuing their treatment, especially for those with low socioeconomic status.

M-FGD4: "There is 150 birr for taxi, and there is some flour and milk. That is all".

M-FGD4: "We get economic support of around 150 birr for transport and some food packages monthly".

M-FGD1: "In my case, they give 100 birr for transport costs, different kinds of food like lentils, milk, flour, and oil".

- **Quick service**

The study identified that one of the enablers to sticking to treatment follow-up was the presence of expedited service in the health facilities for DR-TB patients. This saved time for other daily lively activities and motivated them to adhere to treatment follow-up plans.

M-FGD3: "I come here by Bajaj [rickshaw], and it takes me 20 to 30 minutes to get the medicine, and then I will be back".

M-FGD3: "It takes 10 to 30 minutes.... It is just giving us the medicine".

M-FGD4: "At the health centre the medicine was already prepared in your name. It does not take more than 30 minutes. Here, when we come for our check-up monthly, seeing the doctor and having all examinations and tests does not take more than two hours".

M-FGD5: "In the health centre it takes 30 minutes, but here we get it in 20. If you are taking an x-ray it takes up to 45 minutes".

- **Reimbursement**

The FGD participants mentioned that receiving DR-TB treatment and follow-up services free of charge and reimbursement of services and medication bought out of pocket in case of absence from the government facilities was reducing economic strain on the patients and facilitating treatment success.

M-FGD2: "…If they have the drugs here, they will give you. Otherwise, you buy it from an outside pharmacy and they will refund your money".

M-FGD2: "…Uh... meaning they will give you the laboratory request and prescriptions and tell you that you can use your own money and they will reimburse you upon bringing the receipt… ".

F-FGD2: "If the test is not available in the hospital, we are told to have the test at the private laboratories and they will reimburse our payment upon bringing the receipt".

5.1.3.3.3 Self-efficacy

This category refers to the strength of an individual patient's belief in his or her own ability to respond to difficult situations and to deal with any associated obstacles or setbacks. It is an individual patient's ability to successfully undertake action.

- **Determination**

Besides programme-related facilitation towards treatment success, the determination of the individual to resist hindering factors throughout the treatment duration was mentioned by the study participants to be an important enabling factor to successful treatment completion.

F-FGD2: "There are a lot of problems, as you know, which make you lose hope. But the main thing is your determination".

5.1.3.4 Theme 7: Perceived benefits of treatment completion

Theme 7, perceived benefits of treatment completion, refers to FGD participants' beliefs in the efficacy of treatment completion to make them better from their disease and cure them. In theme 7, two categories were identified. These are namely: (1) Trust in the treatment, and (2) Trust in the service (see Table 5.9).

Table 5.9: Theme 7: Perceived benefits of treatment completion - categories and sub-categories

Theme 7	Categories	Sub-categories
Perceived benefits of treatment completion	Trust in the treatment	Good treatment Brings cure
	Trust in the service	Satisfying services Good care

5.1.3.4.1 Trust in the treatment

This category refers to FGD participants trust in the treatment of DR-TB, believing that if the treatment is taken properly until the end, it is very good and could bring a cure and save lives.

- **Good treatment**

The FGD participants mentioned that if the treatment is taken properly till the end, the treatment is very good. FGD participants stated that:

F-FGD5: "The treatment is very good. When I was admitted here, I was 30 kg. It was a good time. The treatment has been so good".

M-FGD6: "MDR treatment is very good. These drugs save lives. If we take the drug correctly until we finish, it is very good".

F-FGD3: "If you take the treatment correctly, you will have a change".

F-FGD5: "The treatment is very good. It's so expensive, so we cannot afford it on our own and we may not be treated".

- **Brings cure**

The FGD participants indicated that they had a firm belief that if the treatment is taken properly till the end, the treatment is very good and could bring cure to patients and save lives.

M-FGD6: "In my opinion, if a person takes the drug properly, he will be cured".

M-FGD4: "If you have the capacity and properly take it, the drug will bring you cure".

F-FGD3: "I learned that we could recover by taking the treatment properly and it has side-effects if we discontinue the medicine".

M-FGD4: "If you take the medicine perfectly, it will cure you".

5.1.3.4.2Trust in the service

This category refers to FGD participants experience regarding their trust in DR-TB treatment service and patient care during treatment duration.

- **Satisfying services**

FGD participants indicated that they had trust in the treatment service that it had a contribution so that they could finish their treatment till the end. The FGDs participants stated their experience of the perceived benefit of the treatment service as follows:

M-FGD1: "The treatment service is very good. The care of patients is also good".

M-FGD1: The treatment service is very nice. The nurse brings on time as per the doctor order".

F-FGD2: "The service is good in general. There is follow-up. They give care for us. … . And they have contributed a lot so that we could finish our treatment".

M-FGD4: "…The doctor asks you if there are any problems and about side-effects and prescribes you a treatment if you have any problems. They also give you advice on how to take the treatment properly and not to discontinue it. That is all".

M-FGD6: "The treatment process is very good. I am making good progress after I started treatment with continued follow-up".

- **Good care**

FGD participants explained that they had trust in the care provided by HCPs that it had a contribution so that they could finish their treatment till the end. They also mentioned in the discussion that the treatment process was comprehensive and they were confident that it had brought progress in their condition. The FGDs participants stated their experience of the perceived benefit of the HCPs care during treatment duration as follows:

M-FGD3: "…To tell the truth, we are good. They are taking care of us. The first time I came here, I was not just like this. I did not think that I could recover. And after I started this medicine, I have been fine. Thanks to God. If the service and treatment continue like this, we have the chance to fully recover. And we are making good progress, in my opinion".

M-FGD3: "…I discontinued TB treatment many times in the past and have passed through many painful life situations. As a patient, the government and physicians support all patients suffering from this disease by giving follow-up monthly, by examining patients like ears and eyes, and by sending samples to the laboratory for sputum and blood analysis every month. I am happy with the support and am following my medication voluntarily, and I feel confident that I will recover from the disease".

5.1.3.5 Theme 8: Perceived severity of the disease

Theme 8, perceived severity of the disease, refers to FGD participants' perceived belief about DR-TB as a serious disease that has severe consequences. Theme 8 comprises two categories as shown in Table 5.10.

Table 5.10: Theme 8: Perceived severity of the disease - categories and sub-categories

Theme 8	Categories	Sub-categories
Perceived severity of the disease	Physical consequences	Disabling disease Separation
	Social implications	Self-isolation Marginalization

5.1.3.5.1 Physical consequences

This category refers to the severity of DR-TB disease, with the physical consequences of severe illness as well as separation.

- **Disabling disease**

FGD participants mentioned that DR-TB is a serious and disabling disease. The study participants stated their realization of the severity of the disease as follows:

M-FGD3: "This MDR is very difficult".

M-FGD3: "This is a very bad disease. You cannot even work. It is so hard".

F-FGD4: "I became sick almost to death and was admitted to Yekatit hospital".

M-FGD4: "I started the treatment 18 months ago. I was so sick the first time when I started the medicine, I could not be able to walk".

- **Separation**

FGD participants mentioned that DR-TB is a dreadful disease that can result in the physical separation of the family. One FGD participant stated that:

M-FGD3: "I was separated from my marriage and my child. Because of the dreadfulness of the disease and, in fact, its transmissibility [communicability of DR-TB], she [his wife] left me".

5.1.3.5.2 Social implications

This category refers to social implication of DR-TB that are difficult to cope with

- **Self-isolation**

The FGD participants reported that the disease has negative social implications that can oblige someone with the disease to develop self-isolation from the community. One of the study participants reported that:

M-FGD2: "Because of the severity of the disease and that it's transmitted by breathing, I developed the habit of self-isolation and fleeing away from people".

- **Marginalization**

The FGD participants reported that DR-TB is associated with the marginalization of patients in the community. The following sentences were noted by the FGD participants:

M-FGD4: "Since I became sick with TB and the diagnosis was confirmed, my morale has been touched so much. Everybody, including my friends, my relatives, and even the community, discriminated against me. They were not willing to even say hi. They marginalized me from social life and I felt it so much".

M-FGD3: “I cannot move in the community as I like. I cannot interact as I like with people. I faced psychological problems. "That is a serious problem for me”.

M-FGD3: “But in those times of staying on treatment, even people that are close to me did not visit me. Similarly, patients admitted with me did not have anyone to visit them. So the discrimination from the community for such a long time was so hard”.

5.2 THEORETICAL FRAMEWORK

This study used HBM constructs in relation to DR-TB treatment completion. Thus, in that particular instance, perceived severity refers to an individual’s subjective assessment of the severity of the consequences of not completing DR-TB treatment. Perceived susceptibility refers to an individual's assessment of their personal risk of developing problems with regard to not properly taking DR-TB medication. Perceived benefits relate to a subjective assessment of the importance of adherence to second-line regimens. Finally, perceived barriers relate to the patient’s evaluation of the obstacles to taking second-line drugs. These constructs can indicate possible mechanisms that could be triggered to reinforce treatment completion behaviour.

In this study, it was conceptualised in the context of the successful completion of DR-TB treatment. The HBM translates to the desire to achieve successful treatment completion and the belief that completion of DR-TB treatment will improve the patient’s health and bring cure, and this would influence whether or not a patient properly takes the medication and successfully completes their treatment.

In this study exploring barriers to completion of DR-TB treatment through the application of HBM, identified real and perceived barriers to successful completion of treatment regimen. The most commonly reported barriers were related to clinical issues, patient and drug-related factors, programme and health system factors, psychological, and socio-economic factors. Furthermore, barriers that limited DR-TB patients treatment completion were factors associated with proper treatment follow-

up, including supply shortages, inadequate service delivery, and a lack of responsibility by providers.

On the other hand, enablers or facilitators (factors that have enabled patients towards treatment completion) were described under the HBM construct as cues to action. Cues to action factors that motivated patients towards treatment adherence and completion include caring for each other, community and family support, and compassionate care.

In this study the other HMB construct explored and described was perceived benefits. Previously treated DR-TB patients' beliefs in the efficacy of treatment completion to make them better from their disease and cure them. Perceived benefits of treatment completion identified in the study were trust in the treatment and trust in the service. DR-TB patients indicated that they had a firm belief that if the treatment is taken properly till the end, the treatment is very good and could bring change, cure patients and save lives. Furthermore, that they had trust in the service and care of patients.

The perceived severity of DR-TB is the other HBM construct explored in this study. It is the belief that DR-TB is a serious disease that has severe physical and social consequences. It was indicated that DR-TB is a serious and difficult disease with the consequence of severe illness as well as fatality. Furthermore, it was explained that DR-TB is a disease that has negative social implications that are difficult to cope with.

One of the concepts of the HBM, self-efficacy was explored in this study. The strength and determination of previously treated DR-TB patients by themselves to resist hindering factors throughout the treatment duration were explored as an important enabling factor to successful treatment completion.

Modifying factors, including demographic characteristics, clinical characteristics, lifestyle and physical characteristics, health system related factors, personality, socio-economics, of HBM associated with treatment completion of DR-TB treatment were explored and described.

As scholars Mukumbang et al (2017:2) debate, if an individual has a high perceived threat towards a DR-TB disease, low barriers to adopting healthy behaviours, and a high perceived benefit to action that would help avoid the health issue, then there is

an increased likelihood of the individual engaging in the recommended behaviour of treatment completion.

5.3 CONCLUSION

This chapter presented the findings of the qualitative strand of the study. The chapter achieved the objectives of describing the views of experts managing DR-TB patients and the lived experiences of previously treated DR-TB patients on treatment completion, respectively. The next chapter dwells on the discussion of the key findings of the study, supported or refuted by available literature.

CHAPTER SIX

DISCUSSION OF KEY FINDINGS AND LITERATURE CONTROL

6.1 INTRODUCTION

The previous two chapters presented quantitative and qualitative findings of the study. This chapter discusses the core findings of the study from a comparative angle relative to available literature and presents the conclusions. In the discussion of the findings, the quantitative and qualitative results are integrated where appropriate.

This study sought to answer the following research questions:

- What are the views of experts treating DR-TB patients on treatment completion?
- What are the lived experiences of previously treated patients on treatment completion?
- What are the factors associated with DR-TB treatment completion?
- In what ways do qualitative interviews with patients and experts explain factors associated with treatment completion?

6.2 RESEARCH DESIGN AND METHODS

Creswell and Plano Clark (2018:5) define mixed method research as a philosophical assumption and methods of inquiry that guide the direction of the collection and analysis and the mixture of qualitative and quantitative data within a study. Research designs are procedures for collecting, analysing, interpreting, and reporting data in research studies (Creswell & Plano Clark 2018:51).

This study utilised the convergent concurrent (parallel) mixed method design. Polit and Beck (2017:584), state that the purpose of the convergent design (sometimes called a triangulation design) is to obtain different, but complementary, data about the central phenomenon under study - that is, to triangulate data sources. In this design, qualitative and quantitative data are collected simultaneously and with equal priority. The goal of this design is to converge on “the truth” about a problem or phenomenon. The researcher’s job is to link the two data sets, often at the interpretation stage of the project. Likewise in this study, the quantitative data and qualitative data sets were

analysed separately and then brought together at interpretation in the discussion section.

6.3 DISCUSSION ON KEY RESULTS

6.3.1 Treatment completion

Maximising the successful treatment completion in DR-TB is a global health priority and focus area of the End TB strategy, and is also one of the performance indicators in the strategy (Eshetie, Alebel, Wagnew, Geremew, Fasil & Sack 2018b:4). Researchers Law, Daftary, O'Donnell, Pasayatchi, Calzavara and Menzies (2019:2); Ahmad, Javaid, Syed Sulaiman, Afridi, Zainab and Khan (2018:1); Safaev, Parpieva, Liverko, Yuldashev, Dumchev, Gadoev, Korotych and Harries (2021:1) and Girum, Tariku and Dessu (2017:332) emphasised that treatment of DR-TB, in contrast to drug-sensitive tuberculosis, is costlier, more toxic, less effective, more complex and takes a longer time. Consequently, the odds of treatment non-completion are considerably higher and associated with unsuccessful outcomes with second line DR-TB treatment compared to non-DR-TB treatment (Leveri, Lekule, Mollel, Lyamuya & Kilonzo 2019:2; Bhering, Sarubbi Junior, Kritski, Souza & Duarte Duarte 2020:62-63; McNally, de Wildt, Meza & Wiskin 2019:2).

As per WHO's task force strategic plan set to achieve a target of DR-TB treatment success of 75% at the end of 2015, a number of countries including Ethiopia have not yet achieved this milestone (Eshetie, Gizachew, Alebel & van Soolingen 2018b:4). Presently, for drug susceptible and drug-resistant TB combined, the target level of > 90% is set for 2025 at the latest as one of top 10 indicators for monitoring implementation of the End TB Strategy at global and national levels (WHO 2016a:13; WHO 2018:14).

The successful treatment completion in this study was 72.69%, which is comparable to 73.2% and 71.8% reported by Woldeyohannes, Assefa, Aman, Tekalegn and Hailemariam (2019:7) and Baluku, Nakazibwe, Naloka, Nabwana, Mwanja, Mulwana, Sempiira, Nassozi, Babirye, Namugenyi, Ntambi, Namiiro, Bongomin, Katuramu, Andia-Biraro and Worodria (2021:1) in Ethiopia and Uganda respectively. However, it is higher than the 65%, 64.4% and 69.3% reported by Girum et al (2017:334), Baye, Sarhie and Endalew (2018:3) in Ethiopia and Gadallah, Mokhtar, Rady, El-Moghazy, Fawzy and Kandil (2016:1000) in Egypt respectively; but lower than the 75.6% and

78.6% reported by Leveri et al (2019:3-4) and Meressa, Hurtado and Andrews (2015:1183) in Tanzania and Ethiopia respectively. The higher treatment success in Meressa et al (2015:1183) might possibly be attributed to the study being conducted under strict observational study protocols rather than programmatic conditions.

6.3.2 Factors associated with treatment completion

Age, employment, history of alcohol consumption, BMI, comorbidity, registration group at start of treatment, HIV test results, comorbidity, DST technique, psychotic symptoms, drug-induced hepatitis, renal toxicity, electrolyte disturbance and arthritis were factors which had statistically significant association with treatment completion before adjusting the confounders. But, after adjusting the confounders in multiple logistic regression, age, registration group, comorbidity, DST results, psychotic symptoms, drug-induced hepatitis, renal toxicity, electrolyte disturbance and arthritis all had statistically significant association with treatment completion.

6.3.2.1 Age

Ageing reduces the capacity of the immune system and affects the coordinated mechanisms of phagocytic cells and adaptive immune T cell responses important to kill or contain the mycobacteria. Moreover, aged people are prone to develop adverse events from anti-TB drugs because of other existing comorbidities and age-related physiological changes. As a consequence, poor adherence to the regimen and unsuccessful treatment completion may result (Byng-Maddick & Noursadeghi 2016:1-3).

Outcomes of drug resistant tuberculosis are better in younger patients than older clients. Baye et al (2018:3) in their study aimed to determine treatment outcomes of multi-drug-resistant tuberculosis in Boru Meda, Ethiopia, and found that patients in the age group of <30 years were associated with successful treatment outcomes. A study conducted by Leveri et al (2019:2) to determine the proportions of treatment outcomes and their predictors among MDRTB patients in Tanzania also found that age >44 years is associated with unsuccessful treatment outcomes. Similarly, a study in Uzbekistan by Safaev et al (2021:8) reported unfavourable treatment outcomes were significantly higher in patients with increasing age.

In a study conducted in Northern Taiwan, it was reported that age 65 years and above (adjusted OR 27.6, 95% CI 4.8–158.3; p<0.001) was the only risk factor associated

with unfavourable treatment outcomes (Yu, Chen, Chien & Jou 2015:274). In Japan by Kawatsu, Uchimura, Izumi, Ohkado and Yoshiyama (2018:5) showed that low completion rate of 57% was observed due to the large proportion of those aged 65 years old and above. However, when restricting the result to those aged 64 years old and below, the rate improved to 71.6% indicating age may certainly be one of the factors affecting treatment outcome (Kawatsu et al 2018:5). Similarly, the current study also established that patients in the age group of 55-64 years were less likely to successfully complete treatment (AOR=0.16, 95%CI: 0.04 - 0.59) compared to other age groups.

6.3.2.2 Registration group

As defined in Chapter One, lost-to-follow-up (LTFU) refers to a patient who has been on treatment for at least four weeks and whose treatment was interrupted for eight or more consecutive weeks. WHO (2019:34) indicates that treatment interruption decreases treatment success because interruption of second-line drugs (SLDs) exposes to inadequate treatment and has been documented as a significant risk factor for poor treatment outcome due to the development of further drug resistance (Gadallah, et al 2016:1000). A study from India also indicated lost-to-follow-up patients are more likely to die or develop more severe and resistant forms of TB (Shringarpure, Isaakidis, Sagili, Baxi, Das & Daftary 2016:2).

Baluku et al (2021:4), in a study aimed at determining the treatment outcomes of DR-TB patients with poor prognostic indicators in Uganda, reported the association of previous exposure to SLDs with lower odds of treatment success. Patients who have been exposed to SLDs often have fewer retreatment options due to acquired additional resistance and long-term toxicities (Baluku et al 2021:4). Similarly, in Ethiopian study, Eshetie, Gizachew, Alebel and van Soolingen (2018a:9) showed that poor treatment occurrence was 2.17-fold higher (95%CI, 1.55±3.03) in retreated cases compared to newly diagnosed TB cases. Furthermore, a study by Leveri et al (2019: 2) also showed that one of predictors of unsuccessful treatment outcomes is previous history of TB treatment.

Meta-analysis of individual-level treatment patient data from 9 562 pulmonary DR-TB patients from TB programmes from 23 countries identified that LTFU is associated with substance misuse, alcohol abuse, resistance to a high number of anti-TB drugs, poor patient–provider relationships, greater disease severity and occurrence of drug

side-effects (Walker, Shi, Hicks, Elsey, Wei, Menzies & Lan 2019:2; Leveri et al 2019:8). Likewise, in the current study, patients in the registration group after lost-to-follow-up at the start of treatment were less likely to successfully complete treatment (AOR= 0.05, 95%CI: 0.004-0.54) compared to other registration groups in the study.

Similarly, in the qualitative findings of the study, factors exposing patients to treatment interruption and lost-to-follow-up were explained by the health care providers in the in-depth interviews. First, low socioeconomic background of the DR-TB patients was identified as an encumbrance, where they are marginalised, psychologically affected and vulnerable population of the society. Second, pill burden is mentioned as a primary reason patients attribute for their treatment interruption. Third, it emerged that serious side-effects compel patients to interrupt their medication, disappear from follow-up and default from their treatment. Fourth, there was a lack of awareness about the importance of treatment adherence for full duration, completing the treatment to prevent relapse and of the severity of the disease including how much DR-TB is fatal.

6.3.2.3 Comorbidity

A 2017 study by Girum et al (2017:335) assessing the survival status and treatment outcomes of DR-TB treatment in two treatment initiating centres (TICs) in Southern Ethiopia found that the rate of death was 4.3 times higher among patients with comorbidities than patients without. In another mixed methods study by Sanchez-Padilla, Marquer, Kalon, Qayyum, Hayrapetyan, Varaine, Bastard and Bonnet (2014:164) to identify factors related to default from DR-TB treatment in Yerevan, Armenia, reported that comorbidities accounted for the non-return of patients for treatment. In the same vein, Leveri et al (2019:2), Baluku et al (2021:2), McNally, de Wildt, Meza and Wiskin (2019:2), Charyeva, Curtis, Mullen, Senik and Zaliznyak, (2019:2) and Dlodlo et al (2019:11) noted that comorbidities like diabetes and HIV were the predictors of unsuccessful treatment outcomes.

Due to comorbidities, patients are likely to have drug toxicity, and require substitution of the medicine with less efficacious alternatives and successful completion of treatment could be affected by the adverse events or weak (less effective) regimen (Baluku et al 2021:4). The aforementioned studies clearly indicate that there is an inverse relationship between comorbidities and successful treatment completion. In the current study, not having comorbidity (AOR=2.06, 95%CI: 1.06-4.00) was

significantly associated with treatment completion, and patients with comorbidity were less likely to complete treatment compared to their counterparts.

In this regard, the qualitative findings from the in-depth interview of experts explain how comorbidities affect treatment completion. In the first place, most of the HCPs who were participants in this study mentioned that comorbidities like HIV, diabetes, malnutrition, chronic illnesses like renal disease and lung disease complicate treatment. Besides, frustration due to the high pill burden and increased adverse events reduce the success of treatment completion.

6.3.2.4 Adverse events

A number of studies have indicated that treatment of DR-TB is challenging and complicated, takes long, and is associated with frequent adverse events (Leveri et al 2019:2; Jakasania, Shringarpure, Kapadia, Sharma, Mehta, Prajapati & Kathirvel 2020:2; Baye et al 2018:1; Tiberi, Torrico, Rahman, Krutikov, Visca, Silva, Kunst & Migliori 2019:1; Lange, Aarnoutse, Alffenaar, Bothamley, Brinkmann, Costa & Chesov 2019:645,652; Bhering et al 2020:68; Gualano, Mencarini, Musso, Mosti, Santangelo, Murachelli, Cannas, Di Caro, Navarra, Goletti, Girardi & Palmieri 2019:1).

Many studies established that adverse events of second line anti-TB drugs are associated with unsuccessful treatment completion. Jakasania et al (2020:1) stated that while on DR-TB treatment, adverse events are the leading causes of unsuccessful treatment outcomes among patients. In the qualitative study by Shringarpure et al (2016:4), adverse events were identified as a major barrier to adherence in the long and difficult journey of DR-TB treatment. Likewise, McNally et al (2019:2) described that medication side-effects are barriers to optimal outcomes. Furthermore, Sanchez-Padilla et al (2014:162,164) in the analysis of both quantitative and qualitative results, side-effects were reported as reasons for defaulting from treatment.

In a study set out to analyse adverse drug reactions (ADRs) and treatment outcomes of MDR-TB, Dela, Tank, Singh and Piparva (2017:524) explained that ADRs associated with second line drugs, resulting in dropouts, insufficient treatment, and were significantly associated with non-treatment adherence and defaulter outcome, thereby affecting successful treatment completion. Similarly, Bogale, Tsegaye, Abdulkadir and Akalu (2021:1344) in their study aimed at determining the unfavourable treatment outcomes and its predictors among patients with DR-TB in

Southern Ethiopia DR-TB treatment centres concluded that the presence of drug adverse events were significantly associated with unfavourable treatment outcome. Furthermore, a study conducted by Gualano et al (2019:2) in Italy to describe the frequency and type of adverse drug reactions in a cohort of DR-TB patients and their potential impact on treatment outcome verified that adverse events represent a significant barrier to treatment completion and could inversely affect outcome.

In the current study, at multivariate analysis, it was found that not having adverse events; namely, psychotic symptoms (AOR= 2.79, 95% CI: 1.14 - 6.82), drug-induced hepatitis (AOR=12.00, 95%CI: 2.43 - 59), renal toxicity (AOR= 8.31, 95% CI 1.51-45.6) and electrolyte disturbance (AOR= 8.31, 95% CI 1.51- 45.6) were significantly associated with increased chances of treatment completion. Conversely, having an adverse event such as arthritis (AOR= 2.17, 95% CI: 1.20-3.93) had association with treatment completion.

The qualitative results from in-depth interviews with HCPs and focus groups with patients clarified that the second line anti-TB drugs cause untoward adverse events that affect a patient's smooth treatment adherence and completion. The more the side-effects come into picture and exist for longer period of time, the higher the chances of causing reluctance and frustration due to reduced quality of life of the patient. Consequently, patients prefer to quit their regimen or disappear from follow-up. Moreover, due to serious adverse events patients may lose their life.

6.3.2.4.1 Psychotic symptoms

Different scholars have demonstrated that psychiatric disorders such as psychosis and depression are common with second line anti-TB drugs used to treat the drug-resistant form of tuberculosis (Alene, Viney, McBryde, Tsegaye & Clements, 2017:354; Bhering et al 2020:68; Kundu, Basu, Sarkar, Nath & Biswas 2021:393; Meressa et al 2015:1184). As Dela et al (2017:525) indicated, severe psychiatric manifestations have been reported to appear in 9.7-50% of DR-TB patients taking cycloserine. Huque, Elsey, Fieroze, Hicks, Huque, Bhawmik, Walker and Newell (2020:2) further confirmed that psychiatric side-effects with cycloserine are debilitating to the patients.

Cycloserine associated neurotoxicity is attributed to diminished central nervous system (CNS) production of gamma-aminobutyric acid (GABA) caused by the inhibition of glutamic decarboxylase (Dela et al 2017:525). GABA is an inhibitory

neurotransmitter in the brain which exerts inhibitory functions in the nervous system by reducing neuronal excitability and producing a relaxation effect (Gou, Wang & Wang 2012:E75). Further, the concomitant use of ethambutol, INH or fluoroquinolones in the regimen containing cycloserine may increase the risk of CNS toxicity (Dela et al 2017:525).

Kundu et al (2021:392), Dela et al (2017:525) and Huque et al (2020:2) in their studies reported that psychiatric disorders undermine health-seeking behaviour and are associated with poorer adherence to DR-TB therapy and may also trigger loss to follow-up among DR-TB patients. Besides, Baluku et al (2021:2) also reported psychiatric adverse drug effects are among predictors of poor treatment outcomes. Whilst psychotic symptoms are not a finding of this current study, the study did identify that those patients without psychotic symptoms were 2.79 times more likely to complete their treatment successfully than those with psychotic symptoms (AOR= 2.79, 95% CI: 1.14 - 6.82).

6.3.2.4.2 Drug-induced hepatitis

Drug-induced hepatotoxicity (DIH) is a common adverse event in patients treated with first and second line anti-TB drugs (Lee, Lee, Kim, Kim, Lee, Kim, Ha, Kim, Jung, Lee & Kim 2016:800; Song, Yoon, Park, Heo, Kim, Chung & Lee 2019:1; Keshavjee, Gelmanova, Shin, Mishustin, Andreev, Atwood, Furin & Miller 2012:596). DIH reflects direct toxicities of drug metabolites or effects thereof on immune system–mediated pathways (Song et al 2019:1). Among the second line anti-TB drugs, prothiomanide, ethionamide, para-aminosalicylic acid, flouroquinolones and linezolid have been reported to be associated with a high risk of hepatotoxicity (Lee et al 2016:804; Keshavjee et al 2012:597). Researchers Lee et al (2016:800), mention that the incidence of DIH during DR-TB treatment ranges from 1.7% to 16.8%. Comparably, the present study found a frequency of DIH during DR-TB treatment of 3.08%.

In the current study, patients without drug-induced hepatitis during treatment were significantly more likely to complete their DR-TB treatment successfully (AOR=12.00, 95%CI: 2.43 - 59). This finding resonates with a study from Republic of Korea by Lee et al (2016:803) that reported patients without drug-induced liver injury were significantly associated with successful outcomes. Likewise, similar findings were

found in a case control study by Song et al (2019:7) indicating that the successful treatment completion was lower in the group with DIH than the non-DIH group.

6.3.2.4.3 Renal toxicity

In an observational cohort study aimed at evaluating occurrence, management, and risk factors for ADRs in DR-TB patients, and the impact on treatment outcomes in Peshawar, Pakistan, Ahmad et al (2018:1) reported that renal toxicity is one of serious adverse effects of second-line drugs having negative consequences on quality of life of patients.

During treatment of DR-TB with second-line regimen, nephrotoxicity results from the injectable drugs aminoglycosides. These drugs have a propensity to accumulate in the proximal renal tubules resulting in intra-cellular accumulation and through inhibition of mitochondrial ribosomes, they produce nephrotoxic effects and subsequent tubular necrosis (Perumal, Abdelghani, Naidu, Yende-Zuma, Dawood, Naidoo, Singh & Padayatchi 2018:537; Sabur, Brar, Wu & Brode 2021:6-7). Moreover, researchers in the field noted that there is vast documented evidence that nephrotoxicity is one of the adverse events associated with aminoglycosides (Reuter, Tisile, von Delft, Cox, Cox, Ditiu & Garcia-Prats 2017:1115; Shibeshi, Sheth, Admasu, Berha, Negash & Yimer 2019:1). Similarly, in one study aimed to assess the prevalence, management of nephrotoxicity and ototoxic symptoms and treatment outcomes of patients treated for DR-TB with injectable-based regimens in Ethiopia, Shibeshi et al (2019:1) concluded that nephrotoxicity is associated with second-line injectable (SLI) drugs (aminoglycosides and capreomycin) which are administered during the intensive phase of the DR-TB regimen.

In the present study, occurrence of renal toxicity of 2.26% was found to be comparable to that observed in an observational cohort study in Peshawar, Pakistan (2.7%) by Ahmad et al (2018:5). It is slightly higher than 1.2% reported by Yang, Park, Jang, Yang, Kim, Moon, Byun, Lee, Kim and Kang (2017:4) in their study in South Korea, which may be attributable to the advantage of close monitoring and management of side-effects, as all patients in the South Korean study were treated for MDR-TB in the hospital for the whole treatment duration. And yet, it is slightly lower than 3.7% reported by Tag El Din, El Maraghy, and Abdel Hay (2015:939-940) in their study in Egypt at Abbassia Chest Hospital. This slight difference may be explained by the

variations in comorbidities in the two settings and, in the latter study, smaller number of patients in the study (only 107 MDR-TB patients) and covered a shorter study period (January 2009 to January 2012).

In a study to assess rates and risk factors for nephrotoxicity and ototoxicity among tuberculosis patients in Tbilisi, Georgia, Buziashvili et al (2019:1005, 1010) reported that life threatening renal toxicity may necessitate temporary or permanent interruption of the underlying second-line anti-TB drugs. This could lead to reduced treatment efficacy resulting in prolongation of culture conversion and treatment duration. Subsequently, the nephrotoxic adverse effect could seriously jeopardise patients' treatment adherence and lead to poor final treatment outcomes including failure. Similarly, in the current study patients without renal toxicity during treatment were significantly more likely to complete their DR-TB treatment successfully (AOR=12.00, 95%CI: 2.43 - 59).

6.3.2.4.4 Electrolyte disturbance

Merid, Gezie, Kassa Muluneh, Akalu and Yenit (2019:2) and Reuter et al (2017:1115) noted that there is large body of evidence documenting electrolyte disturbance as one of the major adverse events reported in different studies on SLDs. Tag El Din et al (2015:949) in their study aimed to assess adverse reactions of SLDs in patients treated for MDR-TB, reported that screening results for electrolyte abnormalities showed 26.2% had hypokalaemia which corroborates the current study of 27.93% and mentioned that capreomycin injection and low baseline body weight were the underlying factors. Likewise, Meressa et al (2015:1186) described that in their programmatic management of DR-TB, hypokalaemia occurred three times more frequently in patients receiving capreomycin compared to regimens with other injectables.

Second-line anti-TB medication adverse events - whether life threatening adverse events like hypokalaemia and non-life threatening ones like gastrointestinal upsets, have a serious impact upon quality of life of patients. Consequently, patient's adherence and compliance could be seriously affected resulting in unsuccessful treatment completion (Ahmad et al 2018:1). In the present study, it was found that absence of electrolyte disturbance has significant association with increased chances of treatment completion (AOR= 1.75, 95% CI 1.03- 2.95).

Furthermore, Girum et al (2017:335) mentioned that electrolyte disturbance was one of severe forms of adverse drug effects of DR-TB treatment which could make patients experience a fatal outcome and may necessitate withholding the therapy, further adding odds of fatality. In addition, Meressa et al (2015:1186) observed that hypokalaemia has been associated with mortality in other cohorts, lowering chances of successful outcomes by adding odds of unfavourable outcomes.

6.3.2.4.5 Arthritis

A number of prior studies done in Ethiopia and globally noted that arthritis is the most common adverse event encountered during DR-TB treatment (Meressa et al 2015:1186; Yang et al 2017: 5; Ahmad et al 2018:5; Dela et al 2017:523). Likewise, in the current study more than a quarter (29.98%) of patients developed arthritis during their treatment and comparable findings were reported in observational studies in Ethiopia and Pakistan (Meressa et al 2015:1184; Ahmad et al 2018:5). On the other hand, in the present study, arthritis had a statistically significant association with treatment completion (AOR= 2.17, 95% CI: 1.20-3.93), patients with arthritis were more likely to complete treatment compared to those who did not. However, previous studies demonstrating positive or negative relationship of arthritis with treatment outcome outcomes are not available in the literature.

6.3.2.5 DST results

The post-2015 global tuberculosis strategy (The End TB Strategy) calls for early detection and treatment of all persons of all ages with any form of tuberculosis, whether drug susceptible or drug resistant. New WHO recommended molecular platforms would allow early and accurate diagnosis, including universal DST of both drug susceptible and drug resistant tuberculosis. Universal DST is a crucial step for early diagnosis and successful treatment of DR-TB (WHO 2014b:10-11; WHO 2020:6; Molie et al 2019:2; Migliori, Tiberi, Zumla, Petersen, Chakaya, Wejse & Torrico 2020:S17).

Lack of DST is among the possible factors causing inadequate treatment of DR-TB (Molie et al 2019:2). In turn, the use of inadequate treatment could lead to further amplification of resistance and could result in treatment failure, whereas DST facilitates rapid detection of DR-TB in just a couple of days allowing the initiation of

effective treatment regimens and successful treatment completion (Migliori et al 2020:S19; Lange et al 2019:645). Line probe assays (LPAs) are WHO recommended faster DST techniques widely used for the detection of resistance to the key first line drugs rifampicin and isoniazid and second line drugs include the fluoroquinolones and second line injectables (Lange et al 2019: 646; Safaev et al: 2021:2). Likewise, in the current study, patients diagnosed with LPA were more likely to complete treatment compared to the other DST techniques (AOR=2.11, 95%CI: 1.11 - 4.01).

In general, not having comorbidity, not having adverse events, psychotic symptoms, drug-induced hepatitis, renal toxicity, and electrolyte disturbance, having arthritis and diagnosis with LPA were factors which showed significant positive association with treatment completion or lack thereof. On the other hand, age group of 55 – 64 years, registration group after lost-to-follow-up, were factors which showed significant negative association with treatment completion.

6.3.3 Views of experts treating DR-TB patients on treatment completion

6.3.3.1 Barriers to treatment completion

6.3.3.1.1 Clinical issues

- **Delay in management of side-effects**

This study identified that delay in the management of side-effects of the anti-TB drugs were barriers to treatment completion. Patients could quit the drugs and discontinue their treatment before completion, provided quick management of side-effects is not in place.

In line with this, a study aimed to assess adverse reactions of second-line TB drugs in patients treated for DR-TB in Egypt noted that it is essential to manage adverse events timeously and aggressively to prevent the resultant permanent morbidity and mortality and patient non-adherence. Otherwise, without prompt intervention, this could lead to unsuccessful treatment completion and unfavourable treatment outcomes (Tag El Din et al 2015:948).

- **Comorbidity**

This study identified that most of the HCPs who participated in this study mentioned that comorbidities like HIV, diabetes, malnutrition, chronic illnesses like renal disease

and lung disease greatly complicate treatment. Equally, frustration due to the high pill burden and increased occurrence of adverse events associated with comorbidities reduce the success of treatment completion.

This finding resonates with findings from many studies across the world. A 2017 study by Girum et al (2017:335) assessing the survival status and treatment outcome of DR-TB treatment in two TICs in Southern Ethiopia, found that the hazard rate of death was 4.3 times higher among patients with comorbidities than patients without comorbidities. In another quantitative and qualitative study by Sanchez-Padilla et al (2014:164) to identify factors related to default from DR-TB treatment in Yerevan, Armenia, reported that comorbidities were one of the reasons for not returning for treatment. In the same vein, Leveri et al (2019:2), Baluku et al (2021:2), McNally et al (2019:2), Charyeva et al (2019:2) and Dlodlo et al (2019:11) noted that comorbidities like diabetes and HIV were the predictors of unsuccessful treatment outcomes.

As shown in the quantitative results, HIV and diabetes constitute the majority of the comorbidities of the study patients. 117 (68.02%) of the patients have had HIV, while 39 (22.67%) have had diabetes as a comorbid condition at the beginning of their therapy. Also in the current study, not having comorbidity (AOR=2.06, 95%CI: 1.06-4.00) was significantly associated with treatment completion, and patients with comorbidity were less likely to complete treatment compared to their counter parts.

- **Complicated treatment**

From the in-depth interviews, one of the barriers for successful treatment completion of DR-TB was that treatment of DR-TB is a complicated one, compared to that of drug susceptible TB. The participants mentioned that the treatment is given for long times and not as effective as the first line drugs and poses the greater possibility of failure. A study conducted in Tanzania also indicated that DR-TB treatment is complicated, requires long duration, and causes several adverse events, and it is associated with unsuccessful treatment completion compared to drug susceptible treatment (Leveri et al 2019:2). Likewise, another study conducted in Georgia showed that DR-TB treatment compared to the drug susceptible one, is more complex, less effective, and toxic and takes long duration for up to two years (Buziashvili et al 2019:1005). Furthermore, studies conducted in Ethiopia observed that due to less effectiveness

and more side-effects and longer duration of DR-TB treatment compared to drug susceptible regimen, treatment outcomes for the former are poorer as well compared to the drug susceptible regimen (Molie et al 2019:2; Baye et al 2018:1).

This finding is also supported by studies conducted by Law et al (2019:2) and McNally et al (2019:2) where they concluded that treatment of DR-TB with second line treatment is more toxic, less effective and needs longer duration than treatment of drug susceptible tuberculosis. It was also stated that treatment non-completion and interruption are significantly higher in the treatment of DR-TB.

- **Prognosis**

This study demonstrated that prognosis of DR-TB is more fatal than susceptible TB. As some of the health providers informed, DR-TB is highly fatal and the prognosis is not as susceptible TB where some patients survive and some die. In addition, as DR-TB patients are not usually diagnosed timeously and come after multiple first line treatment courses. This creates suitable lodging environment for the bacteria and cavities, which can make the treatment difficult. Further, repeated attack of the lung results in fibrosis [scarring] difficult for the drugs to penetrate the scar tissue and cure challenging.

As indicated in the quantitative strand, only 48 (9.86%) patients were new and had no TB treatment history, while the rest 439 (90.14%) patients had treatment history of TB. In addition, from a total of 242 patients having X-ray examinations, 33 (13.64%) had bilateral cavities, while 199 (82.23%) had fibrosis. These coincide with bad prognostic factors generated in the in-depth interview with the experts.

It has been indicated, in a study conducted in Uganda to determine the treatment outcomes of DR-TB patients with poor prognostic indicators, that cavitary disease and previous exposure to second line drugs are predictors of poor treatment outcomes (Baluku et al 2021:2). Similarly, in other studies by Molie et al (2019:2); Leveri et al (2019:2) and Tok, Liew, Wong, Razali, Loganathan, Chinna, Ismail and Kadir (2020:6-8) it has been shown that lung cavitation at baseline chest X-ray and history of previous TB treatment were factors associated with unfavourable treatment outcomes. Likewise, it was indicated in a study conducted in Estonia that previous TB treatment

had significant association with poor treatment outcomes in DR-TB (Baye et al 2018:1).

- **Delay in diagnosis**

In one study conducted in Peru, Mookherji and Algria-Flores (2018:8), noted that provided the complexity of diagnosis of DR-TB, delays in diagnosis are a common phenomenon despite its pivotal role for successful management of the disease. A study conducted in Tanzania by Mpagama, Ezekiel, Mbelele, Chongolo, Kibiki, de Guex and Heysell (2020:1-2) the researchers similarly stated that a number of factors signal there is a significant delay in the process of diagnosis of DR-TB including a large proportion of MDR-TB patients with previous history of multiple episodes of first line treatment regimen reflecting prior missed opportunities for diagnosis. Similarly in the quantitative section of the current study, 439 (90.14%) patients had treatment histories of TB which is even higher than that of 70% in the Tanzanian study (Mpagama et al 2020:2), signalling missed opportunities and delay of diagnosis.

Poor knowledge amongst health care providers, shortage of rapid molecular tests and unreliable specimen transportation and referral pathways were the major contributors to a delay in diagnosis (Mpagama et al 2020:3). It was also indicated in a systematic review of qualitative literature by De Vries, Cremers, Heuvelings, Greve, Visser, Bélard, Janssen, Spijker, Shaw, Hill, Zumla, van der Werf, Sandgren and Grobusch (2017:e139), that institutional barriers including inadequate diagnostics and infrastructure in the health system, wrong diagnosis and shortage of training of professionals contribute to delays in diagnosis.

Many studies across the world support the notion that delay in diagnosis of DR-TB is one of the factors for unfavourable treatment outcomes. In line with this, a study conducted in Zimbabwe by Matambo, Takarinda, Thekkur, Sandy, Mharakurwa, Makoni, Ncube, Charambira, Zishiri, Ngwenya, Nyathi, Chiteka, Chikaka and Mutero-Munyati (2020:3), and another study conducted in Myanmar by Htun, Khaing, Aung, Yin, Myint, Aung, Soonthornworasiri, Silachamroon, Kasetjaroen and Kaewkungwal (2018:3), together with a study in Armenia by Khachatryan, Grigoryan, Dadu, Kumar, Akopyan, Dumchev, Harutyunyan and Matteelli (2021:2) noted that delay in the process of diagnosis and initiation of treatment may have considerable impact on

disease progression and prognosis finally contributing to unsuccessful treatment outcomes.

- **Badly affected lung (advanced disease)**

This study established that patients with DR-TB generally come with badly affected and deteriorating lungs with advanced and extensive lesions. This makes treatment and cure difficult, becoming a major barrier to successful treatment completion. In a study conducted in Egypt, it was found that extensive lung lesion is a significant predictor of an unsuccessful outcome. It has also been noted that extension of destruction of the lung tissue was a risk factor for poor treatment outcomes owing to its association with a poor bacteriologic response, as documented previously in many studies (Gadallah et al 2016:1000,1002).

- **Surgical management**

It is known that thoracic surgery is one of the interventions recommended for managing patients with DR-TB who do not respond to anti-TB drugs as well as when construction of effective regimen is compromised (Tiberi et al 2019:6; Lange et al 2019:655). Moreover, surgery has a role of alleviating serious complications and clearing the source of infection and increasing chances of effective medical treatment (Lange et al 2019:655). Furthermore, a number of studies confirm that surgical intervention is significantly associated with successful treatment outcomes (Leveri et al 2019:2; Lange et al 2019:655; Tobón, Rueda, Cáceres, Mejía, Zapata, Montes, Ospina, Fadul, Paniagua & Robledo 2020:622).

This study identified that the services of surgical management for patients with DR-TB has been generally weak in the country and patients with DR-TB have not been getting operations, timeously. In addition, there has been no ICU service for DR-TB patients, which is a lifesaving service. Absence or unavailability of surgical and intensive care services create a barrier to successful treatment completion for patients with DR-TB.

6.3.3.1.2 Drug-related factors

- **Side-effects**

As established in the quantitative section of this study, adverse events were significantly associated with decreased chances of treatment completion. The results of in-depth interview with health care providers (qualitative results) corroborated the

quantitative results. Side-effects of the second-line anti-TB drugs were cited as a barrier to successful treatment completion.

The second line anti-TB drugs were reported to bring many adverse events which potentially affect treatment adherence of patients. The study participants also noted that if the side-effects persist for long, occur repeatedly, and necessitate hospitalization, the patients prefer to quit their therapy. In addition, serious side-effects are one of the reasons for patients to interrupt their medication, disappear from follow-up and default from treatment.

Many studies established the fact that adverse events of second line anti-TB drugs are one of the factors associated with unsuccessful treatment completion. Jakasania et al (2020:1) stated that while on DR-TB treatment, adverse events are one of the leading causes of unsuccessful treatment outcomes among patients. In the qualitative study by Shringarpure et al (2016:4), adverse events were pointed out as a major barrier to adherence in the long and difficult journey of DR-TB treatment. Likewise, McNally et al (2019:2) described that medication side-effects are barriers to optimal outcomes. Furthermore, Sanchez-Padilla et al (2014:162,164) in the analysis of both quantitative and qualitative results, reported side-effects as one of the main reasons for defaulting from treatment.

In study set out to analyse ADRs and treatment outcome of DR-TB, Dela et al (2017:524-525) explained that ADRs associated with second line drugs, resulting in dropouts, insufficient treatment, and were significantly associated with non-treatment adherence and defaulter outcome. Similarly, Bogale et al (2021:1344) in their study aimed at determining the unfavourable treatment outcome and its predictors among patients with DR-TB in Southern Ethiopia DR-TB treatment centres emphasised that the presence of drug adverse events were significantly associated with unfavourable treatment outcomes. Furthermore, a study conducted by Gualano et al (2019:2) in Italy to describe the frequency and type of adverse drug reactions in a cohort of DR-TB patients and their potential impact on treatment outcome revealed that adverse events represent a significant barrier to treatment completion and could inversely affect outcomes.

- **Long treatment duration**

This sub-category, long treatment duration, emerged from the HCPs in-depth interview as one of the factors raised to be barriers for treatment completion. Patients on second line anti-TB regimen may get tired and bored over time and interrupt the medication. As the time passes, since most of the patients quit their jobs to take the drugs, it poses stress on living and they may also interrupt their treatment finding work to support themselves.

Similar findings were identified in studies conducted locally and globally. Eshetie, Gizachew, Alebel and van Soolingen (2018a:2-3), Molie et al (2019:2), Eshetie et al (2018b:2,8) and Baye et al (2018:1) argue that long treatment duration could compromise treatment adherence which remains a significant challenge in achieving successful treatment outcomes in Ethiopia. In the same way, a qualitative study conducted in India to understand patients' and providers' perspectives of reasons for lost-to-follow-up, pointed that long duration of treatment was one of major barriers to adherence (Shringarpure et al 2016:4).

- **High pill burden**

This study illuminates that high pill burden was considered the primary barrier to treatment completion. In their interview the health care providers affirmed high pill burden is the primary reason patients attribute for their treatment interruption. This finding resonates with a qualitative study in India to understand patients' and providers' perspectives on reasons for lost-to-follow-up that reported pill burden as one of the major barriers to treatment adherence and stay in care (Shringarpure et al 2016:1,4). Similarly, it was also reported in a study done in Ethiopia that pill burden is one of the significant barriers of treatment adherence. So, treatment non-adherence is one of the risks for treatment failure and occurrence of amplified resistance which could lead to poor treatment outcomes (Tola, Garmaroudi, Shojaeizadeh, Tola, Yekaninejad, Ejeta, Kebede & Kassa 2017:448,455).

- **Fear of injection**

Daily injection, like pill burden, was also reported as a major barrier to treatment adherence (Shringarpure et al 2016:4). Additionally, it has been reported that injectables often times cause adverse events which may compel patients to interrupt treatment (Jakasania et al 2020:2; Khachatryan et al 2021:5). Similarly, in the present

study, fear of injection was also considered to be one of the barriers to treatment completion by study participant health workers. Painful injection sites and higher chances of adverse events associated with injectable anti-TB medications significantly cause boredom and frustration in patients resulting in the interruption of therapy.

- **Effectiveness**

Researchers Law et al (2019:2), Ahmad et al (2018:1), Molie et al (2019:2), Baye et al (2018:1), Buziashvili et al (2019:1005), Safaev et al (2021:1) and Girum et al (2017:332) emphasized that treatment of DR-TB, in contrast to drug-sensitive tuberculosis, is more costly, toxic, less effective, more complex and takes a longer time.

Consequently, the odds of treatment non-completion is considerably higher and associated with unsuccessful outcomes with second line DR-TB treatment compared to non-DR-TB treatment (Leveri et al 2019:2; Bhering et al 2020:62-63; McNally, de Wildt, Meza & Wiskin 2019:2). This idea was also echoed in the in-depth interviews with the expert health care providers. Effectiveness of second line anti-TB drugs are not as recognised as that of first line anti-TB drugs. Second line drugs are considered less potent and suboptimal. Hence, successful treatment completion may not be realized at the end.

6.3.3.1.3 Nature of the disease

- **Extensive resistance**

The present study revealed that the nature of DR-TB disease is quite different from the drug susceptible TB. In DR-TB characteristic of the bacterium is resistance to first line drugs and sometimes with extensive resistance. Hence, the disease results from aggressive type of bacteria, treatment is also hard with available medicines. As a result unfavourable treatment outcomes may occur eventually. This finding is supported by recent studies where it has been indicated that extensive drug resistance is one of the predictors of unsuccessful treatment outcomes (Leveri et al 2019:2; Baluku et al 2021:2; Khachatryan et al 2021:5).

6.3.3.1.4 Patient factors

- **False sense of cure**

It has been noted in this study that false sense of cure, by patients who spent a couple of months on treatment, to be one of the reasons for treatment interruption. At the beginning of treatment patients were quite sick. But after they are put on treatment for a few months and the bacteria load decreases, they feel symptomatic resolution and think they are cured. In such situations, they may interrupt the treatment, despite the treatment should continue for prescribed duration.

The results of qualitative studies done in other places also affirm the situation. A study conducted among patients to assess reasons for defaulting from drug-resistant tuberculosis treatment reported that feeling better or cured was one of themes in qualitative findings in both individual patient interview and FGD with programme staffs. It was noted that patients did not think they needed the treatment any longer after they felt better or cured only after taking a few months of therapy (Sanchez-Padilla et al 2014:162,165). And also the study conducted to understand patients' and providers' perspectives on reasons for LFU in Gujarat reported that patients were prone to quit treatment upon feeling resolution of symptoms and improvement of physical signs (Shringarpure et al 2016:6,9).

- **Addiction**

In this study it was revealed that addiction was one the barriers to treatment completion of patients on DR-TB therapy. It was pointed that substance abuse majorly affects treatment adherence and causes treatment interruption. Furthermore, patients suffering from addition, upon improvement of symptoms, tend to return to their peer groups to practice their addiction soon and not abide by the treatment supervision by health providers. In the quantitative section it was presented that 55 (11.29%) of the study patients has history of using non-prescription drugs including substances like khat and cannabis, (see Figure 4.6). In the in-depth interview with HCPs, it was also noted that there are patients with different kinds of addiction, those who take alcohol, smokers and khat chewers.

Different scholars have noted that addiction restricts smooth treatment completion by affecting adherence and initiating lost-to-follow-up. It is reported that addiction to khat, tobacco, alcohol or cannabis is common in patients, compromising their capacity of

adhere to the prescribed regimen till end of therapy. In addition, substance abuse was associated with defaulting from treatment and one of the reasons for not returning for treatment by those already defaulted from therapy (Shringarpure et al 2016:7; Sanchez-Padilla et al 2014:164-165).

Matambo et al (2020:2-3) asserted that substance use has been found to have association with poor treatment outcomes. Moreover, the evidence from meta-analysis study from 22 countries data set of DR-TB treatment cohorts identified that substance misuse was one of the factors being associated with lost-to-follow-up (Walker et al 2019:2). It was shown in the quantitative findings that patients in the registration group after lost-to-follow-up at the start of treatment were less likely to successfully complete treatment (AOR= 0.05, 95%CI: 0.004-0.54) compared to other registration groups in this study.

- **Patient preference**

The study has also revealed that one of the barriers to DR-TB treatment completion was patients' personal preference of traditional medicines and religious activities like holly water and spiritual things. This finding coincides with a study by McNally et al (2019:6) aimed to explore the experiences and perceptions of DR-TB patients and health care providers in Loreto in the Peruvian Amazon in order to identify barriers and facilitators to achieving optimal outcomes and to help inform future management strategies, in which they reported that distrust of medical advice and pharmaceutical drugs and trust of natural medicines are prevalent which is attributed to strong cultural beliefs in natural medicine and traditional healers.

It was indicated that faith in traditional healers and movement of patients to traditional healers contributes towards lost-to-follow-up. Furthermore, it was reported that while on DR-TB treatment, patients reported visiting their traditional healer receiving alternative treatment, which resulted in some of the cases discontinuation of the standard treatment. In the same vein, faith of patients in the practices of traditional healing was identified as significant barrier to conventional treatment and care (Shringarpure et al 2016:1, 7). In addition, Leveri et al (2019:2) also reported use of traditional medicine was also associated with unsuccessful treatment outcome.

6.3.3.1.5 Health system related

- **Accessibility**

In the current study, accessibility was found to be one of the underlying reasons for treatment interruption. It was also indicated most of health facilities which give DR-TB service were located in cities and zonal towns and most of inpatient admission services are centralised making accessibility difficult for patients located in the country side. This finding was in line with studies conducted by McNally et al (2019:2), Jakasania et al (2020:8) and Benbaba, Isaakidis, Das, Jadhav, Reid and Furin (2015:6) that reported accessibility of care to be one of the important factors for adherence to treatment and better compliance. In addition, the WHO recommends that health systems should endeavour to guarantee accessible DR-TB treatment service corresponding to need of patients and also reiterates the need of addressing significant barriers to accessing DR-TB care like distance (WHO 2019a:31, 55).

6.3.3.1.6 Socio-economic factors

- **Economic problems**

In this study it was revealed that economic problems are an obstacle for achieving successful treatment completion. This finding is alongside with a study done in Ethiopia that reported economic problems are associated with as well as independently predict treatment non-adherence. It was also noted that patients who have financial problems suffer extra transportation costs and living costs in the long treatment duration (Tola et al 2017:448, 455).

It was also described that the disease adds a financial burden to the patients. In the first place, patients will sustain reduced physical ability to work and as a consequence cannot stay in their jobs or unable to continue employment, which in turn, leads to reduced or loss of their income. Second, there are incurred costs due to the treatment process, for instance for transportation, food and accommodation. In general, the financial hardship negatively affects treatment adherence and impacts treatment completion. As McNally et al (2019:2) and Baral, Aryal, Bhattrai, King and Newell (2014:1-2) reported, poor adherence is one of the barriers to successful treatment outcomes. Likewise, in the quantitative section, it was shown that only 183 (37.58%)

patients were employed indicating possible financial hardship in most of the patients. Employment was reported to have association with treatment completion.

- **Stigma**

In a recent study done in Portugal, stigma was mentioned to be one of the most common barriers in TB control and prevention activities (Bhering et al 2020:68). Similarly, in another study, it was reported that high degree of stigma exist in high burden countries during all aspects of the treatment process starting from diagnosis to post treatment. Patients constantly face stigma from their social network including friends, family and health workers (Kumar 2016:S129). In a qualitative study in Kolkata India, people believed that DR-TB is an incurable disease and there were anecdotes of avoidance of patients by their neighbours and friends (Kundu et al 2021:395). Furthermore, in mixed methods study in India, it was reported that going to the clinic for directly-observed therapy (DOT) was difficult for patients, since they were experiencing stigma for being known as DR-TB patient (Benbaba et al 2015:9). In the qualitative study done in Ukraine, it was reported that every interviewed patient did not have interest to be seen in TB clinic by their friends (Charyeva et al 2019:6).

In the current study, stigma was mentioned by the study participants as one of the causes of treatment interruption. A number of studies highlight that stigma hinders treatment adherence and leads to lost-to-follow-up. A systematic review of qualitative literature done by De Vries et al (2017:e136) reported that stigma is a hindrance to treatment adherence. In the same way, it was indicated that fear of stigma is one of factors associated with TB treatment non-adherence (Tola et al 2017:448). Again, in recent qualitative study in India, it was stated that stigma reduces treatment adherence (Kundu et al 2021:395). In addition, in another qualitative study in India, Shringarpure et al (2016:8) concluded that stigma was a discouraging factor for DR-TB patients to adhere to their treatment and on the other hand, an encouraging factor leading to lost-to-follow-up.

- **Social problems**

Study conducted in Nepal by Baral et al (2014:6) stated that DR-TB treatment causes social problems. Social problems comprised loosing social support which results from relocation from their social network, loneliness and stigma. Lack of social support, isolation and helplessness and stigma are adding to psychological problems in

tuberculosis patients (Kundu et al 2021:395). Additionally, it was reported that during DR-TB treatment, psychosocial problems exacerbate psychiatric complications and subsequently negatively influences adherence of patients to therapy (Dela et al 2017:525). In general, lack of social support is associated with TB treatment non-adherence (Tola et al 2017:448).

Qualitative study done by Shringarpure et al (2016:1) revealed that social problems are major barriers to treatment adherence and continuous engagement in care. In addition, it was reported that social problems trigger lost-to-follow-up (Shringarpure et al 2016:6). Likewise, in study done in Italy, unemployment and homelessness, which are social problems, were more prevalent in LTFU group compared to the cured one (Gualano et al 2019:7). In summary, the socioeconomic impact of DR-TB treatment including extra costs for accommodation and food, loss of employment, loss of family and social network support, isolation and boredom negatively influences treatment adherence and successful outcomes (McNally et al 2019:13).

Finally, it was highlighted that it is worth addressing social problems for successful treatment completion of DR-TB treatment. Social support, according to global literature, is instrumental in improving successful DR-TB treatment outcomes by improving treatment adherence and reducing rates of lost-to-follow-up. In systematic review of studies, it was also reported that cohorts that received any form of psychosocial or material support resulted in lower lost-to-follow-up rates than those received standard care, during DR-TB treatment (Charyeva et al 2019:2).

- **Malnutrition**

TB as one of chronic diseases, is known to cause secondary malnutrition. In addition, second line anti-TB drugs also have adverse effects of gastrointestinal (GI) disturbances like nausea and vomiting which further aggravate occurrence of malnutrition. Furthermore, it was reported that most of the DR-TB patients had financial problems and getting adequate nutrition is impossible, leading to poor treatment outcomes (Girum et al 2017:335; Htun et al 2018:15; McNally et al 2019:13). Accordingly, many studies have shown the presence of significant association between having severe malnutrition and poor treatment outcomes (Meressa et al 2015:1183; Leveri et al 2019:5). Similarly, in the quantitative section of this study, it was shown that 315 (64.68%) of the study patients had a BMI of less than 18.5

(underweight) (see Figure 4.8). And it was also identified that BMI has some association with treatment completion.

6.3.3.1.7 Programmatic and provider-related

This study revealed that positive patient provider relationship with friendly approach and empathic concerns are necessary to develop trust and good relationships that can result in good treatment outcomes. Lack of ethical and respectful treatment was indicated to be discouraging for patients to stay on their therapy till completion.

A trustful relationship between health care providers and patients is important to establish good communication, to gain patients' trust and confidence in the treatment process (De Vries et al 2017:e137; McNally et al 2019:11). Similarly, Bhering et al (2020:62) noted that a relationship based on trust with emotional support produces improved adherence and successful treatment completion. On the contrary, it was reported that relationships based on hierarchy, where patients are uncomfortable to express their researvations and complaints negatively affected treatment adherence (McNally et al 2019:2). Likewise, in a qualitative study to understand patients' and providers' perspectives on reasons for lost-to-follow-up in India reported that, on patients perspective, engagement in unfriendly relationship with health providers and feelings of not getting information about one's medical reports and health status progress, resulted in treatment interruption and lost-to-follow-up (Shringarpure et al (2016:6-7).

6.3.3.2 Challenges for patient follow-up

6.3.3.2.1 Weak support

- **Social support**

This study has shown that weak social support was one challenging area which has not been well addressed during the treatment. Moreover, most of the patients were of low socioeconomic status. However, the amount of support rendered to patients during treatment follow-up has been meagre. Thus, the unaddressed social support make treatment difficult for patients and indirectly affects treatment completion.

In the previous theme, the study showed that DR-TB treatment causes social problems. And social problems are major barriers to treatment adherence and continuous engagement in care. It has also been highlighted that it is worth addressing

social problems by providing systematic and continuous social support for successful treatment completion (Kundu et al 2021:395; Shringarpure et al 2016:1; Charyeva et al 2019: 2; WHO 2019a:10, 48, 54).

- **Programme support**

The present study has highlighted the existence of weak programme support from national to the facility level especially with respect to human resource capacity to properly give basic mentorship support to treatment follow-up centres. And in addition, the need to realize improvement of clinical monitoring quality in the service ladder. This finding is supported by different authors across the globe.

Lange et al (2019:653) reported that limited capacity is the reality of DR-TB treatment programmes in resource poor settings. Likewise, Wai, Shewade, Kyaw, Thein, Si Thu, Kyaw, Aye, Phyo, Maung, Soe and Aung (2018:12) pointed out that a lack of trained human resource that can provide timeous care and proper service during follow-up periods. In fact, Jakasania et al (2020:2) explained that the main focus of programmes in developing countries is on diagnosis and initiation of therapy. But, less attention was given to patient follow-up activities including clinical and laboratory monitoring of patients to identify and manage adverse events (AEs) early in the treatment process.

6.3.3.2.2 Supply shortage

- **Ancillary drug supply**

This study identified that there has been a chronic shortage of life saving ancillary drugs used to treat adverse events of anti-TB drugs. In addition, there has been severe interruption of supply of ancillary drugs in the system. Some are not available in the hospitals most of the times. This puts the management of adverse events secondary to anti-TB drugs into a difficult spot. If adverse events are not managed timeously because of lack of ancillary drugs, the patient may die and/or interrupt the treatment, eventually, affecting treatment completion.

Timeous administration of ancillary medication is crucial in preventing and treating adverse events associated with anti-TB drugs (Merid et al 2019:8). Furthermore, Tag El Din et al (2015:948) emphasised that failing to manage adverse events timeously and aggressively could result in further morbidity and mortality, reduced patient compliance and non-adherence to therapy. WHO (2021:114) urges that all DR-TB

patients should have access to appropriate ancillary medications. Thus, health facilities should have adequate and regular supply of ancillary drugs in order to achieve successful outcomes in the treatment of tuberculosis disease especially drug-resistant disease (Dlodlo et al 2019:78).

- **Investigations**

Investigations used to monitor treatment progress and occurrence of adverse events were found to be inadequate during follow-ups. There was lack of equipment, interruption of laboratory service and shortages in the laboratory supply system. There was also unavailability of trained human resource to interpret results. As a result, patient monitoring and care might have been compromised and could result in unsuccessful treatment outcomes. The quantitative section of this study supports the shortage of investigations, in that baseline audiometry was not done for the vast majority of the patients i.e. 480 (98.56%) as shown in Figure 4.18.

Baseline and routine laboratory monitoring tests are required for patients on treatment with second-line anti-TB drugs (WHO 2020a:39). Moreover, laboratory tests can detect occult adverse events that cannot be noted by the patient or health care providers (HCPs) (Tag El Din et al 2015:940; Lange et al 2019:652). At the same time, in resource limited settings, where availability of regular supply of monitoring tests are inadequate, identification and management of adverse events cannot be done as required (Perumal et al 2018:537). Studies show that in Ethiopia, there are periodic deficiencies of constant supplies of laboratory reagents in the public sector (Shibeshi et al 2019:7; Meressa et al 2015:1186).

6.3.3.2.3 Service delivery

- **Delay of culture results**

Culture and DST are instrumental to monitor the response of patients to treatment and to detect the occurrence of additional resistance to the second-line anti-TB drugs during treatment. In addition, it is recommended to perform sputum cultures, monthly (WHO 2021a:114; WHO 2019a:41). On the other hand, delayed sample transport or delayed communication of results due to a poorly functioning sample transport system or specimen referral networks (path ways) will attribute to delayed clinical decision making during DR-TB treatment (Mpagama et al 2020:3).

- **Quality**

Different scholars locally and globally support the decentralization of DR-TB services. Alene et al (2017:360) and Florman et al (2020:1) state that health services decentralization enables patients living far from centralized centres to access and stay on DR-TB treatment. Likewise, researchers Evans, Sineke, Schnippel, Berhanu, Govathson, Black, Long and Rosen (2018:2), further explained that decentralization of services renders advantages of cost reduction and outpatient treatments to patients on DR-TB therapy. On the other hand, Lange et al (2019:653) pointed out that there is a shortage of experienced as well as well-trained providers in decentralized centres. Thus, delivering a comprehensive, quality medical care may be in question.

6.3.4 Experience of previously treated patients on treatment completion

6.3.4.1 Perceived barriers to treatment completion

As explained in chapter three, perceived barriers, as a concept of HBM, refer to one's belief in the tangible and psychological costs of the advised behaviours. There could be several barriers that affect people's decision to take particular actions. Perceived barriers to health actions include phobic reactions, physical as well as psychological barriers, accessibility factors, personal characteristics, possible blocks or hindrances to engage in preventive behaviours, including such factors as cost, inconveniences and unpleasantness (Tarkang & Zotor 2015:5).

Perceived barriers also include costs, duration, complexity of the deserved behaviours and accessibility to services that would support taking and maintaining the required actions. It is only when persons realise that they have the capacity to deal with these barriers, that they would be able to take the necessary actions (Tarkang & Zotor 2015:5).

6.3.4.1.1 Drug-related

- **Discomfort due to the drugs**

The FGDs participants described that discomfort of the second line anti-TB medicines have been one of the perceived barriers to treatment completion. They have experienced pain, vomiting and discomfort while taking the drugs. In order not to feel the pain, patients could quit the medication.

Discomfort due to the second line anti-TB drugs are common and at times may hinder successful treatment completion. It has been revealed, by McNally et al (2019:11) that only the sight of the pills was enough to trigger nausea and vomiting. Moreover, it is explained that the nausea which appear right after swallowing of the tablets was incapacitating for patients (Benbaba et al 2015:10). Consequently, it has been reported, in a study conducted in Ethiopia, that discomfort due to nausea and vomiting, and pain of muscles and joints forced patients to interrupt and quit their treatment before completion (Woldeyohannes et al 2019:7). Again, according to Leveri et al (2019:2), severe cases of vomiting were reported to be one of the predictors of poor treatment outcome (loss-to-follow-up).

- **Adverse events**

Another drug-related perceived barrier to treatment completion explained by FGDs participants are adverse events that affect smooth treatment adherence and completion. In the same vein, adverse events were reported to be as one of the barriers of treatment completion in the in-depth interview results with health care providers. Moreover, these qualitative findings confirm the quantitative findings that reported significant association of not having adverse events with treatment completion.

A number of studies have indicated that treatment of DR-TB is challenging and complicated, takes long duration, and is associated with frequent and several adverse events (Leveri et al 2019:2; Jakasania et al 2020:2; Baye et al 2018:1; Tiberi et al 2019:1; Lange et al 2019:645, 652; Bhering et al 2020:68; Gualano et al 2019:1).

Many studies established the fact that adverse events of second line anti-TB drugs are one of the factors associated with unsuccessful treatment completion. Jakasania et al (2020:1) stated that while on DR-TB treatment, adverse events are one of the leading causes of unsuccessful treatment outcomes among patients. In addition, in the qualitative study by Shringarpure et al (2016:4), adverse events were pointed out as one of a major barriers to adherence in the long and difficult journey of DR-TB treatment. Likewise, McNally et al (2019:2) described that medication side-effects are one of the barriers to optimal outcomes. Furthermore, Sanchez-Padilla et al (2014:162,164) in the analysis of both quantitative and qualitative results, side-effects were reported as one of the main reasons for defaulting from treatment.

- **Pill burden and treatment duration**

It was revealed in the current study that the high pill burden and the long treatment duration were frustrating, boring, bringing loss of hope in patients and may result in quitting therapy. A number of studies conducted locally and globally confirm the situation. Eshetie et al (2018a:2-3), Molie et al (2019:2), Eshetie et al (2018b:2, 8) and Baye et al (2018:1) argue that long treatment duration could compromise treatment adherence which remains a significant challenge in achieving successful treatment outcomes in Ethiopia. Similarly, it was also reported that one of the themes identified for reasons for lost-to-follow-up is struggle with prolonged treatment (Shringarpure et al 2016:4).

In qualitative study to understand patients' and providers' perspectives on reasons for lost-to-follow-up in India, it was reported that pill burden is one of the major barriers to treatment adherence and stay in the care (Shringarpure et al 2016:1). Similarly, a study done in Myanmar by Htun et al mentioned that high pill burden and long treatment duration were the concerns of patients during treatment (Htun et al 2018:14).

6.3.4.1.2 Clinical issues

- **Consulting after long illness**

The participants explained that, coming after long illness (after repeated first line treatments, after attempting treatment by traditional healers) when the disease becomes serious causing harm to their lungs, might hinder successful treatment completion. In line with this, the in-depth interviews with health care providers indicated that DR-TB patients are not usually diagnosed timeously and come after multiple first line treatment courses. This creates suitable lodging environment for the bacteria and cavities which can make the treatment difficult. Further, repeated attack of the lung results in fibrosis [scarring] which makes it difficult for the drugs to penetrate the scar tissue and make a cure difficult (Baluku et al 2021:2; Molie et al 2019:2; Leveri et al 2019:2; Tok et al 2020:6-8).

This situation could explain the findings obtained from the quantitative strand of the study. The majority of patients, 439 (90.14%) had treatment histories of TB and come after long illness before diagnosis of DR-TB. In addition, from a total of 242 patients having X-ray examinations, 33 (13.64%) had bilateral cavities, while 199 (82.23%) had fibrosis, indicating that patients with DR-TB come after long illness often developing

potential structural and parenchymal damage that could be an obstacle for successful treatment completion.

- **Delay in diagnosis**

Like FGD participants experience, in-depth interviews with experts also echoed the same idea of delay in diagnosis of DR-TB as one of the factors related to unsuccessful treatment outcomes. Similar findings were identified in studies conducted in Zimbabwe by Matambo et al (2020:3), in Myanmar by Htun et al (2018:3), as well as in Armenia by Khachatryan et al (2021:2), where it was noted that delay in the process of diagnosis and initiation of treatment may have considerable impact on disease progression and prognosis, finally contributing to unsuccessful treatment outcomes.

6.3.4.1.3 Stigma and discrimination

- **Community and healthcare provider stigma**

In the current study, both in FGD with patients and in-depth interviews with HCPs, stigma was mentioned to be one of the causes of treatment interruption. A number of studies highlighted that stigma hinders treatment adherence and leads to lost-to-follow-up (De Vries et al 2017:e136; Tola et al 2017: 448; Kundu et al 2021:395; Shringarpure et al 2016:8). In a recent Portuguese study stigma was mentioned to be one of the most common barriers in TB control and prevention activities (Bhering et al 2020:68). Similarly, it was also noted that patients constantly face stigma from their social network including friends, family and health workers (Kumar 2016:S129).

In line with this, a qualitative study conducted in Port Harcourt, Nigeria, also showed that patients were treated differently by friends and family members to the extent that they were forbidden from sharing cutlery with other family members and were systematically ostracised by the the community. In addition, health care providers rarely enter DR-TB wards and have a conversation with patients for fear of infection. Hence, such interactions hindered proper service provision and contributed to poor treatment outcomes in a number of cases (Bieh, Weigel & Smith 2017:3-4).

6.3.4.1.4 Economic challenge

The experience of study participant patients of the focus groups revealed the economic burdens and financial strains they faced while on treatment forcing them to the extent of discontinuing their treatment. Furthermore, patients on the DR-TB treatment lose their jobs because of their illnesses and side effects from the drugs. They also do not have any source of income to buy at least the nutritious food available locally and cannot support their dependents at home. In addition, they cannot rent a house to stay near the treatment centre when away from home and also cannot cover transport fees. These economic challenges make continuing the treatment difficult for them.

This finding is supported by the findings from the in-depth interviews with HCPs, where it was revealed that economic problems are an obstacle for achieving successful treatment completion. It was also described that the disease adds a financial burden to the patients. In the first place, patients will sustain reduced physical ability to work and as a consequence cannot stay in their jobs or unable to continue employment, which in turn, leads to reduced or loss of their income. Second, there are incurred costs due to the treatment process, for instance for transportation, food and accommodation. In general, the financial hardship negatively affects treatment adherence and adversely impacts treatment completion.

This finding is supported by a study done in Ethiopia that reported economic problems are associated with as well as independently predict treatment non-adherence. It was also noted that patients who have financial problems suffer extra costs incurred to cover transportation and living costs during the long treatment duration (Tola et al 2017:448, 455). In short, as McNally et al (2019:2, 8, 13) and Baral et al (2014:1-2) reported, poor adherence is one of the barriers to successful treatment outcomes.

6.3.4.1.5 Laboratory service related

Baseline and routine monitoring laboratory tests are required for patients on treatment with second-line anti-TB drugs (WHO 2020a:39). Moreover, laboratory tests can detect occult adverse events that cannot be noted by the patient or HCPs (Tag El Din et al 2015:940; Lange et al 2019:652). At the same time, in resource limited settings, where availability of regular supply of monitoring tests is inadequate, identification and management of adverse events cannot be done as required (Perumal et al 2018:537).

Studies show that in Ethiopia, there is a deficiency of constant supply of laboratory reagents in the public sector periodically (Shibeshi et al 2019:7; Meressa et al 2015:1186).

This study also identified that there has been a chronic shortage of life-saving ancillary drugs used to treat adverse events of anti-TB drugs. In addition, there has been severe interruption of supply of ancillary drugs in the system and they are not available in hospitals most of the time. Furthermore, some investigations, which are necessary for the follow-up, were not available. This lack of follow-up tests has an impact. It is difficult to identify side-effects early and to follow patients' conditions in their absence.

6.3.4.1.6 Patient factors

- **False sense of recovery**

As we have noted in the in-depth interview, when patients take medication for a couple of months, the bacteria load will decrease and the symptoms will start to subside. So, patients may develop a false sense of cure and quit their therapy, in spite of the fact that they should continue medication for the prescribed duration. In this regard, the results of qualitative studies done in other places also affirm the situation. It was noted that patients did not think they needed the treatment any longer after they felt better or cured only after taking a few months of therapy (Sanchez-Padilla et al 2014:162,165). Similarly, it was also reported that patients were prone to quit treatment upon feeling resolution of symptoms and improvement of physical signs (Shringarpure et al 2016:6,9).

- **Returning to habits already quitted**

Different scholars have noted that addiction has been the bottle neck for smooth treatment completion by affecting adherence and initiating lost-to-follow-up. It is reported that addiction to khat, tobacco, alcohol or cannabis is common in patients compromising their capacity of adherence to the prescribed regimen till the end of therapy. In addition, it was also indicated that substance abuse was associated with defaulting from treatment and one of the reasons for not returning for treatment by those already defaulted (Shringarpure et al 2016:7; Sanchez-Padilla et al 2014:164-165).

Matambo et al (2020:2-3) connoted that substance use has been found to have association with poor treatment outcomes. Moreover, the evidence from a meta-analysis study from 22 countries data set of DR-TB treatment cohorts identified that substance misuse was one of the factors associated with lost-to-follow-up (Walker et al 2019:2).

6.3.4.1.7 Provider-related factors

A trustful relationship between health care providers and patients is important to establish good communication, to gain patients' trust and confidence in the treatment process (De Vries et al 2017:e137; McNally et al 2019:11). Likewise, Bhering et al (2020:62) noted that a relationship based on trust with emotional support produces improved adherence and successful treatment completion. On the contrary, it was reported that relationships based on hierarchy, negatively affected treatment adherence (McNally et al 2019:2). Moreover, in a qualitative study to understand patients' and providers' perspectives on reasons for lost-to-follow-up in India reported that, from patients' perspectives, engagement in unfriendly relationships with health providers and feeling not getting information about one's medical reports and health status progress, resulted in treatment interruption and lost-to-follow-up (Shringarpure et al (2016:6-7).

6.3.4.2 Challenges for patient follow-up while on the treatment

6.3.4.2.1 Weak patient follow-up

Regular clinical and laboratory follow-up as well as timeous monitoring and management of adverse events are among the basic principles of DR-TB treatment. Sabur et al (2021:6) stipulated that regular patient follow-up and monitoring decrease occurrence of adverse events. In addition, regular patient follow-ups give a chance to educate patients about the use of each medication and possible adverse events. This enables patients to report adverse events during clinical days, allowing successful treatment completion to eventually take place (Gualano et al 2019:10). Likewise, DOT gives patients a chance to communicate daily for any symptoms related to AEs and to express their concerns. It also allows the health care providers to monitor any signs of AEs and identify other needs of patients, thereby consolidating adherence and

continuation of treatment (Lange et al 2019:652; Bhering et al 2020:68). In general, addressing concerns of patients like socioeconomics and closely monitoring of AEs are essential for good treatment adherence and successful treatment completion (Htun et al 2018:16; Buziashvili et al 2019:1009; Shibeshi et al 2019:8).

The current study has provided a deeper insight into the weak patient follow-up practiced during the treatment period. It was revealed that because of weak DOT practice, patients were not strictly followed and unattended while taking their medication, hence, omitting some of their doses. This could bring suboptimal treatment that may result in unsuccessful treatment outcomes. Moreover, it was also explained that due to weak follow-up, any adverse events, including life threatening ones, may get complicated unnoticed and any patient concerns, could remain unaddressed. As a consequence, unfavourable treatment outcomes could surface.

6.3.4.2.2 Service delivery

- **Interruption and quality of food service**

This study highlighted challenges during treatment follow-up. It was mentioned that due to interruption of food supplements and poor quality of food provided at inpatient services, most of the time, patients complained and stopped treatment. In line with this, McNally et al (2019:13) and Florman et al (2020:1) state that proper nutrition is part and parcel of DR-TB care and treatment. Moreover, inadequate nutrition can lead to extended treatment duration or unsuccessful treatment outcome (treatment failure). Similarly, WHO asserts that food may improve treatment outcomes by combating malnutrition and uplifting the immune function of the body (WHO 2019a:52). Hence, it should be the duty of every DR-TB programme to extend uninterrupted and quality supply of nutritious and quality food for patients during treatment.

- **Not giving adequate information**

The first pillar of the End TB Strategy focuses on patient centred care and prevention. Patient centred care is the shared management between a patient and health care providers. Patient centred care reflects shared decision making during treatment processes by considering needs and desires of patients, for instance how and when to take medications. Many studies have reported that this approach results in improved adherence to treatment of chronic illnesses including DR-TB. Patient centred care demands good communication and partnership between the patient and health service

giver. Since, treatment of DR-TB is given for long duration, patients can benefit from patient centred care and treatment. Patients need information regarding their illness and its therapy in order to successfully complete their treatment course (Dlodlo et al 2019:26; Mookherji & Algria-Flores 2018:2).

6.3.4.3 Enablers for treatment completion

6.3.4.3.1 Cues to action

As described in chapter three, the HBM's cues to action are events or experiences, personal, interpersonal or environmental that motivate a person to take action. It requires motivation on the part of the person to have the desire to comply with the prescribed action or treatment, to have concerns about health matters, to be willing to seek and accept health care and to engage in positive health activities (Tarkang & Zotor 2015:5).

- **Caring for each other and support of family and community**

The current study illuminates how caring for each other, family and community support motivate patients in engaging in efforts towards treatment completion. First, it has been revealed that caring for each other motivated them to stick to the orders of the health providers and prescribed treatment. Second, it has been noted that the community support was explained to be a great enabler to continue with their treatment especially for those who did not have family and social support. Third, it has been indicated that family support was overwhelming in keeping them continuing their medication for such long periods.

Community health workers support through daily visits helped reduce losses to follow-up (Law et al 2019:7). Moreover, community support, be it from a family or community health worker, improved the quality of TB management (Mookherji & Algria-Flores 2018:8). Support and encouragement from family and peers helps patients maintain a positive attitude towards their treatment (McNally et al 2019:13). Furthermore, patients met frequently to provide support to each other and to discuss challenges with treatment and support services. For most patients, the most important source of physical and emotional support was their fellow patients (Bieh et al 2017:5).

- **Compassionate care and counselling**

Healthcare provider's sensitivity to their patients suffering and commitment to relieve that suffering was found to be vital in the treatment process. It was described that compassionate care could motivate patients to stick to their treatment. In addition, HCPs counselling was reported as one of the enabling factors for patients to stay on their treatment despite occurrence of problems while on therapy. It was also identified that counselling helped patients to instil hope in times of problems and hopelessness.

In this regard, McNally et al (2019:11-12) suggest that through effective communication and empathy, HCPs can promote a positive attitude in their patients. The resultant trust between them was described as an important enabler to treatment completion. Furthermore, Law et al (2019:7) reported that risk of lost-to-follow-up can be reduced around 70% by giving counselling sessions tailored to the individual patient. Similarly, according to WHO (2019:53) evidence, higher rates of treatment success as well as lower rates of treatment failure and loss to follow-up were observed in patients who had access to psychological support.

6.3.4.3.2 Programme-related

Availability of programme related assets comprising; presence of smooth linkage between TICs and TFCs, having treatment supporter, provision of monthly social supports, getting quick and free services, were found as enablers to patients during treatment process to complete the recommended therapy. First, the presence of good linkage between treatment initiating and follow-up centres benefited patients to follow their treatment without interruption of any services and supplies. Again, having a nurse treatment supporter during treatment made possible home based DOT and injection whereby facilitating smooth treatment process and completion.

Programme based monthly social support, including transport fee and food packages, was found to be helpful for continuous attendance of treatment, especially for those with low socioeconomic status. And also, the study identified that expedited services allowed patients to save time for other activities of daily living and motivated them to adhere to treatment. Receiving free treatment and service as well as reimbursement for outsourced one, was found to reduce economic strain upon the patients and facilitate towards treatment completion.

Different scholars locally and globally support the decentralization of DR-TB services including building the capacity of TFCs and strengthening the linkage with TICs. Alene et al (2017:360) stated that health services decentralization enables patients living far from centralized centres to access and stay on DR-TB treatment. Likewise, researchers Evans et al (2018:2), further explained that decentralization of services renders advantages of cost reduction and outpatient treatments to patients on DR-TB therapy. On the other hand, Lange et al (2019:653) pointed out that there has been a shortage of experienced as well as well-trained providers in a decentralized centres. For this reason, WHO (2019:56) emphasizes the need of staff training and close treatment supervision where decentralized care is provided.

The WHO recommends treatment adherence interventions to ensure successful TB treatment outcomes. Treatment adherence interventions incorporate treatment supervision (DOT by trained treatment supporter), social support such as material support (food, transport fees), and psychological support (counselling) (WHO 2019a:10, 48, 54). The End TB Strategy calls for relieving the catastrophic economic burden faced by TB patients related to direct and indirect costs due to TB and health care. Even when TB services are given free of charge, the burden of income loss and non-medical costs need to be mitigated through social protection measures including social or material support (WHO 2014b:18; WHO 2019a:11, 48).

6.3.4.3.3 Self-efficacy

Self-efficacy, one of the concepts of HBM, refers to the strength of an individual patient's belief in his/her own ability to respond to difficult situations and to deal with any associated obstacles or setbacks. It is individual patient's ability to successfully undertake action (Tarkang & Zotor 2015:5). Besides programme related facilitation towards treatment successfulness, determination of the individual to resist hindering factors throughout the treatment duration was mentioned by the study participants to be an important enabling factor to successful treatment completion. In line with this, McNally et al (2019:7), in their qualitative study aimed to explore the experiences and perceptions of DR-TB health care providers and patients, reported that belief in one's self and a strong determination to heal was helpful in overcoming the challenges faced during the DR-TB treatment.

6.3.4.4 Perceived benefits of treatment completion

As described in chapter three, the HBM was conceptualized around the individual's beliefs and attitudes captured in four constructs representing the perceived threat and net benefits. These constructs are perceived susceptibility and perceived severity that make up perceived threat and perceived benefits and perceived barriers representing the net benefit (Mukumbang et al 2017:2).

Perceived benefits refer to one's beliefs in the efficacy of the advised action to reduce the risk or seriousness of impact. The person needs to believe that by taking a certain action, it will help one to avoid or prevent a problem from occurring. It is this belief that gives a person confidence to take the action because of the expected outcomes. Perceived benefits are beliefs about the effectiveness of recommended health actions (Tarkang & Zotor 2015:5).

This study identified that FGD participant previously treated DR-TB patients have had a firm belief that treatment completion till the end will bring cure and save lives. Because they have had a trust in the treatment, services and care of patients that completing the treatment course could bring about improved health. On the other hand, Alene et al (2017:359) argued that, compliance of patients may decline due to fatigue from unsuccessful first line anti-TB treatment(s) without any perceived benefit. It was suggested in such cases, to improve treatment outcome, early diagnosis and initiation of effective treatment is of paramount importance.

As reported in the quantitative section of this study, the majority of patients 338 (69.40%) had history of failure of first line anti-TB drug treatment; among which 267 (54.82%) had failure of retreatment first line regimen and 71(14.91%) had failure of new first line regimen (see Figure 4.10). For this reason, it is natural to expect declining compliance as a result of fatigue from the repeated first line regimens without any perceived benefits in the study participants. It is important to enhance compliance of patients by initiating effective DR-TB regimens tailored to the individual patients.

6.3.4.5 Perceived severity of the disease

Li et al (2015:910), in their study aimed to explore the relationships among components of the HBM, patients preventive behaviour of TB and patients intention seeking care, explained that cognition of severity and susceptibility of disease plays

an important role whether patients engage in a health related action or not. The awareness of disease severity provides the impetus for the desired action. The perception of severity of a disease was also mentioned to have a direct and positive impact on intention of health care seeking (Li et al 2015:911).

In the present study it was stated that DR-TB was perceived as serious disease. FGD participants mentioned that DR-TB is a serious and difficult disease with a consequence of severe illness as well as fatality. Further, the FGD participants reported that the disease has negative social implications that were difficult to cope with. In the same way, a similar finding was identified in a systematic review of qualitative literature done by De Vries et al (2017:e138) where it was indicated that participants were generally aware of the potential severity of tuberculosis to the extent of fatality.

On the contrary, health care professionals, in the in-depth interviews, indicated that there has been lack of awareness and low knowledge in the community and among patients on the importance of treatment adherence for the whole duration, about the severity of the disease and how fatal it is. In addition, most of the FGD study participants in the present study received awareness of DR-TB at hospitals after they were diagnosed and put on therapy. Hence, it is advisable to alert patients about their disease, including the severity. Educating patients about the seriousness of DR-TB disease is a serious factor that could mitigate treatment interruption (Yang et al 2017:4).

6.3.5 Contrasts and comparisons between the two groups of participants

From the findings of this study, it was clear that both healthcare providers and previously treated patients agreed on some issues related to barriers to treatment completion for patients with DR-TB. Yet on the other hand, there were contrasting perceptions on other issues.

6.3.5.1 Similarities

Both groups of participants agree on clinical matters including the need to consult after long illness, delay in diagnosis, sub-optimal doses that are barriers to treatment completion for patients with DR-TB. On the other hand, healthcare providers mentioned additional clinical barriers to treatment completion from their professional

perspective including comorbidity, prognosis, extensive resistance and weak surgical management in Ethiopia.

Both groups of participants also concurred on drug-related issues. Adverse events, long duration of treatment, high pill burden and discomfort due to the drugs were perceived as the barriers to treatment completion.

Both groups of participants agree on patient related factors revealed to be barriers to successful treatment completion. These include false sense of cure, addiction (returning to habits already quitted), fear of side-effects and personal preferences.

Both groups of participants agree on health system factors seen as barriers to treatment completion. Accessibility problems, bad facility setup (infrastructure) and competency were mentioned by both healthcare professionals and previously treated DR-TB patients affecting proper patient monitoring as well as follow-up and are the underlying reasons for treatment interruption.

Both groups of participants agree on socio-economic barriers to treatment completion. Low socio-economic background, stigma, malnutrition and psychological challenges were mentioned as affecting successful treatment completion.

6.3.5.1 Contrasts

The two groups of participants disagreed on provider-related factors hindering successful treatment completion. Healthcare provider study participants reiterated that if patients on treatment are not treated in ethical ways and with dignity, these become discouraging factors to continue their treatment. In addition, positive patient-physician relationships characterised by a friendly approach and empathy are necessary for the development of trust. Otherwise, patients are likely to discontinue treatment. On the other hand, previously treated DR-TB patient study participants stated that inpatient wards were unresponsive during their stay in the hospitals, especially during emergency situations. There were perceptions that the ward team was not fast enough in addressing emergency situations. Moreover, it was also stated that there was poor communication from health providers.

The two groups of participants also disagreed on awareness or perceived severity of the disease. Previously treated patients in the FGDs stated that DR-TB was perceived as a serious disease. They understood that DR-TB is a serious disease with possible

consequences of severe illness, even fatality. Further, the FGD participants reported that the disease has negative social implications that were difficult to cope with. On the contrary, health care professionals, in the in-depth interviews, indicated that there was a lack of awareness and low knowledge among patients about the severity of the disease and the fact that it is fatal. Hence it is instructive to educate patients about their disease, including its severity.

6.3.6 Qualitative results explaining quantitative results

6.3.6.1 Registration group lost-to-follow-up

The quantitative results confirmed that patients in the registration group after lost-to-follow-up at the start of treatment were less likely to complete treatment (AOR= 0.05, 95%CI: 0.004-0.54) compared to other registration groups in the study. Similarly, in the qualitative findings of the study, factors exposing patients to interruption in treatment and lost-to-follow-up were explained by the health care providers. This is summed up in an excerpt taken from a healthcare provider:

> *HP2: "There are some factors I consider l[as exposing] patients to treatment interruption, for defaulting on treatment and lost-to-follow-up. In the first place social and economic problems of the patients are the major ones. When we take their history, most of the time patients who come for treatment are those who do not have families, those who live and come from places that expose them [to] communicable diseases, daily labourers, those who come from congregate settings and those who are very poor economically".*

6.3.6.2 Comorbidity

The quantitative results showed that not having comorbidity (AOR=2.06, 95%CI: 1.06-4.00) was significantly associated with treatment completion, and patients with comorbidity were less likely to complete treatment compared to their counterparts. In this regard, the qualitative findings of the in-depth interview of experts explained how comorbidities affect treatment completion. In the first place, most of the study participant HCPs mentioned that comorbidities like HIV, diabetes, malnutrition, chronic illnesses like renal disease and lung disease complicate treatment. Besides, frustration due to the high pill burden and increased occurrence of adverse events

reduce the success of treatment completion. The two data sets are in agreement as it can be concluded that comorbidity is a barrier to treatment completion.

HP15: "If there are comorbidities like HIV, diabetes and others, the treatment becomes complicated. The drugs have interactions. There is also a pill burden. When an HIV positive person get[s] an MDR-TB, the medication he takes will be extremely high. If he takes also for an OI [opportunistic infections] another drugs and again if he takes ancillary drugs for adverse events, that will bring frustration and the patient may stop the drugs. This [is] one of the major barriers to interrupt the treatment".

6.3.6.3 Adverse events

The quantitative results showed that not having adverse events, namely, psychotic symptoms (AOR= 2.79, 95% CI: 1.14 - 6.82), drug-induced hepatitis (AOR=12.00, 95%CI: 2.43 - 59), renal toxicity (AOR= 8.31, 95% CI 1.51- 45.6) and electrolyte disturbance (AOR= 8.31, 95% CI 1.51- 45.6) were significantly associated with increased chances of treatment completion. Conversely, having an adverse event, in this case arthritis, (AOR= 2.17, 95% CI: 1.20-3.93) had an association with treatment completion.

The qualitative results from in-depth interviews with HCPs and focus groups with patients clarified that the second line anti-TB drugs cause untoward side-effects that affect patient's smooth treatment adherence and completion. The more the side-effects manifest and exist for longer times, the higher the chances of inducing reluctance and frustration due to reduced quality of life on the patient's side. Consequently, patients prefer to quit their regimen or disappear from follow-ups. Moreover, due to serious adverse events patients may lose their life. The two data sets are congruent and it could be concluded that adverse events are barriers to treatment completion.

HP6: "Since patients on MDR-TB treatment are taking large number of drugs, there are also a number of side-effects that may come into the picture. This reduces their quality of life. They can have headache, daily gastrointestinal upset, joint pain and others. This brings reluctance and initiate the patients to think that the drugs are causing them harm. The occurrence of adverse events every time can be considered as a barrier [to treatment completion]".

F-FGD6: "The drug is heavy. Sometimes there is a headache. Most of the times it makes me to vomit".

6.3.6.4 Residence

Quantitative results showed that 123 (25.3%) of the study patients were from rural areas by residence. In the quantitative analysis, residence had no statistically significant association with treatment completion.

The in-depth interviews with health-care providers confirmed that patients from rural areas are the hardest hit in that there is no structure to follow their condition. Furthermore, it was explained that in the face of unavailability of diagnostic facilities in rural areas, the disease worsens with severe damage to the lung parenchyma and patients end up with serious illness. Consequently, this results in poor outcomes.

HP6: "Especially on the remote and rural areas there is no structure that can listen to them and solve their problems, follows their condition and gives necessary support".

HP5: "In the rural areas they don't have MDR-TB diagnostic facilities. If MDR-TB is not diagnosed early and the patient treated for susceptible TB while having actually MDR-TB …".

This study established that most of health facilities which provide DR-TB services are located in cities and district towns, making accessibility difficult because of problems of transportation. These accessibility problems are therefore underlying reasons for treatment interruption.

HP14: "With the current MDR-TB treatment service, the policy we have, and the accessibility of the health centres, there is a huge gap. The health centres are found in the cities and district towns. Therefore, most of the patients who discontinue treatment are those who come from countryside or those with very low economic and living conditions."

The study found that community-based DR-TB care has not been established in the country and patients cannot adhere to their treatment from home. The rural patients are the hardest hit in that there is no structure to follow up on their condition.

HP14: "And maybe the principle of community-based DR-TB care in our country is not in place. For drug susceptible TB the patient can follow treatment from home".

In addition, most of the inpatient admissions are centralised and patients should be relocated for a long time from their homes, creating psychosocial pressure on them. Patients may not withstand such pressure and may discontinue their treatment for good.

HP15: "Another barrier I think is that most MDR-TB treatments are centralised. People have to be displaced. They must be admitted. And these things bring a lot of pressure. As I said, a social crisis separates them from their family. This creates high psychological pressure on the patient. So, the patient may go away and never come back and complete the treatment".

6.3.6.5 Employment

Quantitative results showed that 183 (37.58%) were employed and 165 (33.88%) were not employed at the beginning of their therapy. Employment was one of the factors which had statistically significant association with treatment completion before adjusting the confounder.

The qualitative results confirmed that employers were not cooperative with patients [their workers] on DR-TB treatment for long times. They refused to grant patients sick leave. This could push patients discontinue the treatment until completion. The next excerpt was a patient's story narrated by the health-care provider in which denial from employers affected patient's treatment completion.

HP3: "Someone starts treatment after quilting his job because he was critically ill at that time, but after he knows that he is surviving he wants to resume his job to continue his life…There were patients I remember who work on trucks. For example, one employer told his worker that he would not take any sick leave afterwards and he would be fired if he brings a [request for] sick leave again. If he loses that job, he may not find similar jobs. So, it is customary that you find patients who say to you that I am now feeling good and healthy and let me continue my job".

If the patient is a breadwinner of the family, they cannot stay on the treatment for long. They should feed their children and manage the family. In such situations, there may be the tendency to interrupt the medication and return to work. Additionally, they might have lost their jobs due to the illness. The excerpt taken from HCPs dwells on this aspect as follows:

> *HP14: "For example, there was patient who is a mother of children under our follow-up. She was sick and started treatment after diagnosis of MDR-TB. She was admitted and treated in the hospital for some months. As a result, after months of follow-up, her children and her family were in trouble. Then her relatives and family advised her that she had improved and recovered and needed to return to her home. And she returned [to] her children and discontinued treatment".*

> *HP7: "Another challenge is… they lose their job when they get sick. They do not have income. Then if you make them discharge, what would they live on? First, they have no place to live. Second, they have no means to survive. There is no monthly salary."*

Hence, there should be protection of patient rights in the work place and provision of socio-economic support for DR-TB patients on the basis of their employment status.

6.3.6.6 Alcohol consumption (life style)

Quantitative results showed ninety-eight (20.12%) of the study patients had a history of alcohol consumption in the past at the beginning of their treatment. History of alcohol consumption had a statistically significant association with treatment completion before adjusting the confounder.

Qualitative results show that previously treated patients' experience of returning to their old habits and addictions, thereby affecting treatment adherence and eventually causing treatment interruption and unsuccessful outcomes.

> *M-FGD1: "Of course, you know sometimes the drugs make you emotional and patients may start the habits they already quitted like smoking and drinking alcohol. These further destroy their health."*

It was also suggested that substance abuse affects treatment adherence and causes treatment interruption. Furthermore, patients suffering from addiction, upon

improvement of symptoms, tend to return to their addiction and not abide by the treatment supervision recommended by health providers. The healthcare provider explained impacts of addiction on patients receiving treatment as follows:

> *HP14: "… There are patients with different kinds of addiction. Those who take alcohol, smokers and khat chewers. It is very hard to have patients with substance abuse problems to keep track of their treatment. I think they also discontinue because of such problems."*

6.3.6.7 Using non-prescription drugs

Quantitative results showed fifty-five (11.29%) of the study patients had a history of using non-prescription drugs, including substances like khat and cannabis at the beginning of their treatment.

In this study it was confirmed that addiction was a barrier to treatment completion of patients on DR-TB therapy. It was voiced that substance abuse affects treatment adherence and causes treatment interruption. Furthermore, patients suffering from addiction, upon improvement of symptoms, tend to return to their peer groups to engage in their addiction and often they do not abide by the treatment supervision recommended by health providers. One HCP explained impacts of addiction on patients receiving treatment as follows:

> *HP15: "Some patients may have uh…problems with addiction. Substance abusers, alcoholics if there are any of these things, most will not take the medicine unless we address that part."*

6.3.6.8 Treatment supporter

Quantitative results showed four hundred and thirty-five (89.32%) of the study patients have had treatment supporter at the initiation of their treatment, while 52 (10.67%) of them did not have any treatment supporter.

Qualitative results showed that treatment supporter is vital to ensure optimal administration of all doses and support adherence of patients and encourage both family and patients. Lack of treatment supporter negatively affects the course of successful treatment completion.

M-FGD3: "Not having a treatment supporter who is besides you and encourages you".

It was also mentioned by the study participants having treatment supporter during treatment was one of the facilitators for smooth treatment completion.

F-FGD5: "I used to take either the injection or medicine at my home. There was one nurse who [brought] me the medicine at my home. I only came here for the check-up".

6.3.6.9 Body mass index (BMI)

Quantitative results showed that 315 (64.68%) of the study patients had BMI of less than 18.5 (underweight). BMI was one of the factors which had statistically significant association with treatment completion before adjusting the confounder.

Qualitative results showed that most of the patients at the beginning of DR-TB treatment had malnutrition. Consequently, the malnourished patients' successful treatment outcome was affected negatively. Malnourished patients have reduced protein in the blood which is important for some anti-TB drugs to enter the circulation, hence result in lower therapeutic values of the medicines. Symptoms may reappear and patients could lose trust in the medication and resort to stopping the treatment. An excerpt taken from a health-care worker participant illustrates this.

HP14: "Most of the patients at start of treatment are malnourished. There are many patients with severe malnutrition. … at least more than 60% of the patients have moderate malnutrition or enter into severe one in the beginning of treatment. They need nutritional rehabilitation. They need nutritional therapeutic feeding".

6.3.6.10 Delay of second-line drugs treatment

Quantitative results showed that, from the time of diagnosis to initiation of treatment, 217 (44.56%) study patients had delay of treatment initiation of less than 30 days. On the other hand, 46 (9.45%) patients had delays of second-line anti-TB treatment initiation of 30-60 days. Likewise, 51 (10.47%) study patients had to wait for 61-120 days to start second-line treatment, and 173 (35.52%) had to wait for more than 120 days.

The qualitative results from in-depth interview with healthcare providers show that, as the time passes without getting timeously diagnosis and treatment, the disease becomes worse with severe damage to the lung parenchyma and serious illness with poor outcomes.

> *HP11: "It takes a lot of time for most patients to be diagnosed with MDR-TB. So when patients come for treatment, they come with a serious illness so the mortality rate will increase".*

6.3.6.11 Chest x-ray findings

Quantitative results showed that a total of 242 patients had x-ray examinations. Thirty three patients (13.64%) had x-ray findings of bilateral disease with cavities, while 199 (82.23%) and 10 (4.13%) patients had fibrosis and normal findings respectively.

In the in-depth interviews, participant HCPs described that patients with DR-TB generally come with badly affected and deteriorating lungs with advanced and extensive lesions. This makes treatment and cure difficult, becoming a significant barrier to successful treatment completion. This was elaborated in an excerpt taken from a health-care professional:

> *HP15: "In addition, generally these patients have significant or very severe lung problems. The lung is badly affected…and easily exposed to a variety of lung problems. As a result they can easily die. The likelihood that the patients will die in a different condition than the TB is greater."*

6.3.6.12 LPA

The quantitative results revealed that patients diagnosed with LPA were more likely to complete treatment compared to the other DST techniques (AOR=2.11, 95%CI: 1.11 - 4.01). In the qualitative in-depth interviews with healthcare providers, delay of second line DST results were mentioned to be one of the challenges during treatment follow-ups, affecting clinical decision.

> *HP4: "During follow-up, the other thing seen as a challenge and headache for the physicians is delay of culture and DST results."*

6.4 CONCLUSION

In general, the findings of the present study established the barriers to treatment completion for patients with drug-resistant tuberculosis in Ethiopia. Most of the study findings from the qualitative and quantitative strands were discussed from a comparative angle to other studies conducted locally and globally. In the next chapter, best practice guidelines addressing barriers to treatment completion for patients with drug-resistant tuberculosis are developed as they emerge from the findings of the study.

CHAPTER SEVEN

BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS

7.1 INTRODUCTION

The previous chapter discussed the core findings of the study in line with the available literature. This chapter presents best practice guidelines developed by the researcher emerging from the findings of the study and informed by a systematic review of existing evidence. These guidelines are aimed at addressing barriers to treatment completion for patients with drug-resistant tuberculosis in Ethiopia.

7.2 THEORETICAL FRAMEWORK AND MAJOR FINDINGS CONTRIBUTING TO THE DEVELOPMENT OF THE BEST PRACTICE GUIDELINES

The HBM was used as a guide in the whole process of this research undertaking. More importantly, the HBM is a suitable model to assess the views, experiences and other factors that can facilitate or hinder treatment completion. In this study, the health belief model provided the theoretical framework used to explore treatment completion of patients with DR-TB.

This study used HBM constructs in relation to DR-TB treatment completion. Thus, in that particular instance, perceived severity refers to an individual’s subjective assessment of the severity of the consequences of not completing DR-TB treatment. Perceived susceptibility refers to an individual's assessment of their personal risk of developing problems with regard to not properly taking DR-TB medication. Perceived benefits relate to a subjective assessment of the importance of adherence to second-line regimens. Finally, perceived barriers relate to the patient’s evaluation of the obstacles to taking second-line drugs. These constructs can indicate possible mechanisms that could be triggered to reinforce treatment completion behaviour.

In this study, it was conceptualised in the context of the successful completion of DR-TB treatment. The HBM translates to the desire to achieve successful treatment completion and the belief that completion of DR-TB treatment will improve the patient’s health and bring cure, and this would influence whether or not a patient properly takes the medication and successfully completes their treatment.

In this study exploring barriers to completion of DR-TB treatment through the application of HBM, identified real and perceived barriers to successful completion of treatment regimen. The most commonly reported barriers were related to clinical issues, patient and drug-related factors, programme and health system factors, psychological, and socio-economic factors. Furthermore, barriers that limited DR-TB patients treatment completion were factors associated with proper treatment follow-up, including supply shortages, inadequate service delivery, and a lack of responsibility by providers.

On the other hand, enablers or facilitators (factors that have enabled patients towards treatment completion) were described under the HBM construct as cues to action. Cues to action factors that motivated patients towards treatment adherence and completion include caring for each other, community and family support, and compassionate care.

In this study the other HMB construct explored and described was perceived benefits. Previously treated DR-TB patients' beliefs in the efficacy of treatment completion to make them better from their disease and cure them. Perceived benefits of treatment completion identified in the study were trust in the treatment and trust in the service. DR-TB patients indicated that they had a firm belief that if the treatment is taken properly till the end, the treatment is very good and could bring change, cure patients and save lives. Furthermore, that they had trust in the service and care of patients.

The perceived severity of DR-TB is the other HBM construct explored in this study. It is the belief that DR-TB is a serious disease that has severe physical and social consequences. It was indicated that DR-TB is a serious and difficult disease with the consequence of severe illness as well as fatality. Furthermore, it was explained that DR-TB is a disease that has negative social implications that are difficult to cope with.

One of the concepts of the HBM, self-efficacy was explored in this study. The strength and determination of previously treated DR-TB patients by themselves to resist hindering factors throughout the treatment duration were explored as an important enabling factor to successful treatment completion.

Modifying factors, including demographic characteristics, clinical characteristics, lifestyle and physical characteristics, health system related factors, personality, socio-

economics, of HBM associated with treatment completion of DR-TB treatment were explored and described.

As scholars Mukumbang et al (2017:2) debate, if an individual has a high perceived threat towards a DR-TB disease, low barriers to adopting healthy behaviours, and a high perceived benefit to action that would help avoid the health issue, then there is an increased likelihood of the individual engaging in the recommended behaviour of treatment completion.

The findings of this study were used to develop best practice guidelines. The best practice guidelines are to be used as an evidence-based source of information in addressing barriers for treatment completion of patients with DR-TB.

7.3 DEFINITION OF GUIDELINES

Guidelines are systematically developed statements with recommendations aimed at optimising patient care based upon a systematic review of evidence and an assessment of the alternative care options (IOM 2011:4). Guidelines are recommendations about health interventions, either clinical, public health or policy, intended to assist providers and recipients of health care and other stakeholders to make informed decisions (WHO 2012:1). They are systematically developed statements [recommendations] designed to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances (AGREE 2017:1).

Recommendations provide information to the intended end-user of the guidelines about what to do in specific situations to achieve the best health outcomes possible. They equally assist the guideline user in making informed decisions about whether to perform specific interventions, clinical tests, or public health measures, as well as when and where to do so (WHO 2014c:1).

Rosenfeld, Shiffman and Robertson (2013:S3) note that guidelines give healthcare providers the opportunity to translate best evidence into best practice. Likewise, Ansari and Rashidian (2012:1), and NHMRC (1999:9-10) remark that guidelines can improve health care quality and outcomes by linking best available evidence with best clinical practice. In general, as a result of more effective interventions and better standardised

health care, patients benefit through improved outcomes (Rosenfeld et al 2013: S4; Shekelle, Woolf, Grimshaw, Schünemann & Eccles 2012:1).

7.4 DEFINITION OF BEST PRACTICE

The activities, disciplines and methods available to identify, implement and monitor the available evidence in healthcare are referred to as “best practices.” Healthcare, public health activities, and health policy should be advised by the best available evidence (Perleth, Jakubowski & Busse 2001:235).

Having the purpose of organising and providing health services in effective and efficient ways, public health policy and clinical decision making are assisted by various available activities and health research (Perleth et al 2001:236). Perleth et al (2001:237) further elaborate activity to mean a set of actions that are related to the health care system in terms of recommendations and advice developed through systematic research. Best practice in this context means ‘doing things smarter; practices that lead to superior performance, achieving consistent quality in what is done; and evidence-based practice’ (Perleth et al 2001:237).

Best practice in health care entails the best way to identify, collect, evaluate, disseminate, and implement information about, as well as monitoring the outcomes of healthcare interventions. Information is required on the best available evidence on health care interventions. Perleth et al (2001:238) frame the definition of best practice in the health sector as the duly weighted use of all valid and relevant information for health interventions and monitoring of the outcomes of health care interventions.

In general, evidence-based practice in healthcare that integrates the best evidence from research with a healthcare providers’ expertise and a patient’s preferences, expectations, and values an association with higher quality care and better patient outcomes (Wallen, Mitchell, Melnyk, Fineout-Overholt, Miller-Davis, Yates & Hastings 2010:2762). In the current study, a relevant systematic search of current evidence was conducted to provide best practice for the development of guidelines and recommendations for implementation in Ethiopia.

7.5 GUIDELINES DEVELOPMENT PROCESS

The formulation of the best practice guidelines was based on the conclusion and summary of the study findings presented in Chapters Four and Five, discussed in Chapter Six, as well as systematically reviewed evidence from the literature. The draft guidelines and recommendations for implementation were shared with senior clinicians from different specialisation disciplines and programme managers at national and regional levels, as well as healthcare providers working at DR-TB treatment initiating and follow-up centres, including physicians, nurses, pharmacists, laboratory technologists, and social workers, in eliciting their reviews and feedback. The clinicians, programme managers, and healthcare providers were selected based on their programmatic, clinical, and practical experience in the area of drug-resistant tuberculosis management.

7.6 VALIDATION OF THE GUIDELINES

Next, the revised draft of best practice guidelines was presented to public health experts, clinicians, programme managers, and stakeholders who were not involved in the preliminary work to validate the adequacy of the document and make comments for improvement. All invited experts attended the validation workshop prepared on 13 May, 2021. The experts validated the draft best practice guidelines based on the criteria of clarity, acceptability, validity, applicability, reliability, relevance, effectiveness, feasibility, sustainability and achievability by using Likert scale, and put their comments, ideas, suggestions or any amendment of each best practice guidelines.

Table 7.1: Biographic information of Experts

S.No	Qualification	Occupation	Work Experience
1	MPH	PMDT Advisor at MOH	19 years
2	MD, MPH	Lecturer	16 years
3	MD, Internist	Physician	14 years
4	MD	Physician	9 years
5	BSc, MPH	PMDT manager at MOH	17 years
6	BSc, MSc	DR-TB, TB/HIV team leader at RHB	14 years
7	PhD	Senior PMDT Advisor at Partner Org.	19 years
8	MSc	Senior M&E advisor at Partner Org.	16 years

The Likert scale indicated each best practice guideline based on the criteria: strongly disagree (1), disagree (2), agree (3), and strongly agree (4) (Table 7.2). The experts were requested to score each revised draft of the best practice guideline from 40, and

the researcher was to consider the best practice guideline acceptable if the mean score was 30 (75%) points or above (Table 7.3).

Table 7.2: Criteria and scoring for validating guidelines

S. No	Criteria	Score			
		Strongly disagree (1)	**Disagree (2)**	**Agree (3)**	**Strongly agree (4)**
1	Clarity				
2	Acceptability				
3	Validity				
4	Relevance				
5	Reliability				
6	Feasibility				
7	Sustainability				
8	Applicability				
9	Effectiveness				
10	Achievability				

Table 7.3: Score of experts on each guideline

Guidelines	Experts score on each guideline								
	Exp1	Exp2	Exp3	Exp4	Exp5	Exp6	Exp7	Exp8	Average score
Guideline 1	34	37	32	38	33	32	40	32	35
Guideline 2	38	37	34	39	32	32	33	39	36
Guideline 3	40	38	40	40	38	39	39	39	39
Guideline 4	36	33	34	34	36	35	34	35	35
Guideline 5	39	39	38	39	36	36	39	37	38
Guideline 6	40	40	40	38	38	40	37	39	39
Guideline 7	38	40	36	34	38	38	40	40	38
Guideline 8	34	34	34	40	38	38	34	34	36
Guideline 9	37	36	36	38	40	40	37	37	38
Guideline 10	32	35	35	34	33	38	39	38	36
Guideline 11	33	40	33	40	38	37	37	38	37
Guideline 12	40	40	36	34	34	37	39	40	38
Guideline 13	37	37	34	35	39	34	38	40	37
Guideline 14	36	39	34	36	36	33	34	38	36
Guideline 15	35	34	36	38	38	37	37	39	37
Guideline 16	39	36	33	33	40	32	36	35	36
Guideline 17	33	33	35	38	34	39	39	39	36
Guideline 18	40	40	38	39	35	35	38	37	38
Guideline 19	32	34	33	33	36	38	38	38	35
Guideline 20	39	39	37	35	34	34	39	36	37

The researcher thoroughly revised the best practice guidelines based on the experts' comments and suggestions and sent them the revised document by email for review. Subsequently, the researcher arranged a Zoom meeting, and a final consensus was

reached on the final document. Finally, comments and inputs were accepted and incorporated into the final best practice guidelines. Figure 7.1 depicts the process of the development of these best practice guidelines.

7.7 PURPOSE OF THE BEST PRACTICE GUIDELINES

The purpose of the guidelines is to achieve improved DR-TB treatment outcomes by addressing barriers to treatment completion through evidence-based best practices in the delivery of DR-TB care and services and informed decision making.

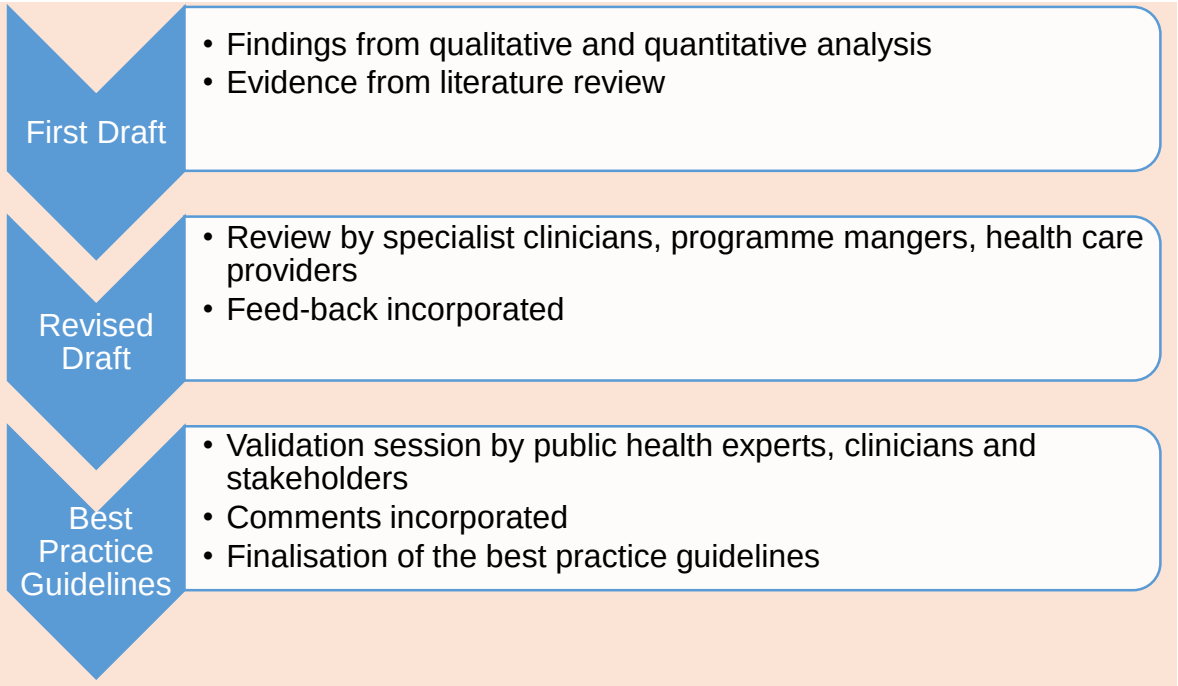


Figure 7.1 Process of the development of best practice guidelines

7.8 SCOPE OF BEST PRACTICE GUIDELINES

The best practice guidelines are to be used as an evidence-based source of information in addressing barriers to treatment completion of patients with DR-TB treatment. They were designed for use as guidance for health care providers involved in DR-TB care and service, programme managers working on DR-TB, and decision and policy makers at different levels of the health system in implementing the programmatic management of DR-TB at health facilities and community level.

7.9 TARGET AUDIENCES

The best practice guidelines were tailored to the following target audiences or end users (end-users are those who will apply the guidelines (WHO 2014c:17) namely, health care providers, programme managers and stakeholders in the programmatic and clinical management of DR-TB, as well as decision- and health policy-makers in the Ethiopian health system.

7.10 BEST PRACTICE GUIDELINES

7.10.1 Best practice guidelines for addressing barriers related to clinical issues

Guideline 1: Consider a collaborative framework for treatment and care of DR-TB and Diabetes

This study found that comorbidities like diabetes complicate treatment and are predictors of unsuccessful treatment outcomes. As shown in the quantitative results, 39 (22.67%) had diabetes as a comorbid condition at the beginning of their therapy. Furthermore, comorbidities like diabetes cause frustration to patients due to the high pill burden and increased occurrence of adverse events which reduce the success of treatment completion.

Rationale on which the best practice guidelines are based

In patients with DR-TB and DM, optimal diabetes management is aimed at reversing DR-TB treatment failure and improving patient outcomes. Optimal diabetes management consists of proper glycaemic control and measures that reduce the risk of cardiovascular disease (Lange et al 2019:654). Similarly, some preliminary evidence suggests that improving glycaemic control in TB patients with DM can lead to better TB treatment outcomes and a reduced risk of relapse and recurrence (Lin et al 2019:35). Furthermore, considering cardiovascular risk assessment to guide management in terms of counselling and prescription of anti-hypertensive, lipid-lowering and anti-platelet treatments is recommended to enhance better outcomes (Lange et al 2019:654).

Recommendations for implementation of the guidelines

- Routine screening of DM in DR-TB patients at the time of diagnosis and registration.
- Provide counselling on appropriate lifestyle management, such as smoking cessation, avoiding excess alcohol consumption, a healthy diet, weight loss, and physical activity.
- Educate clients with DM about their increased risks of TB and the signs and symptoms of TB so that they can present themselves to the clinic.
- Conduct systematic TB screening in clients with DM, preferably with chest radiography.
- Give dietary instructions and medications to optimise glycaemic control.
- Consider cardiovascular risk assessment in TB-DM patients.
- Initiate measures to minimise the risk of cardiovascular problems.
- Work to achieve the recommended targets for glucose control of HBA1c <8% or FBS <180 mg/dl during DR-TB treatment.

Guideline 2: Strengthen the collaboration with ART and PMDT programmes

This study found that comorbidities like HIV complicate treatment and are predictors of unsuccessful treatment outcomes. As shown in the quantitative results, HIV constitutes the majority of the comorbidities of the study patients, in which 117 (68.02%) of the patients had HIV as a comorbid condition at the beginning of their therapy.

Rationale on which the best practice guidelines are based

Many studies indicate that through appropriate implementation of ART programmes, DR-TB treatment success can be enhanced. Likewise, recent studies show that mortality from MDR-TB may be reduced by early initiation of ART (Girum, Tariku & Dessu 2017:335; Meressa et al 2015:1185; WHO 2020a:58). In addition, patients with MDR-TB/HIV coinfection should get early diagnosis, timely access to second-line anti-TB drugs, motivational counselling, and early ART as soon as MDR-TB treatment is tolerated, regardless of CD4 count. Close monitoring of treatment side effects, clinical management and prophylaxis of opportunistic infections, nutritional support, and

additional socioeconomic support are also important for treatment adherence (Htun et al 2018:16).

Recommendations for implementation of the guidelines

- Maintain close monitoring of the toxicity of overlapping drugs, particularly nephron- and hepatotoxicity, as well as drug-drug interactions (DDIs). Possible DDI exists between bedaquiline and several ART regimens, especially those containing efavirenz and/or lopinavir/ritonavir.
- Do not co-administer bedaquiline and efavirenz.
- Offer early screening and diagnosis of TB (DR-TB) to HIV positive clients.
- Extend timely access to second-line anti-TB medications in the case of a diagnosis of DR-TB.
- Provide motivational counselling throughout the treatment process.
- Early initiation of ART as soon as DR-TB treatment is tolerated, regardless of CD4 count, ideally as early as two weeks and no later than eight weeks after initiation of anti-TB.
- Initiate ART within the first two weeks of initiating TB treatment when there is profound immunosuppression (CD4 counts less than 50 cells/mm3).
- Provide close monitoring of adverse events and OIs.
- Provide patients with adherence motivation behavioural counselling.

Guideline 3: **Early recognition and management of comorbidities, organ dysfunction and risk factors associated with unsuccessful treatment outcomes**

Due to comorbidities, patients are likely to have drug toxicity and require substitution of the medicine with a less efficacious one, and successful treatment completion could be affected by the adverse events or weak regimen. Many studies conducted locally and globally, including the current study, clearly indicate that there is an inverse relationship between comorbidities and successful treatment completion. In the current study, patients with comorbidity were less likely to complete treatment compared to their counterparts. It is reported that comorbidities affect treatment completion and significantly complicate treatment. Besides, due to treatment of comorbidities, frustration arising from the high pill burden and increased occurrence of adverse events reduce the success of treatment completion.

Similarly, the current study also verified that patients in the age group 55 – 64 years were less likely to complete treatment successfully (AOR=0.16, 95%CI: 0.04 - 0.59) compared to other age groups. Aged people are prone to developing adverse events from anti-TB drugs because of other existing comorbidities and age-related physiological changes. As a consequence, poor adherence to the regimen and unsuccessful treatment completion may result. Likewise, in the current study, patients in the registration group after lost-to-follow-up at the start of treatment were less likely to complete treatment successfully compared to other registration groups in the study.

Rationale on which the best practice guidelines are based

Patients with comorbidities and organ dysfunction such as hepatic dysfunction and elevated creatinine are likely to experience more drug toxicity, need substitution of less efficacious drugs, and death may arise from the comorbidity or adverse effect. These patients should benefit from review by a panel of experts at the time of treatment initiation, to decide an appropriate regimen and other clinical management recommendations (Baluku et al 2021:4). In addition, the early recognition of factors that could influence treatment outcomes is essential for the successful treatment of patients with DR-TB. Moreover, knowing these factors would help to focus on their care. Similarly, attention should be paid to older DR-TB patients (Tobón et al 2020: 623-24; Baye et al 2018:5).

A cluster randomised study showed that the addition of individually tailored counselling sessions provided by nurses throughout treatment reduced the risk of lost-to-follow-up by 70% (Law et al 2019:7). Hence, patients in the registration group after-lost-to-follow-up at the start of treatment benefit from individually tailored counselling during their treatment periods.

Recommendations for implementation of the guidelines

- A panel of experts should review patients with comorbidities and organ dysfunction.
- Get multidisciplinary evaluation for older patients with DR-TB.
- Attention should be given to the control of comorbidities.
- Offer testing for any other comorbidities.

- Conduct close observation of the serum potassium level and consider prescribing low amounts of potassium and magnesium supplements to prevent hypokalaemia.
- Offer close observation of the serum creatinine level.
- The glomerular filtration rate (GFR) and urine output, serum creatinine, blood urea nitrogen, and albumin should all be monitored.
- Utilise novel biomarkers, including kidney injury molecule-1, neutrophil gelatinase-associated lipocalin and N-acetyl-β-d-glucosaminidase, which may be useful additions in panels of biomarker for early detection of drug-induced AKI.
- Individually tailored counselling should be initiated for DR-TB patients throughout their treatment period.
- Pre-treatment baseline assessment should be conducted to identify factors associated with unsuccessful treatment outcomes.
- Do a proper physical examination (including colour blindness tests, visual acuity tests, and neurologic tests)
- Offer baseline laboratory tests (haematologic, chemistry, electrolyte, hormonal).
- Do hepatitis B virus (HBV) and hepatitis C virus (HCV) tests at baseline.
- Get thorough audiometry, electrocardiogram, and radiologic examinations.

Guideline 4: **Thorough assessment and proactive management of prognosis**

The study confirmed that the prognosis of DR-TB is more fatal than susceptible TB. As DR-TB patients are not usually diagnosed timeously and come after multiple first-line treatment courses, suitable lodging environment for the bacteria can be created, resulting in cavities. As shown in the quantitative strand, only 48 (9.86%) patients were new and had no TB treatment history, while the majority of 439 (90.14%) patients had a treatment history of TB. In addition, from a total of 242 patients having X-ray examinations, 33 (13.64%) had bilateral cavities, while 199 (82.23%) had fibrosis, which are bad prognostic factors associated with poor treatment outcomes.

Rationale on which the best practice guidelines are based

Early diagnosis and immediate initiation of treatment are essential for an effective TB control programme. Delay in diagnosis is significant for disease prognosis at the individual level (Tag El Din et al 2015:940). Delays in diagnosis of TB can result in greater morbidity and mortality and increase the likelihood of long-term organ damage (Sah et al 2021:62). Hence, ensuring early diagnosis has the fundamental advantage of averting a bad prognosis of the disease.

It was indicated in a study conducted at Gondar University Hospital in Ethiopia that a diagnosis of MDR-TB by itself led to a poor prognosis by creating psychosocial problems for patients due to the prospect of long treatment lasting two years and being hospitalised for six months (Alene et al 2017:359). Therefore, sound psychosocial support is essential in the treatment process.

Surgery has been recommended for the treatment of patients with DR-TB who do not respond to drug treatment and have a persistent cavitary well-localised lesion but adequate respiratory function, as well as when not enough active drugs are available for a curative scheme (Tobón et al 2020:622).

Patients who have been exposed to SLDs often have fewer retreatment options due to acquired additional resistance and long-term toxicities. Programmes should therefore aim to optimise DR-TB treatment the first time it is initiated (Baluku et al 2021:4). To this end, results from genotypic testing using LPA/whole-genome sequencing (WGS) and phenotypic DST (pDST) should be available at the earliest opportunity to design an appropriate personalised regimen (Lange et al 2019:649).

Recommendations for implementation of the guidelines

- Ensure the early diagnosis of DR-TB.
- Provide immediate initiation of DR-TB treatment after diagnosis.
- Strict follow-up of clinical and laboratory response throughout the course of treatment.
- In addition to bacteriologic tests, monitor progress through markers of response to treatment or of disease progression, such as the patient's general condition, weight gain over time, resolution of disease manifestations, blood indices, and results of imaging (for example chest radiography).
- Close monitoring of adverse events due to second-line drugs.

- Provide proper counselling as well as social and emotional support to patients to boost their morale and keep them on the treatment.
- Identify any comorbidities and risk factors affecting treatment success and manage them accordingly.
- Provide psychological counselling for patients at the time of DR-TB diagnosis.
- Consider hospitalization of patients for some time, to contain the progress and dissemination of the disease in the body and to assure the success of the treatment.
- Consider pulmonary surgery to improve prognosis as a result of reducing the bulk of lung tissue with intractable pathology and bacterial load.
- Provide patient tailored individualised treatment regimens.
- Have additional molecular tests (LPA/WGS and pDST) in addition to the GeneXpert test before initiating individualized treatment.

Guideline 5: Provide patient tailored or individualised DST guided treatment regimens

The present study established that the nature of DR-TB disease is quite different from that of drug-susceptible TB. In DR-TB, the characteristic bacterium is resistant to first-line drugs and, sometimes with extensive resistance. Hence, the disease results from an aggressive type of bacteria, and treatment is also difficult with available medicines. Consequently, unfavourable treatment outcomes may occur eventually.

Lack of DST is among the possible factors causing inadequate treatment of DR-TB. In turn, the use of inadequate treatment could lead to further amplification of resistance and could result in treatment failure, whereas DST facilitates rapid detection of DR-TB in just a couple of days, allowing initiation of effective treatment regimens and successful treatment completion.

Rationale on which the best practice guidelines are based

A patient-tailored clinical strategy focused on good adherence is necessary to achieve high treatment success rates for DR-TB patients. In particular, the need to individualise treatment regimens has been recently emphasised, taking into account the drug-resistant pattern of the causative MTB strain (Migliori et al 2020:S19-S20).

In addition, as DR-TB strains are often resistant to one or more SLDs, in-depth genotypic and phenotypic DST is needed to construct individualised treatment regimens to improve treatment outcomes (Lange et al 2019:645). In this regard, in addition to the GeneXpert test result, having additional molecular tests that are capable of detecting mutations associated with resistance to other drugs when initiating a DR-TB regimen is needed (Lange et al 2019:648).

Many scholars state that successful diagnosis and treatment of DR-TB relies on universal DST and programmes applying individualised treatment regimens for a duration of more than 18 months, and DOTS strategy throughout this period achieved the highest success rate (Gadallah et al 2016:1000; Migliori et al 2020: S17).

Recommendations for implementation of the guidelines

- Introduce the Xpert system at point of care facilities for rapid detection of RR-TB.
- Facilitate universal access to drug susceptibility testing.
- Extend rapid molecular DST as the initial test to detect DR prior to the initiation of appropriate therapy for all TB patients, including new and previously treated ones.
- Strengthen referral linkage for LPAs.
- Consider building the capacity of laboratories to give second-line DST service and/or LPAs.
- When initiating a DR-TB regimen, have LPA results in addition to GeneXpert test results to guide the initial treatment choice.
- Treatment regimens should always be guided by LPAs or WGS.
- Results from genotypic testing using LPA/WGS and pDST should be available at the earliest opportunity to design an appropriate personalised regimen.
- Let the DR-TB panel team set up at each of the hospitals jointly decide for each patient.
- Whenever possible, the treatment regimen should be discussed by a multidisciplinary board (Consilium) of experts that may include infectious diseases specialists, pulmonologists, thoracic surgeons, clinical microbiologists, and pharmacologists.

- Commission DST for bedaquiline to monitor resistance at the national reference laboratory.

Guideline 6: There should be timely recognition, aggressive monitoring and intensive management of adverse events

The study identified that adverse events were significantly associated with a decreased chance of treatment completion and were cited as a barrier to successful treatment completion. It was reported that adverse events potentially affect treatment adherence of patients and are one of the reasons for patients interrupting their medication, disappearing from follow-up, and defaulting from treatment. Moreover, due to serious adverse events, patients may lose their lives.

In the current study, at multivariate analysis, it was found that having adverse events; namely, psychotic symptoms, drug-induced hepatitis, renal toxicity, and electrolyte disturbance, was significantly associated with a lower chance of treatment completion.

Rationale on which the best practice guidelines are based

Different studies informed us that rapid evaluation, diagnosis, and intensive management of adverse events have a major impact on patient adherence and successful completion of treatment (Meressa et al 2015:1186; Leveri et al 2019:7; Lange et al 2019:652). Likewise, it was also reported that regular follow-up of patients and specific, targeted enquiry into AEs, as well as careful documenting and reporting, are important in achieving better patient compliance and improving treatment outcomes (Jakasania et al 2020:7-8; Gualano et al 2019:7).

Recommendations for implementation of the guidelines

- Extend intensive treatment of adverse events.
- During the early months of treatment, frequent patient monitoring and prompt intervention for AEs are critical.
- Offer information about side effects; it could help patients to tolerate treatment.
- Do clinical examinations and laboratory investigations as per schedule or need throughout the treatment duration.

- Monitor GFR and urine output, serum creatinine, blood urea nitrogen, and albumin.
- Arrange continuous capacity-building training on the monitoring and treatment of AEs.
- During follow-up visits, patients should be thoroughly questioned about the occurrence of AEs.
- The treating team should be trained to apply appropriate mental health assessment tools so that psychiatric disorders can be identified as soon as possible.
- Ensure stringent clinical and laboratory-based active drug safety monitoring with real-time reporting.
- Conduct close observation of the serum potassium level and consider prescribing low amounts of potassium and magnesium supplements to prevent hypokalaemia.
- It is important to check regularly for symptoms and perform laboratory screenings to detect those AEs not reported by the patient or DOT provider.
- Monitor patients daily for signs and symptoms of AEs during DOT sessions.
- Advise spreading consumption of the pills over several hours to reduce discomfort.
- Encourage patients to take pills after a meal to alleviate discomfort.
- Utilise a systematic method of patient interviewing so that patients can report AEs without missing anything.
- Healthcare providers should be trained to screen patients regularly for signs and symptoms of common SLD adverse events.
- Make prompt evaluation, diagnosis, and treatment of any AEs.
- Ensure an adequate supply of essential ancillary drugs at all DR-TB treatment centres.
- Work to integrate and apply all the medical disciplines, as SLDs side effects affect all the systems.
- Consider capacitating and enabling the staff to do all clinical examinations needed for patient monitoring.
- Make sure to collect laboratory results properly.

- Ensure there are laboratory investigations available necessary for patient follow-up in tracking treatment adverse effects systematically.
- Routine maintenance of non-functional chemistry machines.

Guideline 7: Address delays in diagnosis

This study verified that delay in diagnosis of DR-TB is one of the factors related to unsuccessful treatment outcomes. It was noted that delay in diagnosis and initiation of treatment have a considerable impact on disease progression and prognosis, ultimately contributing to unsuccessful treatment outcomes. It was also stated that a number of factors indicate there is a significant delay in the process of diagnosis of DR-TB, including a large proportion of MDR-TB patients with a previous history of multiple episodes of first line treatment regimen reflecting prior missed opportunities for diagnosis. Similarly, in the quantitative section of the current study, 439 (90.14%) patients had a treatment history of TB, indicating missed opportunities and a delay in diagnosis.

Poor knowledge of health care providers, shortage of rapid molecular tests, and unreliable specimen transportation and referral pathways were mentioned as the major findings contributing to a delay in diagnosis. In addition, institutional barriers, including inadequate diagnostics and infrastructure in the health system, wrong diagnosis, and shortage of training of professionals are some of the major factors causing delayed diagnosis.

Rationale on which the best practice guidelines are based

Early detection of tuberculosis improves treatment outcomes by reducing morbidity, the likelihood of long-term organ damage, and mortality. And, lower mortality and a lower rate of treatment failure can be observed in programmes with a shorter delay in treatment commencement for MDR-TB patients (Sah et al 2021:62; Gadallah et al 2016:1000; Alene et al 2017:359).

Recommendations for implementation of the guidelines

- Cut down on missed opportunities (address the 20% of DR-TB cases who visit health facilities for other reasons before being diagnosed with DR-TB).

- Expand rapid molecular DST as the first test to detect DR-TB before initiating appropriate therapy for all TB patients, including new and previously treated.
- Introduce the Xpert system at point of care facilities for rapid detection of RR-TB and strengthen referral linkage for LPAs to diagnose MDR-TB-XDR-TB in just a few days.
- Strengthen the sample referral system.
- Ensure the feedback system works optimally from referral/regional laboratories to TICs.
- Introduce rapid molecular DST as the initial test at point-of-care facilities.
- Consider using innovative ways of reporting DST results to TICs. This may include short message services, emails or the use of web-based mobile applications.
- Address institutional barriers to diagnosis.
- Improve the activities of early contact tracing and active screening of family members and other contacts.
- Reduce diagnostic costs such as travel and other expenses.
- Identify high-risk or difficult-to-reach populations with limited access to TB services.
- Allocate sufficient time for the training of healthcare providers on DR-TB.
- Decentralise diagnostic facilities with ample skilled providers.
- Improve the diagnostic and testing capabilities of the country.
- Offer universal TB symptom screening for all patients at all health facilities.
- Provide urine LAM testing to known HIV infected patients with CD4 counts <100 cells/mm3.
- Identify high-risk populations that have poor access to TB services.
- Consider community-based mass chest radiography screening campaigns using digital radiography with automated computer evaluation.
- Address stigma and discrimination because people who have TB symptoms may refuse screening for TB or avoid going for diagnostic tests due to stigma, discrimination, and fear.
- Routine maintenance and proper service for diagnostic equipment, including microscopes, x-ray machines, and GeneXpert.

- Work in partnership with private health providers, especially traditional healers, by training them and providing incentives for referrals.
- Expand diagnostic facilities.
- Tackle incorrect diagnosis by improving the capacity of the facility and providers.
- Provide sufficient training for health care providers.

Guideline 8: Offer surgery for patients amenable to surgery

This study identified that the service of surgical management for patients with DR-TB has been generally weak in the country and patients with DR-TB have not been getting operations timeously. In addition, there has been no ICU service for DR-TB patients, which is a lifesaving service. The unavailability of surgical and intensive care services creates a barrier to successful treatment completion for patients with DR-TB in the country.

Rationale on which the best practice guidelines are based

The emergence of drug-resistant strains of MTB has recently restored thoracic surgery to a prominent position among interventions designed to combat tuberculosis. When combined with effective drug therapy, surgery has been associated with favourable outcomes in cases of MDR-/XDR-TB. In fact, the main goals of surgery are to eliminate life-threatening complications, to remove the source of infection, and to improve the chances of effective medical treatment (Tiberi et al 2019:6; Lange et al 2019:655).

The largest case series to date was published in 2018 by Giller et al, who documented 5,599 thoracic surgeries in TB patients treated in Russia over a 17-year period. The authors reported an overall mortality rate of 0.1% and treatment success rates of 93.0% and 92.1%, respectively, in patients with MDR-TB and XDR-TB (Tiberi et al 2019:3). Moreover, a systematic review and meta-analysis of data from 24 studies illustrated a significant association between surgical intervention and successful treatment compared to non-surgical interventions (Tobón et al 2020:622).

Surgery has been recommended for the treatment of patients with DR-TB who do not respond to drug treatment and have a persistent localised cavitary lesion but with adequate respiratory function, as well as when there are not enough active drugs

available for a curative treatment. Similarly, in selected patients with a strong risk of relapse and treatment failure (and localised pulmonary sequelae), elective partial lung resection, either lobectomy or wedge resection, has been recommended in addition to an adequately designed MDR-TB regimen. Under optimal conditions and in selected patients, the treatment success rates of combined medical and surgical treatment of patients with DR-TB can approach 90% (Tobón et al 2020:622; Migliori et al 2020:S21; WHO 2020a:60; Lange et al 2019:655).

Recommendations for implementation of the guidelines

- Consider surgical intervention in DR-TB patients with localised pulmonary sequelae or persistent cavitary lesions who do not respond to drug treatment.
- Consider pulmonary surgery to improve prognosis by reducing the bulk of lung tissue with intractable pathology and bacterial load.
- Establish surgical facilities, including operation rooms with laminar air flow and negative air pressure serving DR-TB clients.
- Institute intensive care units serving DR-TB clients.
- Extend referral networks between surgery facilities and TICs.
- Utilise a multidisciplinary Consilium for deciding on the indications of surgery to ensure the best possible outcomes.
- Communicate the time of culture conversion as the optimal time for elective surgery.
- Consider emergency surgery in situations of recurrent haemoptysis, profuse lung haemorrhage, or tension pneumothorax.
- Do not consider surgery for bilateral cavitary disease (subtotal affected lungs), poor cardiorespiratory function, severe comorbidity, and active bronchial TB.
- Offer pre-operative physical exercise and post-operative rehabilitation, including psychological support.
- Engage social workers, counsellors, or psychologists with DR-TB patients having surgery.

Guideline 9: Prevention of complications and provision of palliative care

From the study findings, one of the barriers to the successful treatment completion for patients with DR-TB treatment was that the treatment for DR-TB is a complicated one

compared to that of drug susceptible TB. It was mentioned that the treatment is complex, less effective, toxic, given the long time and not as effective as the first-line drugs and has a high failure. It was also indicated that the treatment causes several adverse events and treatment interruption is significantly higher in the treatment of DR-TB.

The study confirmed that patients with DR-TB generally present with badly affected and deteriorating lungs with advanced and extensive lesions. This makes treatment and curing difficult, becoming a barrier to successful treatment completion. It has also been noted that the extension of destruction of the lung tissue was a risk factor for poor treatment outcomes owing to its association with a poor bacteriologic response.

Rationale on which the best practice guidelines are based

Proper treatment of drug-susceptible TB and early detection and treatment of MDR-TB before complications develop, along with prevention of drug side-effects, are very important. Recent evidence shows that about half of pulmonary TB patients completing treatment suffer from the consequences of sequelae (complications) with obstructive, restrictive, and mixed functional patterns, indicating the necessity of palliative care (Girum et al 2018:11; Migliori et al 2020:S23).

Zero suffering is one of the goals of the End TB Strategy. Palliative care is defined as an approach to improve the quality of life of patients facing a “life-threatening illness, through the prevention and alleviation of suffering utilising early detection and proper assessment and treatment of pain and other physical, psychosocial and spiritual problems" (WHO 2017:25).

Recommendations for implementation of the guidelines

- Provide proper treatment of drug-susceptible TB.
- Provide individualised DST-guided treatment regimens.
- Initiate early detection and treatment of DR-TB before complications developed.
- Prevention and aggressive management of drug side effects.
- Strict follow-up of patients with clinical and laboratory tests throughout the treatment duration.

- Monitor treatment response clinically by checking remission of signs and symptoms and bacteriologically by performing sputum culture and smear microscopy as well as radiological findings compared to the baseline.
- Offer repeat testing for DST in the case of repeated positive cultures.
- Offer HCV screening for DR-TB patients as well as scale up accessible treatment.
- Initiate proactive use of therapeutic drug monitoring (TDM), which can help to prevent drug-related complications.
- Consider setting up a rehabilitation centre for patients with complications.
- Offer respiratory physiotherapeutic interventions.
- Work on capacity building to extend physiotherapy services, including training to staff, rooms, and equipment for therapy.
- Integrate palliative care into the TB programme.
- Offer symptom control and proper infection control measures.
- Make accessible treatment and care for DR-TB patients that relieve suffering and are life-saving.
- Offer lung function tests to determine the baseline level of function and disease.
- Inhaled or long-acting bronchodilators may be prescribed if the lung function tests show airflow obstruction.
- Advise patient to remain active and follow a pulmonary rehabilitation or exercise programme.
- Educate about airway clearance exercises.

7.10.2 Best practice guidelines for addressing barriers related to patient factors

Guideline 10: Increase awareness about the disease and importance of finishing the treatment course

This study indicated that there was a lack of awareness and low knowledge in the community and among patients about the importance of treatment adherence for the whole duration of the treatment. It was also established that when patients take

medication for a couple of months, the bacteria load will decrease and the symptoms will start to subside. So, patients may develop a false sense of cure and could quit their therapy, in spite of the fact that they should continue medication for the prescribed duration of treatment.

Rationale on which the best practice guidelines are based

Many scholars indicate that effective education enables the patient to come to terms with their diagnosis, deal with the side-effects of medication, and take responsibility for their own health. Likewise, good education improves treatment outcomes by helping to reduce wrong health beliefs and myths, promoting patients' belief in their ability to be cured (McNally et al 2019:2, 12). In addition, analysis of the benefit of patient education in RCTs showed that patients who received educational counselling had better rates of successful treatment completion and treatment adherence, and had lower rates of loss to follow-up (WHO 2019a:52). In general, it was reported that educating patients about TB disease helps ensure successful therapy completion (CDC 2021:129).

Recommendations for implementation of the guidelines

- Involve peer educators in raising DR-TB awareness among patients on treatment and the community at large.
- Prepare DR-TB information in a language or format that is understood by the local population.
- Understand TB symptoms and how it is transmitted, prevented, diagnosed, and treated.
- Inform the community where DR-TB services are provided.
- Create awareness of DR-TB through the use of available visual (posters, leaflets, digital messaging on mobile), audio (radio programmes, audio clips through mobile) and audio-visual (TV programmes, short videos, films) materials.
- Involve existing community structures like the women's development army and health extension workers as agents to create awareness of DR-TB.
- Develop information, education, and communication (IEC) materials in local languages and dialects or in pictorial form.

- Create awareness of the importance of completing the treatment; otherwise, the disease will relapse again.
- Render proper advice and continuous counselling supported by a psychologist to convince patients of the importance of finishing the treatment course and the danger of discontinuing the regimen.
- Involve expert patients (those who finished DR-TB treatment) to educate and share their experiences with patients on treatment.
- Provide detailed information at the beginning and then communicate the clinical progress throughout the treatment period to patients.
- Inform patient when they commence treatment, about how long it is necessary, in which month what changes are seen or expected, and for how long they ought to continue.
- Give sufficient awareness during pre-treatment counselling.
- Ensure that each patient has an adequate understanding of the treatment.

Guideline 11: Initiate interventions to treat behavioural problems including substance abuse

In this study, it was verified that addiction was a barrier to treatment completion for patients on DR-TB therapy. It was pointed out that substance abuse significantly affects treatment adherence and causes treatment interruption. Furthermore, patients suffering from addiction tend to relapse to practice their addiction soon after identifying some improvement in symptoms and do not abide by the treatment supervision by health providers. In the quantitative section, it was presented that 55 (11.29%) of the study patients had a history of using non-prescription drugs, including substances like khat and cannabis. In the in-depth interviews with HCPs, it was also noted that there are patients with different kinds of addiction, those who take alcohol, smokers, and khat chewers.

Rationale on which the best practice guidelines are based

It has been proposed that interventions in treating substance abuse during anti-tuberculosis treatment might improve treatment outcomes (Sanchez-Padilla et al 2014:165). In addition, according to WHO evidence, it was noted that patients who

had access to psychological support had higher rates of treatment completion and cure, as well as lower rates of treatment failure and loss to follow-up (WHO 2019a: 53). Moreover, it was also reported that the implementation of comprehensive interventions, focusing on socioeconomic problems like poverty and substance abuse, is essential to improve treatment adherence (Tola et al 2017:456).

A coherent smoking cessation approach, including a wide range of psychosocial and pharmacological interventions, increases the treatment success rates in tuberculosis patients while decreasing the risk of further pulmonary complications. Therefore, the WHO recommends integrating early and effective smoking cessation measures, starting at the primary health care level, into tuberculosis control plans. Because of the similar risk posed by alcohol abuse, comparable interventions have also been recommended for individuals with alcohol dependence (Tiberi et al 2019:6).

Recommendations for implementation of the guidelines

- Initiate a coherent smoking and alcohol cessation intervention.
- Integrate substance abuse interventions with clinical and programmatic management of DR-TB.
- Effectively deal with peer pressure.
- Promote ways to handle stress, like taking up exercise and reading a good book.
- Create integration with a psychiatry unit to seek help for mental illness.
- Offer behavioural change interventions.
- Consider behavioural treatments such as individual, group, and telephone counselling.
- Promote lifestyle interventions.
- Offer psychosocial and pharmacological interventions.
- Make incentive-based interventions available.
- Involve self-help groups.
- Facilitate peer- to-peer counselling.
- Offer alcohol cessation counselling.
- Involve TB clubs in behavioural change interventions.

- Ensure that there are recreational and refreshment areas and a garden for inpatients in the MDR ward.
- Engage social workers, counsellors, or psychologists in the treatment of DR-TB patients.
- Consider comprehensive interventions to tackle psychosocial problems.

Guideline 12: Offer a package of treatment adherence promoting interventions in order to improve retention-in-care and prevent lost to follow-up

For a successful treatment outcome, optimal treatment adherence is mandatory. According to WHO, to be adherent, patients should attend the scheduled visits and take regular medication above 90% of the prescribed doses. However, evidence shows that a considerable number of TB patients interrupt their treatment due to various and interrelated psychological, socio-economic, behavioural, health care system, and health care provider-related factors (Tola et al 2017:454-455; WHO 2020a:63).

The current study found that treatment interruption contributes to decreased treatment success. In the quantitative findings, patients in the registration group after lost-to-follow-up at the start of treatment were less likely to successfully complete treatment (AOR = 0.05, 95%CI: 0.004-0.54) compared to other registration groups.

Similarly, in the qualitative findings of the study, factors exposing patients to treatment interruption and lost-to-follow-up were explained by the health care providers in the in-depth interviews. First, the low socioeconomic background of the DR-TB patients, where they are marginalised, psychologically affected, and vulnerable population of society. Second, pill burden is a primary reason patients attribute for their treatment interruption. Third, serious side-effects compel patients to interrupt their medication, disappear from follow-up, or default from their treatment. Fourth, there is lack of awareness about the importance of treatment adherence for full duration, completing the treatment to prevent relapse, and the severity of the disease, including how much it is fatal.

Rationale on which the best practice guidelines are based

Interventions to improve retention-in-care and treatment adherence and reduce defaulters among DR-TB patients are essential in increasing treatment success rates

(Baye et al 2018:5; Law et al 2019:2). Indeed, a large body of evidence demonstrates that various combinations of treatment adherence interventions, such as patient and staff education, social and psychological support, and tracers in conjunction with DOT, significantly improve treatment outcomes (WHO 2020a:64). Likewise, nutrition and transport reimbursements have been associated with lower rates of non-adherence (Shringarpure et al 2016:9).

Reinforced communication with closer and regular contact between health services and the patient, including substance abuse treatment, during the out-patient phase should help reduce default rates (Sanchez-Padilla et al 2014:165).

Incentives and enablers can be used to ensure adherence to therapy. Incentives are inexpensive rewards given to patients to encourage them to take their medication or to keep their DOT or clinic appointments. Enablers are things that help the patient receive treatment; for instance, bus fare to get to the clinic (CDC 2021:133).

A randomised clinical trial showed that patient-centred TB care, including home-based DOT, had a significant impact on improved adherence and treatment outcomes for TB patients in Armenia (Khachatryan et al 2021:6). A patient-centred approach involves patients in the decision-making process and plays a key role in improving treatment adherence since patients value participating in a pragmatic and individualised treatment plan. Therefore, patients and their family members should be counselled at every opportunity, to address information gaps and to enable informed decision-making (McNally et al 2019:2, 10; Kundu et al 2021:393).

Recommendations for implementation of the guidelines

- Social support in the form of material support like food, financial incentives or transport fees, living allowances, housing incentives may be provided to DR-TB patients to address direct and indirect income losses incurred by them and their families.
- The adherence and pre-treatment counselling must be strong, and the patient should be empowered and well informed about the treatment.
- Provide emotional support.
- Offer incentives and enablers based on the needs of the individual patient.
- Psychological support may be offered to patients in the form of counselling sessions or peer groups.

- Consider financial support to encourage long-term retention in MDR-TB care.
- Provide reinforced communication, with closer and more regular contact with the patient.
- Allocate enough health provider time to each patient during DOT and clinical follow-ups.
- Tracers, according to WHO (2020a:62), communication with the patient, including home visits and use of digital technology like SMS, automated telephone reminders, or phone calls, can be used based on resources and patient needs.
- A digital medication monitor, a device that can remind patients to take medication, may be offered based on resources and conditions for implementation.
- Consider substance abuse treatment.
- Extend free care in all service outlets for DR-TB patients including diagnostics, medication, and procedures.
- Counselling and treatment education should be provided to all patients throughout the treatment duration.
- Patients should be continuously motivated to adhere to treatment, and providers have an important role here.
- Encourage a positive attitude towards DR-TB treatment through effective communication and empathy.
- Patients should be educated about the consequences of non-adherence.
- Utilise a patient-centred approach in which patients are actively involved in the treatment plan and process.
- Provide DR-TB care that responds to individual patient preferences, needs, and values.
- Give comprehensive DR-TB care in a manner that patients feel safe, respected, and engaged in decisions about their care.
- Include patients in the decision-making process during treatment periods.

7.10.3 Best practice guidelines for addressing barriers related to psycho-social factors

Guideline 13: Provide socio-economic support for all DR-TB patients on treatment

In this study, it was shown that economic problems are an obstacle to achieving successful treatment completion. It was also noted that patients who have financial problems suffer extra costs incurred to cover transportation and living costs during the long treatment duration. Similarly, it was confirmed that lack of social support is associated with TB treatment non-adherence. In addition, it was reported that social problems trigger loss-to-follow-up. In summary, the socioeconomic impact of DR-TB treatment, including extra costs for accommodation and food, loss of employment, loss of family and social network support, and isolation, negatively influence treatment adherence and successful outcomes.

Rationale on which the best practice guidelines are based

Scholars note that providing some nutritional and socio-economic support in other programmes brought low loss-to-follow-up rates and conclude that such support is essential for the successful achievement of treatment programmes, particularly where extreme poverty is rampant (Meressa et al 2015:1185). In the same vein, a systematic review found that fewer losses-to-follow-up resulted in DR-TB treatment strategies that used a more comprehensive approach, including financial and nutritional support (Law et al 2019:2). Similarly, in studies conducted in other low-income settings in Nepal and South Africa, financial support in the form of food vouchers or direct income replacement has been proven to improve treatment outcomes (McNally et al 2019:13).

Furthermore, the same systematic review also reported that in addition to standard care, patients who received some form of psychosocial, educational, or material support were less likely to be lost-to-follow-up. Similarly, it was also reported that there is a positive association of losses-to-follow-up with provision of financial support to reimburse rent or travel expenses, as well as to compensate for lost wages during treatment (Law et al 2019:6, 7). Moreover, in another study, it was also identified that nutritional supplementation was associated with successful treatment outcomes (Leveri et al 2019:7). In general, existing research shows that the economic burden

for patients with TB is high and that economic support is important in improving treatment outcomes (Charyeva et al 2019:12).

Recommendations for implementation of the guidelines

- Assess the needs of patients for psychosocial support through conversations and active listening.
- Offer food parcels or food certificates to patients to support their treatment.
- Employment and income generation opportunities should be provided as part of the intervention programme.
- Form a collaborative partnership between DR-TB services and faith-based civil society organisations to offer psychosocial support, including spiritual support.
- Provide financial support to reimburse rent, travel expenses, and compensate for lost income or wages during treatment.
- Provide nutritional supplementation.
- Involve charity organisations to support discharged patients with socio-economic problems.
- Consider designing a permanent social support system within the programme independent of the partners.
- Provide additional support or incentives, such as serving breakfast meals with DOT, to encourage attendance until the end of treatment.
- Consider nutritional therapeutic feeding at the beginning of the treatment, as most DR-TB patients need nutritional rehabilitation.
- Ensure an adequate budget is allocated for the nutrition of inpatients in the MDR ward.
- Expand the options for individualised social support for patients.
- Use legislations to protect people affected by DR-TB from discrimination such as expulsion from workplaces. Right to Employment of Persons with Disability Proclamation No. 568/2008 and Social Health Insurance Proclamation No.690 /2010.

- Expand coverage of social protection schemes to cover the needs associated with illness such as sickness insurance, disability pension, social welfare payments
- Make available a social grant for patients with DR-TB based on their need and situation.

Guideline 14: Provide psycho-emotional support for all DR-TB patients on treatment.

This study revealed that DR-TB treatment creates psychosocial pressure on patients who may not resist such pressure and may discontinue their treatment for good. In addition, psychosocial support during treatment is not well addressed in the country. Furthermore, emotional trauma, feelings of loneliness, and at times, loss of hope make their treatment process painful.

Rationale on which the best practice guidelines are based

In the first place, when patients arrive at a TB clinic, they are already scared, tired, and frustrated with care-seeking and illness. These factors contribute to fear, frustration, and depression, highlighting the crucial need for psychological support. In this regard, it has been revealed by different studies that timely diagnosis and management of psychological problems can enhance successful treatment outcomes and prevent incidences like suicide in patients (Kundu et al 2021:396; Mookherji & Algria-Flores 2018:8).

McNally et al (2019:10) noted that care provided by healthcare providers must be holistic, incorporating a multi-disciplinary team that supports the patient emotionally and psychologically as well as medically. Furthermore, teams involved in treating MDR-TB patients should be trained to apply appropriate mental health assessment tools, especially early on, so that psychiatric disorders can be identified as soon as possible (Bhering et al 2020:68).

According to WHO (2019:53) evidence, higher rates of treatment success as well as lower rates of treatment failure and loss to follow-up were observed in patients who had access to psychological support. Similarly, Bhering et al (2020:62) noted that a

relationship based on trust with emotional support produces improved adherence and successful treatment completion.

It was reported in a systemic review that patients who received some form of psychosocial, educational, or material support, in addition to the standard care, were less likely to be lost-to-follow-up (Law et al 2019:6). Equally important, psychosocial support addresses the psychological, social, and economic factors that can prevent people from accessing diagnosis, adhering to care plans, and successfully completing a course of treatment (Sah et al 2021:15). In summary, a meta-analysis conducted by Hoorn and colleagues showed that psycho-emotional, socio-economic, and a combination of these types of support provided to patients with TB were associated with a significant improvement in successful treatment outcomes (van Hoorn, Jaramillo, Collins, Gebhard & van den Hof 2016: 20).

Recommendations for implementation of the guidelines

- Integrate or link mental health into TB control and care.
- At least a psychological counsellor can be planned at the centres of DR-TB with screening for mental illness at peripheral levels.
- Healthcare providers should make quick referrals to centres when they see psycho-emotional problems, for instance, feelings of loneliness, loss of hope, feelings of isolation, suicidal ideation, and depression.
- Identification of mental health issues should be resumed at treatment initiation and its monitoring should be continued throughout DR-TB care.
- Consider utilizing digital technologies by applying interventions to address mental illness issues in DR-TB care.
- Build health system capacity to identify symptoms of depression and other psychiatric conditions and expand the multidisciplinary team. Members of the team may include from the departments of thoracic surgery, psychiatry, internal medicine, laboratory, dermatology, ophthalmology, cardiology, infectious diseases, pulmonology, dietetic, clinical microbiology, and paediatrics.
- Provide psychological counselling for the patients at the time of DR-TB diagnosis and closely monitor all patients for adverse drug effects, especially at the early stages of treatment.

- Assess the needs of patients for psychosocial support through conversations and active listening.
- Involve peer supporters to provide information on a one-to-one basis or in support groups to alleviate emotional and physical aspects of treatment.
- Arrange peer consultants through an online communication platform to answer any queries and allay anxieties about treatment.
- Render proper advice and continuous counselling supported by a psychologist in order to convince them of the importance of finishing and the danger of discontinuing the regimen.
- Engage social workers, counsellors, or psychologists in the treatment of DR-TB patients.
- Provide detailed information at the beginning and then after communicating the clinical progress throughout the treatment period to patients.
- Provide holistic care incorporating a multidisciplinary team that supports the patient emotionally and psychologically as well as medically.
- Educate family members and empower them to provide emotional and psychological support to patients.
- Collaboratively work to assess the care needs of patients and jointly agree on a care plan that includes clinical, psychological, and social support for patients and their families.
- Engage a multidisciplinary team for the comprehensive management of DR-TB patients. The team may include members from the departments of thoracic surgery, psychiatry, internal medicine, laboratory, dermatology, ophthalmology, cardiology, infectious diseases, pulmonology, clinical microbiology, and paediatrics.
- Patients on DR-TB treatment are isolated from society, feel lonely, and it is of great value that HCPs should provide emotional and motivational support.

Guideline 15: Offer interventions to prevent stigma

In the current study, stigma was mentioned by the study participants as one of the causes of treatment interruption. FGD participants explained their experiences of stigma and discrimination encountered from the community while on their DR-TB treatment. The stigma and discrimination were so pervasive that they were compelled to discontinue their treatments. In addition, HCP stigma and denial of service by HCPs due to stigma were mentioned by participants of the focus group discussions.

Rationale on which the best practice guidelines are based

Stigma is a common barrier in the fight against tuberculosis. It must be identified and addressed through educational interventions (Bhering et al 2020:68). In this regard, many studies indicated improving the knowledge of the patients as well as the community by providing effective education about DR-TB and the engagement of treatment support groups are instrumental in combating stigma. To this end, the findings of a study by McNally et al (2019:12) indicated that improved patient and population knowledge after effective education about the disease could facilitate engagement with treatment by encouraging belief in evidence-based medicine and dispelling stigma. And in another study, it was also identified that TB clubs have proved to be effective in tackling stigma in low and middle-income countries (Sah et al 2021:31).

Recommendations for implementation of the guidelines

- Provide family and community sensitisations, treatment-supporter programmes and counselling.
- Organise interactive community awareness programmes that specifically address stigmatizing attitudes and actions.
- Use existing laws (Right to Employment of Persons with Disability Proclamation No. 568/2008 and Social Health Insurance Proclamation No.690 /2010) and court systems to uphold the rights of DR-TB patients and their families.
- Apply the health policy framework to reduce stigma.
- Clarify that it is illegal to stigmatise anyone with DR-TB, including limiting or preventing access to TB services.

- Make sure service providers (and staff at all levels) are trained on DR-TB and stigma.
- Develop a communication strategy that includes advocacy to reduce stigma.
- Involve TB clubs run by former DR-TB patients in offering psychological as well as emotional support.
- Facilitate DR-TB survivors' sharing of stories.
- Keep all private information of people with DR-TB or in the process of being investigated for DR-TB, confidential.
- Treat clients equally with respect and dignity.
- Extend the care that is provided, upholding the dignity of the individual in a non-stigmatising manner.
- Public banners and health education posters related to TB should be carefully designed to prevent the creation of stigma.
- Create awareness in the community not to discriminate against DR-TB patients and rather to embrace them.
- Work to improve the attitude of health care professionals towards DR-TB.

7.10.4 Best practice guidelines for addressing barriers related to health system and service delivery.

Guideline 16: Establish and promote trustful relationship between patients and health care providers

The study verified that positive patient-provider relationships with a friendly approach and empathic concerns do develop trust and good relationships that culminate in good treatment outcomes. Patients were discouraged from completing their therapy because of a lack of ethical and respectful treatment by some healthcare providers. In addition, the study found that the responsiveness of HCPs was not in place at inpatient wards during their stay in the hospitals, and there was poor communication from health providers in telling patients the level of their problems and explaining their results.

Rationale on which the best practice guidelines are based:

A trustful relationship between healthcare providers and patients establishes good communication and generates patients' trust and confidence in the treatment process (De Vries et al 2017:e137; McNally et al 2019:11). Likewise, Bhering et al (2020:62) noted that a relationship based on trust with emotional support produces improved adherence and successful treatment completion. On the contrary, hierarchical relationships in which patients were uncomfortable expressing their feelings generated a negative impact on treatment adherence.

Recommendations for implementation of the guidelines

Health care providers should:

- Develop interpersonal communication skills like active listening to earn patient trust and build rapport.
- Possess multiple qualities like empathy, respectfulness, and responsiveness that develop trust in patients and promote adherence to treatment.
- Be open, sincere, approachable, responsible, flexible, and open to communication, and have good energy.
- Have excellent interpersonal communication skills and demonstrate active listening.
- Provide unconditional care and service with an understanding of the importance of treating patients as any other society member, as someone equal to them.
- Have unconditional regard when accepting patients (showing complete support and acceptance of a person no matter what that person says or does), understanding their problems, challenges and needs.
- Provide emotional, informational, instrumental (providing tangible assistance, offering a helping hand) and motivational support for their patients.
- Provide continuous information to patients and their family members on facts about DR-TB, which includes side-effects, the importance of staying on treatment, healthy nutrition, recipes, exercise, and personal hygiene.

- Assist with emotional and motivational support during monthly follow up visits.
- Communicate with patients about the level of their problems and update them on how they are responding to therapy.
- We need to ensure we develop good relationships and trust by treating patients with a friendly approach, handling with empathy, discussing problems, sharing concerns, responding to demands and reassuring the future.
- Be responsive to the needs of patients in inpatient care and follow-up monitoring.

Guideline 17: Make sure availability and supply of ancillary drugs and laboratory monitoring tests

The study identified a chronic shortage of life-saving ancillary drugs used to treat adverse events of anti-TB drugs. In addition, there has been severe interruption of supply of ancillary drugs in the system and these are not available in most hospitals most of the time. This puts management of adverse events secondary to anti-TB drugs difficult. And if adverse events are not managed on time because of a lack of ancillary drugs, the patient may die and/or interrupt the treatment, eventually affecting treatment completion.

Investigations used to monitor treatment progress and the occurrence of adverse events were found to be inadequate during follow-ups. There was a lack of equipment, an interruption of laboratory service, and shortages in the laboratory supply system. Trained human resources were unavailable to interpret results. As a result, patient monitoring and care might have been compromised and could have resulted in unsuccessful treatment outcomes.

Rationale on which the best practice guidelines are based

Timeously administration of ancillary medication is very important to prevent and treat adverse events associated with anti-TB drugs (Merid et al 2019:8). Furthermore, Tag El Din et al (2015:948) emphasised that failing to manage adverse events in time and aggressively so could result in further morbidity and mortality, in addition to reduced

patient compliance and non-adherence to therapy. Thus, health facilities should have an adequate and regular supply of ancillary drugs to achieve successful outcomes in the treatment of tuberculosis disease, especially drug-resistant ones (Dlodlo et al 2019:78).

Baseline and routine monitoring laboratory tests are required for patients on treatment with second-line anti-TB drugs (WHO 2020a:39). Moreover, laboratory tests can detect occult adverse events that cannot be noted by the patient or HCPs (Tag El Din et al 2015: 940; Lange et al 2019:652). At the same time, in resource-limited settings, where the availability of regular supplies of monitoring tests is inadequate, the identification and management of adverse events cannot be done as required (Perumal et al 2018:537). Studies show that in Ethiopia, there is a deficiency in the constant supply of laboratory reagents in the public sector periodically (Shibeshi et al 2019:7; Meressa et al 2015:1186).

Recommendations for implementation of the guidelines:

- Ensure there is an ample supply of reagents and kits in the laboratory for monitoring tests.
- Conduct an inventory of ancillary medications and laboratory monitoring tests and machines. For instance, anti-emetics, antacids, antihistamines, pyridoxine, potassium replacement, thyroxine, medicines for psychiatric conditions, medicines for peripheral neuropathy, ECG papers, electrolyte and chemistry tests.
- Check stock at both stores and the DR-TB unit.
- Ensure adequate supply and stock of essential ancillary drugs at all DR-TB treatment centres.
- Utilise the integrated pharmaceutical logistics system (IPLS).
- Follow the requesting and reporting system of IPLS.
- Strengthen the stock monitoring system.
- Establish laboratory equipment and machines (chemistry, electrolyte, and haematology analysers) maintenance capacity at hospital levels.
- Ensure back-up in the laboratory supply system of necessary investigations.
- Maintain a sufficient supply of laboratory items to monitor treatment response.
- Avail a sufficient and regular supply of ancillary medicines for the management of drug side effects (anti-emetics, antacids, antihistamines, pyridoxine,

potassium replacement, thyroxine, medicines for psychiatric conditions, and medicines for peripheral neuropathy, etcetera).

- Routine maintenance of non-functionality of machines/analysers.

Guideline 18: Decentralize DR-TB models of care as well as treatment initiation and follow-up centres to enhance accessibility

This study found that most health facilities which give DR-TB service are located in cities and towns, making accessibility difficult for patients located in the countryside. In addition, most inpatient admissions are centralised, and patients spend a long time away from their homes, creating psychosocial pressure on them. Patients may fail to resist such pressures and may consequently discontinue their treatment for good.

Rationale on which the best practice guidelines are based

Different scholars locally and globally support the decentralisation of DR-TB services, including building the capacity of TFCs and strengthening the linkage with TICs (Alene et al 2017:360; Evans et al 2018:2; Htun et al 2018:2). According to Alene et al (2017:360), health service decentralisation allows patients living far from centralized centres to access and remain on DR-TB treatment. An analysis of a systematic review of the treatment and care of DR-TB patients in decentralized versus centralised systems showed that treatment success and loss to follow-up improved with decentralised care compared to centralised care (WHO 2020a:68).

Likewise, researchers Evans et al (2018:2), further explained that decentralisation of services renders advantages of cost reduction and outpatient treatment options to patients on DR-TB therapy. On the other hand, Lange et al (2019:653) pointed out that there has been a shortage of experienced as well as well-trained providers in decentralised centres. For this reason, WHO (2019a:56) emphasises the need for staff training and close treatment supervision where decentralized care is provided.

Recommendations for implementation of the guidelines:

- Work on scaling up of diagnostic capacity with Xpert MTB/RIF and other molecular WHO-approved rapid diagnostics (mWRDs) at district level hospitals and health centres.

- Train technical human resources on clinical and programmatic management of DR-TB at district level hospitals and health centres.
- Make the expansion of TICs a priority agenda item for central and regional decision-makers through proper advocacy.
- Decentralised care should not be offered to patients with extensive disease, serious comorbidities, and adherence problems.
- Build the capacity of the TICs and TFCs to offer appropriate treatment supervision, patient education and social support, staff training, infection control practices, and quality assurance.
- Commission expansion of infrastructure for DR-TB care and service for wider geographic coverage in the country.
- Expand decentralised laboratory access to DST in the country.
- Increase the capacity of the regional laboratories to do phenotypic DST, which is still needed to confirm the susceptibility of second-line drugs and to construct the optimal final regimen.
- Ensure universal access to TB diagnosis, treatment, and care according to international standards.
- Ensure the decentralisation and availability of sufficient resources in the health system to guarantee access to all commodities and services to deliver proper DR-TB care.
- Extend and maintain basic mentorship service, which is conducted from TIC to TFC and also from hospital to health centre.
- Initiate the principle of community-based DR-TB care in the country.

Guideline 19: Initiate community-based model of DR-TB care in the country.

The study found that the principle of community-based DR-TB care is not in place in the country and patients cannot follow their treatment from home. The rural patients are the hardest hit in that there is no structure that can listen to them and solve their problems, follow their condition and give necessary support. Moreover, the study identified the necessity of extending community-based care in a decentralized fashion

as of the drug susceptible TB care to the lowest structural levels. Hence, decentralizing, in a sense, community-based service for most patients is feasible.

Rationale on which the best practice guidelines are based

A systemic review of interventions to improve retention-in-care and treatment adherence among patients with DR-TB showed that cohorts that received home-based DOT with daily home visits by community health workers had the greatest reduction in losses-to-follow-up when compared to cohorts with standard of care. In the same study, more frequent contact with HCPs throughout treatment, in the form of home visits for DOT or individual counselling, resulted in fewer losses-to-follow-up (Law et al 2019:7).

Khachatryan et al (2021:5) confirmed that when home-based DOT is implemented by HCPs, it has a protective factor against unfavourable treatment outcomes. In the first place, home-based DOT improves adherence because of the shared responsibility for taking medication between HCPs and the patient. Second, home-based DOT gives patients an opportunity to take medications in their own comfortable zones without any inconveniences caused by travel to TFCs. Finally, patients can get the necessary social and psychological support from their family members, which may also contribute to increased adherence (Khachatryan et al 2021:6).

Scholars Bieh, Weigel and Smith (2017:2) describe that home or community-based models of care are favoured by patients, their families, community members, and health workers. In fact, on top of cost effectiveness, community-based care allows easier access to treatment and facilitates psychosocial support for patients from their social network. Likewise, locally adapted community-based, ambulatory DR-TB care has been shown to be cost-effective, as well, from South Africa to Nepal, Pakistan, Bangladesh, and Ethiopia (Mookherji & Algria-Flores 2018:8). Furthermore, the ambulatory model of care could improve the cost-effectiveness of DR-TB care for patients on treatment and has benefits of reduced resource use and avoiding as many deaths compared with hospitalization models (WHO 2019a:55).

Recommendations for implementation of the guidelines

- Provide daily home visits and home-based DOT.
- Adopt patient support measures locally. For instance, the alternative patient-friendly modes of DOT include video-observed DOT (for the evening dose every day and all the doses on Sunday and other holidays).

- Capacitate primary health care units on DR-TB care and allow health centres, health posts, and health extension workers to participate.
- Commission decentralisation to the community-based service from hospital to health centre, from health centre to health post and home.
- Offer continuous support from the health system and community that can be conveyed through regular DOT contacts.
- Initiate community-based ambulatory DR-TB services and care, which offer alternatives to facility-based DOT.
- Integrate community-based interventions into the DR-TB treatment programme
- The ambulatory care model of care rather than the hospitalised one should be extended to treat DR-TB patients in most cases.
- Engage health extension workers (HEWs) in community-based DR-TB care.
- Allow health centres, health posts, and health extension workers to participate.
- Involve HEWs in active patient follow-up routines to trace those patients who stop their treatment, address their concerns, and work together with them to bring them back into care.
- Consider making community-based DR-TB care an essential component of the DR-TB treatment programme.

Guideline 20: Offer quality DR-TB care

The study revealed that there has been a gap in delivering comprehensive quality DR-TB care to all patients at all levels. And there is a minimum quality of treatment service in place.

Rationale on which the best practice guidelines are based

Quality TB care is patient-centred, efficient, effective, equitable, timely, safe, and accessible care consistent with international standards (Naidoo, Gengiah, Singh, Stillo & Padayatchi 2019:4).

Recommendations for implementation of the guidelines

- Offer people-centred care that is tailored to the needs, preferences, experiences, and values of the people seeking care.

- Offer people-centred care based on the right to be treated with respect as well as quality services such as accurate diagnosis, the latest treatment, referral, and follow-up.
- Provide effective evidence-based care and services in line with WHO guidance.
- Offer care in a safe way that avoids harm to the people for whom the care is intended.
- Extend the care that is provided, upholding the dignity of the individual, along with nutrition, financial, and counselling support in a non-stigmatising manner.
- Offer comprehensive care such that clients feel engaged in the decisions about the care.
- Provide DR-TB services with a skilled and competent health workforce.
- Ensure the provision of DR-TB services is based upon accessible facilities and safe, regulated tools and technologies.
- Make sure to address issues like comorbidities, risk factors, and social factors that may impact recovery.
- Provide the best standards of DR-TB care with the best available tools, latest innovations, guidelines, diagnosis, and treatments.
- Work to integrate mental health support services with PMDT to combat depression and other mental health challenges experienced by patients during therapy.

Table 7.4: Summary of Guidelines and Recommendations for implementation

Guideline	Recommendations for implementation
1**: Consider collaborative framework for treatment and care of DR-TB and Diabetes**	• Routine screening of DM in DR-TB patients at the time of diagnosis and registration. • Provide counselling on appropriate lifestyle management, such as smoking cessation, avoiding excess alcohol consumption, a healthy diet, weight loss, and physical activity. • Educate clients with DM about their increased risks of TB and the signs and symptoms of TB so that they can present themselves to the clinic. • Conduct systematic TB screening in clients with DM, preferably with chest radiography. • Give dietary instructions and medications to optimise glycaemic control. • Consider cardiovascular risk assessment in TB-DM patients. • Initiate measures to minimise the risk of cardiovascular problems. • Work to achieve the recommended targets for glucose control of HBA1c <8% or FBS <180 mg/dl during DR-TB treatment.

2: Strengthen the collaboration with ART and PMDT programmes	• Maintain close monitoring of the toxicity of overlapping drugs, particularly nephron- and hepatotoxicity, as well as drug-drug interactions (DDIs). Possible DDI exists between bedaquiline and several ART regimens, especially those containing efavirenz and/or lopinavir/ritonavir. • Do not co-administer bedaquiline and efavirenz. • Offer early screening and diagnosis of TB (DR-TB) to HIV positive clients. • Extend timely access to second-line anti-TB medications in the case of a diagnosis of DR-TB. • Provide motivational counselling throughout the treatment process. • Early initiation of ART as soon as DR-TB treatment is tolerated, regardless of CD4 count, ideally as early as two weeks and no later than eight weeks after initiation of anti-TB. • Initiate ART within the first two weeks of initiating TB treatment when there is profound immunosuppression (CD4 counts less than 50 cells/mm3). • Provide close monitoring of adverse events and OIs. • Provide patients with adherence motivation behavioural counselling.
3: Early recognition and management of comorbidities, organ dysfunction and risk factors associated with unsuccessful treatment outcomes	• A panel of experts should review patients with comorbidities and organ dysfunction. • Get multidisciplinary evaluation for older patients with DR-TB. • Attention should be given to the control of comorbidities. • Offer testing for any other comorbidities. • Conduct close observation of the serum potassium level and consider prescribing low amounts of potassium and magnesium supplements to prevent hypokalaemia. • Offer close observation of the serum creatinine level. • The glomerular filtration rate (GFR) and urine output, serum creatinine, blood urea nitrogen, and albumin should all be monitored.

	• Utilise novel biomarkers, including kidney injury molecule-1, neutrophil gelatinase-associated lipocalin and N-acetyl-β-d-glucosaminidase, which may be useful additions in panels of biomarker for early detection of drug-induced AKI. • Individually tailored counselling should be initiated for DR-TB patients throughout their treatment period. • Pre-treatment baseline assessment should be conducted to identify factors associated with unsuccessful treatment outcomes. • Do a proper physical examination (including colour blindness tests, visual acuity tests, and neurologic tests) • Offer baseline laboratory tests (haematologic, chemistry, electrolyte, hormonal). • Do hepatitis B virus (HBV) and hepatitis C virus (HCV) tests at baseline. • Get thorough audiometry, electrocardiogram, and radiologic examinations.
4: Thorough assessment and proactive management of prognosis	• Ensure the early diagnosis of DR-TB. • Provide immediate initiation of DR-TB treatment after diagnosis. • Strict follow-up of clinical and laboratory response throughout the course of treatment. • In addition to bacteriologic tests, monitor progress through markers of response to treatment or of disease progression, such as the patient's general condition, weight gain over time, resolution of disease manifestations, blood indices, and results of imaging (for example chest radiography). • Close monitoring of adverse events due to second-line drugs. • Provide proper counselling as well as social and emotional support to patients to boost their morale and keep them on the treatment. • Identify any comorbidities and risk factors affecting treatment success and manage them accordingly. • Provide psychological counselling for patients at the time of DR-TB diagnosis. • Consider hospitalization of patients for some time, to contain the progress and dissemination of the disease in the body and to assure the success of the treatment. • Consider pulmonary surgery to improve prognosis as a result of reducing the bulk of lung tissue with intractable pathology and bacterial load. • Provide patient tailored individualised treatment regimens. • Have additional molecular tests (LPA/WGS and pDST) in addition to the GeneXpert test before initiating individualized treatment.

5: Provide patient tailored or individualized DST guided treatment regimens.	• Introduce the Xpert system at point of care facilities for rapid detection of RR-TB. • Facilitate universal access to drug susceptibility testing. • Extend rapid molecular DST as the initial test to detect DR prior to the initiation of appropriate therapy for all TB patients, including new and previously treated ones. • Strengthen referral linkage for LPAs. • Consider building the capacity of laboratories to give second-line DST service and/or LPAs. • When initiating a DR-TB regimen, have LPA results in addition to GeneXpert test results to guide the initial treatment choice. • Treatment regimens should always be guided by LPAs or WGS. • Results from genotypic testing using LPA/WGS and pDST should be available at the earliest opportunity to design an appropriate personalised regimen. • Let the DR-TB panel team set up at each of the hospitals jointly decide for each patient. • Whenever possible, the treatment regimen should be discussed by a multidisciplinary board (Consilium) of experts that may include infectious diseases specialists, pulmonologists, thoracic surgeons, clinical microbiologists, and pharmacologists. • Commission DST for bedaquiline to monitor resistance at the national reference laboratory.
6: There should be timely recognition, aggressive monitoring and intensive management of adverse events.	• Extend intensive treatment of adverse events. • During the early months of treatment, frequent patient monitoring and prompt intervention for AEs are critical. • Offer information about side effects; it could help patients to tolerate treatment. • Do clinical examinations and laboratory investigations as per schedule or need throughout the treatment duration. • Monitor GFR and urine output, serum creatinine, blood urea nitrogen, and albumin. • Arrange continuous capacity-building training on the monitoring and treatment of AEs. • During follow-up visits, patients should be thoroughly questioned about the occurrence of AEs. • The treating team should be trained to apply appropriate mental health assessment tools so that psychiatric disorders can be identified as soon as possible. • Ensure stringent clinical and laboratory-based active drug safety monitoring with real-time reporting.

	• Conduct close observation of the serum potassium level and consider prescribing low amounts of potassium and magnesium supplements to prevent hypokalaemia. • It is important to check regularly for symptoms and perform laboratory screenings to detect those AEs not reported by the patient or DOT provider. • Monitor patients daily for signs and symptoms of AEs during DOT sessions. • Advise spreading consumption of the pills over several hours to reduce discomfort. • Encourage patients to take pills after a meal to alleviate discomfort. • Utilise a systematic method of patient interviewing so that patients can report AEs without missing anything. • Healthcare providers should be trained to screen patients regularly for signs and symptoms of common SLD adverse events. • Make prompt evaluation, diagnosis, and treatment of any AEs. • Ensure an adequate supply of essential ancillary drugs at all DR-TB treatment centres. • Work to integrate and apply all the medical disciplines, as SLDs side effects affect all the systems. • Consider capacitating and enabling the staff to do all clinical examinations needed for patient monitoring. • Make sure to collect laboratory results properly. • Ensure there are laboratory investigations available necessary for patient follow-up in tracking treatment adverse effects systematically. • Routine maintenance of non-functional chemistry machines.
7: Address delay in diagnosis	• Cut down on missed opportunities (address the 20% of DR-TB cases who visit health facilities for other reasons before being diagnosed with DR-TB). • Expand rapid molecular DST as the first test to detect DR-TB before initiating appropriate therapy for all TB patients, including new and previously treated. • Introduce the Xpert system at point of care facilities for rapid detection of RR-TB and strengthen referral linkage for LPAs to diagnose MDR-TB-XDR-TB in just a few days. • Strengthen the sample referral system. • Ensure the feedback system works optimally from referral/regional laboratories to TICs. • Introduce rapid molecular DST as the initial test at point-of-care facilities.

	• Consider using innovative ways of reporting DST results to TICs. This may include short message services, emails or the use of web-based mobile applications. • Address institutional barriers to diagnosis. • Improve the activities of early contact tracing and active screening of family members and other contacts. • Reduce diagnostic costs such as travel and other expenses. • Identify high-risk or difficult-to-reach populations with limited access to TB services. • Allocate sufficient time for the training of healthcare providers on DR-TB. • Decentralise diagnostic facilities with ample skilled providers. • Improve the diagnostic and testing capabilities of the country. • Offer universal TB symptom screening for all patients at all health facilities. • Provide urine LAM testing to known HIV infected patients with CD4 counts <100 cells/mm3. • Identify high-risk populations that have poor access to TB services. • Consider community-based mass chest radiography screening campaigns using digital radiography with automated computer evaluation. • Address stigma and discrimination because people who have TB symptoms may refuse screening for TB or avoid going for diagnostic tests due to stigma, discrimination, and fear. • Routine maintenance and proper service for diagnostic equipment, including microscopes, x-ray machines, and GeneXpert. • Work in partnership with private health providers, especially traditional healers, by training them and providing incentives for referrals. • Expand diagnostic facilities. • Tackle incorrect diagnosis by improving the capacity of the facility and providers. • Provide sufficient training for health care providers.
8: Offer surgery for patients amenable to surgery.	• Consider surgical intervention in DR-TB patients with localised pulmonary sequelae or persistent cavitary lesions who do not respond to drug treatment. • Consider pulmonary surgery to improve prognosis by reducing the bulk of lung tissue with intractable pathology and bacterial load.

	• Establish surgical facilities, including operation rooms with laminar air flow and negative air pressure serving DR-TB clients. • Institute intensive care units serving DR-TB clients. • Extend referral networks between surgery facilities and TICs. • Utilise a multidisciplinary Consilium for deciding on the indications of surgery to ensure the best possible outcomes. • Communicate the time of culture conversion as the optimal time for elective surgery. • Consider emergency surgery in situations of recurrent haemoptysis, profuse lung haemorrhage, or tension pneumothorax. • Do not consider surgery for bilateral cavitary disease (subtotal affected lungs), poor cardiorespiratory function, severe comorbidity, and active bronchial TB. • Offer pre-operative physical exercise and post-operative rehabilitation, including psychological support. • Engage social workers, counsellors, or psychologists with DR-TB patients having surgery.
9: Prevention of complications and provision of palliative care.	• Provide proper treatment of drug-susceptible TB. • Provide individualised DST-guided treatment regimens. • Initiate early detection and treatment of DR-TB before complications developed. • Prevention and aggressive management of drug side effects. • Strict follow-up of patients with clinical and laboratory tests throughout the treatment duration. • Monitor treatment response clinically by checking remission of signs and symptoms and bacteriologically by performing sputum culture and smear microscopy as well as radiological findings compared to the baseline. • Offer repeat testing for DST in the case of repeated positive cultures. • Offer HCV screening for DR-TB patients as well as scale up accessible treatment. • Initiate proactive use of therapeutic drug monitoring (TDM), which can help to prevent drug-related complications. • Consider setting up a rehabilitation centre for patients with complications. • Offer respiratory physiotherapeutic interventions. • Work on capacity building to extend physiotherapy services, including training to staff, rooms, and equipment for therapy.

	• Integrate palliative care into the TB programme. • Offer symptom control and proper infection control measures. • Make accessible treatment and care for DR-TB patients that relieve suffering and are life-saving. • Offer lung function tests to determine the baseline level of function and disease. • Inhaled or long-acting bronchodilators may be prescribed if the lung function tests show airflow obstruction. • Advise patient to remain active and follow a pulmonary rehabilitation or exercise programme. • Educate about airway clearance exercises.
10: Increase awareness about the disease and importance of finishing the treatment course	• Involve peer educators in raising DR-TB awareness among patients on treatment and the community at large. • Prepare DR-TB information in a language or format that is understood by the local population. • Understand TB symptoms and how it is transmitted, prevented, diagnosed, and treated. • Inform the community where DR-TB services are provided. • Create awareness of DR-TB through the use of available visual (posters, leaflets, digital messaging on mobile), audio (radio programmes, audio clips through mobile) and audio-visual (TV programmes, short videos, films) materials. • Involve existing community structures like the women's development army and health extension workers as agents to create awareness of DR-TB. • Develop information, education, and communication (IEC) materials in local languages and dialects or in pictorial form. • Create awareness of the importance of completing the treatment; otherwise, the disease will relapse again. • Render proper advice and continuous counselling supported by a psychologist to convince patients of the importance of finishing the treatment course and the danger of discontinuing the regimen. • Involve expert patients (those who finished DR-TB treatment) to educate and share their experiences with patients on treatment. • Provide detailed information at the beginning and then communicate the clinical progress throughout the treatment period to patients. • Inform patient when they commence treatment, about how long it is necessary, in which month what changes are seen or expected, and for how long they ought to continue.

	• Give sufficient awareness during pre-treatment counselling. • Ensure that each patient has an adequate understanding of the treatment.
11: Initiate interventions to treat behavioural problems including substance abuse	• Initiate a coherent smoking and alcohol cessation intervention. • Integrate substance abuse interventions with clinical and programmatic management of DR-TB. • Effectively deal with peer pressure. • Promote ways to handle stress, like taking up exercise and reading a good book. • Create integration with a psychiatry unit to seek help for mental illness. • Offer behavioural change interventions. • Consider behavioural treatments such as individual, group, and telephone counselling. • Promote lifestyle interventions. • Offer psychosocial and pharmacological interventions. • Make incentive-based interventions available. • Involve self-help groups. • Facilitate peer- to-peer counselling. • Offer alcohol cessation counselling. • Involve TB clubs in behavioural change interventions. • Ensure that there are recreational and refreshment areas and a garden for inpatients in the MDR ward. • Engage social workers, counsellors, or psychologists in the treatment of DR-TB patients. • Consider comprehensive interventions to tackle psychosocial problems.
12: Offer a package of treatment adherence promoting interventions in order to improve retention-in-care and prevent lost to follow-up	• Social support in the form of material support like food, financial incentives or transport fees, living allowances, housing incentives may be provided to DR-TB patients to address direct and indirect income losses incurred by them and their families. • The adherence and pre-treatment counselling must be strong, and the patient should be empowered and well informed about the treatment. • Provide emotional support. • Offer incentives and enablers based on the needs of the individual patient. • Psychological support may be offered to patients in the form of counselling sessions or peer groups.

	• Consider financial support to encourage long-term retention in MDR-TB care. • Provide reinforced communication, with closer and more regular contact with the patient. • Allocate enough health provider time to each patient during DOT and clinical follow-ups. • Tracers, according to WHO (2020a:62), communication with the patient, including home visits and use of digital technology like SMS, automated telephone reminders, or phone calls, can be used based on resources and patient needs. • A digital medication monitor, a device that can remind patients to take medication, may be offered based on resources and conditions for implementation. • Consider substance abuse treatment. • Extend free care in all service outlets for DR-TB patients including diagnostics, medication, and procedures. • Counselling and treatment education should be provided to all patients throughout the treatment duration. • Patients should be continuously motivated to adhere to treatment, and providers have an important role here. • Encourage a positive attitude towards DR-TB treatment through effective communication and empathy. • Patients should be educated about the consequences of non-adherence. • Utilise a patient-centred approach in which patients are actively involved in the treatment plan and process. • Provide DR-TB care that responds to individual patient preferences, needs, and values. • Give comprehensive DR-TB care in a manner that patients feel safe, respected, and engaged in decisions about their care. • Include patients in the decision-making process during treatment periods.
13: Provide socio-economic support for all DR-TB patients on treatment	• Assess the needs of patients for psychosocial support through conversations and active listening. • Offer food parcels or food certificates to patients to support their treatment. • Employment and income generation opportunities should be provided as part of the intervention programme. • Form a collaborative partnership between DR-TB services and faith-based civil society organisations to offer psychosocial support, including spiritual support. • Provide financial support to reimburse rent, travel expenses, and compensate for lost income or wages during treatment. • Provide nutritional supplementation. • Involve charity organisations to support discharged patients with socio-economic problems.

	• Consider designing a permanent social support system within the programme independent of the partners. • Provide additional support or incentives, such as serving breakfast meals with DOT, to encourage attendance until the end of treatment. • Consider nutritional therapeutic feeding at the beginning of the treatment, as most DR-TB patients need nutritional rehabilitation. • Ensure an adequate budget is allocated for the nutrition of inpatients in the MDR ward. • Expand the options for individualised social support for patients. • Use legislations to protect people affected by DR-TB from discrimination such as expulsion from workplaces. Right to Employment of Persons with Disability Proclamation No. 568/2008 and Social Health Insurance Proclamation No.690 /2010. • Expand coverage of social protection schemes to cover the needs associated with illness such as sickness insurance, disability pension, social welfare payments • Make available a social grant for patients with DR-TB based on their need and situation.
14: Provide psycho-emotional support for all DR-TB patients on treatment	• Integrate or link mental health into TB control and care. • At least a psychological counsellor can be planned at the centres of DR-TB with screening for mental illness at peripheral levels. • Healthcare providers should make quick referrals to centres when they see psycho-emotional problems, for instance, feelings of loneliness, loss of hope, feelings of isolation, suicidal ideation, and depression. • Identification of mental health issues should be resumed at treatment initiation and its monitoring should be continued throughout DR-TB care. • Consider utilizing digital technologies by applying interventions to address mental illness issues in DR-TB care. • Build health system capacity to identify symptoms of depression and other psychiatric conditions and expand the multidisciplinary team. Members of the team may include from the departments of thoracic surgery, psychiatry, internal medicine, laboratory, dermatology, ophthalmology, cardiology, infectious diseases, pulmonology, dietetic, clinical microbiology, and paediatrics. • Provide psychological counselling for the patients at the time of DR-TB diagnosis and closely monitor all patients for adverse drug effects, especially at the early stages of treatment.

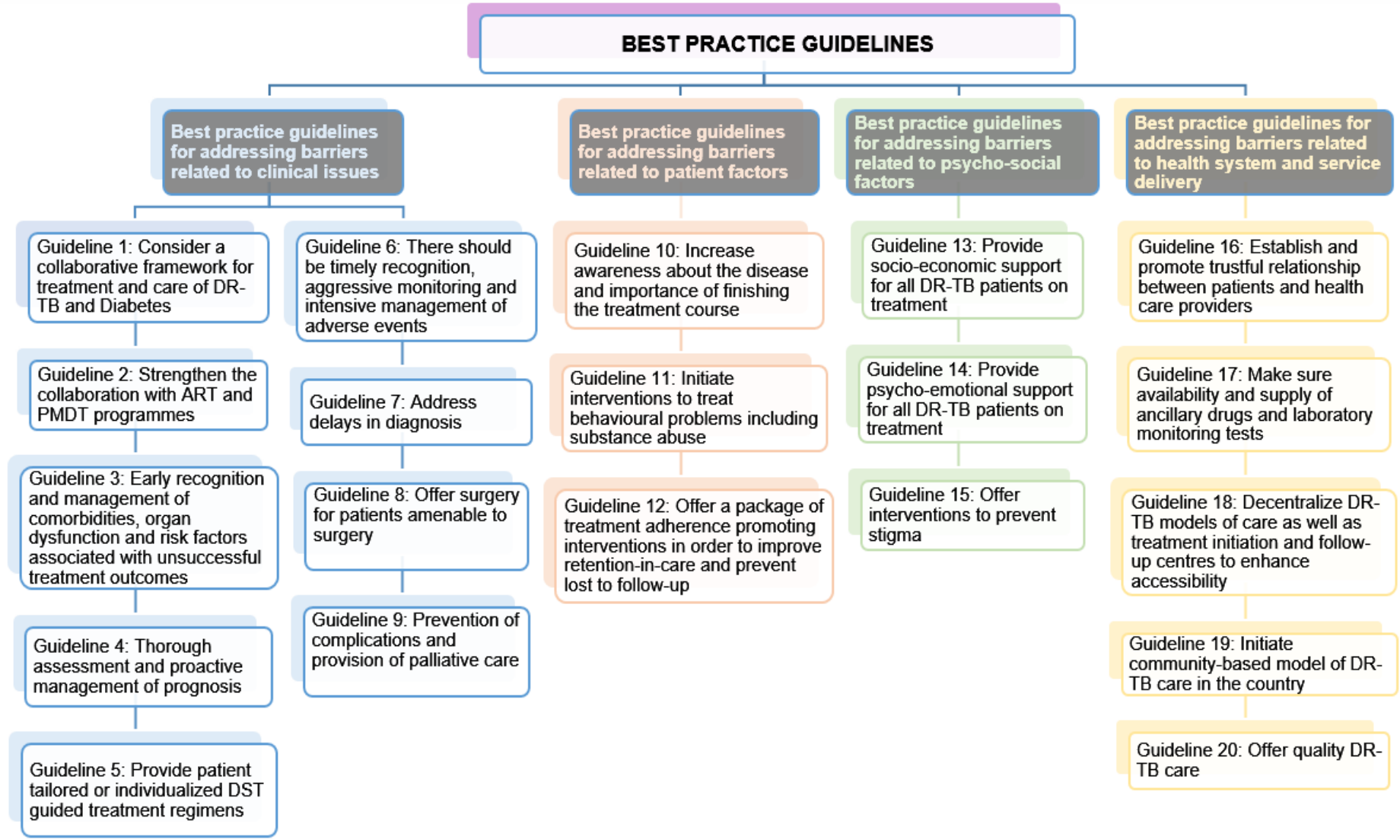
	• Assess the needs of patients for psychosocial support through conversations and active listening. • Involve peer supporters to provide information on a one-to-one basis or in support groups to alleviate emotional and physical aspects of treatment. • Arrange peer consultants through an online communication platform to answer any queries and allay anxieties about treatment. • Render proper advice and continuous counselling supported by a psychologist in order to convince them of the importance of finishing and the danger of discontinuing the regimen. • Engage social workers, counsellors, or psychologists in the treatment of DR-TB patients. • Provide detailed information at the beginning and then after communicating the clinical progress throughout the treatment period to patients. • Provide holistic care incorporating a multidisciplinary team that supports the patient emotionally and psychologically as well as medically. • Educate family members and empower them to provide emotional and psychological support to patients. • Collaboratively work to assess the care needs of patients and jointly agree on a care plan that includes clinical, psychological, and social support for patients and their families. • Engage a multidisciplinary team for the comprehensive management of DR-TB patients. The team may include members from the departments of thoracic surgery, psychiatry, internal medicine, laboratory, dermatology, ophthalmology, cardiology, infectious diseases, pulmonology, clinical microbiology, and paediatrics. • Patients on DR-TB treatment are isolated from society, feel lonely, and it is of great value that HCPs should provide emotional and motivational support.
15: Offer interventions to prevent stigma	• Provide family and community sensitisations, treatment-supporter programmes and counselling. • Organise interactive community awareness programmes that specifically address stigmatizing attitudes and actions. • Use existing laws (Right to Employment of Persons with Disability Proclamation No. 568/2008 and Social Health Insurance Proclamation No.690 /2010) and court systems to uphold the rights of DR-TB patients and their families. • Apply the health policy framework to reduce stigma.

	• Clarify that it is illegal to stigmatise anyone with DR-TB, including limiting or preventing access to TB services. • Make sure service providers (and staff at all levels) are trained on DR-TB and stigma. • Develop a communication strategy that includes advocacy to reduce stigma. • Involve TB clubs run by former DR-TB patients in offering psychological as well as emotional support. • Facilitate DR-TB survivors' sharing of stories. • Keep all private information of people with DR-TB or in the process of being investigated for DR-TB, confidential. • Treat clients equally with respect and dignity. • Extend the care that is provided, upholding the dignity of the individual in a non-stigmatising manner. • Public banners and health education posters related to TB should be carefully designed to prevent the creation of stigma. • Create awareness in the community not to discriminate against DR-TB patients and rather to embrace them. • Work to improve the attitude of health care professionals towards DR-TB.
16: Establish and promote trustful relationship between patients and health care providers.	Health care providers should: • Develop interpersonal communication skills like active listening to earn patient trust and build rapport. • Possess multiple qualities like empathy, respectfulness, and responsiveness that develop trust in patients and promote adherence to treatment. • Be open, sincere, approachable, responsible, flexible, and open to communication, and have good energy. • Have excellent interpersonal communication skills and demonstrate active listening. • Provide unconditional care and service with an understanding of the importance of treating patients as any other society member, as someone equal to them. • Have unconditional regard when accepting patients (showing complete support and acceptance of a person no matter what that person says or does), understanding their problems, challenges and needs. • Provide emotional, informational, instrumental (providing tangible assistance, offering a helping hand) and motivational support for their patients. • Provide continuous information to patients and their family members on facts about DR-TB, which includes side-effects, the importance of staying on treatment, healthy nutrition, recipes, exercise, and personal hygiene.

	• Assist with emotional and motivational support during monthly follow up visits. • Communicate with patients about the level of their problems and update them on how they are responding to therapy. • We need to ensure we develop good relationships and trust by treating patients with a friendly approach, handling with empathy, discussing problems, sharing concerns, responding to demands and reassuring the future. • Be responsive to the needs of patients in inpatient care and follow-up monitoring.
17: Make sure availability and supply of ancillary drugs and laboratory monitoring tests.	• Ensure there is an ample supply of reagents and kits in the laboratory for monitoring tests. • Conduct an inventory of ancillary medications and laboratory monitoring tests and machines. For instance, anti-emetics, antacids, antihistamines, pyridoxine, potassium replacement, thyroxine, medicines for psychiatric conditions, medicines for peripheral neuropathy, ECG papers, electrolyte and chemistry tests. • Check stock at both stores and the DR-TB unit. • Ensure adequate supply and stock of essential ancillary drugs at all DR-TB treatment centres. • Utilise the integrated pharmaceutical logistics system (IPLS). • Follow the requesting and reporting system of IPLS. • Strengthen the stock monitoring system. • Establish laboratory equipment and machines (chemistry, electrolyte, and haematology analysers) maintenance capacity at hospital levels. • Ensure back-up in the laboratory supply system of necessary investigations. • Maintain a sufficient supply of laboratory items to monitor treatment response. • Avail a sufficient and regular supply of ancillary medicines for the management of drug side effects (anti-emetics, antacids, antihistamines, pyridoxine, potassium replacement, thyroxine, medicines for psychiatric conditions, and medicines for peripheral neuropathy, etcetera). • Routine maintenance of non-functionality of machines/analysers.
18: Decentralise DR-TB models of care as well as treatment initiation and follow-up centres to enhance accessibility.	• Work on scaling up of diagnostic capacity with Xpert MTB/RIF and other molecular WHO-approved rapid diagnostics (mWRDs) at district level hospitals and health centres. • Train technical human resources on clinical and programmatic management of DR-TB at district level hospitals and health centres.

	• Make the expansion of TICs a priority agenda item for central and regional decision-makers through proper advocacy. • Decentralised care should not be offered to patients with extensive disease, serious comorbidities, and adherence problems. • Build the capacity of the TICs and TFCs to offer appropriate treatment supervision, patient education and social support, staff training, infection control practices, and quality assurance. • Commission expansion of infrastructure for DR-TB care and service for wider geographic coverage in the country. • Expand decentralised laboratory access to DST in the country. • Increase the capacity of the regional laboratories to do phenotypic DST, which is still needed to confirm the susceptibility of second-line drugs and to construct the optimal final regimen. • Ensure universal access to TB diagnosis, treatment, and care according to international standards. • Ensure the decentralisation and availability of sufficient resources in the health system to guarantee access to all commodities and services to deliver proper DR-TB care. • Extend and maintain basic mentorship service, which is conducted from TIC to TFC and also from hospital to health centre. • Initiate the principle of community-based DR-TB care in the country.
19: Initiate community-based model of DR-TB care in the country.	• Provide daily home visits and home-based DOT. • Adopt patient support measures locally. For instance, the alternative patient-friendly modes of DOT include video-observed DOT (for the evening dose every day and all the doses on Sunday and other holidays). • Capacitate primary health care units on DR-TB care and allow health centres, health posts, and health extension workers to participate. • Commission decentralisation to the community-based service from hospital to health centre, from health centre to health post and home. • Offer continuous support from the health system and community that can be conveyed through regular DOT contacts. • Initiate community-based ambulatory DR-TB services and care, which offer alternatives to facility-based DOT.

	• Integrate community-based interventions into the DR-TB treatment programme • The ambulatory care model of care rather than the hospitalised one should be extended to treat DR-TB patients in most cases. • Engage health extension workers (HEWs) in community-based DR-TB care. • Allow health centres, health posts, and health extension workers to participate. • Involve HEWs in active patient follow-up routines to trace those patients who stop their treatment, address their concerns, and work together with them to bring them back into care. • Consider making community-based DR-TB care an essential component of the DR-TB treatment programme.
20: Offer quality DR-TB care.	• Offer people-centred care that is tailored to the needs, preferences, experiences, and values of the people seeking care. • Offer people-centred care based on the right to be treated with respect as well as quality services such as accurate diagnosis, the latest treatment, referral, and follow-up. • Provide effective evidence-based care and services in line with WHO guidance. • Offer care in a safe way that avoids harm to the people for whom the care is intended. • Extend the care that is provided, upholding the dignity of the individual, along with nutrition, financial, and counselling support in a non-stigmatising manner. • Offer comprehensive care such that clients feel engaged in the decisions about the care. • Provide DR-TB services with a skilled and competent health workforce. • Ensure the provision of DR-TB services is based upon accessible facilities and safe, regulated tools and technologies. • Make sure to address issues like comorbidities, risk factors, and social factors that may impact recovery. • Provide the best standards of DR-TB care with the best available tools, latest innovations, guidelines, diagnosis, and treatments. • Work to integrate mental health support services with PMDT to combat depression and other mental health challenges experienced by patients during therapy.


BEST PRACTICE GUIDELINES
Best practice guidelines for addressing barriers related to clinical issues
Guideline 1: Consider a collaborative framework for treatment and care of DR-TB and Diabetes
Guideline 2: Strengthen the collaboration with ART and PMDT programmes
Guideline 3: Early recognition and management of comorbidities, organ dysfunction and risk factors associated with unsuccessful treatment outcomes
Guideline 4: Thorough assessment and proactive management of prognosis
Guideline 5: Provide patient tailored or individualized DST guided treatment regimens
Guideline 6: There should be timely recognition, aggressive monitoring and intensive management of adverse events
Guideline 7: Address delays in diagnosis
Guideline 8: Offer surgery for patients amenable to surgery
Guideline 9: Prevention of complications and provision of palliative care
Best practice guidelines for addressing barriers related to patient factors
Guideline 10: Increase awareness about the disease and importance of finishing the treatment course
Guideline 11: Initiate interventions to treat behavioural problems including substance abuse
Guideline 12: Offer a package of treatment adherence promoting interventions in order to improve retention-in-care and prevent lost to follow-up
Best practice guidelines for addressing barriers related to psycho-social factors
Guideline 13: Provide socio-economic support for all DR-TB patients on treatment
Guideline 14: Provide psycho-emotional support for all DR-TB patients on treatment
Guideline 15: Offer interventions to prevent stigma
Best practice guidelines for addressing barriers related to health system and service delivery
Guideline 16: Establish and promote trustful relationship between patients and health care providers
Guideline 17: Make sure availability and supply of ancillary drugs and laboratory monitoring tests
Guideline 18: Decentralize DR-TB models of care as well as treatment initiation and follow-up centres to enhance accessibility
Guideline 19: Initiate community-based model of DR-TB care in the country
Guideline 20: Offer quality DR-TB care

7.11 CONCLUSION

This chapter presented the best practice guidelines aimed at addressing barriers to treatment completion for patients with DR-TB in Ethiopia. The best practice guidelines emerged from the findings of the study and they are informed by a systematic review of existing evidence in the literature. The best practice guidelines covered a wide range of barriers to DR-TB treatment completion. The next chapter proffers conclusions, limitations, and recommendations derived from the study to develop the best practice guidelines, as well as the researcher's reflections during the journey of conducting this study.

CHAPTER EIGHT

CONCLUSION, LIMITATIONS, RECOMMENDATIONS AND RESEARCHER'S REFLECTIONS

8.1 INTRODUCTION

Chapter seven presented best practice guidelines developed by the researcher based on the findings and informed by a systematic review of existing evidence, aimed at addressing barriers to treatment completion for patients with drug-resistant tuberculosis in Ethiopia. This final chapter presents the conclusion, limitations, and recommendations of the study, as well as researcher's reflections whilst conducting the study.

8.2 THE PURPOSE OF THE STUDY

The purpose of this study was to develop best practice guidelines for the completion of treatment of patients with drug-resistant tuberculosis in Ethiopia. This was achieved through the formulation of best practice guidelines derived from the conclusion and summary of the study findings presented in chapters four and five, and discussed in chapter six, as well as systematically reviewed evidence from the literature. The purpose of these best practice guidelines is to achieve improved DR-TB treatment outcomes by addressing barriers to treatment completion through evidence-based best practices in the delivery of DR-TB care and services and informed decision-making.

8.3 RESEARCH SUMMARY

This study used a convergent concurrent mixed method design to get an in-depth understanding of the lived experiences of patients using focus group discussions and the views of healthcare providers through an in-depth interview regarding barriers to treatment completion. Further, the researcher had a comprehensive understanding of factors associated with treatment completion of patients taking DR-TB treatment garnered from a review of the DR-TB unit registers and patient charts.

The study settings were DR-TB treatment-initiating hospitals in Ethiopia. Hospitals A, B, C, and D were the study settings for this study. For the quantitative strand, data

from 487 patients were collected retrospectively from DR-TB registers and patient charts using a pre-tested questionnaire (Annexure G).

For the qualitative strand, data collection tools were focus group discussion guides for FGDs (Annexure I) and interview guides for in-depth interviews (Annexure J). In both focus groups and in-depth interviews, open-ended probing questions were utilised to delve further into the emerging discussions. Focus group interviews were conducted with 42 purposively selected DR-TB patients with a history of unsuccessful previous treatment and then on a retreatment regimen in Saint Peter, Alert, Adama, and Bishoftu Hospitals. A group of seven patients was assembled for a discussion in each focus group session. A total of six FGD sessions were conducted.

In-depth interviews with healthcare providers who have been working in clinical and programmatic management of DR-TB were conducted. In total, fifteen experienced healthcare providers, including senior internal medicine specialist physicians, general practitioner physicians, health officers, and nurses, participated in the interviews.

The quantitative data were analysed using SPSS version 24 for Windows, whereas the qualitative data were coded and sorted using ATLAS.ti 8 software, and a conventional content analysis approach was used, focusing on both the manifest and latent content of the narratives.

From the in-depth interview with healthcare providers, three themes emerged, which comprised: barriers to treatment completion; challenges for patient follow-up; and cross-cutting issues influencing treatment completion. Accordingly, the first theme comprised six categories and numerous subcategories, as illustrated in Table 5.3. Likewise, theme two had six categories with a number of subcategories and theme three had seven categories with a few subcategories, as shown in Table 5.4 and 5.5, respectively.

From the focus group discussions with previously treated DR-TB patients, five themes emerged, which were: perceived barriers to treatment completion; challenges for patient follow-up while on treatment; facilitators and enablers for completing treatment; perceived benefits towards treatment completion; and perceived severity of the problem.

8.4 RESEARCH OBJECTIVES

A summary of the research findings is presented based on the objectives of the research.

8.4.1 To determine factors associated with treatment completion of patients on DR-TB treatment.

This objective was achieved quantitatively by retrospective chart review of unit DR-TB registers and patient charts. The study established that patients with comorbidity and adverse events such as psychotic symptoms, drug-induced hepatitis, renal toxicity, and electrolyte disturbance, as well as those in the age group of 55–64 years and in the registration group after lost-to-follow-up at the start of treatment, were less likely to complete treatment. On the other hand, patients with arthritis and those who were diagnosed with LPA were more likely to complete treatment. The detailed logistic regression analysis is illustrated in Table 4.6.

8.4.2 To describe the views of experts managing DR-TB patients on treatment completion.

This objective was accomplished by in-depth interviews with health care professionals working in clinical and programmatic management of DR-TB. During in-depth interviews, the HCPs were asked about their views regarding barriers to DR-TB treatment completion. This study identified and categorised a number of barriers to treatment completion. The barriers identified are classified under seven categories: clinical issues, drug related challenges, extensive resistance, patient factors, health system related factors, socio-economic, and programmatic as well as provider-related factors.

Under clinical issues, barriers identified were delay in the management of side effects; comorbidities; complexity of treatment; long illness before treatment; bad prognosis; delay in diagnosis; and lack of proper surgical management. Besides, drug-related barriers identified were side effects, long treatment duration, high pill burden, fear of injection, and ineffectiveness of SLDs. In addition, the study also confirmed that a false sense of cure, substance abuse, and lack of awareness are patient factors posing a barrier for treatment completion. Similarly, accessibility, bad facility infrastructure, and absence of community-based DR-TB service were categorised as health system

barriers to treatment completion. Further, low socio-economic conditions, stigma, and malnutrition were identified as factors erecting barriers to treatment completion. Lastly, the manner of handling patients, inadequacy of pre-treatment counselling, and weak monitoring of patients were identified as programmatic and provider-related barriers that hinder treatment completion.

8.4.3 To describe experiences of previously treated DR-TB patients on treatment completion.

This objective was achieved because the lived experiences of previously treated patients on DR-TB treatment completion were identified in the thick descriptions offered. The experiences of patients were described in terms of HBM concepts. From the focus group discussions, five themes emerged, namely, perceived barriers to treatment completion; challenges for patient follow-up while on treatment; enablers for completing treatment; perceived benefits towards treatment completion; and perceived severity of the problem. The categories and subcategories of each of the five themes were presented and discussed in chapters five and six.

8.4.4 To explain factors associated with treatment completion with findings from qualitative strand.

In the qualitative findings of the study, factors affecting and posing barriers to treatment completion were explained and clarified by the healthcare providers in the in-depth interviews and by the patients in the focus group discussions. In addition, in the discussion of the findings, the quantitative and qualitative results are integrated where appropriate.

8.4.5 Develop best practice guidelines aimed at addressing barriers to treatment completion for patients with DR-TB in Ethiopia.

This objective was achieved by developing best practice guidelines aimed at addressing barriers to treatment completion for patients with DR-TB in Ethiopia. The best practice guidelines emerged from the findings of the study and were informed by a systematic review of existing evidence in the literature. Furthermore, the best practice guidelines were validated by experienced experts in the field of programmatic and clinical management of drug-resistant tuberculosis.

8.5 RECOMMENDATIONS

The following recommendations are proffered as derived from the results of the study.

Recommendations for the Federal Ministry of Health

- Initiate the principle of community-based DR-TB care in Ethiopia.
- Guide the decentralisation of community-based services from hospitals to health centres and from health centres to homes.
- Decentralise DR-TB treatment supported by policy-level direction.
- Extend adequate supply and distribution of nutritional therapeutic feeding to TICs and TFCs.
- Plan backup in the laboratory supply system for all necessary investigations.
- Work to achieve good programme support at the national, regional, and health facility levels to focus on and improve clinical monitoring quality.
- Plan to train and prepare physicians every year to replace those going to specialisation training.
- Extend continuous on-the-job and/or online training to HCPs.
- Focus on practical skills development systems in the training process of HCP.
- Commission a stringent system of pharmacovigilance.
- Mitigate fund limitations for PMDT.
- TB programmes should prioritise ensuring that communities receive appropriate and consistent education regarding MDR-TB,
- TB programmes should prioritise ensuring that patients receive psychosocial support, especially during the waiting times for diagnosis and treatment initiation, and
- TB programmes should prioritise ensuring that nutritional education and assistance are appropriate and consistent, early on and throughout the treatment process.
- Strengthen central laboratory infrastructure and capacity to accommodate new technologies.
- Advocate for increased funding to attain the national funding targets.
- Integrate mental health care into PMDT at policy and implementation levels.
- Integrate community-based DR-TB care into an essential component of PMDT.

- Establish a surgical treatment centre for patients with DR-TB.

Recommendations for Regional Health Bureaus

- Facilitate and make sure there is an adequate supply of essential ancillary drugs at all DR-TB treatment centres.
- Support treatment centres to improve treatment service quality and programme monitoring.
- Support TICs to implement and maintain basic mentorship services for TFCs.
- Make health centres, health posts and health extension workers participatory in a decentralised community-based DR-TB care.
- Capacity building of human resources who can provide timeously referrals and manage adverse effects properly.
- Continuous skill and competency training for all HCPs at any service point to vigilantly investigate DR-TB from any suspected site.
- Expand the limited infrastructure for DR-TB care and service for wider geographic coverage in the country.
- Support the undertaking of ambulatory community-based TB care.
- Prioritise consistent education regarding DR-TB in the community.
- Extend and ensure free ancillary medication supply at all levels.
- Revitalise the specimen referral system in order to improve access to culture and DST for patients.
- Organise interactive sensitisation programmes with the community to mitigate the stigma related to DR-TB.
- Strengthen public-private partnerships and communication with traditional healers.
- Craft income generation opportunities for patients on DR-TB treatment.
- Provide strong programmatic support for drug-susceptible TB management to avoid relapse and amplification of resistance.

Recommendations for national and regional culture and DST laboratories

- Use an innovative feedback system to notify culture and DST results on time. In this regard, telehealth, which is the use of digital information and communication technologies (computers and smartphones) to access health care information remotely, can be a good option.

- Improve access to testing by the expansion of decentralised laboratory service.
- Consider uptake of currently available tools as per WHO recommendations and optimise DR-TB diagnostic networks.
- Work to bring whole genome sequencing (WGS), a genotypic DST technology that allows the simultaneous detection of knowing resistance mutations to all drugs, to the level of sub-national laboratories.
- Increase the capacity of the regional laboratories to do phenotypic DST, which confirms the susceptibility of second-line drugs and to construct an optimal treatment regimen.
- Monitor that a feedback system for culture and DST works optimally.
- Initiate a therapeutic drug monitoring (TDM) investigation.

Recommendations for treatment-initiating centres

- Capacitate the staff do all the clinical examinations needed for patient monitoring.
- Integrate all the medical disciplines in DR-TB care.
- Improve the competence of staff continuously in all aspects and parameters of PMDT.
- Allocate access to prompt surgical and high-quality respiratory care evaluation and interventions for serious patients with advanced disease, both virtually and in person.
- Provide clinical and laboratory tools and equipment needed for baseline assessment.
- Extend and maintain basic mentorship services to TFCs.
- Support the MDR-TB panel team to jointly decide for each patient.
- Ensure proper clinical and laboratory monitoring of patients on treatment.
- A package of treatment adherence interventions may be offered to patients on DR-TB treatment.
- Carry out proper maintenance of infrastructure in the TICs to provide adequate sanitary and refreshment services for inpatients.

Recommendations for treatment follow-up centres

- Educate each patient so that they have a thorough understanding of DR-TB, treatment, and the significance of completion of therapy.

- Equip the patient with a strong foundation of understanding about the complexity of DRTB treatment and a routine reminder throughout the duration of treatment.
- Equip the patient with a solid understanding of the complexities of DR-TB treatment, as well as providing a routine reminder throughout the course of treatment.
- Strengthen adherence and pre-treatment counselling
- Inform and empower patients about the treatment and side effects.
- Offer adherence-promoting interventions.
- Assign adequate human resources for DR-TB care and service.
- Provide family, community, and employer sensitisation to enhance DR-TB awareness.
- Allocate enough health provider time to each patient

Recommendations for healthcare providers

- Ensure daily home visits and home-based DOT by community health workers.
- Provide patients with timeous feedback of results.
- Referral should be carried out as soon as possible.
- Manage side effects immediately and extensively.
- Perform routine screening of common comorbidities.
- Systematically screen for lab and clinical abnormalities regularly to pick up side-effects and to intervene before patients develop symptoms.
- Provide DOT that is patient-centred and locally optimized.
- Track feedback for bacteriology results on time
- Undertake close monitoring of the treatment response during the follow-up period.
- Ensure all patients' clinical and laboratory results are duly recorded.
- Trace patients missing treatment follow-up and lost-to-follow-up.
- Ensure early initiation of ART in DR-TB patients with HIV co-infection.
- Provide continuous health education that is adapted to the needs of patients.
- Give continuous counselling and need-based psychosocial support.
- Provide compassionate care and establish a good relationship with the patient.
- Actively involve patients in the treatment plan and process.

- Encourage families and peers to support patients to maintain a positive attitude towards their treatment.

Recommendations for partner organizations in DR-TB care

- Participate in enhancing the capacity of laboratories in treatment monitoring.
- Support the establishment of a surgical treatment centre for patients with DR-TB.
- Cooperation in TB financing and mobilising funding for TB diagnostic and treatment services.
- Mobilise funding for operational research and innovation of newer drug combination regiments which are easier to implement.
- Designing and building wards and units with enough capacity to provide surgical and post-surgical care.
- Renovation of the existing infrastructures in the DR-TB treatment facilities.
- Provision of clinical equipment for DR-TB care and services.

Recommendations for further research

- Measuring and mitigating catastrophic costs due to DR-TB treatment in Ethiopia.
- Observational study to assess adherence interventions that are more or less likely to lead to successful treatment completion.
- Operational research of newer and repurposed drug combinations to test the more effective and novel treatment regimens which are easier to implement.

8.6 CONTRIBUTION OF THE STUDY

This study provided a robust description of the experiences of the previously treated patients and views of the healthcare professionals, as well as factors associated with treatment completion. The best practice guidelines developed in the study have many potential applications for clinical practice and programmatic management of DR-TB, thereby contributing to the provision of a standard of care for patients. The best practice guidelines also benefit the programme by clarifying the possible best recommendations for solving barriers to treatment completion and contributing to the alleviation of economic, social, psychological, and physical suffering related to the disease. In addition, the knowledge generated from the study helps the healthcare

leadership and programme managers in making practical problem-solving decisions at the national level. Furthermore, the findings of the study could serve as background and recent literature for other researchers in the field.

8.7 LIMITATIONS OF THE STUDY

- The views of healthcare providers working in the treatment-initiating hospitals were gathered in the study. The views of healthcare providers working in the treatment follow-up health centres, whose views might have broadened the findings related to barriers to treatment completion, were not gathered in the study.
- Recall bias: previously treated patients are likely to have forgotten their past treatment experiences and may not have shared adequate information about their previous treatments.
- Since retrospective data were collected from patients' charts, some information might be missed due to incomplete records.

8.8. RESEARCHER'S REFLECTIONS

It has been a difficult but fascinating journey. During this time, I have learned and grown, and I am now better prepared to pursue a career that will fulfil me. Moreover, this journey has taught me that I am more resilient and determined than I previously thought. I have also realized that the more you learn, the more you realize how little you know.

I learned how to step out of my comfort zone with the help of my professor, friends, and family. I discovered that completing the journey could be rewarding. As a result, I managed to do scientific writing, statistical analysis, and editing all on my own before giving it to experts. I also specialize in writing and submitting manuscripts to peer-reviewed journals.

In conclusion, as Marian Wright Edelman once said, "Education is for improving the lives of others and for leaving your community and world better than you find them." I believe the best practice guidelines will improve programmatic management of drug-resistant tuberculosis and help patients complete their treatments successfully.

8.9. CONCLUSION

This chapter presented the research summary of the study and the recommendations provided for the target stakeholders in the clinical and programmatic management of drug resistant tuberculosis in the country, including the Federal Ministry of Health, Regional Health Bureaus, national and regional culture and DST laboratories, treatment initiating and follow-up centres, health-care providers and partners. In addition, recommendations for future research, the contributions and limitations of the study were presented as well.

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Annexure A: Ethical clearance certificate from the Research Ethics Committee: Department of Health Studies, UNISA

UNISA

RESEARCH ETHICS COMMITTEE: DEPARTMENT OF HEALTH STUDIES
REC-012714-039 (NHERC)

7 February 2018

Dear Ahmed Reshid Tusho

Decision: Ethics Approval

HSHDC/834/2018
Ahmed Reshid Tusho
Student no:6212-190-1
Supervisor: Prof TS Mokoboto-Zwane
Qualification: D Litt et Phil
Joint Supervisor: -

Name Ahmed Reshid Tusho

Proposal: Best practice guidelines to address barriers to treatment completion for patients with drug resistant tuberculosis

Qualification: **DPCHS04**

Thank you for the application for research ethics approval from the Research Ethics Committee: Department of Health Studies, for the above mentioned research. Final approval is granted from 7 February 2018 to 7 February 2023.

The application was reviewed in compliance with the Unisa Policy on Research Ethics by the Research Ethics Committee: Department of Health Studies on7 February 2018.

The proposed research may now commence with the proviso that:

1) The researcher/s will ensure that the research project adheres to the values and principles expressed in the UNISA Policy on Research Ethics.

2) Any adverse circumstance arising in the undertaking of the research project that is relevant to the ethicality of the study, as well as changes in the methodology, should be communicated in writing to the Research Ethics Review Committee, Department of Health Studies. An amended application could be requested if there are substantial changes from the existing proposal, especially if those changes affect any of the study-related risks for the research participants.

RECEIVED
2018 -02- 14
Executive Dean
College of Human Sciences

University of South Africa
Preller Street, Muckleneuk Ridge, City of Tshwane
PO Box 392 UNISA 0003 South Africa
Telephone: +27 12 429 3111 Facsimile: +27 12 429 4150
www.unisa.ac.za

3) The researcher will ensure that the research project adheres to any applicable national legislation, professional codes of conduct, institutional guidelines and scientific standards relevant to the specific field of study.

4) [Stipulate any reporting requirements if applicable].

Note:
The reference numbers [top middle and right corner of this communiqué] should be clearly indicated on all forms of communication [e.g. Webmail, E-mail messages, letters] with the intended research participants, as well as with the Research Ethics Committee: Department of Health Studies.

Kind regards,

pp
Prof JE Maritz
CHAIRPERSON
maritje@unisa.ac.za

Prof MM Moleki
ACADEMIC CHAIRPERSON
molekmm@unisa.ac.za

Prof A Phillips
DEAN COLLEGE OF HUMAN SCIENCES

Annexure B: Approval letter from AHRI/ALRET Ethics Review Committee

	AHRI/ALERT Ethics Review Committee	Date: October 01 No: _____

ANNEX 4
Form AF-10-015.1

AAERC approval letter

Protocol number PO36/18

Investigators: Ahmed Reshid

Protocol Title: "Best Practice Guidelines to Address Barriers to Treatment Completion for Patients with Drug-resistant Tuberculosis"

Study Site(s): Saint Peter, ALERT, Adama and Bishoftu Hospitals.

Application Type: Initial ■ Amendment ☐ Renewal ☐

Review Procedure: Full Board ■ Expedited ☐ Secretariat ☐

Review Date: September 4, 2018

Final Decision: ■ Approved" Approval Date: October 01, 2018

Approval period: October 01, 2018 to September 30, 2019

I. Elements approved- 1. Protocol Version No. Version Date

II. Obligations of the Principal Investigator-
1. Should comply with standard international & national scientific and ethical guidelines.
2. All amendments and changes made in protocol and consent form need AAERC approval.
3. End of the study, including manuscripts and thesis works should be reported to the AAERC.

III. Does the protocol need to be reviewed by the National ERC (NRERC)? Yes ☐ No ■

Follow up report expected in:

3 Months ___ 6 Months ___ 9 Months ___ One year ✓

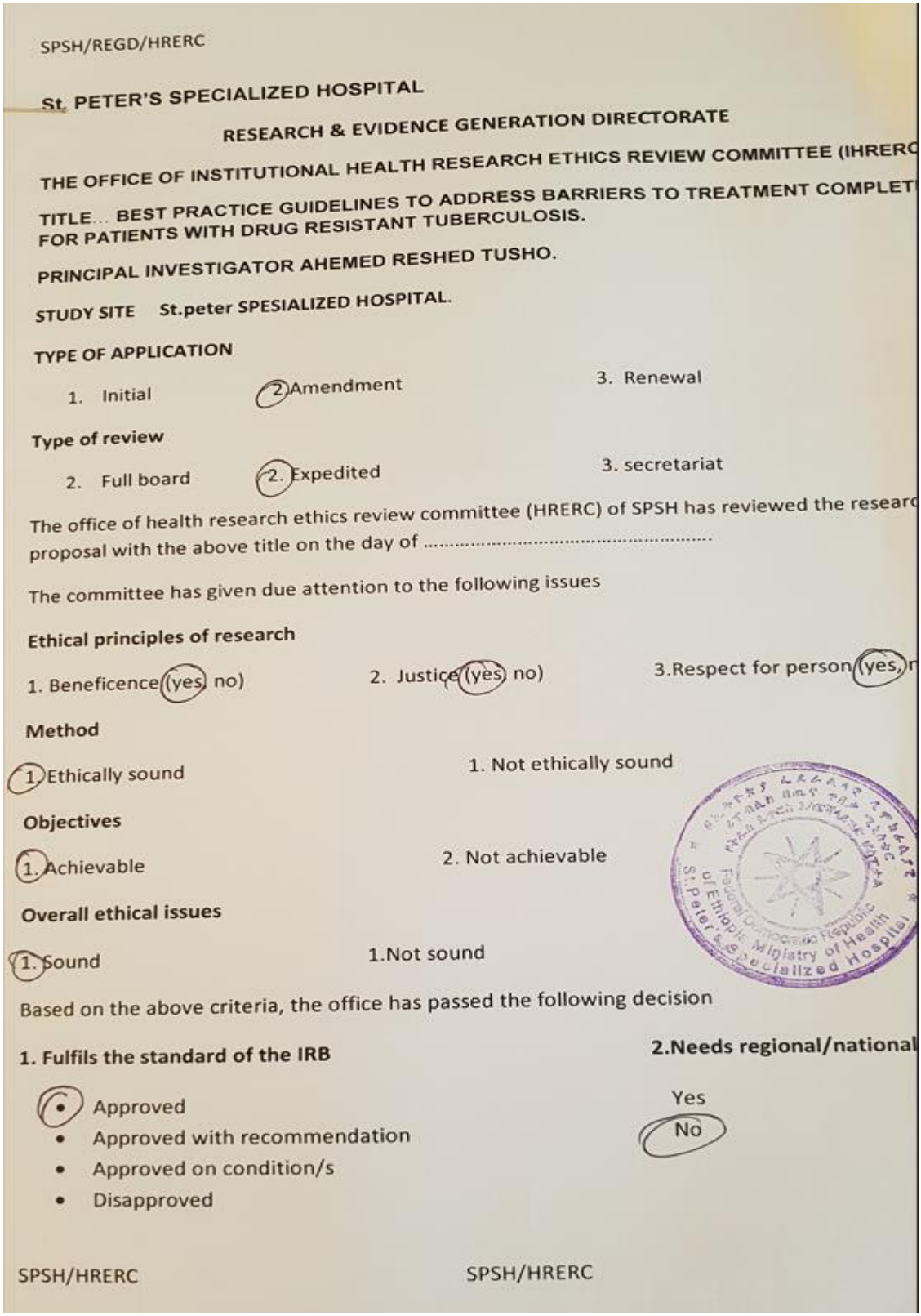
Name: Mr. Hailemichael Getachew Dr. Geremew Tarekegne

Signature: _____ _____

Date: 01/10/18 01/10/18

AAERC Secretary AAERC Chairperson

Annexure C: Approval letter from SPSH Ethics Review Committee



SPSH/REGD/HRERC

St. PETER'S SPECIALIZED HOSPITAL

RESEARCH & EVIDENCE GENERATION DIRECTORATE

THE OFFICE OF INSTITUTIONAL HEALTH RESEARCH ETHICS REVIEW COMMITTEE (IHRERC

TITLE... BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLET FOR PATIENTS WITH DRUG RESISTANT TUBERCULOSIS.

PRINCIPAL INVESTIGATOR AHEMED RESHED TUSHO.

STUDY SITE St.peter SPESIALIZED HOSPITAL.

TYPE OF APPLICATION

1. Initial (2) Amendment 3. Renewal

Type of review

2. Full board (2.) Expedited 3. secretariat

The office of health research ethics review committee (HRERC) of SPSH has reviewed the researc proposal with the above title on the day of .....

The committee has given due attention to the following issues

Ethical principles of research

1. Beneficence (yes, no) 2. Justice (yes, no) 3.Respect for person (yes, n

Method

(1.) Ethically sound 1. Not ethically sound

Objectives

(1.) Achievable 2. Not achievable

Overall ethical issues

(1.) Sound 1.Not sound

Federal Democratic Republic of Ethiopia Ministry of Health St.Peter's Specialized Hospital

Based on the above criteria, the office has passed the following decision

1. Fulfils the standard of the IRB **2.Needs regional/national**

- (•) Approved
- Approved with recommendation
- Approved on condition/s
- Disapproved

Yes
(No)

SPSH/HRERC SPSH/HRERC

decision is valid for the coming 3-6 months period taking the approval date as day 1, & the proposal should be implemented as presented to the office with the incorporated comments. If there is any plan to make changes in any part of the approved protocol, it is highly obligatory to inform the office to have another revision otherwise the office will not allow any activity as it is against the National ethics review guideline & Good clinical practice is the researcher duty & responsibilities to inform & submit a summary of each & every activity of the study every 2 months to the office. The researcher is also expected to submit the final completed work of the research to the office.

Name Artayt Nigse	Name Bru-A	Name
Signature	Signature	Signature
Date 13/09/10	Date 13/09/10	Date 13/09/10
Secretary	Chairperson	Research and evidence generation Director

Annexure D: Permission letter from Federal Ministry of Health

የኢትዮጵያ ፌዴራላዊ ዲሞክራሲያዊ
ሪፐብሊክ
የጤና ጥበቃ ሚኒስቴር

Federal Democratic Republic of
Ethiopia
Ministry of Health

ቀን 05-08-2010
Date
ቁጥር መጠ/14148/109
Ref. No.

ለቅዱስ ጴጥሮስ ስፔሻላይዝድ ሆስፒታል
ለአለርት ሆስፒታል
አዲስ አበባ
ለአዳማ ሆስፒታል
አዳማ
ለቢሾፍቱ ሆስፒታል
ቢሾፍቱ

ጉዳዩ፡- ትብብር እንዲደረግላቸው ስለመጠየቅ፤

አቶ አህመድ ረሺድ ቱሾ በ Best practice guidelines to address barriers to treatment completion for patients with drug resistant tuberculosis በሚል አርእስት ጥናት እያደረጉ ስለሆነ በእናንተ በኩል አስፈላጊው ትብብር እንዲደረግላቸው እንጠይቃለን።

ከሰላምታ ጋር

ብሩክ ከበደ ነጋሽ
የበሽታዎች መከላከልና መቆጣጠር
ዳይሬክቶሬት ተ/ዳይሬክተር

ግልባጭ፡-

- ለበሽታዎች መከላከልና መቆጣጠር ዳይሬክቶሬት
  ጤና ጥበቃ
- ለአቶ አህመድ ረሺድ
  አዲስ አበባ

251-(0)11-5517011
251-(0)11-5515425
Fax 251-(0)11-5519366
251-(0)11-5159657
E-mail:moh@ethionet.et
Web site: www.moh.gov.et
1234
Addis Ababa

Annexure E: Informed consent form for in-depth interview

QUALITATIVE

My name is Ahmed Reshid, and I thank you for agreeing to participate in this study. The purpose of this study is to explore barriers to treatment completion of patients with drug resistant TB and propose best practice guidelines to improve programmatic management of drug resistance TB in Ethiopia. I have requested you to participate in this study because you can provide valuable information on this matter. I therefore urge you to answer the following questions to the best of your knowledge.

This study is important because it will assist us to get a better understanding of the barriers involved during treatment of MDR-TB and the impact they have on patients in completing treatment and getting cured. The purpose of this study is to explore and describe barriers to treatment completion of patients with drug resistance TB and propose best practice guidelines to improve programmatic management of drug resistance TB in Ethiopia. However, you may experience some discomfort or distress during the focus group discussions. If that happens, please let me know and if needs be, that we discontinue the discussion.

The discussion will be recorded using a tape recorder and this is to ensure that the researcher captures what you say accurately. Because your name is not required, what you say will not be linked to you. All the information will be kept in a safe cupboard and will only be used for research.

If you agree to participate, you will be required to participate in an in-depth interview which will take approximately 30 minutes to one hour.

If you have any questions about the study or about participating, please feel free to ask me now. If you have questions after completing the session or any time, you can call me at +251911381328.

I understand that my participation is voluntary and that I may refuse to participate or withdraw my consent and stop taking part at any time without penalty. I understand the risks/benefits associated with this study and I was given an opportunity to ask questions. I understand that all study data will be kept confidential. I therefore freely consent to take part in this research project.

Signature of participant _____ Date _____

It is my opinion that the participant understands the nature of the study, as well as related risks and benefits

Signature of Investigator _____ Date _____

Signature of the Witness_____ Date _____

Confidentiality agreement

I ..... having agreed to participate in the study entitled “BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS” hereby pledge not to divulge any information related to this study including other participants who took part in this study. I will apply the ethical principles of confidentiality on all information that I might know.

Signature _____ Date _____

Researcher’s signature _____ Date_____

Annexure E 1: Informed consent form - Amharic version

የጥናቱ መረጃ ቅ□

ሰላምታ፣ አህመድ ረሺድ እባላለሁ ። የዚህ ጥናት አላማ መድሃኒት የተላመደ ቲቢ ህክምና ተግዳሮቶችና ተግባራዊ መፍትሃዎቻቸውን ተረድቶ በኢትዮጵያ ያለውን መድሀኒት የተላመደ ቲቢ ህክምና ፕሮግራም አገልግሎት ለማሻሻል ነው።

በዚህ ጥናት እንዲሳተፉ የጋበዝኩዎት በዚህ ሀሳብ ዙሪያ ጠቃሚ መረጃ እንደሚሰጡኝ ስለማምን ነው። በዚሁ መሠረት የሚያውቁትን እንዲያካፍሉን እጠይቃለው።

ይህ ጥናት አስፈላጊነቱ መድሃኒት የተላመደ ቲቢ ህክምና ተግዳሮቶችን ይበልጥ እንድናውቅና በበሽተኞች ላይ ህክምናውን ጨርሰው እንዳይድኑ የሚያስከትለውን **ተጽዕኖ ለማወቅ ነው**።: የዚህ ጥናት ዓላማ ተግዳሮቶቹን በጥልቀት ለማጥናትና ለመመርመር እንዲሁም ተግባራዊ የመፍትሃ ፅንጸ ሀሳቦችን ለማመንጨት ነው።

በውውይታችን ወክት በማንኛውም ምክንያት የሚያስጨንቆትና ጤናዎ ከታወከ ይህንኑ ያሳውቁኝና ቃለ-መጠይቁን ማቁዋረጥ እንችላለን።

 ቃለመጠይቁ ሲከናወን በድምጽ መቅጃ ይቀዳል። ይህም መረጃውን በትክክል ሳይቆራረጥ ለመያዝ ነው።

ስምዎን መጥቀስ ስለማያስፈልግ የተናገሩት ሀሳብ ከእርስዎ ጋር አይያያዝም። ሁሉም መረጃዎች በጥብቅ ቁልፍ ባለው ሳጥን ውስጥ ይቀመጣሉ። ለዚህ ጥናት ዓላማ ብቻ ይውላሉ።

በጥናቱ ለመሳተፍ ፈቃደኛ ከሆኑ ከ30 ደቂቃ እስከ 1 ሰዓት የሚቆይ ጥልቅ ቃለ ምልልስ ይኖረዋል። ማንኛውም ጥያቄ ካለዎት እባክዎ ይጠይቁኝ። ቃለ መጠይቁ ካለቀ በኋላም ጥያቄ ካለዎት በ0911381328 ይደውሉልኝ።

የጥናቱ መረጃ ቅ□

ሰላምታ፣ አህመድ ረሺድ እባላለሁ በዚህ ጥናት ለመሳተፍ ፈቃደኛ በመሆንዎ አመሰግናለሁ። የዚህ ጥናት አላማ መድሃኒት የተላመደ ቲቢ ህክምና ተግዳሮቶችና ተግባራዊ መፍትሃዎቻቸውን ተረድቶ በኢትዮጵያ ያለውን መድሀኒት የተላመደ ቲቢ ህክምና ፕሮግራም አገልግሎት ለማሻሻል ነው።

በዚህ ጥናት እንዲሳተፉ የጋበዝኩዎት በዚህ ሀሳብ ዙሪያ ጠቃሚ መረጃ እንደሚሰጡኝ ስለማምን ነው። በዚሁ መሠረት የሚያውቁትን እንዲያካፍሉን እጠይቃለው።

ይህ ጥናት አስፈላጊነቱ መድሃኒት የተላመደ ቲቢ ህክምና ተግዳሮቶችን ይበልጥ እንድናውቅና በበሽተኞች ላይ ህክምናውን ጨርሰው እንዳይድኑ የሚያስከትለውን **ተጽዕኖ ለማወቅ ነው**።: የዚህ ጥናት ዓላማ ተግዳሮቶቹን በጥልቀት ለማጥናትና ለመመርመር እንዲሁም ተግባራዊ የመፍትሃ ፅንጸ ሀሳቦችን ለማመንጨት ነው።

በውውይታችን ወክት በማንኛውም ምክንያት የሚያስጨንቆትና ጤናዎ ከታወከ ይህንኑ ያሳውቁኝና ውይይቱን ማቁዋረጥ እንችላለን።

ውይይቱ ሲከናወን በድምጽ መቅጃ ይቀዳል። ይህም መረጃውን በትክክል ሳይቆራረጥ ለመያዝ ነው።

ስምዎን መጥቀስ ስለማያስፈልግ የተናገሩት ሀሳብ ከእርስዎ ጋር አይያያዝም። ሁሉም መረጃዎች በጥብቅ ቁልፍ ባለው ሳጥን ውስጥ ይቀመጣሉ። ለዚህ ጥናት ዓላማ ብቻ ይውላሉ።

በጥናቱ ለመሳተፍ ፈቃደኛ ከሆኑ ከ30 ደቂቃ እስከ 1 ሰዓት የሚቆይ ጥልቅ ቃለ ምልልስ ይኖረዋል። ማንኛውም ጥያቄ ካለዎት እባክዎ ይጠይቁኝ። ቃለ መጠይቁ ካለቀ በኋላም ጥያቄ ካለዎት በ0911381328 ይደውሉልኝ።

የጥናት ተሳትፎ የፈቃደኝነት ቅ□

እኔ ከታች የፈረምኩት ግለሰብ ስለጥናቱ የተገነዘብኩ ሲሆን ተሳትፎዬም በፈቃደኝነት ላይ የተመረኮዘ ነው። ውይይቱን ማቋረጥ ከፈለኩ ምንም ምክንያት መስጠት ሳያስፈልገኝ ወይም የመቀጠል ግዴታ ሳይኖርብኝ ውይይቱን ማቋረጥ እችላለው። ጥያቄ ለመጠየቅም መብት ተሰቶኛል። በመሆኑም በሙሉ ፈቃደኝነት በዚህ ጥናት ለመሳተፍ ተስማምቻለሁ።

የተሳታፊ ፊርማ---------- ቀን----------

Annexure F: Informed consent form for focus group discussion

QUALITATIVE

My name is Ahmed Reshid, and I thank you for agreeing to participate in this study. The purpose of this study is to explore barriers to treatment completion of patients with drug resistance TB and propose best practice guidelines to improve programmatic management of drug resistance TB in Ethiopia. I have requested you to participate in this study because you can provide valuable information on this matter. I therefore urge you to answer the following questions to the best of your knowledge.

This study is important because it will assist us to get a better understanding of the barriers involved during treatment of MDR-TB and the impact they have on patients in completing treatment and get cured. The purpose of this study is to explore and describe barriers to treatment completion of patients with drug resistance TB and propose best practice guidelines to improve programmatic management of drug resistance TB in Ethiopia. However, you may experience some discomfort or distress during the focus group discussions. If that happens, please let me know and if needs be, that we discontinue the discussion.

The discussion will be recorded using a tape recorder and this is to ensure that the researcher captures what you say accurately. Because your name is not required, what you say will not be linked to you. All the information will be kept in a safe cupboard and will only be used for research.

If you agree to participate, you will be required to participate in a focus group discussion which will take approximately 1 hour and 30 minutes.

If you have any questions about the study or about participating in the study, please feel free to ask me now. If you have questions after completing the session or any time, you can call me at +251911381328.

I understand that my participation is voluntary and that I may refuse to participate or withdraw my consent and stop taking part at any time without penalty. I understand the risks/benefits associated with this study and I was given an opportunity to ask questions. I understand that all study data will be kept confidential. I therefore freely consent to take part in this research project.

Signature of participant _____ Date _____

It is my opinion that the participant understands the nature of the study, as well as related risks and benefits

Signature of Investigator _____ Date _____

Signature of the Witness_____ Date _____

Confidentiality agreement

I ..... having agreed to participate in the study entitled “BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS” hereby pledge not to divulge any information related to this study including other participants who took part in this study. I will apply the ethical principles of confidentiality on all information that I might know.

Signature _____ Date _____

Researcher’s signatures _____ Date_____

Annexure G: Questionnaire

Best Practice Guidelines to Address Barriers to Treatment Completion for Patients with Drug-resistant Tuberculosis. Questionnaire.

1. Age
    a. 18-24
    b. 25 – 34
    c. 35 – 44
    d. 45 – 54
    e. 55 – 64
    f. 65 and above
2. Gender
    a. Male
    b. Female
3. Address
    a. Urban
    b. Rural
4. Marital status
    a. Married
    b. Single
    c. Divorced
    d. Widowed
5. Employment
    a. Employed
    b. Unable to work
    c. Student
    d. Unemployed
    e. Other_____
6. History of alcohol consumption
    a. Yes
    b. No
7. History of non-prescription drugs (cannabis etc)
    a. Yes
    b. No

8. Weight at start of treatment----------
9. Height----------
10. BMI----------
11. Treatment Supporter
    a. Has had
    b. Did not have
12. Comorbidity
    a. Yes
    b. No
13. If yes, specify
    a. Diabetes

b. Chronic liver disease
c. Chronic renal failure
d. Hypertension
e. CNS disorder
f. HIV
g. Other, specify----------

14. Registration group at start of treatment
    a. New
    b. Relapse
    c. After lost to follow up
    d. After failure of new first line drug regimen
    e. After failure of retreatment first line drug regimen
    f. Transfer in (from another treatment site)
    g. Other
15. Classification of TB types
    a. Pulmonary
    b. EPTB specify----------
16. Resistance type
    a. MDR TB
    b. Pre-XDR TB
    c. XDR-TB
17. Bacteriology results
    a. Bacteriologically confirmed
    b. Clinically diagnosed
18. Prior TB drug use (more than one month)
    a. First-line drugs
    b. Second-line drugs
19. What is the outcome of most recent TB treatment?
    a. Cured
    b. Completed
    c. Failed
    d. Lost to follow up
    e. Not evaluated
20. HIV testing done
    a. Yes
    b. No
    c. Unknown
21. HIV test results
    a. Reactive
    b. Nonreactive
22. If reactive, started CPT
    a. Yes
    b. No
23. If reactive, started ART
    a. Yes
    b. No

24. Base line audiometry
    a. Normal
    b. Abnormal
    c. Not done
25. Drug-susceptibility testing (DST) results
    a. DST technique_____
        i. Xpert MTB/RIF
        ii. LPA
        iii. Culture
        iv. Other WRD
    b. Resistant_____
    c. Susceptible_____
26. Date of diagnosis_____
27. Date treatment started_____
28. Intensive phase duration_____
29. Treatment regimen and dose_____
30. Missed days (number of days patient did not take any of the prescribed treatment) _____
31. Incomplete days (number of days patient did not take all prescribed TB drugs) _____
32. Treatment outcome
    a. Cured
    b. Completed
    c. Died
    d. Failed
    e. Lost to follow up
    f. Not evaluated
33. Treatment outcome date_____
34. Chest X-ray
    a. Bilateral disease with cavities
    b. Fibrosis

35. Smear and culture results

Month	Smear	Culture	Month	Smear	Culture
Baseline			13		
1			14		
2			15		
3			16		
4			17		
5			18		
6			19		
7			20		
8			21		
9			22		
10			23		
11			24		
12					

36. Monthly monitoring schedule

Tests	Routinely done			
	Yes	No		
Weight				
CBC				
Serum Electrolyte				
LFT				
Urea/Creatinine				
TSH				
Audiometry				

37. Adverse events encountered during treatment
    a. Nausea & vomiting
    b. Gastritis
    c. Peripheral neuropathy
    d. Seizures
    e. Hearing impaired
    f. Depression Anxiety
    g. Psychotic symptoms
    h. Hypothyroidism
    i. Drug induced hepatitis
    j. Renal Toxicity
    k. Electrolyte disturbance
    l. Optic neuritis
    m. Arthralgia, Arthritis
    n. Other, Specify_____

Annexure H: Turnitin digital receipt and report

turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	A R TUSHO
Assignment title:	Complete dissertation/thesis submission for examination
Submission title:	BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREA...
File name:	TUSHO_THESIS.docx
File size:	1.33M
Page count:	344
Word count:	98,350
Character count:	560,865
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Submission ID:	1925954955

BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS.

by

AHMED RESHID TUSHO

submitted in accordance with the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in the subject

PUBLIC HEALTH

at the

UNIVERSITY OF SOUTH AFRICA

SUPERVISOR: PROF SHEILA THERESA MOKOBOTO-ZWANE

OCTOBER 2022

Annexure I: FGDs guide

Focus group discussions guide for DR-TB patients

Participant information

THE FOLLOWING QUESTIONS ARE ABOUT YOUR PERSONAL INFORMATION

Participant's code	Age	Sex	How long has it been since you started receiving DR-TB treatment?

THE FOLLOWING QUESTIONS ARE ABOUT YOUR EXPERIENCES AND VIEWS REGARDING THE DR-TB TREATEMENT PROGRAM

GRAND TOUR QUESTION

- What are your experiences and views regarding the DR-TB treatment?

FOLLOW UP QUESTIONS

1. On what days of the week do you come to receive DR-TB treatment services?
2. Approximately how much time do you spend at the facility while seeking DR-TB treatment services?
3. State the DR-TB services that are offered to you at the facility?
4. Is DR-TB treatment always available at the facility?
5. Is all the laboratory service available and how do you see the follow up services?
6. Do you think the staff at the facility is adequate to provide DR-TB treatment services?
7. What were the adverse events you experienced to you?
8. Are you generally satisfied with the way the DR-TB treatment services are offered?
9. What were the challenges that you faced while on DR-TB treatment?
10. Why did you interrupt the previous DR-TB treatment?
11. What was difficult for you while you were on treatment?
12. How did you get help in your work/job during treatment?
13. Did you face any challenging for you at home, work places or other places while on treatment?
14. Do you have any suggestions for improvement?

Annexure J: In-depth interview guide

In depth interview guide for Physicians/ clinicians/program managers

Participant information

THE FOLLOWING QUESTIONS ARE ABOUT YOUR PERSONAL INFORMATION

Participant's code	Age	Sex	How long have you been involved in the provision of DR-TB treatment service?

THE FOLLOWING QUESTIONS ARE ABOUT YOUR VIEWS REGARDING THE BARRIERS TO TREATMENT COMPLETION OF DR-TB TREATMENT.

GRAND TOUR QUESTION

What are your views regarding the DR-TB treatment service?

FOLLOW UP QUESTIONS

1. What are the factors contributing to low treatment outcome of DR-TB program?
2. What are the barriers to completion of DR-TB treatment in general?
3. Why do patients default from treatment in your view?
4. State the DR-TB treatment services offered at your facility?
5. Tell me about ancillary drugs Availability at this facility.
6. What are the main challenges to patient follow up?
7. How is the allocation of sufficient staff to DR-TB treatment services?
8. How you feel about competency of staff in providing DR-TB treatment services effectively?
9. Are you satisfied with the DR-TB treatment services that you are currently providing?
10. Are there any other challenges that you are currently facing in the provision of DR-TB treatment services?
11. Do you have any suggestions for improvement of the DR-TB treatment services and treatment completion and success?

Annexure K: Language editing certificate

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Date: 31st October, 2022

TO WHOM IT MAY CONCERN

CERTIFICATE OF EDITING

I, **Muchativugwa Liberty Hove**, confirm and certify that I have read and edited the entire thesis, **BEST PRACTICE GUIDELINES TO ADDRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS**, submitted by **AHMED RESHID TUSHO**, Student number **62121901**, in accordance with the requirements for the degree of **DOCTOR OF PHILOSOPHY in PUBLIC HEALTH** at the **UNIVERSITY OF SOUTH AFRICA.**

AHMED RESHID TUSHO was supervised by PROFESSOR SHEILA THERESA MOKOBOTO-ZWANE.

I hold a PhD in English Language and Literature in English and am qualified to edit such a thesis for cohesion and coherence. The views expressed herein, however, remain those of the researcher/s.

Yours sincerely

Professor M.L. Hove (PhD, MA, PGDE, PGCE, BA Honours – English)

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Annexure L: A quantitative findings verification letter from a statistcian

አርማወር ሐንሰን የ ምርምር ኢንስቲትዩት (አህሪ)
Armauer Hansen Research Institute (AHRI)
ALERT Compound, Federal Ministry of Health

Date: November 11, 2022

To Whom It May Concern

I, Tsegaye Hailu, a statistician at Armauer Hansen Research Institute, confirm that I assisted Mr Ahmed Reshid with the quantitative strand of his thesis, **"BEST PRACTICE GUIDELINES TO ADRESS BARRIERS TO TREATMENT COMPLETION FOR PATIENTS WITH DRUD RESISTANT TUBERCULOSIS,"** and that the findings are correct.

Yours Sincerely

Tsegaye Hailu(MSC, PhD candidate)
10/11/2022

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Annexure M: Legal Translation Certificate

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July 5, 2023

Reference Number: ATBS/07/204/2023

To Whom It May Concern

Subject: Issuance of Evidence

We herby certify that our company Atlantic Business and Translation Service have assisted Mr. Ahmed Reshid with translation of consent forms and interview script of his thesis "Best Practice Guidelines to Address Barriers to Treatment Completion for Patients with Drug Resistant Tuberculosis in Ethiopian" from English to Amharic and back to English.

Any assistance extended to him in this regards is highly appreciated

Sincerely Yours

Ebrahim Haji Bati
G/MANAGER
ኢብራሂም ሃጂ ባቲ
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