(COMPLETED RESEARCH)

THE EPIDEMIOLOGY AND TREATMENT OUTCOMES OF TUBERCULOSIS CASES IN LESOTHO BETWEEN 2009 AND 2019

by

SELLO MONTSI

MINI-DISSERTATION

Submitted in fulfilment of the requirements for the degree of

MASTER OF PUBLIC HEALTH

in

EPIDEMIOLOGY

In the

FACULTY OF HEATH SCIENCES

(School of Healthcare Sciences)

Department of Public Health

at the

UNIVERSITY OF LIMPOPO

Supervisor: Prof E. Maimela

2021

DEDICATION

I dedicate my dissertation work to my family and many friends. A special feeling of gratitude to my loving wife, my mother and my children. Matsitso, Mamotete,Tsitso, and Katleho. Lastly Mokonyana family whose words of encouragement and push for tenacity ring in my ears

DECLARATION

I Sello Montsi declare that the work presented for assessment in this dissertation titled "The epidemiology and treatment outcomes of tuberculosis cases in Lesotho between 2009 and 2019" is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references. I confirm that it has not previously been presented for another assessment, and that my debts (for words, data, arguments and ideas) have been appropriately acknowledged

Sello Montsi	15 August 2021
…….	……..
Full names	Date

ACKNOWLEDGEMENTS

Two years ago when I was accepted to study at University of Limpopo for MPH the desire to finish on time was too great to conceive. Thanks to the Almighty for it is such a privilege and honor to have made it thus far.

I wouldn't have made it this far without the following people who became my support system to complete my studies and for their respective contributions to this dissertation:

- God Almighty for giving me the strength, knowledge, ability, and opportunity to undertake this research study. Without His Grace, this achievement would not have been possible.
- My supervisor Professor Eric Maimela, whose insight and knowledge into the subject matter steered me through this research.
- Ministry of Health TB Monitoring and Evaluation Office team dedicated their time in supporting me during data collection.
- My partner Mrs. Matsitso Montsi – I simply couldn't have done this without you, you set me off on the road to this MPH a long time ago, special thanks.
- Finally, dear friends and family especially Mr. Molikeng Mokonyane for all the support throughout my tough monthly travels to Limpopo.

Abstract

The epidemiology and treatment outcomes of Tuberculosis cases in Lesotho between 2009 to 2019

Background: Tuberculosis (TB) is a fatal disease globally, if not managed well, with a million or more people dying by the disease annually in low and middle-income countries (LMIC). Around two billion people are thought to be asymptomatically (latently) infected with Mycobacterium tuberculosis, putting them at risk of acquiring active tuberculosis. Tests that identify immunoreactivity to mycobacterial antigens rather than live bacteria, as well as mathematical modelling, are used to estimate the prevalence of latent tuberculosis infection. According to reports, tuberculosis (TB) was the cause of 1.3 million fatalities among HIV-negative people in 2016, surpassing the global number of HIV/acquired immune deficiency syndrome (AIDS) deaths. In addition, TB was a factor in 374,000 HIV-related deaths. Despite the effectiveness of chemotherapy over the last seven decades, tuberculosis remains the world's leading infectious killer. In 2016, 10.4 million new cases were reported, a number that has remained constant since the dawn of the twenty-first century, confounding public health specialists tasked with designing and implementing measures to lessen the global burden of tuberculosis disease. As a result, the current study aims to look into the epidemiology of tuberculosis in Lesotho in order to help policymakers make decisions on TB control in the country.

Methodology:. In the current investigation, a cross-sectional, retrospective descriptive study design was used, as well as a probability sampling strategy. The National TB-Database from the Ministry of Health in Lesotho was used as the source of data for this quantitative investigation, which was analyzed using STATA statistical software version 12 for Windows (STATA Corporation, College Station, Texas). A Chi-Squared test was used to compare categorical variables, while a t-test was used to examine continuous variables. A statistically significant P-value of 0.05 was used.

Results: A total of 18 836 TB patient records were recovered, with 45 percent of the TB patients being females. The average age of the TB patients was 35.9 years, with a standard deviation of 12.7%, and the ages ranged from one year to 84 years. There

was a statistically significant difference between the age groups (p value 0.001), with 33.1 percent of TB patents being in the age group 25–34 years, followed by 29 percent, 15.4 percent, 11.2 percent, and 5.5 percent in the age groups 35–44 years, 45–55 years, 15–24 years, and 55–64 years 65 years.. There has been a fluctuating treatment outcome of TB from 63.5% for cured patients in 2012 to 57.2% in 2013 and this rose to 60.4% in 2014 then eventually reached 76.7% in 2019. The TB treatment success rate in Lesotho also showed a similar trend as the cure rate. The overall TB death rates in the current study was found to be increasing on an annual basis from 7.4% in 2012 to 9.2% in 2018 then dropped to 8.5% in 2019. The TB patients who have not been evaluated for treatment outcomes have been decreasing annually from 4.4% in 2012 to 0.8% in 2019. The proportion of TB patients with known HIV status increased from 22.3% in 2015 to 90.5% in 2019 and similarly to the proportion of TB patients with HIV status positive increased from 15.1% in 2015 to 60.4% in 2019. The proportion of TB patients with HIV status positive increased with increasing age group all age groups.

Conclusion: TB is still a concern in Lesotho, where treatment target goals have not yet been fulfilled, the findings of this study underline the importance of addressing the underlying socio-economic causes of TB. The most important goal in TB control is to detect 70% and cure at least 85% of sputum smear positive cases. If these goals are met, the prevalence, incidence, transmission, and medication resistance to tuberculosis (TB) could all decrease. Despite the National Tuberculosis Control Programme's attempts to enhance TB patients' access to treatment and adherence to therapy, the percentage of patients who have good treatment outcomes remains low. Despite having an 84 percent detection rate and using the DOTS technique, the available data did not identify the types of tuberculosis, therefore we were unable to forecast multidrug-resistant tuberculosis (MDR-TB).

Key concepts

Acquired immune deficiency syndrome,(AIDS) Epidemiology, Human Immunodeficiency Virus(HIV), Tuberculosis(TB), Treatment outcomes,

Table of Contents

DEFINITION OF CONCEPTS

Characteristics - a distinguishing trait, quality, or property (Oxford concise colour Medical Dictionary, 2015). In the context of this study, characteristics of tuberculosis patients will be the socio-demographics of the TB patients.

Directly Observed Treatment Short Course (DOTS) - a strategy, which allows patients to take their daily drugs under the observation of health professionals, thereby improving treatment compliance, and has been known to increase TB cure rates (Gebrezgabiher, Romha, Ejeta, Asebe, Zemene & Ameni, 2016). In the context of this study, directly observed treatment short course will be as defined above.

Epidemiology - is the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems (Dicker, Coronado, Koo & Parrish, 2006; Aschengrau & Seage, 2013). In the context of this study, epidemiology will be defined as the distribution of tuberculosis cases and the determinants of treatment outcomes.

Tuberculosis treatment outcomes - are the results after treatment, which are categorised according to the National TB guidelines as either cured, treatment completed, died, defaulted, treatment failure, transferred out or treatment success (Adejumo, Daniel, Adebayo, Adejumo, Jaiyesimi, Akang & Awe, 2016). In the context of this study, tuberculosis treatment outcome will be as defined above.

Tuberculosis - a contagious infection that mainly attacks the lungs, which can also attack other parts of the body like kidney, spine, and brain. It is caused by *mycobacterium tuberculosis*, the bacteria is spread from one person to the next through tiny droplets released into the air via coughs and sneezes. A small percentage of human cases are caused by *M. africanum, M. canetti, M. caprae, M. microti*, and *M. pinnipedii* (Floyd, Glaziou, Zumla & Raviglione, 2018). In this context of study, tuberculosis will be used as the definition above.

ABBREVIATIONS

ART	Antiretroviral therapy
DHIS2	District Health Information System 2
DOTS	Directly Observed Treatment Short Course
HBCs	High-Burden Countries
HIV	Human Immunodeficiency Virus
IPT	Isoniazid Preventive Therapy
LAC	Latin America and the Caribbean
LMIC	Low and Middle-Income Countries
MDGs	Millennium Development Goals
MD-R TB	Multi Drug Resistant Tuberculosis
SSA	Sub-Saharan Africa
TB	Tuberculosis
TI	Transfer in
TO	Transfer out
TREC	Turf loop Research and Ethics Committee
WHO	World Health Organization
XDR-TB	Extensively Drug Resistance Tuberculosis
PTB	Pulmonary TB
FHDC	Faculty Higher Degree Committee
SREC	School of Healthcare Sciences Research Committee
CPT	Co-trimoxazole Preventive therapy
SCC	Standardised short-course chemotherapy
NTCP	National Tuberculosis Control Programme

1. CHAPTER 1: INTRODUCTION

If left untreated, tuberculosis (TB) kills about 1 million people per year in low and middle-income countries (LMICs) (Honeyborne, Lipman, Zumla, & McHugh, 2019). According to the World Health Organization (WHO), there were 10.4 million new tuberculosis cases worldwide in 2015, with six countries accounting for 60% of the disease burden: Indonesia, India, Pakistan, China, Nigeria, and South Africa (Pai & Memish, 2017) In 2015, an estimated 1.8 million people died of tuberculosis (TB), with 0.4 million of those infected with the human immunodeficiency virus (HIV) (Rendon, Centis, Zelleweger, Solovic, Torres-Duque et al., 2017). Incidence of tuberculosis has decreased slightly over the last decade, but it remains uncontrolled in several parts of the world, including Asia and Africa (Dheda, Gumbo, Maartens, Dooley, McNerney, Murray et al., 2017)

There is another global health threat which is multi drug resistant TB (MDR-TB) and in 2014, approximately 5% of TB cases in the world were MDR-TB (WHO, 2014). This makes TB a major challenge among highly burdened communities worldwide (Tiberi, Muñoz-Torrico, Duarte, Dalcolmo, D'Ambrosio et al., 2018). A report from drug resistant surveillance data indicates that about 480,000 individuals who were on TB treatment developed MDR-TB and 190,000 died from MDR-TB (Girum, Tariku & Dissu, 2017). In 2014, approximately 9.7% of those who had MDR-TB had Extensively Drug-Resistant TB (XDR-TB) (Velayati, Farnia & Farahbod, 2016; Girum et al., 2017). Patients who recover from MDR-TB get lung damage at some point and continue to suffer from functional disability due to long-term lung damage (Rao, Ippolito, Mfinanga, Ntoumid, Yeboah-Manuf, Vilaplana, Zumla & Maeurer, 2019). There were about half (50%) of MDR-TB patients who were cured globally in 2017, and the others had their lungs damaged which led to them being sick with other conditions due to damaged lungs (Rao et al., 2019).

Amongst people who migrate to other countries, TB is still a life-threatening condition, especially in the countries that have very low TB incidences (Castelli & Sulis, 2017). TB still remains a major problem in Sub-Saharan African countries, even though there are major controls put in place for this disease in other African states such as Egypt,

and other North African countries (Girardi, Schepisi, Goletti, Bates, Mwaba et al., 2017).

According to O'Connor, Frederix, Saito, Maama, Hirsch-Moverman et al. (2017), tuberculosis has surpassed HIV as the greatest cause of death from an infectious disease worldwide. A twin epidemic is ravaging Sub-Saharan Africa, with high rates of HIV and tuberculosis coinfections leading to substantial morbidity and mortality (Tiam, Machekano, Gounder, Maama-Maime, Ntene-Sealiete et al., 2014).

Lesotho has one of the highest rates of tuberculosis (TB) and tuberculosis-HIV co-infection in the world (Luba, Tang, Liu, Gebremedhin, Kisasi & Feng, 2019). In 2015, Mugomeri, Chatanga, Lefunyane, Ruhanya, Nyandoro, and Chin'ombe reported a high incidence of tuberculosis in Lesotho, with 402 cases per 100,000 HIV-positive people (Mugomeri, Chatanga, Lefunyane, Ruhanya, Nyandoro, & Chin'ombe, 2015). In 2017, the prevalence of TB grew to 788 per 100,000, with roughly 72 percent of TB patients also having HIV (Hirsch-Moverman, Howard, Frederix, Lebelo, Hesseling et al., 2017). Because of their weakened state, active tuberculosis is the most common illness among HIV-positive people (Mugomeri et al., 2015). In Lesotho, however, the epidemiology of patients diagnosed with tuberculosis and treatment outcomes have not been studied. In the light of Lesotho's TB situation, this is an important study project. The research problem, literature evaluation on the topic of study, purpose of the study, research question, goal, and objectives were all underlined in the research proposal. Furthermore, the study's methodology was discussed, as well as how ethics were taken into account.

1.2 PROBLEM STATEMENT

Data on tuberculosis epidemiology and treatment outcomes should be thoroughly understood in order to accurately depict the proportion of mean treatment outcomes and types of tuberculosis in a given area (Mekonnen, Derbie, Mekonnen & Zenebe, 2016).As a public health student and health care worker at a district office in Lesotho. The researcher has realised that the epidemiological aspects of TB cases have not

been characterised and the treatment outcomes also not evaluated. This is an important component of epidemic-ending tactics that aids in a greater focus on local-level strategies and has been critical in the elimination of infectious diseases such as smallpox and polio across Africa, including Lesotho, in earlier years. Unfortunately, the country lacks systematic reporting of tuberculosis cases and identification of disease clusters or hotspots, as well as treatment outcomes at the local level where continuing transmission occurs. In view of this challenge, the current study focused on investigating the epidemiology of TB cases and their treatment outcomes.

1.3 PURPOSE OF THE STUDY

1.3.1 Aim

The aim of this study was to investigate the epidemiology of tuberculosis and treatment outcomes of TB cases in Lesotho between 2009 and 2019.

1.3.2 Objectives

The objectives of this study were:

- To describe the socio-demographics characteristics of TB cases in Lesotho between the years 2009 and 2019
- To investigate the epidemiology of TB in Lesotho between the years 2009 and 2019
- To determine the treatment outcomes of TB cases in Lesotho between the years 2009 and 2019

1.4 RESEARCH QUESTION

The research question for this study was “What is the epidemiology and treatment outcomes of TB cases in Lesotho from the years 2009 to 2019”?

1.5 METHODOLOGY

The procedures or strategies used to find, select, process, and analyze information about a topic are referred to as research methodology. To answer the research question stated in this study, a cross-sectional, retrospective descriptive study method was used; the study is quantitative (Detels, Gulliford, Karim & Tan, 2015). The current study used the probability sampling method, which is also known as random sampling. This is a form of sampling in which the researcher must be aware of the sample universe from which the sample is drawn. Every item in the universe had an equal probability of being included in the sample under this

sampling scheme (Elfil & Negida, 2017; Sharma, G., 2017). The STATA statistical program version 12 for Windows was used to analyze the data (STATA Corporation, College Station, Texas 2017). In chapter 3, a full description of the technique is offered, including how data reliability and validity were accomplished, as well as data analysis and bias reduction measures.

1.6 ETHICAL CONSIDERATIONS

Permission to conduct the study was sought from the University of Limpopo's Turfloop Research Ethics Committee and then from the Ministry of Health in Lesotho to ensure that ethical considerations were taken into account. A storage system was also built to retain the acquired data, and records were preserved in such a way that the patients' identities were not revealed, ensuring their confidentiality, privacy, and anonymity. Because this study used secondary data, there were no known dangers connected with participating. In the archives, the storage is permanent.

1.6 SIGNIFICANCE OF PROPOSED RESEARCH

The study could help Lesotho's Ministry of Health better understand tuberculosis epidemiology and treatment outcomes in order to plan for better health service delivery. Understanding transmission dynamics will help researchers learn more about the elements that promote illness spread, which will aid in the development of preventive measures. Molecular epidemiological studies might also be planned, as they are particularly beneficial in a number of countries for identifying at-risk groups and high-transmission areas, as well as providing a lot of information about the prevalence of different Mycobacterium TB strains. The study of characteristics that influence treatment results may aid in improving DOTS service performance and providing relevant knowledge for disease control program decision-making. In addition, robust tuberculosis surveillance data is required to evaluate the impact of new or improved tuberculosis interventions such as diagnostic assays, enhanced case-detection programs, isoniazid preventive therapy (IPT), and the expansion of antiretroviral therapy (ART) to HIV-positive individuals. As a result of this research, it will be easier to avoid the spread of tuberculosis cases because the epidemiology will be better known.

2. CHAPTER 2: LITERATURE REVIEW

3.1 Introduction

This chapter addresses a review of the relevant literature on the what tuberculosis is, the global epidemiology of tuberculosis, the burden of tuberculosis in Africa and Lesotho. The epidemiology of tuberculosis cases will be explored with respect to sociodemographic characteristics (age, gender, work status and educational level) and the distribution of TB cases by years and geographical areas. Studies focusing on the current trends in the treatment outcomes of tuberculosis will be described within and between different populations. Furthermore, the association between the socio-demographics and tuberculosis treatment outcomes will be discussed. Lastly, the global and regional agendas focussing on the prevention and control of tuberculosis will be reviewed with a focus on rural Sub-Saharan (SSA).

3.2 What is tuberculosis?

Tuberculosis (TB) is an infectious disease that mostly affects the lungs but can also affect the kidneys, spine, bones, and brain (Bidaisee, 2018). It is caused by Mycobacterium tuberculosis, a pathogen that is passed from one person to the next through minute droplets discharged into the air via coughs and sneezes (Mohajan, 2014). (Turner & Bothamley, 2015). M. africanum, M. canetti, M. caprae, M. microti, and M. pinnipedii are responsible for a small percentage of human cases (Floyd et al., 2018). Tuberculosis is a main cause of death among individuals in the most economically productive age groups and HIV-positive people, and even those who are cured of TB might be left with long-term consequences that significantly degrade their quality of life (Glaziou, Sismanidis, Floyd & Raviglione, 2015).

3.3 The global epidemiology of tuberculosis

Tuberculosis has likely afflicted humans for much of their history (Glaziou, et al., 2015), and it is the leading cause of death from infectious disease worldwide, with drug-resistant strains posing a significant threat to global health security (Floyd et al., 2018). Despite the fact that effective and economical anti-TB medicine was discovered more than 50 years ago, this continues to be the case (Glaziou, et al., 2015). Globally, the incidence of tuberculosis is declining at a rate of roughly 2% per year, with new cases per 100 000 people per year (Brode, Daley & Marras, 2014). Although there has been

a decline in TB incidence, prevalence and death have increased over the previous decade, eradicating the illness at a worldwide level remains a long way off, and enormous resource commitment is still necessary (Sulis, Roggi, Matteelli & Raviglione, 2014).

According to the World Health Organization, roughly 8.6 million cases (8.3–9.0 million) were expected to have occurred worldwide in 2012, with approximately 2.9 million of those being women. The majority of cases are thought to be in Asia and Africa (58 percent and 27 percent, respectively), with India (range 2.0–2.4 million) and China (0.91.1 million) accounting for 38 percent of the overall number of cases (Sulis et al., 2014). TB incidence in Europe is diverse, as many countries in Europe make progress in TB control; in low-incidence countries, the TB burden is increasingly borne by specific risk groups, such as migrants from high- to low-incidence countries, people with social risk factors such as homelessness, and people who have come into contact with a TB patient (Jackson & Abubakar, 2017).Recently some European countries such as Germany and Sweden have experienced a substantial increase in TB rates after decades of gradual decline that was associated with a large influx of refugees and other migrants from TB endemic countries (Lönnroth, Mor, Erkens, Bruchfeld, Nathavitharana, Van Der Werf & Lange, 2017).

3.4 Tuberculosis in Africa

The high prevalence of tuberculosis among Africans during European colonialism in the late 19th and early 20th centuries led to the theory that Africa had a "virgin soil," especially conducive to the disease's spread among previously uninfected populations (Comas, Hailu, Kiros, Bekele, Mekonnen, Gumi, Tschopp, Ameni, Hewinson, Robertson & Goig, 2015). Due to inadequate laboratory and diagnostic infrastructures, case detection, recording, and reporting systems throughout Africa, the true scope of the TB problem remains unknown (Zumla, Petersen, Nyirenda & Chakaya, 2015). According to the WHO Global Tuberculosis Report 2015, the WHO Africa area accounts for 28% of the world's 9.6 million new TB cases, with yearly case detection rates more than double the global average of 133 per 100 000. (Ansumana, Keitell, Roberts, Ntoumi, Petersen, Ippolito & Zumla, 2017). The worldwide HIV and tuberculosis epidemics, which have strained health systems and destroyed people in

the region, have hit Sub-Saharan Africa hardest (Telisinghe, Charalambous, Topp, Herce, Hoffmann, Barron, Schouten, Jahn, Zachariah, Harries & Beyrer, 2016.)

Compared to any other region, Africa has the highest rate of tuberculosis in children and adolescents (Sullivan, Esmaili & Cunningham, 2017.). In 2015, 4,092 instances were discovered in Benin, West Africa (Affolabi, Sanoussi, Codo, Sogbo, Wachinou, Massou, Kehinde & Anagonou, 2017). South Africa (SA) has one of the world's worst tuberculosis (TB) epidemics, which is fueled by HIV (Churchyard, Mametja, Mvusi, Ndjek, Hesseling, Reid & Babatunde, 2014; Nanoo, Izu, Ismail, Ihekweazu, Abubakar, Mametja Madhi, 2015).

South Africa had the third largest absolute number of new cases worldwide in 2012, according to the WHO, with 400 000 new cases (Nanoo et al., 2015). As a result, the World Health Organization (WHO) has identified 22 high-burden countries (HBCs), which account for 81% of all estimated incident tuberculosis infections worldwide (Churchyard et al., 2014). SA has the third most reported incident cases and the fifth most estimated prevalent (undiagnosed active TB) cases among the HBCs (Churchyard, Mametja, Mvusi, Ndjek, Hesseling, Reid & Babatunde, 2014).

3.5 Tuberculosis in Lesotho

Lesotho, a lower-middle-income country in Sub-Saharan Africa with a population of 2.1 million, has the world's second highest TB incidence. The estimated prevalence of tuberculosis in the country is now 581 per 100,000. (WHO 2020 Global TB report). Approximately 72% of people with tuberculosis and HIV are co-infected (Hirsch-Moverman et al., 2017). Lesotho has one of the highest per capita tuberculosis (TB) incidence rates in the world (Malangu & Adebanjo, 2015). Because of their weakened state, active tuberculosis is the most common illness among HIV-positive people (Mugomeri et al., 2015). Children account for 5–7% of TB cases in Lesotho, which is low when compared to similar contexts such as neighboring South Africa, where the proportion of paediatric cases is at least 10%–20%. (Hirsch-Moverman et al., 2017). Only 80 countries had achieved good rifampicin testing coverage before 2015, according to WHO, which is defined as documentation of a rifampicin test result for at

least 80% of persons with bacteriologically proven pulmonary TB. Over the last five years, significant progress has been made: by the end of 2019, 113 countries had achieved good testing coverage, including 17 of the 40 countries on WHO's lists of high TB and/or high MDR-TB burden nations for the period 2016–2020, as well as Lesotho (Harding, 2020; WHO, 2020).

3.6 Multidrug-resistant tuberculosis (MDR-TB)

MDR-TB, defined as in vitro resistance to both rifampicin and isoniazid, with or without resistance to other TB treatments, is a major threat to worldwide tuberculosis control (Cain, Marano, Kamene, Sitienei, Mukherjee et al., 2015; Gehre, Otu, Kendall, Forson, Kwara et al., 2016). Since the earliest clinical trials of anti-TB treatment in the 1940s, anti-tuberculosis medication resistance has been identified as a result of poor or interrupted TB treatment (Cain et al., 2015).. Hargreaves, Lönnroth, Nellums, Olaru, Nathavitharana et al. (2017) identified MDR-TB as a public health priority in Europe, with major health and financial repercussions connected with the expensive and lengthy treatment often required. MDR-TB is more common among migrants than among natives in low-incidence nations in Europe (Lönnroth, Migliori, Abubakar, D'Ambrosio, De Vries et al., 2015; Hargreaves et al., 2017). A framework for efforts in low-incidence nations to eliminate TB , (*European Respiratory Journal*, *45*(4), pp.928-952.).

Adequate management necessitates knowledge of the incidence of medication resistance at the outset (Gehre et al., 2016). Ineffective TB control efforts and interruptions in drug supplies, typically due to political and other societal disruptions, encourage the emergence of drug resistance (Cain et al., 2015). MDR-TB is a global public health concern, particularly in Sub-Saharan Africa (SSA), where it adds to the burden of other infectious and non-communicable diseases plaguing the continent (Musa, Adamu, Galadanci, Zubayr, Odoh & Aliyu, 2017). MDR-TB has emerged as a result of ineffective TB control initiatives and poor TB patient management. Due to its low resources and lack of skilled TB health workers, this awareness is more acute in SSA (Mekonnen, Tessema, Moges, Gelaw, Eshetie & Kumera, 2015). MDR-TB affects roughly 480,000 persons worldwide each year, with 170,000 deaths (Cain et al., 2015). WHO estimates a global prevalence of 3.6 percent and 20.2 percent for primary and

acquired multidrug resistant tuberculosis (MDR-TB), respectively, among notified TB cases, with considerable country and regional variations (Mekonnen et al., 2015). In comparison to other locations, the prevalence of multidrug-resistant tuberculosis (MDR-TB) is said to be low in Sub-Saharan Africa (SSA) (Lukoye, Ssengooba, Musisi, Kasule, Cobelens et al., 2015.)

3.7 Tuberculosis treatment outcome

Treatment outcomes are an essential indicator of TB control initiatives, and the Directly Observed Treatment Short Course (DOTS) strategy includes monitoring and evaluating treatment results of TB patients (Gebrezgabiher et al., 2016). Controlling tuberculosis is largely dependent on how well patients are treated. According to the MDGs, the global target for TB treatment success is 85%. This target can be used as a normal target as well. Treatment success rates in the six WHO areas were as follows: western Pacific, Southeast Asian, and east Mediterranean in African, American, and European patients. Ethiopia had the highest success rate, with an 89 percent success rate (Biruk, Yimam, Abrha, Biruk Amdie, 2016). The worldwide target rate for a successful treatment outcome was established at 85%, and treatment outcomes were defined as cured, treatment completed, treatment failed, died, lost to follow-up, not evaluated, and treatment success, which included the sum of cured and treatment completed. Treatment outcomes are influenced by socioeconomic and demographic characteristics, as well as nutrition, HIV, MDR-TB, and TB management techniques such as Directly Observed Therapy Short-course (DOTS) (Ali, Karanja & Karama, 2017). DOTS was suggested as the global TB control approach, which calls for the patient to be treated for eight months: two months of intense therapy under the watch of a trained observer, and six months of maintenance treatment (Atekem, Tanih, Ndip & Ndip, 2018).

3.8 Association of socio-demographics and tuberculosis treatment outcome

Understanding the treatment outcomes and associated factors in a population may aid in improving TB management (Sinshaw, Alemu, Fekadu & Gizachew, 2017). Foreign nationality, male gender, and illiteracy were found to be risk factors for failed TB treatment outcomes in a Malaysian study (Atif, Sulaiman, Shafie, Ali Asif,

2014). In Cameroon, Atekem et al (2018) discovered that marital status, educational level, HIV status, and therapy category all had an impact on treatment outcome. Concurrent diabetes (Siddiqui, Khayyam, & Sharma, 2016), the presence of lung cavities at the commencement of treatment, and smoking have all been linked to a prolonged TB treatment duration (Atif et al., 2014)

3. CHAPTER 3: METHODOLOGY

The procedures or strategies used to find, select, process, and analyze information about a topic are referred to as research methodology. This is a methodical approach to solving problems in a scientific manner, as it examines how research should be conducted. As a result, the methodology section enables the researcher to objectively assess the overall validity and dependability of a study (Kumar, 2019). Making selections concerning the types of procedures to use while designing the study is necessary (Choy, 2014)

3.1 Research Approach and Design

The current research is quantitative in nature and was conducted using a cross-sectional, retrospective, quantitative research approach. Quantitative research is an investigation into a social or human problem based on putting a theory made up of variables to the test, measuring them with numbers and analyzing them with statistical processes to see if the theory's prediction generalizations hold true or not (Tavakol & Sandars, 2014). A research design is a blueprint for setting up the conditions for data collecting and analysis (Bell, 2014; Blaikie & Priest, 2019.). This design was chosen because it generates data that may be used to establish relationships between variables and outcomes. By independently duplicating the analysis, others should be able to validate the original findings (Choy, 2014). A cross-sectional study is a sort of observational research that examines data on variables collected across a sample population at one point in time (Ferguson, Rowlands, Olds & Maher, 2015). The goal of a retrospective study is to establish relationships between variables by measuring the subject only once (Setia, 2016). The study analyzed data from tuberculosis patients recorded in the Lesotho Ministry of Health database between January 2009 and December 2019 to investigate the epidemiology and treatment results of TB cases in Lesotho.

3.2 Study site

Study site is a geographical area where the study will be conducted. The study was conducted in the office of the Ministry of Health in the Maseru City in Lesotho, using national secondary data from Ministry of Health TB database. Maseru is the capital

city of Lesotho located in the western side of the country. Lesotho has 10 districts in which comprehensive and integrated primary health care services are provided.

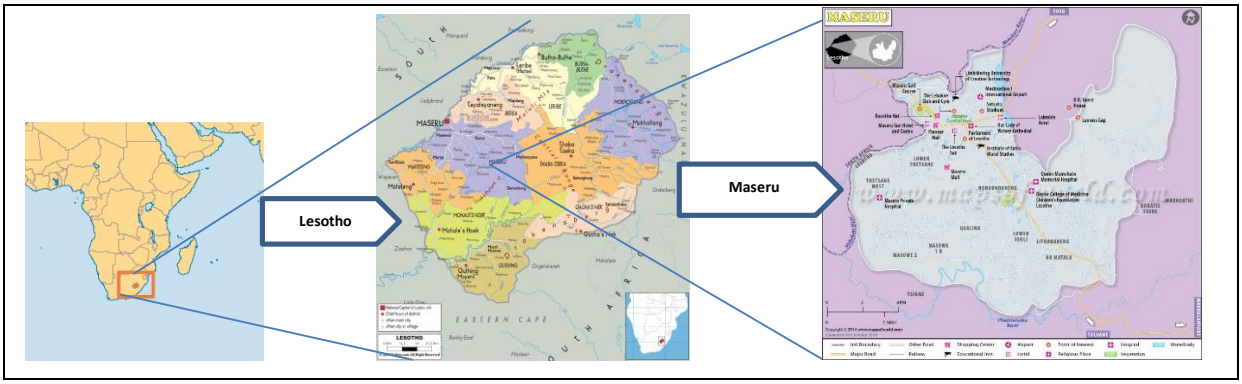


Figure 1 Maps of Africa and Lesotho showing the districts and Maseru Capital Town

Lesotho is divided into two regions which are lowlands and highlands, some facilities are located in the lowlands and others are located on the highlands. The lowlands districts are Butha-Buthe, Leribe, Berea, Maseru, Mafeteng, Mohale's hoek and Quthing.Highlands districts are Qacha'snek, Thaba-Tseka and Mokhotlong. Each district has its own health facilities. The data is collected from each district and captured into the national data base, district health information system 2 (DHIS2) then it can be accessed nationally.

3.3 Population and sampling

3.3.1 Population

A study population is a group of people selected from the broader population who have similar characteristics such as age, sex, or health problems (Setia, 2016).The researcher focused on all patient records with a TB diagnosis in different health facilities in Lesotho. The number of patient records were unknown.

3.3.2 Sampling technique and sample size

The sample technique is selecting a representative sample of the population and using the information gathered as research data (Aydin, Kaplan, Atilgan, & Gürel, 2019). It's also known as a representative of a group because it assures that the sample is representative of the entire population (Mooney & Garber, 2019). Sampling allows the researcher to make a precise estimate of the standard error, which aids in the gathering of information about a population feature (Singh, 2015; Chaudhuri & Dutta,

2018). In this investigation, the non-probability sampling approach, often known as random sampling, was applied. This is a form of sampling in which the researcher must be aware of the sample universe from which the sample is drawn. This sampling strategy allowed us to gain deep insights into the phenomenon we were interested in, and because the population of interest was so large, there was less of a chance of missing valuable insights from people who were not included.

3.3.3 *Inclusion Criteria*

The important characteristics of the target population that the researcher will employ to answer their research question are defined as inclusion criteria. Demographic, clinical, and regional factors are common inclusion criteria (Patino & Ferreira, 2018). The researcher used the following criteria to include all TB patient records in the database, based on treatment outcomes:

Criteria Number	**Criteria**
1	Diagnosed with TB
2	Put on TB treatment
3	Complete TB-treatment & Cured
4	Completed but not cured
5	Died irrespective of completing TB treatment or not
6	Treatment defaulters.
7	Transferred out to another health facility or transferred in from another health facility

3.3.4 Exclusion Criteria

Exclusion criteria are characteristics of potential study participants who meet the inclusion criteria but have extra traits that may jeopardize the study's success or raise their likelihood of a negative outcome (Patino & Ferreira, 2018). TB patient records with missing information, such as treatment outcomes, were eliminated from this investigation.

3.4 Data collection

Data collection is the systematic process of acquiring and measuring information on variables of interest in order to answer specified research questions, test hypotheses,

and evaluate outcomes. (A dictionary of epidemiology, 2014). The data was collected from the National TB-Database from the Ministry of Health in Lesotho using a data extraction tool (Appendix 1) developed using literature on investigating the epidemiology and treatment outcomes of tuberculosis. From Appendix 1, the demographic epidemiological information which was planned for extraction includes age, gender, marital status, educational status, geographical area or district of diagnosis and nationality. However, most variables were not recorded in the available data (Marital status, educational status, geographical area or district of diagnosis and nationality). The treatment outcomes as highlighted in table 1 below were collected using Appendix 1 as Bacteriological coverage, Cured, Lost-to-follow, Died, Successfully Completed, Relapse, Defaulter and transfer out.

Table 1: Tuberculosis treatment outcomes

Cured	A pulmonary tuberculosis patient who had bacteriologically confirmed TB at the start of treatment but was smear- or culture-negative in the last month of treatment and at least once before.
Treatment completed	A tuberculosis patient who finished therapy without showing signs of failure but had no record that sputum smear or culture findings were negative in the last month of treatment and on at least one preceding occasion, either because tests were not done or because results were unavailable.
Treatment failed	During treatment for tuberculosis, a patient's sputum smear or culture is positive during month 5 or later.
Died	A tuberculosis patient who dies before or during treatment for any cause.
Lost to follow-up	A tuberculosis patient who has previously been treated for the disease and was deemed lost to follow-up at the end of their most recent round of therapy, or whose treatment was discontinued for two months or more.
Not evaluated	A tuberculosis patient for whom no treatment outcome has been determined. This covers instances that have been "transferred out" to another treatment unit as well as those for which the reporting unit has no knowledge of the treatment outcome.

Treatment success	The total number of people who have been cured and whose treatment has been completed
Relapse patients	Patients who were previously treated for tuberculosis and were declared cured or had their treatment completed at the end of their most recent course of treatment have now been diagnosed with a recurrent TB episode (either a true relapse or a new episode of TB caused by reinfection).
Bacteriological coverage	defined as the proportion of pulmonary TB (PTB) cases with sputum smear test results (excluding children aged 0–7), is a measure both of the availability of laboratory services and of compliance with TB guidelines.

3.5 Data analysis

During research, data analysis is a continuous process that involves analyzing participant information using analytic guidelines or software (Creswell, 2013). Data was extracted into a Microsoft Excel spreadsheet and then transferred to STATA statistical software version 12 for Windows (STATA Corporation, College Station, Texas) for analysis. Assistance in analyzing the results was obtained from the University of Limpopo's Statistician. Percentages and frequencies are used to represent categorical variables. Furthermore, a Chi-Squared test was used to compare categorical variables, while a t-test was used to analyze continuous variables. A statistically significant P-value of 0.05 was used.

3.6 Reliability, Validity

3.6.1 Reliability

Reliability is concerned with consistency of a measure, an instrument has to give the same results every time used (Bastos, Duquia, Ganzalez-Chica, Mesa & Bonamigo, 2014; Heale & Twycross, 2015). The data extraction tool was cross-checked by the supervisor for consistency in the results. Reliability was also maintained through excluding patients records that are incomplete and has errors. The data extraction tool was not changed to maintain reliability in the current study

3.6.2 Validity

Validity refers to how well a notion can be measured in a quantitative investigation. Content validity, construct validity, and criterion validity are the three categories. The extent to which a research instrument accurately measures all facets of a construct is known as content validity. Construct Validity refers to a condition in which inferences regarding test scores can be derived based on the study topic and criterion. Any other instrument that measures the same variable is referred to as valid (Heale & Twycross, 2015).

3.6.2.1 Internal validity

The degree to which a study is free of bias or systematic errors is known as internal validity (A Dictionary of Epidemiology, 2014). The data collecting tool was reviewed for internal validity by the researcher's supervisor to confirm its authenticity.

3.6.2.2 External validity

This is the degree to which a study's findings can be applied to different populations and circumstances (Cozby & Bates, 2015). Because the sample size in this study was representative of TB cases reported in Lesotho from 2009 to 2019, the data collection tool had good external validity. Furthermore, the use of the data extraction tool was piloted on 10% of the sample before it was utilized to guarantee that it measures what it claims to measure. The sample selection did not include the patient records used in the pilot.. Sample size was total population.

3.7 Bias

Any propensity that precludes a fair consideration of a research question is referred to as bias (Pannucci & Wilkins, 2010). Possible biases in the study include selection bias, sample bias, recording bias, unavoidable prejudice, and reporting bias. Selection bias was a problem for the researcher, but it was minimized by randomly selecting the records to reduce selection bias, and sampling bias was avoided by using the random sample technique. To prevent inevitable bias, the researcher followed the research methodology and worked with a statistician to double-check the data analysis to ensure that it accurately reflected the data received from the database.

3.8. ETHICAL CONSIDERATIONS

3.8.1 Ethical clearance to conduct the study

The proposal for this study was presented at the Department of Public Health Research Committee then submitted to the School of Healthcare Sciences Research Committee (SREC) and Faculty Higher Degree Committee (FHDC) for ethical reviews and ethical approval was requested from the Turfloop Ethics Research Committee (TREC) before the commencement of data collection.

3.8.2 Permission to conduct the study

Permission to conduct the study was also requested from the Ministry of Health in Lesotho (**Appendix B**).

3.8.3 Informed consent and voluntary participation

The current study did not involve patients or people therefore, informed consent and voluntary participation did not apply.

3.8.4 Confidentiality

To maintain confidentiality, the extracted data was kept safe in a computer password protected mode and only the researcher together with supervisor had access to the data.

3.8.4.1 Anonymity

Each patient record was assigned unique identifier number to maintain confidentiality.

3.8.5 Harm

The study used secondary data and no harm was applicable to anyone , each patient record was assigned unique identifier number to maintain confidentiality.

4. CHAPTER 4: RESULTS

4.1. Introduction

The methodology used in the current investigation, which comprised the research design, study population, and sample procedure, was explained in the previous chapter of this study. The goal of this study was to look into the tuberculosis epidemiology and treatment outcomes in Lesotho between 2009 and 2019. The data was collected using a quantitative retrospective cross-sectional study design, and the current chapter discusses the study's findings, which are presented in the form of tables and graphs that include socio demographics, treatment outcomes, and the number of participants, in order to highlight and interpret all statistical and descriptive associations.

4.2 Study Population and completeness of the data

The study population consisted of 18 836 TB patients records which were extracted from the National TB database in Lesotho.

4.3 The epidemiology of TB in Lesotho between the years 2009 and 2019

Table 4.1:
Baseline characteristics, overall and stratified by gender

	Both sexes (n=18 836) n (%)	**Female (n=8 424) n (%)**	**Male (n=10 412) n (%)**	**p-value for trend**
Age in years				
0 – 14	698 (3.7)	329 (3.9)	369 (3.5)	*<0.001*
15– 24	2115 (11.2)	1321 (15.7)	794 (7.6)	
25 – 34	6242 (33.1)	3231 (38.4)	3011 (28.9)	
35 – 44	5461 (29.0)	2110 (25.1)	3351 (32.2)	
45 – 55	2892 (15.4)	933 (11.1)	1959 (18.8)	
55 – 64	1035 (5.5)	341 (4.1)	694 (6.7)	
≥65	393 (2.1)	159 (1.9)	234 (2.3)	
TB Case findings				
2009	1484 (7.9)	675 (8.0)	809 (7.8)	*<0.001*
2010	1748 (9.3)	832 (9.9)	916 (8.8)	
2011	1633 (8.7)	734 (8.7)	899 (8.6)	
2012	1622 (8.6)	733 (8.7)	889 (8.5)	
2013	1681 (8.9)	672 (8.0)	1009 (9.7)	
2014	1938 (10.3)	932 (11.1)	1006 (9.7)	
2015	1603 (8.5)	700 (8.3)	903 (8.7)	
2016	1576 (8.4)	707 (8.6)	869 (8.4)	

2017	1749 (9.3)	726 (8.6)	1023 (9.8)	
2018	1727 (9.2)	798 (9.5)	929 (8.9)	
2019	2075 (11.0)	915 (10.9)	1160 (11.1)	

Approximately forty-five percent of the TB patients records retrieved in the database were females and the mean age was 35.9 years with standard deviation ±12.7 and age ranged from 1 to 84 years. Using stagger's rule there was a statistical significance difference between the age groups (*p value <0.001*) and the majority of TB patents were in the age group 25 – 34 years at 33.1% followed by those in age group 35 – 44 years, 45 – 55 years, 15 – 24 years and 55 – 64 years 65 years at 29%, 15.4%, 11.2% and 5.5% respectively. The least number of TB patients were in the age group 65 years and above at 2.1% followed by those in age group zero to 14 years at 3.7%. Considering the TB case findings by year, majority of the cases were in 2019 at 11% followed by 2014, 2010, 2017 and 2018 at 10.3%, 9.3% 9.3% and 9.2% respectively as presented in Table 4.1 above.

The current study revealed that the Directly Observed Treatment, Short-course (DOTS, also known as TB-DOTS) coverage increased in years from 72% in 2013 to 89.9% in 2019 as presented in Figure 4.1 below.

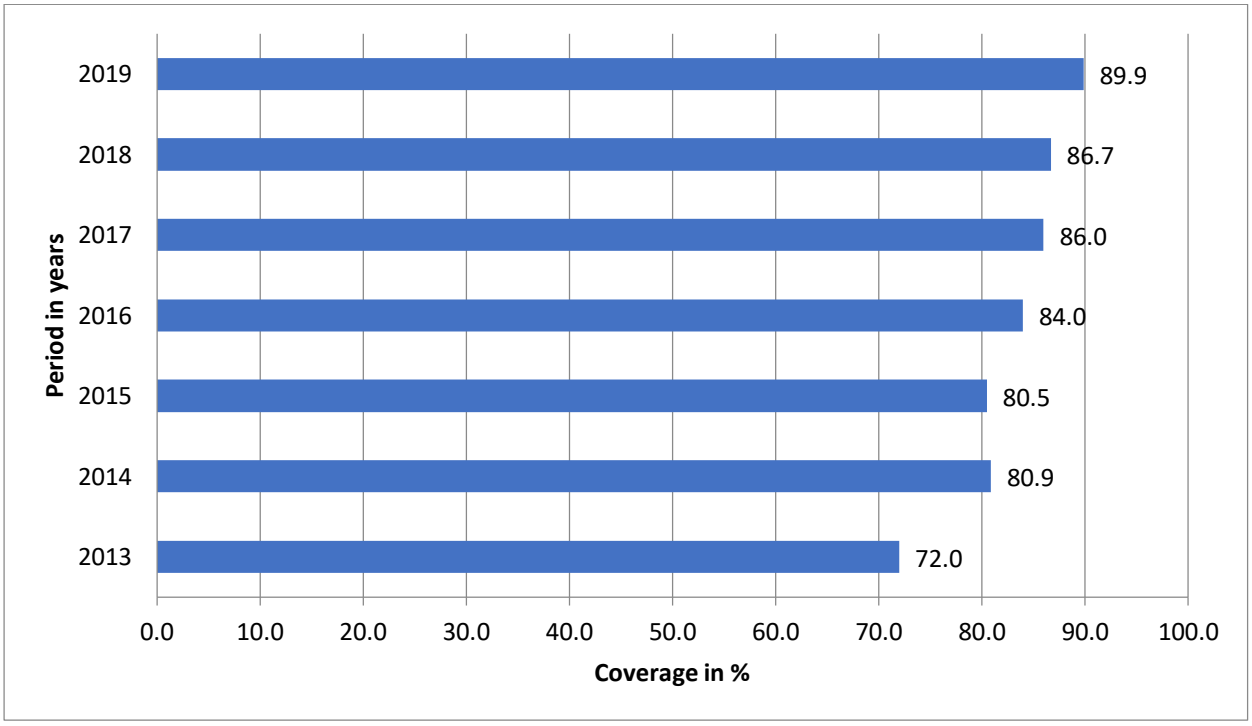


Figure 4.1: DOTS coverage in Lesotho, 2013 – 2019

The smear conversion rates in the available data were for 2 months during the period 2011 to 2019. The study findings revealed that the smear conversion improved on an annual basis from 54.8% in 2011 to 67.3% in 2015 but dropped to 63% and 65.9% in the years 2016 and 2017 respectively. The smear conversion increased to 70.2% in 2018 and dropped to 68.3% in 2019 as presented in Figure 4.2 below.

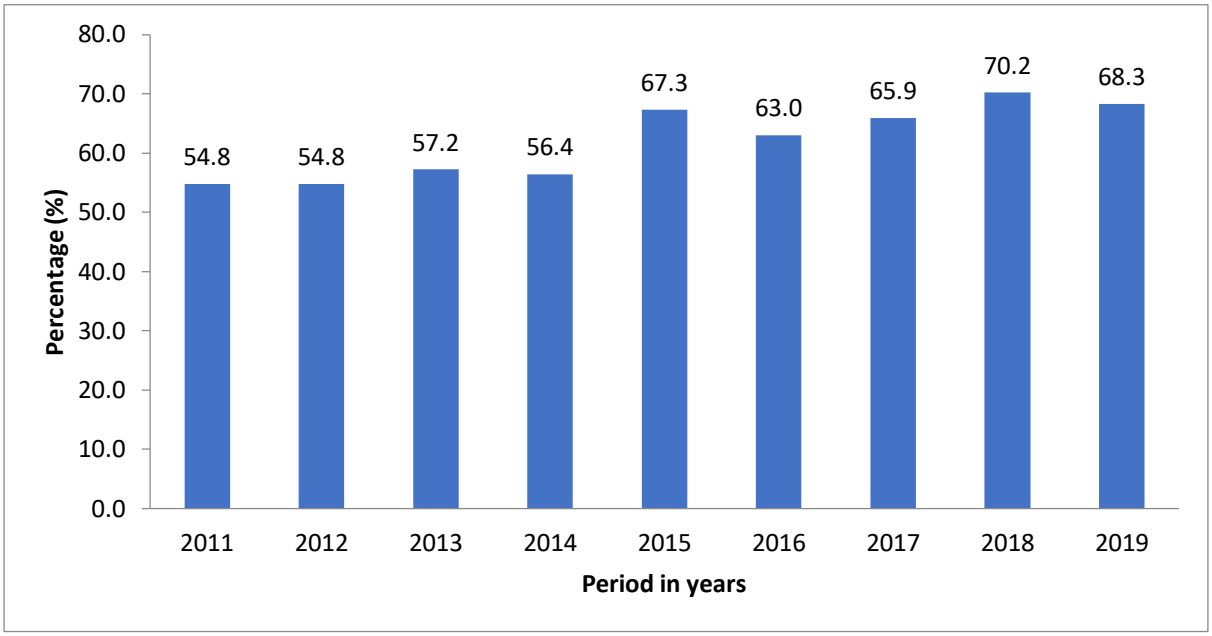


Figure 4.2: TB smear conversions for new smear positive at 2 months in Lesotho, 2011 – 2019

4.4 The treatment outcomes of TB cases in Lesotho between the years 2009 and 2019

The overall treatment outcome of TB was found to be 63.5% for cured patients in 2012 which dropped to 57.2% in 2013. However, from 2014 there has been an improved cure rate of TB patients on an annual basis in Lesotho from 60.4% to 76.7% in 2019. The TB treatment success rate in Lesotho also showed a similar trend as the cure rate. It was 74.8% in 2012 then dropped to 68.6% in 2013 but from 2013 there has been an improvement in the rate of treatment success from 70.4% in 2014 to 78.8% in 2019 as presented in Figure 4.3 below.

The overall TB death rates in the current study was found to be increasing on an annual basis from 7.4% in 2012 to 9.2% in 2018 then dropped to 8.5% in 2019. A fluctuating tread has been reported on TB treatment failure rates from 1.4% in 2012 to 2% in 2013 then dropped to 1.7% in 2014 and increased to 2.5% in 2015. A slight declined in TB treatment failure rate has been reported in 2016 to 2.3% to 1.9% in 2017 but this increased to 2.6% in 2018 and lastly dropped by 0.5% to 2.1% in 2019. The TB defaulter rates has shown a fluctuating trend from 5.1% in 2012 to 8.6% in 2013 but this dropped to 7.4% in 2015 and increased 8.1% in 2016. From 2017 a steady declined in defaulter rate has been reported from 7.7% to 4.8% in 2019. The TB transfer rates has also shown a fluctuating trend from 6.9% in 2012 to 8.8% in 2013. From 2014 a consistent decrease in TB transfer rates has been reported annually from 8.7% to 5.1% in 2019. The TB patients who have not been evaluated for treatment outcomes have been decreasing annually from 4.4% in 2012 to 0.8% in 2019 as presented in Figure 4.3 below.

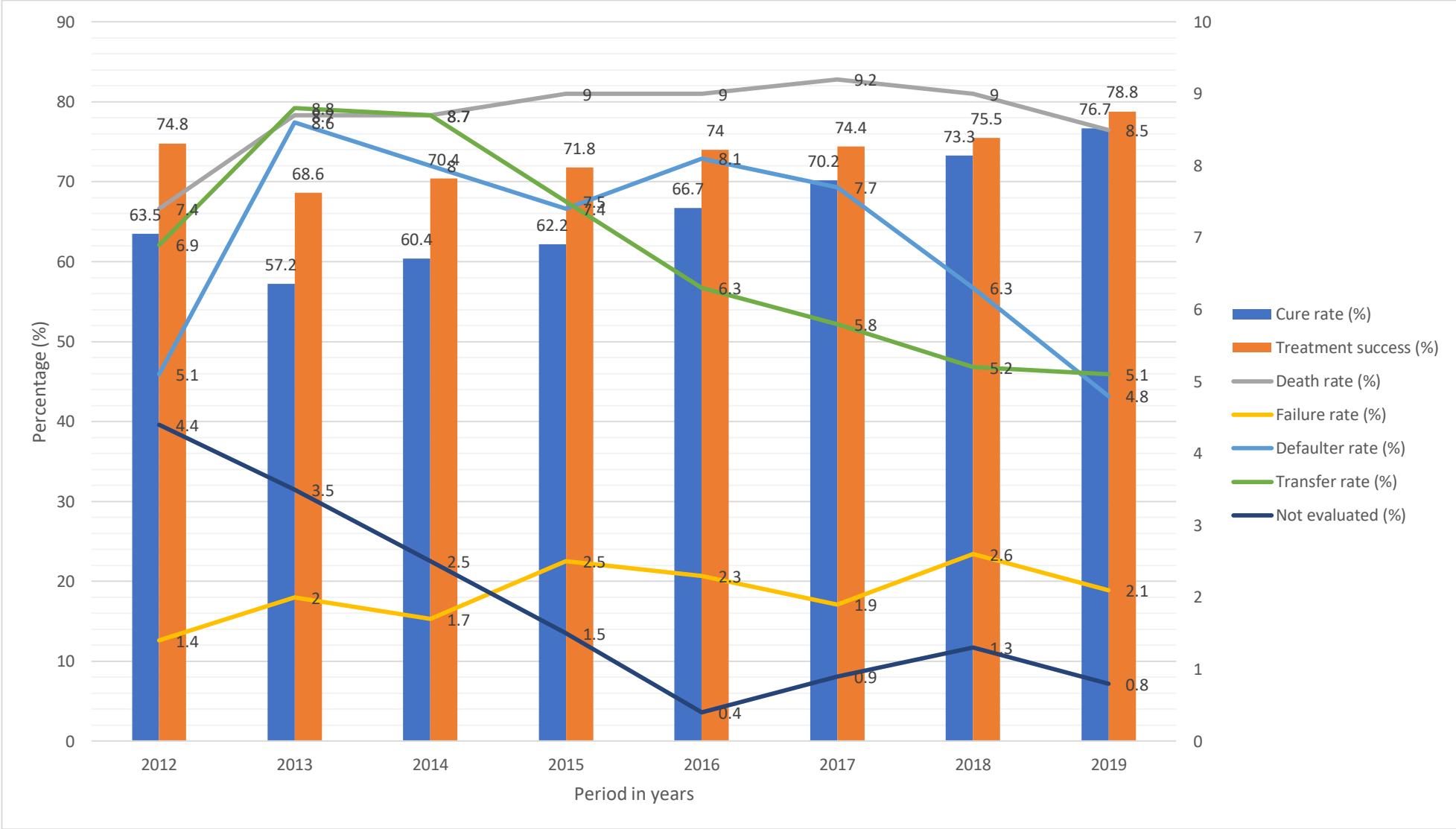
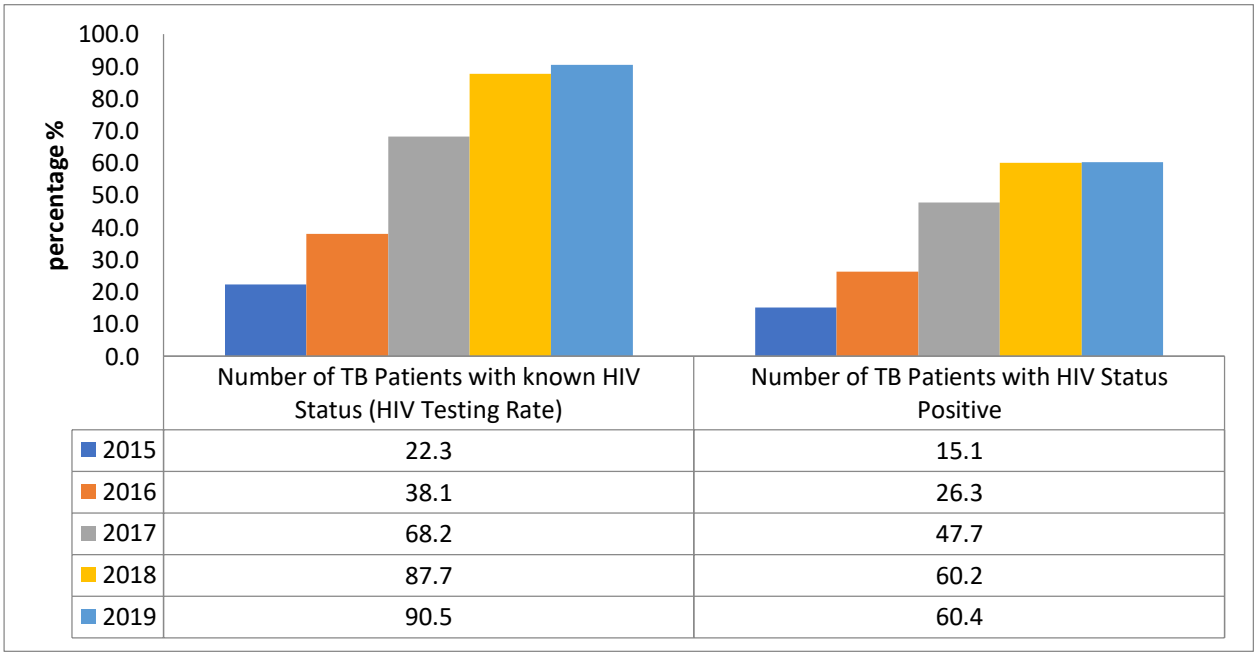


Figure 4.3: TB treatment outcomes in Lesotho, 2012 – 2019

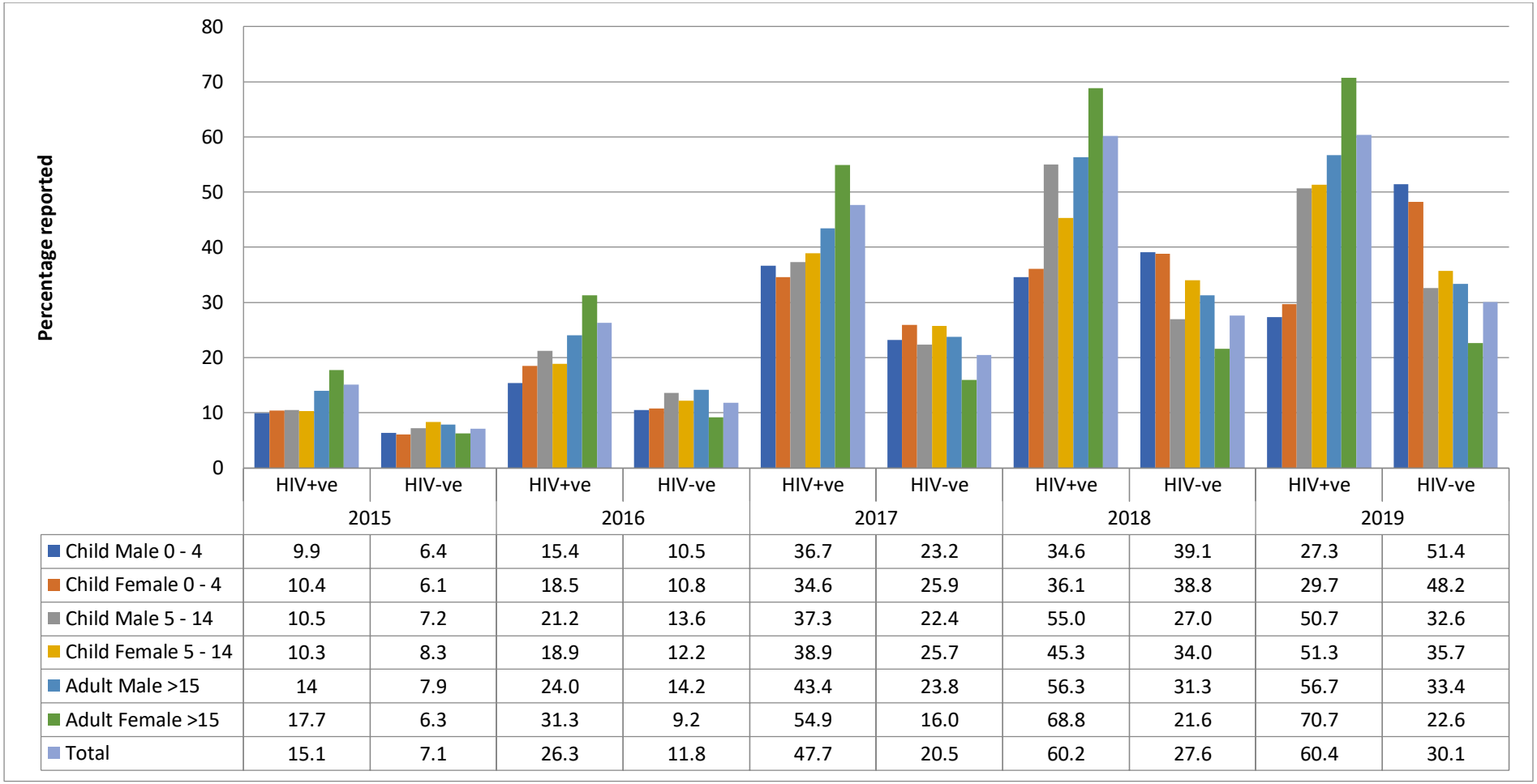
Tuberculosis is more common in HIV-positive people (TB). TB is also the most common opportunistic infection, accounting for around a third of all deaths in this population. The number of TB patients with known HIV status climbed from 22.3 percent in 2015 to 90.5 percent in 2019, according to the current study, while the proportion of TB patients with HIV status positive increased from 15.1 percent in 2015 to 60.4 percent in 2019 as presented in Figure 4.4 below.



	Number of TB Patients with known HIV Status (HIV Testing Rate)	Number of TB Patients with HIV Status Positive
2015	22.3	15.1
2016	38.1	26.3
2017	68.2	47.7
2018	87.7	60.2
2019	90.5	60.4

Figure 4.4: Case finding indicators for TB/HIV in Lesotho, 2014 – 2019

The proportion of TB patients with HIV status positive increased with increasing age in all age groups. In age group 0 – 4 years the prevalence of HIV increased from 9.9% in 2015 to 36.7% in 2017 dropped to 34.6% and 27.3% in 2018 and 2019 respectively. Females in this age group had a prevalence of HIV from 10.4% in 2015 which increased to 36.1% in 2018 and decreased to 29.7% in 2019. A similar trend was witnessed in age group 5 – 14 years for males as the prevalence of HIV increased from 10.5% in 2015 to 55% in 2018 then dropped to 50.7% in 2019. However, females in this age group have shown an HIV prevalence of 10.3% in 2015 which increased to 19.9%, 38.9%, 45.3% and 51.3% in 2016, 2017, 2018 and 2019 respectively. Both adult males and females have shown an increasing HIV prevalence from 2015 to 2019 as presented in Figure 4.5 below.



	2015		2016		2017		2018		2019	
	HIV+ve	HIV-ve	HIV+ve	HIV-ve	HIV+ve	HIV-ve	HIV+ve	HIV-ve	HIV+ve	HIV-ve
Child Male 0 - 4	9.9	6.4	15.4	10.5	36.7	23.2	34.6	39.1	27.3	51.4
Child Female 0 - 4	10.4	6.1	18.5	10.8	34.6	25.9	36.1	38.8	29.7	48.2
Child Male 5 - 14	10.5	7.2	21.2	13.6	37.3	22.4	55.0	27.0	50.7	32.6
Child Female 5 - 14	10.3	8.3	18.9	12.2	38.9	25.7	45.3	34.0	51.3	35.7
Adult Male >15	14	7.9	24.0	14.2	43.4	23.8	56.3	31.3	56.7	33.4
Adult Female >15	17.7	6.3	31.3	9.2	54.9	16.0	68.8	21.6	70.7	22.6
Total	15.1	7.1	26.3	11.8	47.7	20.5	60.2	27.6	60.4	30.1

Figure 4.5: Case finding indicators for TB/HIV in Lesotho, 2014 – 2019 stratified by age group

The proportion of HIV-positive TB patients who are started or continue previously initiated Co-trimoxazole preventive therapy, during TB treatment, expressed as a percentage of all HIV-positive TB patients registered over the reporting period have increased from 67.1% in 2013 to 84.1% in 2016 in Lesotho. This then dropped to 83.1% in 2017 and increased to 85.6% in 2018 and lastly dropped by 11.1% to 74.5% in 2019 as presented in Figure 4.6 below.

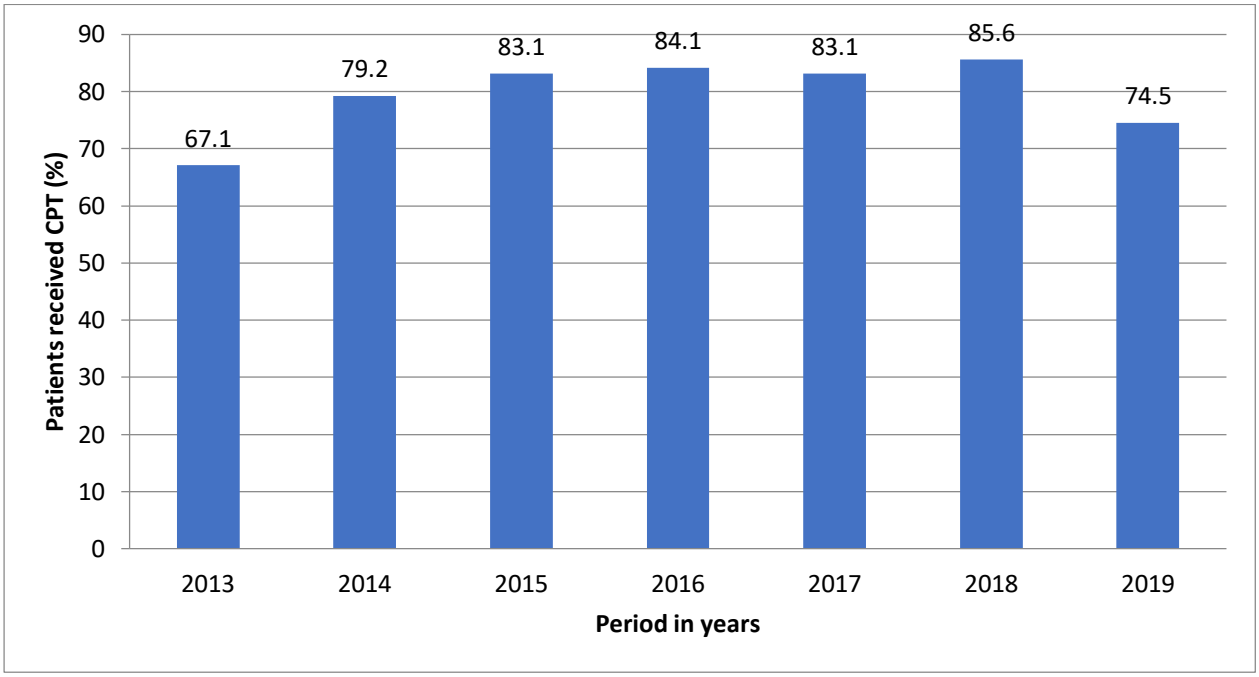
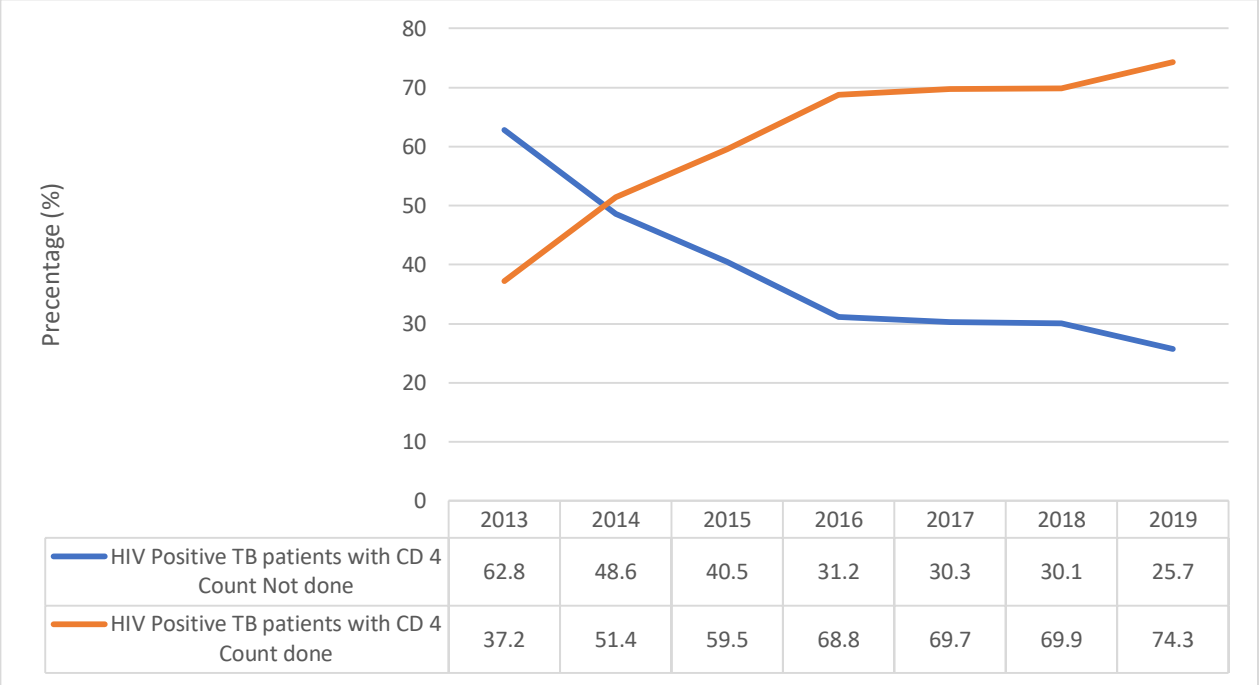


Figure 4.6: During TB treatment in Lesotho, the proportion of HIV-positive TB patients who are started on or continue already commenced Co-trimoxazole preventative medication (CPT)

The proportion of HIV-positive TB patients with CD4 count done has increased from 37.2% in 2013 to 74.3% in 2019 as presented in Figure 4.7 below.



	2013	2014	2015	2016	2017	2018	2019
HIV Positive TB patients with CD 4 Count Not done	62.8	48.6	40.5	31.2	30.3	30.1	25.7
HIV Positive TB patients with CD 4 Count done	37.2	51.4	59.5	68.8	69.7	69.9	74.3

Figure 4.7: Proportion of HIV positive TB patients with CD4 count done and not done

5 CHAPTER 5: DISCUSSION AND CONCLUSION

5.1 Introduction

The outcomes of this study were reported and evaluated in accordance with the study objectives in the preceding chapter. The findings of this investigation are described and compared to the relevant literature in this chapter. The following sections make up the chapter: Introduction, Tuberculosis Epidemiology, Tuberculosis Treatment Outcomes, TB/HIV Co-infection, Study Limitations, Conclusion, and Recommendation.

5.2 Epidemiology of tuberculosis

The current study found that the average age of TB patients was 35.9 years, which is much lower than the 53.5 years reported in a study conducted in Poland (Korzeniewska-Kosea, 2015) and 59.9 years reported in a study conducted in Taiwan (Korzeniewska-Kosea, 2015). (Lin, Lin, Kuo, Wang, Hsu & Chen et al., 2014). The mean age of TB patients in a research conducted in India's Rajkot district (Thakkar, Piparva, & Lakkad, 2019) was identical to the current study. The fact that older persons are more susceptible to tuberculosis has long been recognized in high-income nations, but it is rarely considered in low-income ones (Negin, Abimbola & Marais, 2015). This is different in the current study since TB was most commonly reported among adults aged 25 to 44 years old. This could be because most people in this age range are sexually active or work in mines, and the disease spreads to other family members. TB prevalence rates grew progressively with age in a national tuberculosis prevalence survey done in Asia from 1990 to 2012, and the survey found that TB prevalence rates peaked in the oldest age group of 65 years old in all nations (Onozaki, Law, Sismanidis, Zignol, Glaziou & Floyd, 2015). This pattern differs from that found in Lesotho, where the oldest persons, those aged 65 and up, have the fewest TB cases.

The current study found a year-on-year increase in the incidence of microbiologically confirmed tuberculosis from 2009 to 2019, which is consistent with incidences reported in South Africa (Nanoo, Izu, Ismail, Ihekweazu, Abubakar, Mametja & Madhi, 2015) and Nigeria (Nanoo, Izu, Ismail, Ihekweazu, Abubakar, Mametja & Madhi, 2015). (Adejumo, Daniel, Abdur-Razzaq, Shogbamimu, Femi-Adebayo & Adepoju et al.,

2017). Lesotho's TB epidemic evolved differently than Kenya's, with the Kenyan TB pandemic marked by an increase in TB cases peaking in 2007, followed by a fall that began to accelerate in 2011 (Kipruto, Mung'atu, Ogila, Adem, Mwalili & Masini et al., 2015). However, according to the findings of the current study, the TB pandemic in Lesotho has been expanding year after year. The benefits of combining TB and HIV services can be linked in part to the decrease in TB cases, and these advantages should be maintained. The apparent epidemiologic shift in age, showing lower transmission in the younger age groups, is also noteworthy. The reemergence of tuberculosis in the early 1990s, accompanied by the introduction of HIV and a decline in many people's economic situation, sparked interest in the epidemiology of tuberculosis. An enormous TB pandemic erupted as a result of the fatal mix of HIV and poverty (Kipruto et al., 2015).

5.3 Tuberculosis treatment outcomes

Directly observed treatment short-course (DOTS), a WHO TB control strategy, consists of five components, including the administration of standardized short-course chemotherapy regimens with first-line drugs (isoniazid, rifampicin, pyrazinamide, and streptomycin or ethambutol or both) under direct observation, at least during the intensive treatment phase, regardless of patient drug-susceptibility pattern (Espinal, Kim, Suarez, Kam, Khomenko & Migliori et al., 2000). Lesotho, like other countries throughout the world, has adopted this method since it is one of the most cost-effective human health initiatives (Keshavjee, Seung, Satti, Furin, Farmer & Kim et al., 2007; Adebanjo, & Malangu, 2015).

In Africa, nations with high prevalence of TB/HIV co-infection are the focus of increased efforts to expand DOTS (directly observed treatment short-course) (Khan, Mirza & Qadeer, 2017). Lesotho is one of the top 30 countries with the highest TB burden (Sooro, Malikelle, Leteka, Kobo & Ramathebane, 2021). According to the current study, coverage of Directly observed therapy, short-course (DOTS, commonly known as TB-DOTS) rose over time from 72 percent in 2013 to 89.9% in 2019, which is still less than 100 percent. These findings are similar to those of South Africa, which had 89 percent DOTS coverage (Ershova, Podewils, Bronner, Stockwell, Dlamini & Mametja, 2014), and Uganda, which had 75.1 percent DOTS coverage (Kirirabwa, Kimuli, DeJene, Nanziri, Birabwa & Okello et al., 2018). (Khan et al., 2017).

DOTS is a powerful positive sign that can be used to eradicate tuberculosis. This can be accomplished by actively seeking out new smear-positive TB cases. This could lead to an earlier diagnosis and, as a result, a shorter period of infectiousness before effective chemotherapy can be started (WHO, 2014). This is the only method that can reach a cure rate of more than 85% while saving millions of lives and reducing the risk of drug-resistant tuberculosis strains emerging, thus all nations, including Lesotho, should implement DOTS without fail. Although passive case finding, as implemented through the DOTS technique, has been found to improve case detection in high-burden nations such as Vietnam, Peru, and Ethiopia, there is still room for improvement. Its utility is restricted by patient and health-care system delays, as well as possible underlying HIV infections, which might cause diagnostic delays. The delay is concerning for public health since it raises the risk of TB transmission to patients' contacts and death, particularly in TB-HIV co-infected individuals (Sekandi, Neuhauser, Smyth & Whalen, 2009).

The study found that smear conversion improved annually in Lesotho from 54.8 percent in 2011 to 68.3 percent in 2019. This is a much better performance than Nigeria, where new smear-positive pulmonary TB cases were at 46.5 percent (Gidado, Obasanya, Habib, & Nasiru, 2017), but not as good as a study conducted in South Africa, where the smear conversion rate was high, with only 12.8 percent classified as (Mlotshwa, Abraham, Beery, Williams, Smit & Uys et al., 2016).

Treatment results are an essential indicator of TB control initiatives, and the DOTS strategy includes monitoring and evaluating TB patient treatment outcomes (Gebrezgabiher, Romha, Ejeta, Asebe, Zemene & Ameni, 2016). The primary outcome in this study was the assessment of treatment success (cure and treatment completion) as defined by the 2016 WHO criteria. The assessment of death and loss to follow-up rates during the treatment period were secondary outcomes. Similar to South Africa (Ershova, et al., 2017), the total TB treatment outcome for cured increased from 63.5 percent to 76.7 percent from 2012 to 2019, resulting in these two countries failing to meet the WHO objective of 89 percent. According to a study conducted in Uganda, the cure rate was 41% (Kirenga, Levin, Ayakaka, Worodria, Reilly, & Mumbowa et al., 2014), which could be due to Uganda's high HIV prevalence. The current study's TB treatment success rate improved from 74.8 percent in 2012 to

78.8 percent in 2019, which is lower than treatment success rates in studies in Southern Ethiopia (Gebrezgabiher et al., 2016) and Namibia (Kibuule et al., 2018).

TB is the tenth most common cause of mortality worldwide, and it has been the most common cause of death from a single infectious agent since 2007. In the WHO South-East Asia and African areas, almost 85% of TB deaths occurred (Osei, Oppong & Der, 2020). The overall TB death rates in were found to be increasing on an annual basis from 7.4 percent in 2012 to 8.5 percent in 2019, which is higher than the TB death rates reported in studies conducted in South Africa (Kaplan, Caldwell, Bekker, Jennings, Lombard & Enarson et al., 2014) and Northeast Ethiopia (Kaplan, Caldwell, Bekker, Jennings, Lombard & Enarson et al., 2014.) (Tesfahuneygn, Medhin & Legesse, 2015). However, it is lower than the TB death rate reported in a Ghanaian study (Osei et al., 2020). On the other hand, a study conducted in Zimbabwe revealed a significantly higher TB death rate of 22 percent, the highest in Africa (Takarinda, Sandy, Masuka, Hazangwe, Choto & Mutasa-Apollo et al., 2017).

One of the dangers to TB control is treatment failure, which is defined as a patient who is sputum smear or sputum culture positive at least 5 months after starting anti-TB treatment (Namukwaya, Nakwagala, Mulekya, Mayanja-Kizza & Mugerwa, 2011). This is due to its link to multidrug-resistant tuberculosis (MDR TB) and the fact that infected patients continue to spread the disease (Namukwaya, 2011; Niaz, 2021). Treatment failure rates in the current study increased from 1.4 percent in 2012 to 2.1 percent in 2019, which is greater than Ghana's reported TB treatment failure rate (Hayibor, Bandoh, Asante-Poku & Kenu, 2020) and also greater than the TB treatment failure rate reported in a study conducted in Zimbabwe (Ncube, Takarinda, Zishiri, Van den Boogaard, Mlilo & Chiteve et al., 2017) and Nigeria (Ncube, Takarinda, Zishiri, Van den Boogaard, Mlilo & Chiteve et al., 2017). (Gidado et al., 2017).

Failure to finish the 6-month or longer treatment regimen is a major barrier to TB management. The World Health Organization (WHO) defines treatment default as a two-month treatment stoppage (Cherkaoui, Sabouni, Ghali, Kizub, Billioux & Bennani et al., 2014; Ruru, Matasik, Oktavian, Senyorita, Mirino & Tarigan et al., 2018). TB defaulter rates in the current study were 5.1 percent in 2012 and 4.8 percent in 2019,

which is lower than the TB defaulter rate reported in 2012. A study conducted in South Africa (Kigozi, Heunis, Chikobvu, Botha & Van Rensburg, 2017).

But similar to the TB defaulter rate recorded in Nigeria (Kigozi, Heunis, Chikobvu, Botha & Van Rensburg, 2017). (Gidado et al., 2017). When compared to a study conducted in Kampala, Uganda (Robsky, Hughes, Kityamuwesi, Kendall, Kitonsa & Dowdy et al., 2020), the current study's TB transfer rates were high, which could be related to the fact that the majority of Basotho people travel to South Africa for better job possibilities (Mokoena & Balkaran, S., 2018). The number of TB patients who have not been reviewed for treatment outcomes has been dropping year after year, from 4.4 percent in 2012 to 0.8 percent in 2019, which is lower than the number of TB patients in Uganda who have no documented treatment outcomes (Robsky et al., 2020)

5.4 Tuberculosis/HIV co-infection

People living with HIV (PLHIV) are more likely to get tuberculosis (TB). TB is also the most common opportunistic infection, accounting for around a third of all deaths in this population (Owiti, Onyango, Momanyi & Harries, 2019). The number of TB patients with known HIV status jumped from 22.3 percent in 2015 to 90.5 percent in 2019, according to the current study, which is greater than the findings of a South African study (van der Heijden, Karim, Mufamadi, Zako, Chinappa & Shepherd et al., 2017).

5.5 Limitations of the study

There are a few flaws in this study. The analysis has to focus on the available data due to missing information on socio-demographics of the TB records, TB treatment regimen, DOT coverage for some years, and treatment result for the years 2009 to 2011. As a result, representative sampling is less of a concern, and the results given accurately reflect the situation in this sample. F Tuberculosis (TB) is a primary cause of death worldwide, especially when it is associated with HIV. The proportion of TB patients with HIV status positive increased from 15.1 percent in 2015 to 60.4 percent in 2019, according to the current study, which is higher than the proportion reported in a Chinese study (Qian, Nguyen, Lyu, Albers, Bi & Graviss, 2018). Lesotho's tuberculosis epidemiology is similar to that of other developing countries, where the

disease is connected to widespread poverty, poor living conditions, and a weakened immune system, especially among HIV and AIDS patients (Gulland, 2016.; Ali, Karanja Karama, 2017; Sabiiti, 2017). Furthermore, the information was gathered retrospectively from medical and surveillance papers that were gathered as part of programmatic surveillance rather than as part of a research investigation. As a result, it's probable that information recording hasn't been harmonised across Lesotho's many health facilities.The database provided did not include critical socio-demographics such as marital status, employment position, or educational status. Some crucial variables in the database were also missing information, such as dot coverage, which lacked data from 2009 to 2012; smear conversion, and treatment result (cure rate vs treatment success rate), which lacked data from 2009 to 2010. Finally, during the years 2009 to 2014, there was no information on TB/HIV coinfection based on the available data.

5.6 Conclusion

Because tuberculosis remains an issue in Lesotho, where treatment target goals have not yet been fulfilled, the findings of this study underline the need to address the underlying socio-economic causes of TB. The greatest priority for TB control is to detect at least 70% of sputum smear positive cases and to cure at least 85% of sputum smear positive cases. If these goals are met, the prevalence, incidence, transmission, and medication resistance to tuberculosis (TB) may decrease. Despite the National Tuberculosis Control Programme's attempts to enhance TB patients' access to treatment and adherence to therapy, the percentage of patients who have good treatment outcomes remains low. Despite having an 84 percent detection rate and using the DOTS technique, the available data did not identify the types of tuberculosis, therefore we were unable to forecast multidrug-resistant tuberculosis (MDR-TB).

5.7 Recommendations

The current study findings suggest the need for monitoring of proper information and record keeping at health facility level as there are missing information in the available data. Lesotho's national TB programs should emphasize the need of sputum microscopy at two months after therapy to identify those at risk and follow up with them regularly. To avoid treatment failure, patients with poor adherence to treatment should be regularly monitored. Studies are needed to see how prolonging the intensive phase of treatment affects those who have positive sputum smears after two months.

9. REFERENCES

Adebanjo, O.D. and Malangu, N., 2015. Knowledge and practices about multidrug-resistant tuberculosis amongst healthcare workers in Maseru. *African Journal of Primary Health Care and Family Medicine*, *7*(1), pp.1-5.

Adejumo, O.A., Daniel, O.J., Abdur-Razzaq, H.A., Shogbamimu, Y.O., Femi-Adebayo, T., Adepoju, V.A., Adebayo, B.I. and Sodipo, O.O., 2017. Trend of tuberculosis case notification and treatment outcome in Lagos State, Nigeria: a 5-year retrospective study. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *111*(7), pp.300-307.

Adejumo, O.A., Daniel, O.J., Adebayo, B.I., Adejumo, E.N., Jaiyesimi, E.O., Akang, G. and Awe, A., 2016. Treatment outcomes of childhood TB in Lagos, Nigeria. *Journal of tropical pediatrics*, *62*(2), pp.131-138.

Affolabi, D., Sanoussi, N., Codo, S., Sogbo, F., Wachinou, P., Massou, F., Kehinde, A. and Anagonou, S., 2017. First insight into a nationwide genotypic diversity of Mycobacterium tuberculosis among previously treated pulmonary tuberculosis cases in Benin, West Africa. *Canadian Journal of Infectious Diseases and Medical Microbiology*, *2017*.

Ali, M.K., Karanja, S. and Karama, M., 2017. Factors associated with tuberculosis treatment outcomes among tuberculosis patients attending tuberculosis treatment centres in 2016-2017 in Mogadishu, Somalia. *Pan African Medical Journal*, *28*(1).

Ansumana, R., Keitell, S., Roberts, G.M., Ntoumi, F., Petersen, E., Ippolito, G. and Zumla, A., 2017. Impact of infectious disease epidemics on tuberculosis diagnostic, management, and prevention services: experiences and lessons from the 2014–2015 Ebola virus disease outbreak in West Africa. *International Journal of Infectious Diseases*, *56*, pp.101-104.

Aschengrau, A. and Seage, G.R., 2013. *Essentials of epidemiology in public health*. Jones & Bartlett Publishers.

Atekem, K.A., Tanih, N.F., Ndip, R.N. and Ndip, L.M., 2018. Evaluation of the tuberculosis control program in South West Cameroon: Factors affecting treatment outcomes. *International journal of mycobacteriology*, *7*(2), p.137.

Atif, M., Sulaiman, S.A.S., Shafie, A.A., Ali, I. and Asif, M., 2014. Treatment outcome of new smear positive pulmonary tuberculosis patients in Penang, Malaysia. *BMC infectious diseases*, *14*(1), p.399.

Aydin, B., Kaplan, M., Atilgan, H. and Gürel, S., 2019. A Preliminary Study to Evaluate the Reproducibility of Factor Analysis Results: The Case of Educational Research Journals in Turkey. *Eğitimde ve Psikolojide Ölçme ve Değerlendirme Dergisi*, *10*(1), pp.1-11.

Bell, J., 2014. *Doing Your Research Project: A guide for first-time researchers*. McGraw-Hill Education (UK).

Bidaisee, S.P.S., 2018. Combatting the Obstinate Killer: Tuberculosis. *International Invention of Scientific Journal*, *2*(08).

Biruk, M., Yimam, B., Abrha, H., Biruk, S. and Amdie, F.Z., 2016. Treatment outcomes of tuberculosis and associated factors in an Ethiopian University Hospital. *Advances in Public Health*, *2016*.

Blaikie, N. and Priest, J., 2019. *Designing social research: The logic of anticipation*. John Wiley & Sons.

Brode, S.K., Daley, C.L. and Marras, T.K., 2014. The epidemiologic relationship between tuberculosis and non-tuberculous mycobacterial disease: a systematic review. *The International journal of tuberculosis and lung disease*, *18*(11), pp.1370-1377.

Cain, K.P., Marano, N., Kamene, M., Sitienei, J., Mukherjee, S., Galev, A., Burton, J., Nasibov, O., Kioko, J. and De Cock, K.M., 2015. The movement of multidrug-resistant tuberculosis across borders in East Africa needs a regional and global solution. *PLoS Med*, *12*(2), p.e1001791.

Castelli, F. and Sulis, G., 2017. Migration and infectious diseases. *Clinical Microbiology and Infection*, *23*(5), pp.283-289

Chaudhuri, A & Dutta, T. 2018 'Determining the Size of a Sample to take from a Finite Population', 16(1), pp. 37–44.

Cherkaoui, I., Sabouni, R., Ghali, I., Kizub, D., Billioux, A.C., Bennani, K., Bourkadi, J.E., Benmamoun, A., Lahlou, O., Aouad, R.E. and Dooley, K.E., 2014. Treatment default amongst patients with tuberculosis in urban Morocco: predicting and explaining default and post-default sputum smear and drug susceptibility results. *PloS one*, *9*(4), p.e93574.

Choy, L.T., 2014. The strengths and weaknesses of research methodology: Comparison and complimentary between qualitative and quantitative approaches. *IOSR Journal of Humanities and Social Science*, *19*(4), pp.99-104.

Churchyard, G.J., Mametja, L.D., Mvusi, L., Ndjek, N., Hesseling, A.C., Reid, A. and Babatunde, S., 2014. Tuberculosis control in South Africa: Successes, challenges and recommendations. *South African Medical Journal*, *104*(3), pp.244-248.

Comas, I., Hailu, E., Kiros, T., Bekele, S., Mekonnen, W., Gumi, B., Tschopp, R., Ameni, G., Hewinson, R.G., Robertson, B.D. and Goig, G.A., 2015. Population genomics of Mycobacterium tuberculosis in Ethiopia contradicts the virgin soil hypothesis for human tuberculosis in Sub-Saharan Africa. *Current Biology*, *25*(24), pp.3260-3266.

Creswell, J.W., 2014. Educational research: Planning, conducting, and evaluating quantitative and qualitative research (Fourth; Pearson new international ed.). *Harlow, Essex*, *4*.

Dheda, K., Gumbo, T., Maartens, G., Dooley, K.E., McNerney, R., Murray, M., Furin, J., Nardell, E.A., London, L., Lessem, E. and Theron, G., 2017. The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant, extensively drug-resistant, and incurable tuberculosis. *The lancet Respiratory medicine*, *5*(4), pp.291-360

Dicker, R.C., Coronado, F., Koo, D. and Parrish, R.G., 2006. Principles of epidemiology in public health practice; an introduction to applied epidemiology and biostatistics.

Doody, O. and Bailey, M.E., 2016. Setting a research question, aim and objective. *Nurse Researcher (2014+)*, *23*(4), p.19

Elfil, M. and Negida, A., 2017. Sampling methods in clinical research; an educational review. *Emergency*, *5*(1).

Ershova, J.V., Podewils, L.J., Bronner, L.E., Stockwell, H.G., Dlamini, S. and Mametja, L.D., 2014. Evaluation of adherence to national treatment guidelines among tuberculosis patients in three provinces of South Africa. *South African Medical Journal*, *104*(5).

Espinal, M.A., Kim, S.J., Suarez, P.G., Kam, K.M., Khomenko, A.G., Migliori, G.B., Baéz, J., Kochi, A., Dye, C. and Raviglione, M.C., 2000. Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries. *Jama*, *283*(19), pp.2537-2545.

Ferguson, T., Rowlands, A.V., Olds, T. and Maher, C., 2015. The validity of consumer-level, activity monitors in healthy adults worn in free-living conditions: a cross-sectional study. *International Journal of Behavioral Nutrition and Physical Activity*, *12*(1), p.42.)

Floyd, K., Glaziou, P., Zumla, A. and Raviglione, M., 2018. The global tuberculosis epidemic and progress in care, prevention, and research: an overview in year 3 of the End TB era. *The Lancet Respiratory Medicine*, *6*(4), pp.299-314.

Gebrezgabiher, G., Romha, G., Ejeta, E., Asebe, G., Zemene, E. and Ameni, G., 2016. Treatment outcome of tuberculosis patients under directly observed treatment short course and factors affecting outcome in southern Ethiopia: a five-year retrospective study. *PloS one*, *11*(2), p.e0150560.

Gehre, F., Otu, J., Kendall, L., Forson, A., Kwara, A., Kudzawu, S., Kehinde, A.O., Adebiyi, O., Salako, K., Baldeh, I. and Jallow, A., 2016. The emerging threat of pre-extensively drug-resistant tuberculosis in West Africa: preparing for large-scale tuberculosis research and drug resistance surveillance. *BMC medicine*, *14*(1), p.160.

Gidado, M., Obasanya, J., Habib, A.G. and Nasiru, S., 2017. TB control in Nigeria. In *Handbook of Global Tuberculosis Control* (pp. 61-73). Springer, Boston, MA.

Girardi, E., Schepisi, M.S., Goletti, D., Bates, M., Mwaba, P., Yeboah-Manu, D., Ntoumi, F., Palmieri, F., Maeurer, M., Zumla, A. and Ippolito, G., 2017. The global dynamics of diabetes and tuberculosis: the impact of migration and policy implications. *International Journal of Infectious Diseases*, *56*, pp.45-53.

Girum, T., Tariku, Y. and Dessu, S., 2017. Survival status and treatment outcome of multidrug resistant tuberculosis (MDR-TB) among patients treated in treatment initiation centers (TIC) in South Ethiopia: a retrospective cohort study. *Annals of Medical and Health Sciences Research*, *7*(5).

Glaziou, P., Sismanidis, C., Floyd, K. and Raviglione, M., 2015. Global epidemiology of tuberculosis. *Cold Spring Harbor perspectives in medicine*, *5*(2), p.a017798.

Gulland, A., 2016. More cases of tuberculosis than previously thought, WHO reports.

Hargreaves, S., Lönnroth, K., Nellums, L.B., Olaru, I.D., Nathavitharana, R.R., Norredam, M. and Friedland, J.S., 2017. Multidrug-resistant tuberculosis and migration to Europe. *Clinical Microbiology and Infection*, *23*(3), pp.141-146.

Hayibor, K.M., Bandoh, D.A., Asante-Poku, A. and Kenu, E., 2020. Predictors of Adverse TB Treatment Outcome among TB/HIV Patients Compared with Non-HIV Patients in the Greater Accra Regional Hospital from 2008 to 2016. *Tuberculosis research and treatment*, *2020*.

Heale, R, & Twycross, A. 2015 'Validity and reliability in quantitative studies', *Evidence Based Nursing*, 18(3), pp. 66–67.

Hirsch-Moverman, Y., Howard, A.A., Frederix, K., Lebelo, L., Hesseling, A., Nachman, S., Mantell, J.E., Lekhela, T., Maama, L.B. and El-Sadr, W.M., 2017. The PREVENT study to evaluate the effectiveness and acceptability of a community-based intervention to prevent childhood tuberculosis in Lesotho: study protocol for a cluster randomized controlled trial. *Trials*, *18*(1), pp.1-11.

Honeyborne, I., Lipman, M., Zumla, A. and McHugh, T.D., 2019. The changing treatment landscape for MDR/XDR-TB-can current clinical trials revolutionise and inform a brave new world?. *International Journal of Infectious Diseases*.

Huynh, G.H., Klein, D.J., Chin, D.P., Wagner, B.G., Eckhoff, P.A., Liu, R. and Wang, L., 2015. Tuberculosis control strategies to reach the 2035 global targets in China: the role of changing demographics and reactivation disease. *BMC medicine*, *13*(1), p.88

Jackson, C. and Abubakar, I., 2017. Ending tuberculosis in risk groups in Europe: challenges from travel and population movement. *Eurosurveillance*, *22*(12), p.30489.
Johnson, R.B. and Christensen, L., 2019. *Educational research: Quantitative, qualitative, and mixed approaches*. SAGE Publications, Incorporated.

Kaplan, R., Caldwell, J., Bekker, L.G., Jennings, K., Lombard, C., Enarson, D.A., Wood, R. and Beyers, N., 2014. Integration of TB and ART services fails to improve TB treatment outcomes: comparison of ART/TB primary healthcare services in Cape Town, South Africa. *South African Medical Journal*, *104*(3), pp.204-208.

Keshavjee, S., Seung, K., Satti, H., Furin, J., Farmer, P., Kim, J.Y. and Becerra, M., 2007. Building capacity for multidrug-resistant tuberculosis treatment: health systems

strengthening in Lesotho. *Innovations: Technology, Governance, Globalization*, *2*(4), pp.87-106.

Khan, M.A., Mirza, S. and Qadeer, E., 2017. Tb control in pakistan. In *Handbook of Global Tuberculosis Control* (pp. 15-25). Springer, Boston, MA.

Kibuule, D., Verbeeck, R.K., Nunurai, R., Mavhunga, F., Ene, E., Godman, B. and Rennie, T.W., 2018. Predictors of tuberculosis treatment success under the DOTS program in Namibia. *Expert review of respiratory medicine*, *12*(11), pp.979-987.

Kigozi, G., Heunis, C., Chikobvu, P., Botha, S. and Van Rensburg, D., 2017. Factors influencing treatment default among tuberculosis patients in a high burden province of South Africa. *International Journal of Infectious Diseases*, *54*, pp.95-102.

Kipruto, H., Mung'atu, J., Ogila, K., Adem, A., Mwalili, S., Masini, E. and Kibuchi, E., 2015. The epidemiology of tuberculosis in Kenya, a high TB/HIV burden country (2000-2013). *International Journal of Public Health and Epidemiology Research*, *1*(1), pp.2-13.

Kirenga, B.J., Levin, J., Ayakaka, I., Worodria, W., Reilly, N., Mumbowa, F., Nabanjja, H., Nyakoojo, G., Fennelly, K., Nakubulwa, S. and Joloba, M., 2014. Treatment outcomes of new tuberculosis patients hospitalized in Kampala, Uganda: a prospective cohort study. *PLoS One*, *9*(3), p.e90614.

Kirirabwa, N.S., Kimuli, D., DeJene, S., Nanziri, C., Birabwa, E., Okello, D.A., Suarez, P.G., Kasozi, S., Byaruhanga, R. and Lukoye, D., 2018. Response to anti-tuberculosis treatment by people over age 60 in Kampala, Uganda. *Plos one*, *13*(12), p.e0208390.

Korzeniewska-Koseła, M., 2015. Tuberculosis in Poland in 2013. *Przegl Epidemiol*, *69*(2), pp.277-82.

Lin, C.H., Lin, C.J., Kuo, Y.W., Wang, J.Y., Hsu, C.L., Chen, J.M., Cheng, W.C. and Lee, L.N., 2014. Tuberculosis mortality: patient characteristics and causes. *BMC infectious diseases*, *14*(1), pp.1-8.

Lönnroth, K., Migliori, G.B., Abubakar, I., D'Ambrosio, L., De Vries, G., Diel, R., Douglas, P., Falzon, D., Gaudreau, M.A., Goletti, D. and Ochoa, E.R.G., 2015. Towards tuberculosis elimination: an action framework for low-incidence countries. *European Respiratory Journal*, *45*(4), pp.928-952.

Lönnroth, K., Mor, Z., Erkens, C., Bruchfeld, J., Nathavitharana, R.R., Van Der Werf, M.J. and Lange, C., 2017. Tuberculosis in migrants in low-incidence countries: epidemiology and intervention entry points. *The International Journal of Tuberculosis and Lung Disease*, *21*(6), pp.624-636.

Luba, T.R., Tang, S., Liu, Q., Gebremedhin, S.A., Kisasi, M.D. and Feng, Z., 2019. Knowledge, attitude and associated factors towards tuberculosis in Lesotho: a population based study. *BMC infectious diseases*, *19*(1), p.96.

Lukoye, D., Ssengooba, W., Musisi, K., Kasule, G.W., Cobelens, F.G., Joloba, M. and Gomez, G.B., 2015. Variation and risk factors of drug resistant tuberculosis in sub-Saharan Africa: a systematic review and meta-analysis. *BMC public health*, *15*(1), p.291.

Malangu, N. and Adebanjo, O.D., 2015. Knowledge and practices about multidrug-resistant tuberculosis amongst healthcare workers in Maseru. *African journal of primary health care & family medicine*, *7*(1), pp.1-5.

Mekonnen, D., Derbie, A., Mekonnen, H. and Zenebe, Y., 2016. Profile and treatment outcomes of patients with tuberculosis in Northeastern Ethiopia: a cross sectional study. *African Health Sciences*, *16*(3), pp.663-670.

Mekonnen, F., Tessema, B., Moges, F., Gelaw, A., Eshetie, S. and Kumera, G., 2015. Multidrug resistant tuberculosis: prevalence and risk factors in districts of metema and west armachiho, Northwest Ethiopia. *BMC infectious diseases*, *15*(1), p.461.

Mlotshwa, M., Abraham, N., Beery, M., Williams, S., Smit, S., Uys, M., Reddy, C. and Medina-Marino, A., 2016. Risk factors for tuberculosis smear non-conversion in Eden

district, Western Cape, South Africa, 2007–2013: a retrospective cohort study. *BMC infectious diseases*, *16*(1), pp.1-12.

Mohajan, H., 2014. Tuberculosis is a fatal disease among some developing countries of the world.

Mokoena, S.K. and Balkaran, S., 2018. An exploration of constraints for free movement of people in Africa-a case of Lesotho and South Africa. *African Journal of Public Affairs*, *10*(2), pp.109-126.

Mooney, S. J. and Garber, M. D. 2019 'Sampling and Sampling Frames in Big Data Epidemiology', *Current Epidemiology Reports*. Current Epidemiology Reports, 6(1), pp. 14–22.

Mugomeri, E., Chatanga, P., Lefunyane, M., Ruhanya, V., Nyandoro, G. and Chin'ombe, N., 2015. Adherence to tuberculosis infection control guidelines by nurses in Lesotho. *American journal of infection control*, *43*(7), pp.735-738.

Munayco, C.V., Mújica, O.J., León, F.X., Granado, M.D. and Espinal, M.A., 2015. Social determinants and inequalities in tuberculosis incidence in Latin America and the Caribbean. *Revista Panamericana de Salud Pública*, *38*, pp.177-185.

Musa, B.M., Adamu, A.L., Galadanci, N.A., Zubayr, B., Odoh, C.N. and Aliyu, M.H., 2017. Trends in prevalence of multi drug resistant tuberculosis in sub-Saharan Africa: a systematic review and meta-analysis. *PLoS One*, *12*(9), p.e0185105.

Naing, L., Winn, T. and Rusli, B.N., 2006. Practical issues in calculating the sample size for prevalence studies. *Archives of orofacial Sciences*, *1*, pp.9-14.
Namukwaya, E., Nakwagala, F.N., Mulekya, F., Mayanja-Kizza, H. and Mugerwa, R., 2011. Predictors of treatment failure among pulmonary tuberculosis patients in Mulago hospital, Uganda. *African health sciences*, *11*, pp.105-111.

Nanoo, A., Izu, A., Ismail, N.A., Ihekweazu, C., Abubakar, I., Mametja, D. and Madhi, S.A., 2015. Nationwide and regional incidence of microbiologically confirmed

pulmonary tuberculosis in South Africa, 2004–12: a time series analysis. *The Lancet infectious diseases*, *15*(9), pp.1066-1076.

Ncube, R.T., Takarinda, K.C., Zishiri, C., Van den Boogaard, W., Mlilo, N., Chiteve, C., Siziba, N., Trinchán, F. and Sandy, C., 2017. Age-stratified tuberculosis treatment outcomes in Zimbabwe: are we paying attention to the most vulnerable?. *Public health action*, *7*(3), pp.212-217.

Negin, J., Abimbola, S. and Marais, B.J., 2015. Tuberculosis among older adults–time to take notice. *International Journal of Infectious Diseases*, *32*, pp.135-137.

Niaz, A.B., 2021. *Predictors of initial treatment failure among pulmonary tuberculosis patients in two Specialized Hospitals in Afghanistan* (Doctoral dissertation, Bangladesh Health Professions Institute, Faculty of Medicine, the University of Dhaka, Bangladesh.).

O'Connor, D.E., Frederix, K., Saito, S., Maama, L.B., Hirsch-Moverman, Y., Pitt, B., Hayes-Larson, E., Lebelo, L., Shale, M. and Howard, A.A., 2017. Pulmonary tuberculosis diagnostic practices among people living with the human immunodeficiency virus in Lesotho. *The International Journal of Tuberculosis and Lung Disease*, *21*(10), pp.1133-1138.

Onozaki, I., Law, I., Sismanidis, C., Zignol, M., Glaziou, P. and Floyd, K., 2015. National tuberculosis prevalence surveys in Asia, 1990–2012: an overview of results and lessons learned. *Tropical Medicine & International Health*, *20*(9), pp.1128-1145.

Osei, E., Oppong, S. and Der, J., 2020. Trends of tuberculosis case detection, mortality and co-infection with HIV in Ghana: A retrospective cohort study. *Plos one*, *15*(6), p.e0234878.

Owiti, P., Onyango, D., Momanyi, R. and Harries, A.D., 2019. Screening and testing for tuberculosis among the HIV-infected: outcomes from a large HIV programme in western Kenya. *BMC Public Health*, *19*(1), pp.1-11.

*Oxford concise colour Medical Dictionary.*2015. New edition.New York: Oxford University Press.

Pai, M. and Memish, Z.A., 2017. New tuberculosis estimates must motivate countries to act. *Journal of epidemiology and global health*, *7*(2), pp.97-98

Patino, C. M. and Ferreira, J. C. (2018) 'Inclusion and exclusion criteria in research studies: definitions and why they matter', *Jornal Brasileiro de Pneumologia*, 44(2), pp. 84–84.

Qian, X., Nguyen, D.T., Lyu, J., Albers, A.E., Bi, X. and Graviss, E.A., 2018. Risk factors for extrapulmonary dissemination of tuberculosis and associated mortality during treatment for extrapulmonary tuberculosis. *Emerging microbes & infections*, *7*(1), pp.1-14.

Rao, M., Ippolito, G., Mfinanga, S., Ntoumi, F., Yeboah-Manu, D., Vilaplana, C., Zumla, A. and Maeurer, M., 2019. Improving treatment outcomes for MDR-TB—novel host-directed therapies and personalised medicine of the future. *International Journal of Infectious Diseases*, *80*, pp.S62-S67.

Rendon, A., Centis, R., Zellweger, J.P., Solovic, I., Torres-Duque, C.A., Cordeiro, C.R., de Queiroz Mello, F.C., Manissero, D. and Sotgiu, G., 2018. Migration, TB control and elimination: whom to screen and treat. *Pulmonology*, *24*(2), pp.99-105.

Robsky, K.O., Hughes, S., Kityamuwesi, A., Kendall, E.A., Kitonsa, P.J., Dowdy, D.W. and Katamba, A., 2020. Is distance associated with tuberculosis treatment outcomes? A retrospective cohort study in Kampala, Uganda. *BMC infectious diseases*, *20*(1), pp.1-9.

Ruru, Y., Matasik, M., Oktavian, A., Senyorita, R., Mirino, Y., Tarigan, L.H., van der Werf, M.J., Tiemersma, E. and Alisjahbana, B., 2018. Factors associated with non-adherence during tuberculosis treatment among patients treated with DOTS strategy in Jayapura, Papua Province, Indonesia. *Global health action*, *11*(1), p.1510592.

Sabiiti, W., 2017. Beyond the numbers: interpreting WHO's Global Tuberculosis Report 2016 to inform TB policy and practice in the East African community. *EA Health Research Journal*, *1*(1), pp.2-7.

Sekandi, J.N., Neuhauser, D., Smyth, K. and Whalen, C.C., 2009. Active case finding of undetected tuberculosis among chronic coughers in a slum setting in Kampala, Uganda. *The International Journal of Tuberculosis and Lung Disease*, *13*(4), pp.508-513.

Setia, M.S., 2016. Methodology series module 3: Cross-sectional studies. *Indian journal of dermatology*, *61*(3), p.261.

Sharma, G., 2017. Pros and cons of different sampling techniques. *International journal of applied research*, *3*(7), pp.749-752.

Siddiqui, A.N., Khayyam, K.U. and Sharma, M., 2016. Effect of diabetes mellitus on tuberculosis treatment outcome and adverse reactions in patients receiving directly observed treatment strategy in India: a prospective study. *BioMed research international*, *2016*.

Singh, S.K., 2015. Advantages and disadvantages of probability sampling methods in social research. In *National Conference on Innovative Research in Chemical, Physical, Mathematical Sciences, Applied Statistics and Environmental Dynamics* (pp. 14-18).

Sinshaw, Y., Alemu, S., Fekadu, A. and Gizachew, M., 2017. Successful TB treatment outcome and its associated factors among TB/HIV co-infected patients attending Gondar University Referral Hospital, Northwest Ethiopia: an institution based cross-sectional study. *BMC infectious diseases*, *17*(1), p.132.

Sooro, M.A., Malikelle, T., Leteka, R., Kobo, L. and Ramathebane, M., 2021. A Preliminary Study on Lung Cancer Prevalence Among Patients with Tuberculosis in Lesotho. *Cancer Research Journal*, *9*(3), p.148.

Sulis, G., Roggi, A., Matteelli, A. and Raviglione, M.C., 2014. Tuberculosis: epidemiology and control. *Mediterranean journal of hematology and infectious diseases*, *6*(1).

Sullivan, B.J., Esmaili, B.E. and Cunningham, C.K., 2017. Barriers to initiating tuberculosis treatment in sub-Saharan Africa: a systematic review focused on children and youth. *Global health action*, *10*(1), p.1290317.

Takarinda, K.C., Sandy, C., Masuka, N., Hazangwe, P., Choto, R.C., Mutasa-Apollo, T., Nkomo, B., Sibanda, E., Mugurungi, O., Harries, A.D. and Siziba, N., 2017. Factors associated with mortality among patients on TB treatment in the southern region of Zimbabwe, 2013. *Tuberculosis research and treatment*, *2017*.

Tavakol, M. and Sandars, J., 2014. Quantitative and qualitative methods in medical education research: AMEE Guide No 90: Part I. *Medical Teacher*, *36*(9), pp.746-756.

Telisinghe, L., Charalambous, S., Topp, S.M., Herce, M.E., Hoffmann, C.J., Barron, P., Schouten, E.J., Jahn, A., Zachariah, R., Harries, A.D. and Beyrer, C., 2016. HIV and tuberculosis in prisons in sub-Saharan Africa. *The Lancet*, *388*(10050), pp.1215-1227.

Tesfahuneygn, G., Medhin, G. and Legesse, M., 2015. Adherence to Anti-tuberculosis treatment and treatment outcomes among tuberculosis patients in Alamata District, northeast Ethiopia. *BMC research notes*, *8*(1), pp.1-11.

Thakkar, D., Piparva, K.G. and Lakkad, S.G., 2019. A pilot project: 99DOTS information communication technology-based approach for tuberculosis treatment in Rajkot district. *Lung India: Official Organ of Indian Chest Society*, *36*(2), p.108.

Theron, G., Jenkins, H.E., Cobelens, F., Abubakar, I., Khan, A.J., Cohen, T. and Dowdy, D.W., 2015. Data for action: collection and use of local data to end tuberculosis. *The Lancet*, *386*(10010), pp.2324-2333.

Tiam, A., Machekano, R., Gounder, C.R., Maama-Maime, L.B., Ntene-Sealiete, K., Sahu, M., Isavwa, A., Oyebanji, O., Ahimbisibwe, A., Mokone, M. and Barnes, G.L.,

2014. Preventing tuberculosis among HIV-infected pregnant women in Lesotho: the case for rolling out active case finding and isoniazid preventive therapy. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *67*(1), pp.e5-e11.

Tiberi, S., Muñoz-Torrico, M., Duarte, R., Dalcolmo, M., D'Ambrosio, L. and Migliori, G.B., 2018. New drugs and perspectives for new anti-tuberculosis regimens. *Pulmonology*, *24*(2), pp.86-98.

Turner, R.D. and Bothamley, G.H., 2015. Cough and the transmission of tuberculosis. *The Journal of infectious diseases*, *211*(9), pp.1367-1372.

van der Heijden, Y.F., Karim, F., Mufamadi, G., Zako, L., Chinappa, T., Shepherd, B.E., Maruri, F., Moosa, M.Y., Sterling, T.R. and Pym, A.S., 2017. Isoniazid-monoresistant tuberculosis is associated with poor treatment outcomes in Durban, South Africa. *The international journal of tuberculosis and lung disease*, *21*(6), pp.670-676.

Velayati, A.A., Farnia, P. and Farahbod, A.M., 2016. Overview of drug-resistant tuberculosis worldwide. *International Journal of Mycobacteriology*, *5*, p.S161.

World Health Organization, 2014. *Toolkit to develop a national strategic plan for TB control: prevention, care and control: methodology on how to develop a national strategic plan* (No. WHO/HTM/TB/2015.08). World Health Organization.

World Health Organization, 2018 Tuberculosisi Global Report

Zumla, A., Petersen, E., Nyirenda, T. and Chakaya, J., 2015. Tackling the tuberculosis epidemic in sub-Saharan Africa–unique opportunities arising from the second European Developing Countries Clinical Trials Partnership (EDCTP) programme 2015-2024. *International Journal of Infectious Diseases*, *32*, pp.46-49.

APPENDIX 1: DATA EXTRACTION TOOL

Unique ID | | | |

SECTION A: SOCIO-DEMOGRAPHICS

A1	Date of birth			
		dd	mm	yy

A2 Age _____ Years

A3.	Gender	Male	Female			
A4	Marital status	Single	Married	Divorced	Widowed	
A5	Educational level	No schooling	primary	Secondary	Tertiary	

A6 Nationality _____

A7 District of diagnosis

SECTION B: TB TREATMENT

B1	Date started			
		dd	mm	yy

B2 On treatment | Yes | No |

B3 Completed treatment | Yes | No |

B4 Treatment outcome

Bacteriological coverage
Cured
Lost to follow
Died
Successfully Completed
Relapse
Defaulted
Transfer out

B5 HIV co-infected | Yes | No |

B6 If HIV co-infected

CD4 count	
Viral load	
WHO staging	

APPENDIX 2: Work plan

Activities	Jun2019 – Sep2020	Sep-Oct 2020	Oct-Nov 2020	Nov-Dec 2020	Dec 2020-Jan 2021	Jan-Feb 2021
Proposal writing						
Ethics approval						
Pilot study						
Data collection and collation						
Report writing						
First draft of dissertation submission						
Final report submission						

APPENDIX 3: Letter for requesting permission to use secondary data

Department of Public Health
Faculty of Health Sciences
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 4113/4614 Fax: (015) 268 3384

Dear District Manager

Thank you for taking the time to read this information letter. I am a Master of Public Health Student from the University of Limpopo and I am busy conducting a research study to assess characteristic and treatment outcome of TB in Lesotho 2009 to 2019

The objectives of the study are as follows:

- To describe the socio-demographics characteristics of tuberculosis cases in Lesotho 2009 to 2019
- To determine the characteristics of tuberculosis and treatment outcome of Tuberculosis cases in Lesotho 2009 to 2019 in Lesotho
- To determine the TB rate in Lesotho 2009 to 2019
- To determine the association of socio-demographics, with tuberculosis treatment outcomes

Information will be collected from the existing database which has all TB records. To ensure confidentiality, information gathered will be stored in a storage system which is only accessible to the researcher and research supervisor. There will be no direct harm and rewards to participants as secondary data will be used.

Thank you for considering this request and the current study does not require a consent form as secondary data will be used.

Please forward any question or concern you may have regarding this research to the contact details provided below.

Student researcher:

Montsi S at sellomontsi@hotmail.com and **Research supervisor:** Dr Maimela E eric.maimela@ul.ac.za

APPENDIX: 4 Approval from Turfloop Research Ethics Committee (TREC)

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email:makoetja.ramusi@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: 10 December 2020

PROJECT NUMBER: TREC/393/2020: PG

PROJECT:

Title:	The epidemiology and treatment outcomes of Tuberculosis cases in Lesotho between 2009 and 2019
Researcher:	S Montsi
Supervisor:	Dr E Maimela
Co-Supervisor/s:	N/A
School:	Health Care Sciences
Degree:	Master of Public Health

PROF P MASOKO
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE
The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:

i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**

ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**

iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

Finding solutions for Africa

APPENDIX 5: Approval from Lesotho Ministry of Health

LESOTHO

Ministry of Health
P.O. Box 514
Maseru 100

Category of Review:
[x] Initial Review
[ ] Continuing Annual Review
[ ] Amendment/Modification
[ ] Reactivation
[ ] Serious Adverse Event
[ ] Other _____

REF: ID 125-2020
Date: March 16, 2021
To
Mr. Sello Montsi
Student #: 201824701
University of Limpopo

Dear Mr. **Montsi**

RE: The Epidemiology and Treatment Outcomes of Tuberculosis Cases in Lesotho between 2009 and 2019

This is to inform you that the Ministry of Health Research and Ethics Committee reviewed and **APPROVED** the above named protocol and hereby authorizes you to conduct the study according to the activities and population specified in the protocol. Departure from the approved protocol will constitute a breach of this permission.

This approval includes review of the following attachments:
[x] Protocol
[x] **Data Collection Tool:** Data Extraction Tool
[ ] **Participant materials**
[x] Other materials: letter of permission to conduct a study dated 08th February 2021

This approval is **VALID** until March 16, 2022.

Please note that an annual report and request for renewal, if applicable, must be submitted at least 6 weeks before the expiry date.

All serious adverse events associated with this study must be reported promptly to the MOH Research and Ethics Committee. Any modifications to the approved protocol or consent forms must be submitted to the committee prior to implementation of any changes.

We look forward to receiving your progress reports and a final report at the end of the study. If you have any questions, please contact the Research and Ethics Committee at reumoh@gmail.com (or) 59037919/58800246.

Sincerely,

DR. 'NYANE LETSIE
Director General Health Services

DR. LLANG BRIDGET MAAMA-MAIME
Member of National Health Research
Ethics Committee (NH-REC)

APPENDIX 6: Evidence of language editing

Tiyiselani & Rapetsoa scientific services

Article Publishing • Proof-reading • Editing

85 Compensatie Street,
Duplex Park No 5,
Polokwane, 0699
Postnet Suite 179 • Private Bag X9307 • Polokwane •
0700 Tel: 072 190 2999 • Fax: 0864154022

Date: 15 August 2021

To Whom it May Concern

I hereby confirm that I have proof-read the document entitled: **"The epidemiology and treatment outcomes of tuberculosis cases in Lesotho between 2009 and 2019"** authored by Mr Montsi S with student number 201824701. The document has been edited and proofread for grammar, spelling, punctuation, overall style and logical flow. Considering the suggested changes that the author may or may not accept, at his discretion, each of us has our own unique voice as far as both spoken and written language is concerned. In my role as proof-reader, I try not to let my own "written voice" overshadow the voice of the author, while at the same time attempting to ensure a readable document.

Please refer any queries to me.

Rapetsoa DB