PREDICTORS OF RIFAMPICIN-RESISTANT TUBERCULOSIS AMONG INFECTED PATIENTS IN NAIROBI COUNTY

BY

GEORGE GIATHI KAMAU

THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENT OF THE AWARD OF DEGREE OF MASTERS OF SCIENCE IN FIELD EPIDEMIOLOGY SCHOOL OF PUBLIC HEALTH MOI UNIVERSITY

© 2024

DECLARATION

I declare that this is my original work. It has not been submitted to Moi University or any other institution in whole, part, or any other form for an award of academic qualifications or other purposes.

Signature_____ Date_____

George Giathi Kamau

FELTP/5435/21

SUPERVISORS DECLARATION

This research proposal will be submitted for examination with the approval of the candidate's supervisors.

Signature_____ Date_____

Dr Samson Ndege

Department: Epidemiology and Medical Statistics School of Public Health

University: Moi University, Eldoret, Kenya

Signature_____ Date_____

Dr. Ahmed Abade, Bsc, Msc, Ph.D.

Department: Epidemiology and Medical Statistics School of Public Health

University: Moi University, Eldoret, Kenya

DEDICATION

This thesis is dedicated to my perseverance and determination. It stands as a testament to the countless late nights, sacrifices, and challenges I faced throughout this academic journey. I take pride in my resilience and the invaluable lessons I've learned along the way. This degree is not just a reflection of hard work but also a symbol of my unwavering commitment to both personal and intellectual growth.

To my wife Jane Nginya, Daughter Michelle Wairati, and friends, your unwavering love and support have been my pillars of strength. This accomplishment is also dedicated to each of you for believing in me and pushing me to reach my fullest potential. Thank you for being my constant source of inspiration

ABSTRACT

Background: Rifampicin-resistant tuberculosis (RR-TB) poses a significant threat to tuberculosis (TB) control in Kenya, particularly within Nairobi County, where it accounted for a 12% portion of new cases in 2019. The emergence of RR-TB strains has amplified the urgency of addressing this pressing public health crisis. Monitoring the risk factors for RR-TB to inform policy development and design effective interventions catering to the country's specific needs.

Objectives: To determine sociodemographic, behavioural, and clinical factors associated with RR-TB among patients attending health facilities in Nairobi County.

Methods: A case-control study for patients on TB treatment between January 2021 and March 2023 was conducted in Nairobi County. Data was collected using a free and open-source questionnaire for field data collection, KOBO application. Descriptive analysis was used to summarise participants' characteristics. Bivariate and multivariate logistic regression were used to determine the predictors for RR-TB. Associations were reported using Odds Ratio (OR) and 95% Confidence level (CI). Statistical significance was considered for $p < 0.05$.

Results: 72 cases and 144 controls were enrolled; cases had a mean age of 38 years ±11 standard deviation (SD), while the control had a mean age of 36 years ±10 SD. Male gender contributed the highest proportion for both cases, 52 (72%) and controls 93 (65%). The odds of developing RRTB were 70 times higher among those patients who had a previous history of TB treatment compared to the new patients (aOR=69.909; p >0.001). Those who do not practice cough hygiene had five times increased odds of developing RRTB (aOR=5.265; p=0.002), and the co-infected TB/HIV patients had three times increased odds of developing RRTB (aOR=3.326; p=0.032). The odds of developing RRTB for those with chronic lung conditions were two times higher compared to those who did not have (aOR=1.682; p=0.778). The odds of developing RRTB for those who smoked cigarettes were two times more than those who did not smoke (aOR=1.512; p=0.463). Those admitted to hospitals had three times more odds of developing RRTB than those not admitted (aOR=2.982; p=0.139). No statistically significant differences were observed between age, gender, marital status, religion and the development of RRTB.

Conclusion: Those patients who were previously treated for TB, those not practising cough hygiene, and those with HIV infection had a higher risk of developing RRTB.

Recommendations

There is a need for stronger partnerships between HIV and TB control programs in Nairobi County and Kenya in general to facilitate early detection and management of individuals with both diseases. This will effectively address the dual burden of HIV and TB

LIST OF ABBREVIATIONS

AFB	Acid Fast Bacilli
AOR	Adjusted Odds Ratio
BCG	Bacille Calmette Guérin
COR	Crude Odds Ratio
COVID	Coronavirus Disease
CXR	Chest X-Ray.
DLTLD	Division of Leprosy Tuberculosis and Lung Disease
DOT	Directly Observed Therapy
DRTB	Drug-Resistant Tuberculosis
DST	Drug Susceptibility Test
EPTB	Extra Pulmonary Tuberculosis
FELTP	Field Epidemiology and Laboratory Training Program
GDP	Gross Domestic Product
HP	isoniazid (INH) and RifaPentine (RPT)
HR	Isoniazid mono-resistant Tuberculosis
KEMRI	Kenya Medical Research Institute
RR	Rifampicin resistant
MTB/Rif	Mycobacterium tuberculosis complex/ Rifampicin
MTBC	Mycobacterium tuberculosis complex
MDRTB	Multidrug resistant Tuberculosis
MSF	Médecins Sans Frontières International
NACOSTI	National Commission For Science, Technology and Innovation
NTP	National TB Control Program
NTRL	National TB Reference Laboratory

OR	Odds Ratio
PCR	Polymerase chain reaction.
PTB	Pulmonary Tuberculosis
RR.	Rifampicin Resistant
SD	Standard deviation
SDG	Sustainable Development Goals
TBHIV	Tuberculosis Human Immunodeficiency Virus
USD	United States Dollar
WHO	World Health Organization
XDR	Extensively drug-resistant
XDR-TB	Extensively Drug-Resistant Tuberculosis
LTBI	Latent TB infection
	Any person with bacteriologically confirmed TB that has exhibited resistance to rifampicin, either with or without isoniazid resistance
Case	
Control	Any person with bacteriologically confirmed TB who is susceptible to rifampicin and had a negative smear after completion of the intensive phase in the second month
Rif	Rifampicin
BPaLM	Bedaquiline, Pretomanid, Linezolid and Moxifloxacin
BPaL	Bedaquiline, Pretomanid, Linezolid
DNA	Deoxyribonucleic acid
NAATS	Nucleic Acid Amplification Tests
KENPHIA	Kenya Population-based HIV Impact Assessment

LPA	Line Probe Assay
MTBC	Mycobacterium tuberculosis complex
IREC	Institution Research & Ethics Committee
MOH	Ministry of Health
PI	Principal Investigator
OR	Odds Ratio
CI	Confidence Interval
TIBU	A digital solution dedicated to digitalizing sustainable lung health reporting and routine surveillance as well as continuous capacity-building
CD4+	T-helper cells
CD8+	Cytotoxic T-lymphocytes
IGRAs	Interferon-Gamma Release Assay
TST	Tuberculin Skin Test
CNR	Case Notification Rate
NTLD-P	National Tuberculosis, Leprosy and Disease Program
FBO	Faith-Based Organization
NGO	Non-Government Organization

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENT

I express my deepest appreciation to my esteemed supervisors, Dr. Samson Ndege, and Dr. Ahmed Abade. Their unwavering guidance, support, and expertise have been instrumental throughout the course of my study. Their valuable input and able guidance during the development of the study protocol have significantly contributed to the success of this research.

I am profoundly grateful to County and sub-county TB and Leprosy coordinators for their invaluable assistance during the study. Their support and expertise have been indispensable in the implementation of this research, and I am thankful for their guidance and input.

I extend my gratitude to the Nairobi County Health Services Research Ethics Committee for granting permission for patient interviews and the use of records during the study. Their cooperation and support have been crucial in obtaining the necessary data for this research.

I would like to express my appreciation to the Head Division of the National TB Leprosy and Lung Control Program (D-NTLD-P) for granting permission to involve program staff in the study implementation. Special thanks go to the research assistants for their exceptional work during the data collection period.

Furthermore, I would like to acknowledge the Centers for Disease Control and Prevention (CDC) for their financial support for this study through the FELTP. Their funding has been pivotal in conducting this research.

Lastly, I offer my heartfelt gratitude to everyone mentioned above. Your contributions, support, and encouragement have been immeasurable. God bless every one of you.

.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background Information

The *Mycobacterium Tuberculosis* Complex (MTBC) bacteria in the air is the primary cause of tuberculosis (TB). It is an air droplet infection spread by people with pulmonary TB when they cough, sneeze, speak, spit, or sing, and a contact person breathes in the small particles. The typical presentation of TB is pulmonary TB, which infects the lungs and is contagious; also known as Active TB, TB can affect any body part except hair or nails. (MedlinePlus, n.d.) . Active Tuberculosis's characteristic symptoms are a prolonged cough with blood-containing sputum, fever, night sweats, numerous extrapulmonary TB (EPTB), and weight loss. (American Lung Association, 2020). However, symptoms might be vague and vary depending on the affected boy part. Drug sensitive Tuberculosis (DSTB) is TB that is susceptible to first-line critical medicines of treatment, which are Rifampicin (Rif) and Isoniazid (INH) (Médecins Sans Frontières, 2018). Around 1.5 million estimated individuals passed away due to TB in 2020 (HIV causing 214,000 individuals) globally. Latent TB infection (LTBI) is when the bacteria in one's body are inactive; one is not sick and cannot spread the disease to others. LBTI is usually harmless, but it can sometimes progress to active TB disease. The risk of LTBI progressing to active TB depends on various factors like overall health, age, and presence of comorbidities. 5-10% of LTBI cases are estimated to progress without treatment.

After COVID-19, tuberculosis is the second most common infectious killer in the world and the thirteenth top cause of death overall. The number of TB patients who became ill globally in 2020 was estimated to be 10 million. Out of 10 million, 3.3 million are

women, 1.1 million are children, and 5.6 million are Men. Tuberculosis is found in all nations as well as diverse age groups; TB is also treatable and then escapable globally. In 2020, TB affected 1.1 million children with TB (Humayun et al., 2022). Healthcare caregivers, in most cases, overlook children as well as adolescents with TB, which can be challenging to diagnose and treat. Thirty high TB-burden nations reported 86 per cent of new TB scenarios as of 2020. About eight nations are responsible for two-thirds of the total, India being the lead, the Philippines, China, Indonesia, Nigeria, Pakistan, Bangladesh, and South Africa following the count (World Health Organization, 2024).

The WHO states that Drug-Resistant Tuberculosis (DR TB) poses asignificant public health threat globally. (World Health Organization, 2020). The Global Surveillance Data 2018 estimates a total of 558,000 cases diagnosed with RR TB, a treatment success rate (TSR) of 56 per cent, and a total of 240,000 deaths. (World Health Organization, 2018). This TB occurs when the Mycobacteria tuberculosis bacilli undergo mutations, enabling them to survive exposure to anti-TB drugs. (WHO, 2017) 3.3% of the new TB incidents and 17.7 % of 2019 formerly controlled scenarios had RRTB. The highest proportions were in former Soviet Union nations. Cases of Tuberculosis are reducing at a rate of 2 per cent yearly worldwide, and from 2015 to 2020, this reduction totalled 11 per cent. (World Health Organization, 2023).

The Sustainable Development Goals and the WHO's End TB Plan both include global goals and benchmarks for decreasing the impact of tuberculosis infection. By 2030, SDG aims to end the worldwide TB pandemic, with the incidence rate of the disease serving as a gauge of success. The End TB Strategy's 2030 aims call for a 90 per cent decrease in TB-related mortality and an 80 per cent decrease in the incidence rate of the disease from levels in 2015. The End TB Approach further includes milestones for

2020 to 2025 as well as ambitions for 2035 (Global Tuberculosis Report, 2021) . Such goals included a 90% drop in TB cases and a 95% drop in TB deaths by the year 2035, in comparison to 2015, and a 20% drop in tuberculosis cases and a 35 per cent drop in the total number of TB deaths by 2020 (Menzies et al., 2020).

According to WHO recommendations, RR diagnosis for TB calls for bacteriological confirmation of the disease and drug resistance testing utilising quick molecular tests, culture techniques, and sequencing technologies. Rapid molecular testing, such as sputum smear microscopy, is among the diagnostic procedures for tuberculosis disease. Methods like Gene Xpert or culture testing are still the best for diagnosing Tuberculosis ((Piatek et al., 2000). Rapid assays, culture techniques, as well as Polymerase Chain Reaction technologies can all be applied to recognize tuberculosis resistance to first and second-line anti-tuberculosis medications. (Kavindhran Venel ey al., 2021).

WHO applauds the expansion of all oral regimen access to RR TB testing, detection, and treatment, which all improved from 2018 to 2019. In 2019, 61% of patients with TB who had a positive bacteriological test underwent testing for rifampicin resistance, up from 51% and 7% in 2012. For new and 81 per cent of earlier treated TB individuals, reporting of testing was present. Two hundred six thousand thirty global total RRTB cases were identified and reported in 2019, up 10 per cent from 186,883 cases in 2018, while 177,099 cases were registered for treatment, up from 156,205 cases. (Jeremiah Chakaya et al., 2021). Despite these developments, the number of people who signed up for treatment in 2019 corresponds to only 38% of the projected number of those who contracted RRTB in 2019.

It is necessary to improve TB detection, increase bacteriological validation among hypothetical instances, expand the testing coverage for drug resistance among those

with bacteriologically confirmed TB, and ensure that all patients diagnosed with RRTB are registered in treatment to close this enormous gap. The number of tuberculosis fatalities number worldwide could increase by about 0.2–0.4 million in 2020 alone if the health systems are disrupted to the level where the proportion of tuberculosis patients who are identified and treated reduces by 25–50% over three months. Forty-four per cent of Tuberculosis (TB) infections globally are reported in four nations: India, South Africa, Indonesia, and the Philippines. Between the middle of January and June 2020, the reported number of cases significantly decreased. Total decreases in India, the Philippines, and Indonesia were between 25 and 30 per cent lower than over the same six-month period in 2019. The economic effects of the pandemic are anticipated to increase two of the critical causes of TB incidence marginally: low GDP per capita as well as undernutrition. According to modelling, between 2020 and 2025, there may be an additional 1 million individuals in the developing world each year. The impact on lives following lost wages or unemployment may increase the number of TB patients and their families dealing with catastrophic costs (Jeremiah Chakaya et al., 2021).

Negative influences on essential TB services are seen in the shift of services, such as human resources and finance, to cover COVID-19 response teams. Reports from most countries show the utilisation of Gene Xpert equipment for testing COVID-19 rather than diagnostic testing for TB, reassignment and relocation of TB medical staff, and budget to other duties relating to the COVID-19 pandemic treatment. Further, minor but still substantial countries reported a decrease in the number of health amenities provided outpatient and inpatient care for persons with TB (35 and 32 countries, respectively). In most nations, data collection and recording have correspondingly been impacted.(Zimmer et al., 2022)

Rifampicin-resistant tuberculosis infections prove to be more problematic to treat compared to drug-susceptible ones and impede worldwide advancement toward the goals established by the WHO's End TB Strategy. Therefore, it is crucial to provide policy recommendations based on the best and most up-to-date available knowledge regarding the predictors of RRTB and the treatment and care of individuals with RRTB. The WHO consolidated procedures on drug-resistant tuberculosis cure to fulfil its responsibility to notify health specialists in the Member nations on progressing with treatment and management for individuals with RRTB. Thus, this study is critical in weighing predictors for drug-resistant TB amongst patients in particular health services in Nairobi County.

1.2 Statement of the Problem

Tuberculosis (TB) remains a significant public health threat globally, with the emergence of drug-resistant forms posing a severe challenge to TB control efforts. (WHO, Global tuberculosis report 2020). Early detection and treatment are critical for preventing its spread and improving patient outcomes. However, diagnosing RR-TB is generally tricky and time-consuming, resulting in treatment delays, increased transmission, and higher mortality.

Nairobi County, a densely populated urban area, is particularly vulnerable to RR-TB spread. Despite ongoing efforts to control the disease, there is limited understanding of the factors that contribute to drug resistance among TB patients in this region. In 2019, respiratory infections, including TB and cardiovascular diseases, were among the leading causes of death in Kenya, with mortality rates of 76 and 81 deaths per 100,000 people, respectively.(*GUIDELINES-ON-THE-PROGRAMMATIC-MANAGEMENT-OF-DRUG-RESISTANT-TUBERCULOSIS-2021.Pdf*, n.d.)

The study intends to fill a significant knowledge vacuum by exploring the predictors of drug-resistant tuberculosis in the local setting. Understanding the factors associated with treatment resistance is critical for creating targeted interventions and improving the efficiency of TB control efforts in Nairobi County, identifying specific predictors such as patient demographics, treatment adherence, comorbidities, and socioeconomic factors. This study hopes to provide insights that can help policymakers, improve diagnostic strategies, and optimise treatment procedures. This could entail treating modifiable risk factors such as poor treatment adherence, malnutrition, or co-infections with HIV.

Like in many other countries, the emergence of COVID-19 in Kenya sent shockwaves through the healthcare system, causing a domino effect that impacted various essential services, including TB control programs. In 2020, there was a 15% estimated reduction in TB case finding, attributable primarily to the pandemic and subsequent responses. Laboratory diagnosis for TB also went down, negatively affecting case finding. (*DNTLDP_Annual-Report-2020_Final.Pdf*, n.d.)

The study's findings are expected to add valuable information to the existing body of knowledge on Rifampicin-resistant tuberculosis, eventually assisting healthcare professionals, policymakers, and public health practitioners in implementing evidence-based measures to reduce the impact of drug-resistant TB in Nairobi County.

The findings of this study can inform similar research in other resource-limited contexts, helping to fight RR-TB globally.

1.3 Study Justification

Despite ongoing efforts to control *TB* in Kenya, the emergence and spread of RRTB remains a critical public health challenge. Nairobi County, a densely populated urban

centre and the capital city of Kenya, with a population of over 4.3 million inhabitants, is particularly vulnerable to the spread of RRTB due to poverty, urbanisation, and overcrowding. (Total population of Kenya in 2019, by county, n.d.). Despite efforts to control TB, the emergence of drug resistance has compromised treatment outcomes and increased morbidity and mortality rates.

The selection of Nairobi County for this study is justified by its high TB prevalence, the complex epidemiological profile, and the availability of existing health data. Additionally, conducting the study in an urban setting like Nairobi will provide valuable insights into the challenges and opportunities for DR-TB control in similar environments. The feasibility of the study is supported by the presence of established healthcare facilities, research institutions, and collaborations with government and non-governmental organisations, which can facilitate data collection and analysis.

In Kenya, Nairobi had the highest number of MDR/RR cases at 12 % (97/804). Over 60% of the population lives in low-income settlements, which is why there is a risk of overcrowding. In 2021, the World Bank reported that 34.3 % (18.8 million) lived below the poverty line of $1.9 a day, while 80% had no access to health care services. HIV prevalence is at 4.9% (Kenya Final Report 2018 - PHIA Project., 2018). The patient-to-doctor ratio was 1:16,000, which is against the WHO recommendation of 1 1,000. (World Health Organization, 2022)

1.4 Research Questions

1. What sociodemographic factors are associated with Rifampicin-resistant tuberculosis among patients in Nairobi County?
2. What behavioural factors increase the risk of Rifampicin-resistant tuberculosis among patients in Nairobi County?

3. What clinical factors are linked to developing Rifampicin-resistant tuberculosis among patients in Nairobi County?

1.4.1 Broad Objective

To identify the predictors of RR tuberculosis among patients infected with tuberculosis who are attending health facilities in Nairobi County**.**

1.4.2 Specific Objectives

1. To determine sociodemographic factors related to Rifampicin-resistant tuberculosis among patients attending health facilities in Nairobi County.
2. To determine patient behavioural factors related to Rifampicin-resistant Tuberculosisamong Patients attending health facilities in Nairobi County.
3. To examine Clinical factors linked to Rifampicin-resistant Tuberculosis among patients attending health facilities in Nairobi County

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Global Impact of TB and Rifampicin Resistance Tuberculosis

In the global context, tuberculosis (TB) stands as the 13th leading cause of death, and it remains the second most significant infectious killer after coronavirus (World Health Organization, 2023). In 2021, approximately 10.6 million individuals fell sick with TB universally, affecting 1.2 million children, six million men, and 3.4 million women. TB is primarily transmitted through air-borne infection, as individuals with lung TB can expel the Mycobacterium tuberculosis (MTB) bacterium into the air, propagating the illness via coughing, spitting, sneezing, and speaking. Surprisingly, about one-third of the global population has contacted MTB; nonetheless, they remain asymptomatic and cannot spread the sickness, known as latent TB. Those with MTB infection face a 10% lifetime risk of developing active TB. (Gill et al., 2022).

More than 80% of TB incidents as well as deaths happen in low- as well as middle-income nations, contributing to global health inequality. Poverty, congested living conditions, and inadequate access to healthcare services all contribute to an increased prevalence of tuberculosis in these locations. RRTB frequently occurs in environments with little healthcare infrastructure, making diagnosis and treatment difficult. The universal distribution of Tuberculosis is widespread, with WHO's Southeast Asian Region accounting for 46% of new TB incidents as of 2021, while the African Region comes second with 23%, and the Western Pacific region with an estimated 18%. The latest national TB patient cost survey data reveals that nearly half of TB-affected households universally incur costs surpassing 20% of their household salaries while coping with the disease. (World Health Organization, 2023).

Tuberculosis is an airborne disease with profound public health implications. RRTB, which is resistant to conventional medications, spreads more quickly and is difficult to control. People's global migration and community connections increase the possibility of RRTB strains spreading internationally.

While TB predominantly affects adults during their most productive years, leading to productivity losses. However, diverse age groups are susceptible to the disease. The costs of tuberculosis diagnosis, treatment, and care may pose an enormous financial strain on affected individuals and their families. RRTB, with its more extensive and complicated therapy, exacerbates economic hardships.

Individuals with weak immune systems, including those infected with HIV, facing undernutrition as well as diabetes, or using tobacco, marginalized communities, and individuals in congregate settings (prisons, refugee camps) are at increased risk of developing active TB and RRTB. The impact is frequently more severe in these populations due to barriers to getting healthcare, stigma, and poor finances. In 2021, there were approximately 2.2 million new TB incidents linked to undernutrition, 740,000 associated with alcohol use disorder, and 690,000 linked to smoking. (World Health Organization, 2023).

The development of drug resistance is a big encounter in TB management, caused by inappropriate use of TB medicines, including incorrect prescription, poor-quality drugs, or premature treatment cessation by patients. Rifampicin Resistant Tuberculosis (RRTB) is treatable with second-line medicines; however, these choices are costly and toxic. RRTB remains a public health crisis and a health security hazard. In 2021, approximately one in three individuals with drug-resistant Tuberculosis could access treatment. RRTB has higher mortality rates compared to drug-susceptible TB,

especially in resource-limited settings where access to proper diagnosis and treatment is limited. The overuse or misuse of antibiotics contributes to the global AMR crisis, affecting not only TB but also other infectious diseases.

TB and RRTB are acknowledged as impediments to meeting various Sustainable Development Goals (SDGs), particularly those pertaining to health, poverty, and inequality. International efforts, such as the World Health Organization's End TB Strategy, seek to reduce TB deaths by 90% and TB incidence by 80% by 2030, highlighting the importance of a multisectoral strategy and worldwide collaboration to solve these issues (World Health Organization, n.d.).

2.2 Epidemiology of Tuberculosis

Statistics in 2019 show that the worldwide record of TB cases was 9 million and about 1.4 million deaths. However, a population of 430,000 people who died were living with HIV. The menace of TB makes it a significant concern for public health, which calls for the employment of successful actions to manage and eliminate the illness (Cole, B, 2020). Consequently, four out of five infected people with HIV who suffer from TB cases comprise the African religion. According to the 2019 statistics from the WHO, Kenya is among the 22 countries that articulate a high burden making it among the top five countries in Sub-Saharan Africa. In 2020, Kenya recorded TB cases to be 89,796, with 16% being HIV positive (WHO, 2019) . According to the statistics, it is evident that concurrent HIV infection with TB in patients contributed to the burden of TB disease. Information from 2015 statistics outlines that 38% of patients with TB have a coefficient with HIV, which amplified the values from 88% to 94% from 2015 to 2017, (MINISTRY OF HEALTH REPUBLIC OF KENYA ANNUAL REPORT, 2020).

In 2022, an estimated 10.6 million people fell ill with TB globally, resulting in 1.3 million deaths, making it the second leading infectious killer after COVID-19 (Lindmeier. C, 2022). Over 80% of cases and deaths victims reside in low- and middle-income countries, where access to healthcare and basic necessities is challenging. This creates a deadly combination of poverty and disease, disproportionately impacting adults in their prime, leaving families shattered and communities reeling. But the vulnerable aren't just defined by income. Children, whose defenses are still developing, are easy prey. Those battling compromised immune systems, like those living with HIV/AIDS, face an even fiercer fight. And living in crowded, unsanitary conditions become an open invitation for TB to spread, fueling a vicious cycle of illness and despair.

The global Corona Virus has had a significant effect on the number of tuberculosis (TB) cases, leading to a substantial increase worldwide. The response to the COVID-19 pandemic, including lockdowns, travel restrictions, and reallocation of healthcare resources, led to disruptions in TB services. This includes reduced access to TB diagnosis, treatment, and follow-up care, which can lead to delays in TB detection and the treatment initiation (Falzm et al., 2023). The focus on COVID-19 testing and healthcare system overload led to a decrease in TB case detection.

TB is a substantial public health issue in Kenya, the fourth cause of death among infectious diseases. In 2016 Kenya reported a TB incidence rate of 426 per 100,000 for all age groups. Kenya had 2,300 incident RR TB cases in 2018; nevertheless, the country reported 485 MDR/RRTB cases, omitting the detection of 79% of the projected incident cases. Rifampicin-resistant TB remains a paramount public health concern in Kenya. In 2020, the country reported approximately 804 cases of MDR/RRTB; Nairobi

County accounted for 12% (97/804) of these cases (MINISTRY OF HEALTH REPUBLIC OF KENYA ANNUAL REPORT, 2020). The advance of RRTB can result in the emergence of a more lethal costlier variant that is difficult to treat XDRTB. Despite the existing concerns, there has been a lack of systematic determination of the prevalence of Rifampicin-resistant tuberculosis (RRTB) in Kenya. One of the contributing factors to this gap is the limited laboratory capacity. Only two laboratories in Kenya, namely Kisian Hospital in Kisumu and the National TB Reference Lab (NTRL), are equipped to perform culture tests for TB. This presents a significant issue that needs to be addressed, as detecting RRTB cases and identifying possible predisposing aspects are crucial for notifying the implementation of appropriate tactics to stop resistance development, enhance treatment costs, as well as reduce the burden of hostile drug reactions related to RRTB management.

Such actions call for developing evidence-based and economical public health interventions to accommodate the country's needs. Additionally, the appropriate formulation of policies and establishment interventions to facilitate RRTB control requires the team to properly understand the factors associated with RRTB.

2.3 Aetiology of TB

Tuberculosis, primarily caused by the human tubercle bacillus *Mycobacterium tuberculosis*, continues to pose a significant global health threat. This pathogen's distinctive characteristics, including acid-fast staining properties and slow growth due to its unique cell wall composition, have been instrumental in its identification and diagnostic processes. (Shahinda, S Alsayed; Hendra, Gunosewoyo;, 2023).

Robert Koch's groundbreaking work in 1890 provided conclusive evidence of the infectious nature of tuberculosis. His pioneering research demonstrated that tuberculous

changes were not confined to isolated nodules but spread throughout various organs, solidifying the understanding of tuberculosis as an infectious disease. Subsequent research by various scientists supported this finding. (Lakhtakia, 2014); (Robert Koch - Studies of tuberculosis and cholera, n.d.)

Recent advances in genome sequencing have illuminated the intricacies of M. tuberculosis, uncovering a notable abundance of cytochromes P450 enzymes, pivotal for its metabolism. Studies have further revealed that specific P450-inhibiting azole drugs exhibit potent anti-mycobacterial activity, suggesting potential novel therapeutic avenues. The pathogen's remarkable adaptability and metabolic flexibility contribute to its unparalleled spread within the human population (Leena Hussein Bajrai et al., 2022). These adaptive traits enable the bacterium to evade the host immune response and establish latent tuberculosis infections in some individuals.

M. tuberculosis's success as a pathogen can be attributed to its elusive nature, allowing it to remain undetected for extended periods and reactivate when the host's immune system weakens. This stealthy behavior enables the bacteria to establish chronic infections, leading to diverse clinical presentations and posing challenges in diagnosis and treatment. A single cell division may take up to 18hrs to 24 hours in media that is enriched with a long incubation period of up to 60 days (Waman et al., 2019)

Understanding the intricate biology of M. tuberculosis, from its unique cell wall composition to its metabolic adaptability, provides crucial insights for developing practical diagnostic tools and therapeutic interventions. The ongoing research into this pathogen's genomic and biochemical aspects holds promise for advancing our understanding of tuberculosis and improving strategies for its control and management.

2.4 Microbiology of tuberculosis causative agent

Mycobacterium tuberculosis (M. tuberculosis), the causative agent of tuberculosis, is described by its slow growth, making diagnosing and treating the disease challenging. Visible colonies on culture media may take several weeks to develop, necessitating specific culture techniques and prolonged incubation periods for detection.

Additionally, M. tuberculosis is a facultative anaerobe, allowing it to thrive in both oxygen-rich and oxygen-poor environments. This enables infections in various parts of the human body, notably the lungs, where oxygen levels fluctuate.

Within the host, M. tuberculosis has evolved mechanisms to evade the immune system, particularly within macrophages, which are crucial in defending against bacterial infections. By inhibiting phagosome-lysosome fusion, M. tuberculosis can survive and replicate within macrophages, contributing to its ability to persist in the host for extended periods.

The unique cell wall of M. tuberculosis contains lipids, such as mycolic acids, which play significant roles in its pathogenicity and drug resistance. (Leena Hussein Bajrai et al., 2022). These lipids contribute to the formation of a waxy layer in the cell wall, rendering the bacterium resistant to various antibiotics and host defense mechanisms. This adds further complexity to TB treatment. The thick cell wall also contributes to the bacterium’s ability to survive in the lungs for extended periods.

Genetic diversity is another characteristic of M. tuberculosis, leading to the classification of different strains or lineages. (Tortoli, E., 2006). The sequencing of the M. Tuberculosis genome has been accomplished, aiding researchers in devising novel diagnostic tests and treatments. This genetic diversity significantly influences tuberculosis's epidemiology, virulence, and drug resistance profiles. Consequently, the

essential task of monitoring and studying various strains becomes imperative for the formulation of effective control measures against the disease.

Tuberculosis is highly contagious, spreading by microscopic droplets released when someone with the infection coughs, sneezes, or even talks. (Coleman et al, 2022). These droplets can remain airborne for a long time, making it essential for people with TB to wear a mask and practice good coughing/ sneezing hygiene to prevent potentially infecting others.

2.5 Pathology of tuberculosis

TB, the insidious, persistent, and often devastating infectious disease, leaves its mark not just on the lungs but on the very fabric of the human immune system. The primary route of infection is through inhalation of airborne droplets containing M. tuberculosis. The germs primarily affect the lungs. Once in the alveoli, the bacterium is metabolized by alveolar macrophages. This causes the establishment of a primary lesion or Ghon focus, usually found in the lower lobe of the lung (Tierney Dylan , 2018).

The defining feature of TB's pathology lies in the unique formation of granulomas, a cluster of immune cells acting as shields and weapons against the invading Mycobacterium tuberculosis bacteria. These miniature battlefields, teaming with macrophages, lymphocytes, epithelioid cells, and giant cells, aim to wall off the infection, creating a barrier of scar tissue like a fortress under siege. However, this effort leaves scars, manifesting as tissue damage and fibrosis, a form of scarring that stiffens and weakens the lungs (Tiwari & Martineau, 2023).

While some bacteria are captured within inactive macrophages, others, like cunning warriors, exploit the lymphatic system as their escape route, infiltrating nearby lymph nodes. Here, a new chapter unfolds, with T lymphocytes, the elite soldiers of the immune system, taking center stage. They orchestrated a fierce cell-mediated immune response after a tense stand-off lasting a week. Often, the primary battlefield, the initial site of infection, heals through calcification or fibrosis, a testament to the body's resilience. However, the fight can sometimes escalate, with inflammation spilling over to the pleura and lung tissue, leaving behind a smoldering fire.

However, the fight does not stop there. Some crafty bacteria manage to evade the initial containment within inactive macrophages. They find their way through the lymphatic system to the regional lymph nodes, acting like Trojan horses infiltrating a strategic outpost. (Hwang & Actor, 2019). There a waiting army of T lymphocytes, alerted by the alarm bells of the immune system, launched a counteroffensive after weeks of preparation. T cells, particularly CD4+ and CD8+ T cells, play an important role in managing infection. This cell-mediated immune response aims to neutralize the threat, potentially destroying the bacteria before they can cause further damage.

TB spreads through a more insidious method: the inhalation of infected droplets coughed or sneezed by an infected individual. The ability of the immune system to contain the bacterial invaders and the number of bacteria released determine the contagiousness of the disease. Breaking this chain of transmission requires a multi-pronged approach: stopping the spread from infected individuals and addressing the environmental, clinical, and personal factors that provide fertile ground for the bacteria to flourish (Diel, R; Nienhaus, A, 2023)

But the complexity of TB goes beyond the mere physical battlefield. The center of granulomas often undergoes a chilling transformation known as caseous necrosis, a cheese-like accumulation of dead tissue where bacteria find refuge, shielded from the immune system's complete annihilation. The immune system, though valiant, faces a formidable foe. The bacteria employ cunning tactics, evading and suppressing the immune response, contributing to the chronic and persistent nature of the disease.

Active tuberculosis may occasionally lead to the process of development of cavities inside the lung tissue. These cavities can be triggered by the necrosis of infected tissue, which contributes to bacterial spread and transmission to others. The destruction of lung tissue may result in respiratory symptoms and long-term pulmonary damage.

The fight against TB takes place not just on the battlefield of the lungs, but also within the microscopic world of granulomas. Understanding this complex pathology is crucial for developing effective strategies to combat this persistent and challenging infectious disease.

2.6 Diagnosis of Tuberculosis

Medical practitioners can diagnose TB in adults through a systematic physical examination and assessment of their medical history. TB symptoms present themselves in numerous ways, such as coughing, fever, wheezing, and inability to gain additional weight (Mayo Clinic, 2023). On the other hand, clinical signs include frequent crepitation or wheezes over the affected lung field. Consequently, the signs as well as symptoms of extrapulmonary TB are stated to the involved organ. A detailed medical history is gathered, including any known tuberculosis exposure, prior tuberculosis treatment, and risk factors such as immunosuppression.

Radiological examinations, particularly chest X-rays, are frequently used to detect lung abnormalities linked with tuberculosis. Common findings include lung infiltrates, cavities, and pleural effusions. Chest X-rays are essential for detecting pulmonary tuberculosis, although they may not be sufficient on their own.

The Mantoux test tool screens for *Mycobacteria tuberculosis* infection through purified protein derivative and measures the reaction in millimeters between 48 and 72 hours. An affirmative outcome will show the rate of TB exposure. Consequently, other tests are necessary to approve the existence of TB disease in a patient (Nayak & Acharjya). When an induration of 5 mm or more occurs in immunosuppressed children and a recording of 10 mm in other children, it is well thought out to be positive. Mantoux test can be negative regardless of TB disease in a child, especially malnutrition, HIV,or severe disseminated Tuberculosis. Other tests also detect TB, including the culture of mycobacterium tuberculosis, Acid-fast bacilli staining, and molecular methods, which identify species-specific genes (Bayot, M L; Sharma, S;, 2018)

Confirmation through microbiological methods remains a crucial element in the diagnosis of tuberculosis. Various laboratory techniques are employed to identify the presence of Mycobacterium tuberculosis. Sputum Smear Microscopy, an expedient and cost-effective approach, involves staining sputum samples, which are then microscopically examined for acid-fast bacilli (AFB) presence. Mycobacterial cultures serve as a highly specific method for isolating and identifying M. tuberculosis from clinical samples; however, this approach is characterized by a prolonged turnaround time, often taking several weeks to yield results. Nucleic Acid Amplification Tests (NAATs), specifically Polymerase Chain Reaction (PCR) tests, offer an alternative diagnostic option by amplifying and detecting specific DNA sequences of M.

tuberculosis, which is particularly beneficial in scenarios where culture-based results may be delayed.

When medical practitioners confirm the existence of Pulmonary TB in a patient, they are placed on first-line drugs. The treatment phase has two divisions; the two-month intensive phase comprises Rifampicin, isoniazid, pyrazinamide, and ethambutol. Before administration of these drugs, medical practitioners should ensure the safety profile, interaction of the drug, and side effects. The next phase is the continuous phase which includes the use of isoniazid and Rifampicin (Chida et al, 2018).It is also recommended that the administrator assesses drug resistance. Resistance can either be mono resistance, called resistance to any first-line drug, or polyresistance, which is resistance to 2 first-line drugs or more but not isoniazid and Rifampicin combination. Multi-drug resistance is also typical in patients, which defines the resistance to Rifampicin and isoniazid, while rifampicin-resistant (RR) Tb demonstrates resistance to Rifampicin. Therefore, all assessments should be based on poor drug adherence, the prevalence of MDR/RRTB, and exposure to MDR/RRTB. At least five agents constitute the treatment regimen for MDR/RRTB, including pyrazinamide and at least four other second-line drugs (Rendon et al, 2016).

GeneXpert MTB/RIF is a popular molecular test that identifies M. tuberculosis and measures rifampicin resistance. It is a nucleic acid amplification test with in-built DNA extraction and real-time PCR. It is a quick and automated procedure that produces results within a few hours.

Blood diagnostics, such as interferon-gamma release assays (IGRAs) and tuberculin skin tests (TST), can assist in identifying M. tuberculosis patients. However, these tests fail to distinguish between latent infection and active disease. Tissue biopsies may be conducted in situations with extrapulmonary tuberculosis or the absence of sputum

samples. Molecular techniques like PCR can be used to detect M. tuberculosis DNA in biopsy material.

2.7 Management of TB

Tuberculosis (TB) remains a significant global health challenge, and numerous intervention strategies have been devised to combat its spread effectively. These strategies aim to detect TB cases early, provide effective treatment, reduce transmission, and address the social determinants associated with the disease. Based on WHO guidelines, detecting Multi-Drug Resistant (MDR) or Rifampicin-Resistant (RR) TB requires confirming TB bacteriologically and conducting drug resistance testing using rapid molecular tests or culture methods (WHO, 2021).

In 2022, new WHO guidelines prioritized a 6-month treatment regimen called BPaLM/BPaL for eligible patients. This novel regimen offers shorter treatment duration, reduced pill burden, and high efficacy, which can alleviate pressure on healthcare systems and allocate valuable resources to expand diagnostic and treatment coverage for all individuals in need. In the past, RRTB treatment used to last at least 9 to 20 months, making the adoption of all-oral regimens highly recommended by WHO (World Health Organization, 2023).

While a slightly effective TB vaccine exists, its primary role is to provide mild protection against TB infection transmission. Preventing transmission among adults is a vital prevention measure, accomplished by identifying and curing patients with active TB. Moreover, identifying individuals with latent TB and preventing the development of active infectious TB is another crucial aspect of prevention. Tuberculosis infection control plays a critical role in preventing transmission in various settings, including hospitals, and pasteurizing milk also helps prevent humans from contracting bovine TB.

Proactively searching for TB cases in high-risk populations and utilizing rapid molecular diagnostic tools for early detection and prompt treatment are key strategies to improve TB control. This involves actively seeking TB cases in high-risk populations, such as close contacts of known TB patients, individuals living with HIV/AIDS, and other vulnerable groups. Contact tracing is essential in identifying and testing individuals who have been in close contact with confirmed TB patients, enabling early case detection and preventing further transmission. The publication on Mathematical models and intervention strategies for mitigating tuberculosis in the Philippines demonstrates that prioritizing active case-finding control over case-holding control, along with implementing distancing measures and latent case-finding control, has considerable potential for effectively curbing the spread of TB (Kim et al., 2018). Active case finding is instrumental in achieving early diagnosis and timely treatment, thereby reducing further transmission of TB. Ensuring that TB patients complete their treatment under direct observation is also critical in enhancing treatment adherence and reducing the risk of drug resistance.

The internationally recommended Directly Observed Treatment Short Course (DOTS) strategy, adopted in 1996, has shown significant progress in the TB control effort (Genet, Melese, & Worede). DOTS involves healthcare workers or community members directly observing TB patients taking their medications, thereby improving treatment adherence and overcoming challenges, such as treatment supporters fearing infection or healthcare workers facing difficulties in following up due to heavy workloads in high-burden health systems.

Patients require assistance and information throughout their treatment. This contains information on medication adherence, probable side effects, and treatment length.

Support from healthcare practitioners, community health workers, and patient support organizations is critical for patients to complete their therapy effectively. Individuals with latent tuberculosis infection (LTBI) who are at risk of acquiring active tuberculosis may benefit from preventive medication to lower the risk of disease progression. This frequently entails the administration of isoniazid for a set period.

TB control programs use public health strategies, such as active case discovery, health education campaigns, and the building of healthcare infrastructure, to guarantee timely diagnosis and treatment.

Regular monitoring and evaluation of tuberculosis programs is critical for assessing treatment outcomes, identifying obstacles, and making required changes to improve overall program efficacy.

2.8 Socio-Cultural Factors and RRTB

Socio-cultural variables contribute significantly to the development and spread of RRTB. The combination of social and cultural elements can impact many aspects of tuberculosis prevention, diagnosis, and treatment, potentially leading to the establishment and persistence of drug-resistant strains.

Individuals' comprehension of tuberculosis, treatment, and the need for adherence is influenced by their level of education and health literacy. Lack of understanding or misconceptions about the condition might contribute to poor health-seeking behavior and treatment outcomes. Certain groups may first turn to traditional healers or alternative cures before seeking mainstream healthcare, potentially delaying accurate diagnosis and treatment. In British Columbia, numerous cases posed a risk factor for RRTB, such as young age, Pulmonary TB (PTB), and reactivated TB (Akm Moniruzzaman, 2019). The fundamental reason why TB transmission has never been

reduced, especially in areas where people are congested, such as the slums and refugee camps. When people know what TB is about, from the cause to the prevention, it is easy to curb the number of MDR/RRTB cases from increasing (Abyot Meaza et al, 2023). An analysis done by Hesseling, states that many people have no idea about the cause, signs and symptoms, treatment, and prevention of Tuberculosis. Knowledge is the key to all challenges. Movan describes how knowledge of something givesone the primary line to understand what one has and how to handle it. Lack of knowledge is equivalent to failure and ignorance (Le Morvan, P, 2021).

According to Daley, insecurity is the state of being subject, open, or vulnerable to danger or threat; therefore, one lacks protection. When a state faces many incidences of insecurity, fear is prone to wander among the citizens. In turn, this suppresses other development sectors in a country, such asthe economy, health, and education. Paralyzing the health sector means no peaceful environment for personnel to work or supply medical equipment. As a result, people resist drugs due to using other means of medication. A study on pathways and system response strategies in the Eastern Democratic Republic of the Congo concludes that insecurity negatively impacts health service delivery and quality in the region through three primary channels: violence, mobility restrictions, and resource availability. (Altare et al., 2021). In the recent past, Kenya has faced the challenges of insecurity. In the North Eastern, many inter-clan wars have disrupted the people's peace, making them always live in fear. When there is a lack of peace due to insecurity, people fail to access essential healthcare services. For this reason,TB patients opt to use any available medication, even substandard ones leading to the developmentof MDR/RRTB cases. (A Comprehensive Study of Health Gaps and Needs in the Mandera Triangle The Cross-Border Health for Peace Programme., 2021)

In 2017 study detailing people's lifestyles, refers to people constantly moving about with their families. This movement and change of geographical regions put the refugees at risk as they interact with many people, and in the course,the TB patients are re-infected. When they use other drugs, they develop resistance, and so do MDR/RRTB results (Olowe et al, 2017). Population migration, particularly in metropolitan areas, can contribute to the spread of tuberculosis and RRTB. Movement within and between communities might provide a challenge to good case tracking and management.

We appreciate the cultural diversity of the many ethnic groups in the world, each holding on to a unique belief. Each culture has a myth regarding using a particular item in their community. Just like some communities hold on to beliefs such as not taking any drugs when sick, as their gods will answer their prayers, so do specific communities among the refugees who believe that the consumption of TB drugs adds weight. With such a mythin mind, people practice irregularities in taking TB drugs, and as a result, they develop resistanceover time. (Matakanye et al, 2021). Cultural ideas regarding the origins of sickness and the role of spirituality can influence attitudes about tuberculosis and RRTB. Understanding and responding to different cultural perspectives is critical for good communication and collaboration between healthcare practitioners and patients. Language barriers, healthcare practitioners' cultural competency, and providing services in culturally sensitive settings may also affect access to healthcare services.

Gender roles and power dynamics within households can shape the ability to access healthcare services. In specific communities, women may encounter challenges in obtaining medical care, leading to delays in the commencement of diagnosis and treatment. Moreover, societal expectations may influence women's ability to adhere to

lengthy and demanding treatment regimens for Rifampicin-resistant tuberculosis (RRTB). In many low-income countries, the reported cases of tuberculosis (TB) among men are twice as high as those among women. This observed difference is often attributed to biological and epidemiological factors and socioeconomic and cultural barriers hindering women's access to healthcare services. A study on Gender differentials of pulmonary tuberculosis transmission and reactivation in an endemic area shows that Higher rates of transmitted and reactivated disease and poorer treatment outcomes among men are indicators of gender differentials in the diagnosis and treatment of pulmonary TB and suggest specific strategies in endemic settings. (Van Den Hof et al., 2010). Women have a greater likelihood of severe forms of TB, and TB-HIV coinfection compared to men has important implications for women's health in TB-HIV high-burden settings (Boah et al., 2021).

The stigma associated with tuberculosis can hinder people from obtaining prompt medical care or following treatment plans. Fear of societal discrimination may drive some people to conceal their tuberculosis status, resulting in a delayed diagnosis and an increased risk of developing medication resistance. (TB Stigma Measurement Guidance, 2019).

Studies reveal a link between family overcrowding and higher tuberculosis transmission. This is because overcrowding encourages close contact and poor ventilation, facilitating the spread of airborne tuberculosis bacteria. While not directly addressing RRTB, more extraordinary TB transmission in congested environments may increase the chance of drug-resistant strains arising if treatment adherence is poor. Poor ventilation in homes can trap tuberculosis bacteria in the air, making people more prone to inhale them. This can raise the risk of tuberculosis infection and possibly contribute

to the development of RRTB in the long run, mainly if adequate treatment is not provided. (Lee et al., 2022)

Limited access to clean water, sanitation facilities, and proper hygiene practices might raise the risk of infectious diseases like tuberculosis. While not directly related to RRTB, poor hygienic conditions can promote TB transmission, potentially leading to the establishment of drug-resistant strains.

2.9 Behavioral Factors and RRTB

Humans are fond of purchasing drugs over the counter whenever they feel unwell, be it a simple cough or persistent headache. Frigate described patients saying they continued using drugs for a specific condition for some time; they developed a resistance to the drugs due to the continuous dosage. Similarly, substandard TB drugs bought over the counter led to the development of RRTB cases over time. The immune system adapts to the drugs and can also mutate to other forms, making it resistant to the drugs used against TB (Koch, A; Cox, H; Mizrahi, V, 2018).

Human behavior on drug usage, he asserts that as smokers share a cigar puff, people share drugs among other goods in their day-to-day lifestyle. Human beings tend to depend on one another and, as a result, share day-to-day products from food and shelter to clothing. Concerning this, TB patients are neither spared. (Olowe et al, 2017).

Adherence to the prescribed treatment regimen is critical in TB therapy, especially for RRTB, which frequently necessitates extended and complex drug regimens. Behavioral factors, such as patients' perception of the value of adherence, motivation, and support systems, substantially impact treatment success. Poor adherence to treatment can increase the risk of recurrence and of developing drug-resistant tuberculosis, as shown in previous studies.

In this sector, various studies have indicated that many patients share their prescribed drugs withothers. Patients, therefore, do not fully undertake their doses, leading to the high prevalence rates ofRRTB cases being recorded. (Bykov et al.,, 2022). A survey conducted in the Samara region of Russia (Granich et al., 2018) identified associations between imprisonment, smoking, recreational drug use, and drug resistance. Similar patterns of increasing multidrug-resistant and extensively drug-resistant tuberculosis (MDR/RR-TB) have been observed in the former Soviet Union states and Asia. (Mehra et al., 2017).

Consistent study reports show that the development of RRTB results from previous historic treatments. (Prasad et al., 2018); (Soedarsono et al., 2023); (Li et al., 2022). Meanwhile, Hong Kong reports that the independent predictors of MDR/RRTB originate from a young age and frequent travel. (Law, 2018). The same study also shows that RRTB patients were less likely to have received directly observed treatment during the previous treatment.

Stigmatization linked with tuberculosis, including RRTB, can prevent people from seeking timely diagnosis and treatment. Fear of social isolation and prejudice may cause people to delay seeking healthcare, leading to the disease's spread. Stigma against tuberculosis patients is high in China, and female patients and those with moderate or severe disease should receive special attention in TB stigma-related interventions. (Chen et al., 2021).

2.10 Clinical Factors and RRTB

Elements heavily influence RRTB prevalence, identification, and management in the healthcare system. These factors include healthcare infrastructure components that affect tuberculosis services' delivery and efficacy. RRTB has been termed as a

manufactured problem resulting from insufficient drug regimens that pick drug-resistant tubercle bacilli, inadequate supervision of treatment by TB control initiatives, as well as non-adherence by the particular patient (Chakaya, 2018). Several parts of the world have conducted numerous research to investigate the risk factors accompanying drug-resistant tuberculosis development. RRTB is more challenging to treat than drug-susceptible tuberculosis, necessitating the use of second-line anti-TB medications that frequently have more significant adverse effects and are less effective. RRTB treatment is often more time-consuming and complex, putting a strain on both the individual and the healthcare system.

Directly Observed Therapy (DOT) is the most effective strategy to endure treatment adherence (Center of Disease Control and Prevention, n.d.). The successful completion of TB therapy is critical in preventing the recurrence of TB with drug-resistant strains. It entails a healthcare worker or trained observer closely monitoring the patient as they take each dose of their TB treatment (Directly Observed Therapy (DOT) for the Treatment of Tuberculosis, 2022). The goal of DOT is to improve medication adherence, lower the chance of treatment failure, and limit the spread of drug resistance, especially RRTB. Implementation and monitoring of DOT programs ensures that patients follow their treatment plans. DOT is an essential component in the management of RRTB to prevent future drug resistance. DOT is intended to improve treatment adherence by physically seeing patients taking their prescribed drugs. Adherence is essential for preventing the development of drug resistance. If a patient routinely takes only a portion of their medication or misses doses, they are more likely to acquire drug-resistant tuberculosis. RRTB frequently occurs when TB treatment is not completed as advised. By having a healthcare provider directly see the patient taking each dose, DOT hopes to prevent incomplete treatment and ensure that the entire course of medication

is finished. Direct observation of treatment aids in identifying and resolving any concerns that may result in incomplete or inadequate treatment. By treating these concerns early on, DOT can lower the chance of drug resistance and the emergence of RRTB. DOT enables healthcare providers to quickly assess the patient's reaction to treatment and identify any problems or side effects. Early intervention can help avoid the need for treatment adjustments that could lead to medication resistance.

Individuals with lower Body Max Index (BMI) may be more susceptible to tuberculosis infection. This could be related to compromised immune systems or hunger that impair their ability to combat microorganisms. However, these studies may not necessarily focus on RRTB. When someone with a lower BMI develops tuberculosis, they may have a more difficult time sticking to treatment due to variables such as exhaustion, dietary inadequacies, or pharmaceutical side effects. This could contribute to the development of RRTB if treatment is insufficient or inconsistent.

Individuals who are HIV positive are more likely to acquire RRTB than those who are HIV negative. There is a well-established link between HIV and tuberculosis, and co-infection presents distinct diagnostic, treatment, and preventative issues. Controlling RRTB hinders the progression of the disease to a virtually untreatable form of the disease, namely XDRTB (Sultana et al., 2021) . HIV impairs the immune system, reducing the body's ability to regulate and eliminate tuberculosis infection. This decreased immune response increases the risk of TB disease progression and can contribute to treatment resistance. HIV-positive people may struggle to complete the entire course of TB treatment due to variables such as drug interactions, side effects, or limited access to healthcare facilities. Incomplete or inadequate therapy can result in the development of drug-resistant tuberculosis strains. HIV-positive people are more

susceptible to a variety of illnesses, including tuberculosis. Co-infection with tuberculosis in an already immunocompromised state increases the likelihood of developing medication resistance. A merger of XDRTB and HIV in patients is 98% fatal. As a result, the treatment for XDRTB and RRTB is expensive and prolonged as it is associated with low cure rates and heightened reaction to drugs, which makes it a less widely resource in most countries (World Health Organization, 2014). The diagnosis and monitoring of tuberculosis in HIV-positive people can be more complicated. TB symptoms can overlap with those of HIV-related infections, resulting in a delayed diagnosis and treatment start. This delay may contribute to the development of medication resistance. HIV-positive people with active tuberculosis may have a more significant bacterial burden in their respiratory secretions, which increases the risk of spreading drug-resistant TB strains to others.

Brazil has implemented strategies that provide the most advanced care worldwide for patients with HIV. Brazil stands in a comparative resource-poor region as a paradigm for introducing ART. Despite a high number of 170,000 patients, Brazil can still manage to supply them with an ART mix at no charge and operate a testing infrastructure and comprehensive health, which fosters treatment monitoring and accurate prescription of drugs. Brazil has put in place recommendations for HIV and TB that stress conducting TST testing in all infected adolescents and children and giving IPT to patients with latent infection. However, the application of these rules is still indistinct. (Montenegro et al, 2019).

Unlike Brazil, Siera Leone is facing numerous challenges related to healthcare, including inadequate training facilities, a lack of logistics to finance the training, inadequate government staff, missing IPT administration for evaluation and monitoring

of the systems, stigma, poor infrastructure, and a negative attitude of the staff that reduces patient care. (Caviglia et al, 2021)

Being admitted to a TB unit does not automatically enhance your chances of developing RRTB. However, variables in a TB ward setting may contribute to the transmission of drug-resistant strains if effective infection control measures are not implemented. Individuals with active tuberculosis may be close together in a TB ward. If someone has RRTB and necessary isolation and infection control procedures are not followed, the drug-resistant strain may spread to others. Longer stays in healthcare settings raise the risk of infection with various types of tuberculosis. Prolonged contact with individuals who have RRTB may increase the chance of transmission. Individuals with suspected or confirmed RRTB should be housed in well-ventilated isolation rooms to reduce the risk of transmission.

Skipping TB medicines may lead to the development of RRTB. TB treatment usually consists of antibiotics administered over an extended period, usually six months or more. Consistent and thorough adherence to the prescribed drug regimen is critical for effectively killing TB germs and preventing drug resistance. When people skip doses or stop taking TB medicine early, it creates an environment in which some germs can survive exposure to the antibiotics. These surviving bacteria may contain modifications that render them resistant to one or more anti-TB medications. As a result, insufficient treatment permits drug-resistant forms of tuberculosis to arise and spread.

The BCG vaccine is generally used to protect against tuberculosis and other mycobacterial infections. This vaccine was first administered to human beings in 1921. BCG is the only vaccine against TB. The BCG vaccine is most effective in preventing severe forms of tuberculosis in children, especially miliary and meningeal TB, and thus

is part of the routine newborn immunization schedule in most parts of the globe (Okafor, Chika N.; Rewane, Ayesan ; Momodu, Ifeanyi I., 2023). However, its effectiveness in preventing pulmonary tuberculosis, the most common disease, varies depending on geographical location and TB strain prevalence. While the BCG vaccine is essential for preventing certain types of tuberculosis, it is not directly linked to developing treatment resistance. RRTB is often caused by poor or incomplete treatment of drug-susceptible tuberculosis rather than immunization. Understanding that the BCG vaccine does not provide lifetime protection is crucial, and its protective benefits may fade with time. Furthermore, the vaccination is not uniformly available in all countries, and coverage may vary.

When TB medicine is taken as prescribed, the body receives a high enough dose of antibiotics to kill all bacteria. However, if medicine doses fail to be administered or the treatment term is not completed, the antibiotic concentration drops below the amount required to kill all bacteria. This results in selective pressure, promoting the survival of germs that have previously transformed resistance to at least one antibiotic. These bacteria grow and eventually become the dominant strain, resulting in treatment failure and/or RRTB development. The history of past TB therapy increases the likelihood of developing RRTB. RRTB is a type of tuberculosis that is resistant to one of the most effective first-line anti-TB medications, rifampicin. This is a substantial difficulty because treatment choices for RRTB are more complex, costlier, and have severe side effects. When people receive TB therapy and do not finish the entire course of meds as prescribed, or if there are problems with the quality or consistency of treatment, certain TB bacteria may survive the drugs. These surviving bacteria may develop mutations that render them resistant to the specific anti-TB drugs employed during the incomplete therapy. Incomplete or inadequate treatment can result in the selection and spread of

drug-resistant forms of tuberculosis. If a person with a history of insufficient tuberculosis treatment becomes re-infected with tuberculosis or the existing illness persists, the new infection or persistent infection is more likely to contain drug-resistant strains. If the resistant strain becomes dominant enough, the remaining antibiotics in your regimen may lose their effectiveness, resulting in treatment failure. This indicates you will still have active tuberculosis after finishing the therapy course. (Soedarsono et al, 2023);

2.11 Summary Gap in Literature Review

The reviewed studies have distinguished that particular variables play a substantial part in prompting the RRTB. However, some studies have portrayed the limitations and weaknesses in various aspects. The current study's case to fill them is based on these. For instance, the study in Zambia on the movement of people in and out of rural and urban areas increases the chance of spreading TB (Mutembo et al., 2019). While the Hong Kong control report affiliates young age and frequent travel to be independent factors that contribute to RRTB (CC Leung et al., 2015); These studies give data from various contexts and TB prevalence rates in each nation. This research showcases a contextual gap that the current research aims to contextualize in Kenya. The Addis Ababa presented a contextual and conceptual gap since the aim was only on health system-based features, isolating the influence of behavior and cultural influences on RRTB (Assefa et al., 2017).

A literature review indicates that most research emphasized the risk factors for TB and RRTB. Nevertheless, in Kenya, besides various interventions being implemented to decrease RRTB, such factors still pose an alarmingly high rate of RRTB infections despite the services being offered for free in most public hospitals, which has prompted

the need to carry out this study to assess and determine such factors in Nairobi County and recommend strategies for improvement.

2.12 Conceptual Framework

In this study, a conceptual framework representation, as depicted in Figure one, is provided to illustrate the interconnectedness among the various independent and dependent variables under investigation. The framework highlights the intricate relationship among sociodemographic factors, individual factors, and health factors, which collectively influence the happening of Rifampicin-resistant tuberculosis (RRTB) within chosen health amenities in Nairobi County.

The independent variables encompassed a range of factors that might impact the growth and spread of RRTB. Sociodemographic factors took into account elements such as age, gender, educational level, religion, and residence, which can influence an individual's susceptibility to RRTB. Patient behavioral and socioeconomic factors considered, history of default, smoking, alcohol use, illicit drug use, being in prison, no of rooms in the house, average monthly income, and history of alternative treatment, all of which play a crucial function in the risk of developing drug-resistant tuberculosis. Clinical system-based factors taken into account were the distance from the health facility, treatment facility level (dispensary vs level 4/5 hospitals, stock out of Anti TB drugs, patient BMI, HIV status, account of previous treatment, history of interaction with TB patient, non-communicable disease e.g. Hypertension, diabetes Additionally, the health factors encompass the access to diagnostics and treatment and adherence to infection control practices. This affinity is reflected below

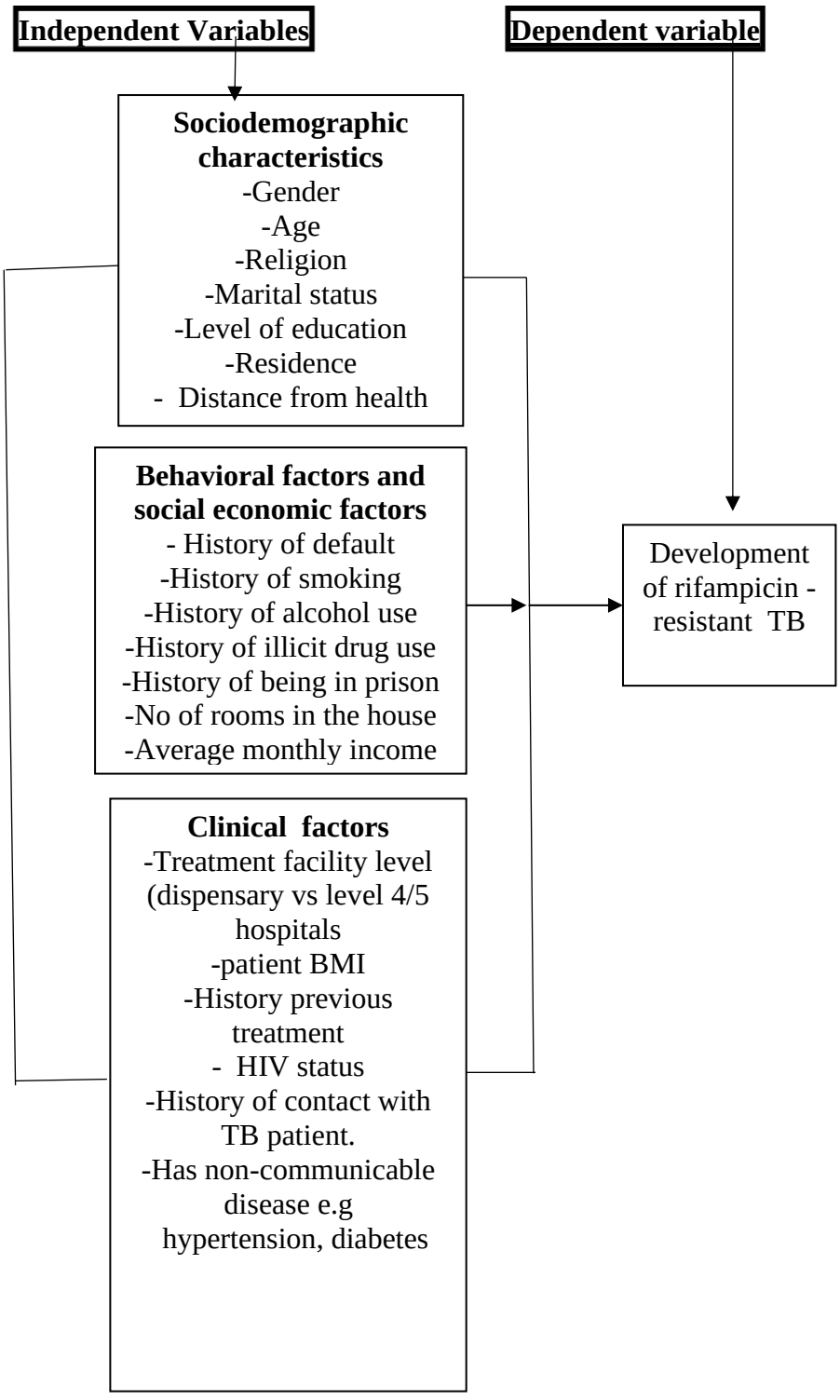

Figure 1: Conceptual Framework

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Site

The study site was in Nairobi County, which has an area of about 700 km2. It hosts a population of over 4 million and has 10 Administrative Subcounties with 17 constituencies (Figure two). It has 23.6% (255/1079) TB treatment registered facilities and 17 Gene Xpert sites (15 public and two private facilities), with a Case Notification Rate (CNR) of 215/100,000 in 2020, up from 284/100,000 in 2019.

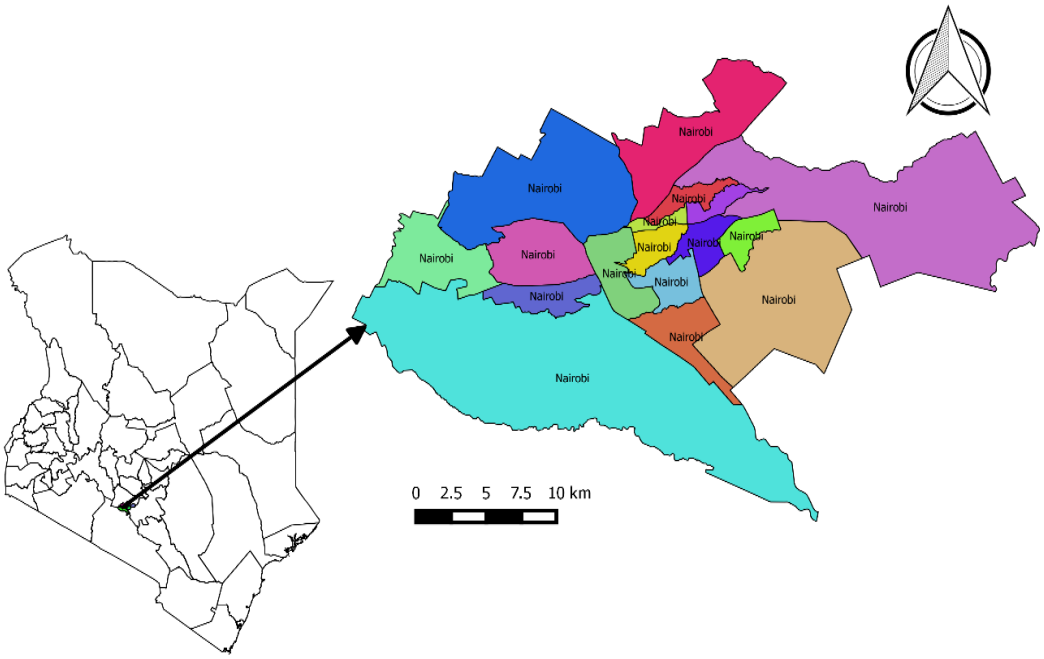

Figure 2: Map showing Nairobi TB control Zones

3.2 Study Population

The primary goal of this research was to undertake a complete and extensive investigation of patients diagnosed with tuberculosis in Nairobi County. The study focused on the total population of Nairobi County who received a TB diagnosis between

January 2021 and March 2023. This broad timeframe allowed for a two-year evaluation of the epidemiological landscape of tuberculosis in the designated region.

The study's spatial focus on Nairobi County emphasizes the importance of knowing the local dynamics of tuberculosis prevalence, transmission, and risk factors in an urban setting. Nairobi, Kenya's capital and central economic hub, provides a unique context with various socio-cultural elements, healthcare facilities, and demographic dynamics that can influence tuberculosis occurrence and management.

By randomly selecting individuals diagnosed with tuberculosis during the given time frame, the study attempted to capture a representative sample of cases, giving a solid foundation for assessing patterns, trends, and potential risk factors linked with tuberculosis in Nairobi County. The broad breadth of the inquiry aimed to discover nuanced insights into the dynamics of tuberculosis in this particular metropolitan milieu.

Furthermore, the study's focus on the period between January 2021 and March 2023 provides a current and relevant view of the tuberculosis situation in Nairobi County. This temporal scope enables the investigation of prospective changes, trends, or variations in tuberculosis transmission. It features over two years, contributing to the current understanding of the illness in the region.

3.2.1 Case definition

In this study, patients underwent laboratory testing for Mycobacterium tuberculosis complex (MTBC) using reliable diagnostic measures, including Genexpert, Truenat, Line Probe Assay (LPA), or culture. Additionally, the patient's drug susceptibility testing (DST) results confirmed resistance to Rifampicin, either with or without isoniazid resistance. The cases included in the study were identified within the

geographic boundaries of Nairobi County, and the data collection spanned from January 2021 to March 2023. (Falzon et al, 2011)

3.2.2 Control definition

A control was defined as a patient undergoing laboratory testing for Mycobacterium tuberculosis complex (MTBC) using methods such as Genexpert, Truenat, Line Probe Assay (LPA), or culture. However, in contrast to the cases, the DST results of the controls confirmed susceptibility to Rifampicin. Furthermore, the controls were smear-negative at the two-month follow-up mark, indicating a lack of detectable tuberculosis bacilli in their sputum samples. Similar to the cases, the controls were identified within Nairobi County, and the data collection period was extended from January 2021 to March 2023. (Falzon et al, 2011)

3.3 Study Design

The case-control study design was chosen as the research methodology for this investigation because it effectively investigates and assesses the potential connections and relationships between numerous factors and the occurrence of Rifampicin-resistant tuberculosis (RRTB). The case-control approach enabled comprehensive research into the factors contributing to the emergence and dissemination of this drug-resistant strain of tuberculosis.

Persons with RRTB (cases) were compared to a carefully selected sample of persons who did not have RRRTB (controls). This comparative technique offered a solid foundation for investigating differences between the two groups in aspects such as demographic features, clinical history, treatment adherence, socioeconomic level, and other important variables. The study aimed to discover factors related to the

development of RRTB and contribute to a better understanding of the complex dynamics of drug resistance in tuberculosis.

The methodology proved ideal for investigating numerous risk factors at once, providing a thorough picture of the complicated interplay between diverse variables and the analyzed outcome.

3.3.1 Sample Size Determination

A minimum sample size of (72cases and 144 controls) was determined through the Fleiss formula.(Workicho et al,, 2017).

The following assumptions were made;

Z - Score for the two-tailed test based on α level (z α/2) 1.96

Z - Score for the one-tailed test based on β level (z 1-β) 0.80

The ratio of controls: cases (r).....1:2

Z - Score for the two-tailed test based on α level (z α/2) 1.96

The proportion of cases (RRTB) with HIV exposure (P1) .....50% (Workicho et al., 2017)

The proportion of controls (Drug sensitive TB) with HIV exposure (P2) ...29 % (Workicho et al., 2017)

P1 .....0.50

P2…….....0.29

OR…….2.4

Number of cases (n1) .....65 + 10% for non-response= 72

Number of controls (n2) .....130 + 10% for non-response= 144

Total sample size (n1+ n2) .....195+10% for non-response= 216

Fleiss formula

$$n_1 = \frac{[n_{\alpha/2}\sqrt{(r+1)\bar{p}\bar{q}} + z(1-\beta)\sqrt{rp_1q_1 + p_2q_2}]2}{r*(p_1 - p_2)^2}$$

$$n_2 = rn_2$$

3.4 Sampling Technique

The process of selecting participants for the study involved several steps and considerations, including using secondary data. Between January 2021 and March 2023, all patients who visited TB care health facilities were initially line-listed, creating a comprehensive list of potential participants was derived from the Treatment information from Basic Unit (TIBU) system, which is an electronic system used to register all patients on TB treatment and house the data at the National level. This Sampling frame divided the data set into two groups: Rifampicin-resistant (RRTB) and drug-sensitive TB (DSTB). In each data set, numbering was done from (1-n), and a random number generator was used using the Random function in Excel to select 72 cases randomly. For the controls, the selection was done by first matching with age ±5 years and assigning numbers from (1-n). A random number generator selected two cases per case for each facility until we reached the 144 controls. Patients who consented to participate were gradually enrolled in the research until the desired sample size was reached.

The recruitment process involved selecting patients from all tuberculosis treatment facilities across 14 sub-counties within Nairobi County. The sub-counties included in the study were Langata, Westland, Kibra, Roysambu, Dagoretti North, Kasarani, Embakasi South, Embakasi East, Embakasi West, Ruaraka, Makadara, Mathare, Kamukunji, and Starehe. These sub-counties were randomly selected from the random generation of cases, which ensured a representative sample from various regions within

Nairobi County. A significant proportion of the participants originated from the regions of Embakasi South and Kamukunji, whereas Makadara had the fewest number of participants.

For each case, two controls were selected from the same facility, ensuring a comparative analysis within the facility itself. This approach allowed for a more accurate evaluation of the factors being studied. However, in cases where there was a scarcity of suitable controls within a particular facility, additional controls were chosen from other facilities that specialize in treating ordinary Tuberculosis individuals referred from the RRTB handling health organizations. This was done to ensure adequate controls for each case and to maintain the integrity of the study.

A simple random sampling technique was employed to ensure a fair and unbiased selection process. This method used a randomisation process to select 72 cases and 144 controls from the pool of potential participants. Using a random sampling technique, the study aimed to minimise selection bias and increase the generalizability of the findings to the larger population.

Following this systematic and rigorous participant selection process, the study aimed to gather a representative sample of individuals from TB-Care health facilities, allowing for robust analysis and meaningful insights into the research objectives.

3.5 Data Collection

A designed structured questionnaire was entered into an electronic form using the Kobo Collect tool application. This digital tool facilitated the efficient and accurate gathering of information. The questionnaire played a vital role in capturing a range of essential variables, including independent sociodemographic, behavioural, and clinical factors.

Face-to-face interviews were conducted with both the cases and controls to ensure the data's reliability and validity. These interviews provided a direct means of obtaining primary data from the participants, enabling a deeper understanding of their experiences and circumstances. The interviews were thoughtfully designed to cover various aspects relevant to the study objectives.

Besides the primary data collected through interviews, secondary data was obtained by meticulously reviewing patient registration records sourced from the national surveillance system, specifically the Treatment Information from Basic Unit (TIBU). The interviews were conducted while patients were in the hospital. This valuable secondary data source provided a comprehensive overview of the cases and controls, further enriching the dataset and contributing to the robustness of the study.

The dependent variable of interest in this research was the development of Rifampicin-resistant TB. This outcome was carefully monitored and analyzed throughout the research to assess its occurrence and potential influencing factors. By focusing on this specific outcome, the study aimed to gain insights into the factors related to the development of Rifampicin-resistant TB.

Before the full-scale implementation of the data collection procedure, a pilot test of the tool was conducted in two non-study health facilities (Embakasi Health Centre and Marurui Health Center). This pilot phase was essential in evaluating the effectiveness and functionality of the questionnaire and the electronic data collection tool. The insights and feedback from the pilot test informed any necessary adjustments and improvements to ensure the smooth execution of the data collection process during the main study.

By accurately implementing data collection methods and the pilot testing phase, the study aimed to gather high-quality, reliable, and relevant data necessary to address the research objectives and draw meaningful conclusions.

3.6 Data Management

The collected data was downloaded into Microsoft Excel for further analysis. To ensure data integrity and accuracy, a comprehensive data cleaning and validation process was conducted. This involved reviewing and verifying the different variables within the database, addressing any discrepancies or errors, and ensuring the consistency and quality of the data.

Access to the data was strictly restricted to prioritise confidentiality and protect the sensitive information gathered during the study. Only the principal investigator had access, which was facilitated through the use of passwords. By implementing stringent security measures, the study aimed to safeguard the privacy and confidentiality of the participant's data, ensuring compliance with ethical standards and data protection regulations.

3.7 Data Analysis

Data analysis was conducted using R Studio version 13. The software facilitated comprehensive statistical computations and visualisation, enabling efficient dataset processing. Through its robust features, R Studio was instrumental in executing various analyses, including descriptive statistics, bivariate analysis, and model fitting, which provided deeper insights into the research findings. A comprehensive univariate analysis was conducted to examine the continuous variables, employing measures of dispersion and measures of central tendency. Categorical data were analyzed by

calculating proportions, rates, and percentages. Dummy tables were utilized to direct the investigation process.

The study population was divided into two groups: subjects with RRTB (cases) and those subjects who had drug-sensitive TB (controls). Various statistical measures were applied to examine the link between factors and RRTB. These included the Crude Odds Ratio (OR), Yates corrected chi-square test, as well as Fisher precise test (in cases where cell counts in the tables were less than 5). The analysis was carried out with a 95% confidence interval (CI) and a 0.05 alpha level of significance. The odds ratio (OR) 1 was considered protective in relation to RRTB risk factors, whereas an odds ratio > 1 was considered a risk factor. Additionally, an odds ratio of 1 indicated that there was no difference between the cases and the controls. The confidence interval was used to assess the odds ratio's fluctuation. If the 95% confidence interval included 1, it was assumed to be completely non-significant. The risk factor factors were shown to be significantly related to RRTB when their P-values were less than 0.05.

A stratified assessment was also carried out to find any confounding factors and effect modifiers. The Chi-square for contradicting odds ratios by stratum (interaction) was examined to see if it was statistically significant (P-value 0.05). The unconditional logistic regression included sociodemographic characteristics discovered by a stratified analysis. Risk factors having a probability level of less than 10% (P-value 0.1) in the bivariate evaluations were added to the logistic regression model. To create the ultimate "Best" model, a stepwise backward elimination logistic regression technique was used. Only statistically significant elements at the alpha level of 0.05 were included in the final model. The variables that were first removed from the model were reentered for retesting, and if they failed to help the model go forward, they were removed. This

comprehensive analysis approach aimed to recognise and evaluate the significant factors related to the RRTB, ensuring the statistical robustness of the findings.

3.8 Dissemination Plan

The Principal Investigator (PI) has organised a complete dissemination strategy to share the study's findings and insights. The distribution process followed the FELTP (Field Epidemiology and Laboratory Training Program) Standards of Practice guidelines, ensuring a methodical and transparent information-sharing approach. Within 90 days of receiving clearance, a final dissemination report was created and released in English on a publicly accessible website. This report provides a detailed outline of the research methodology, key findings, and implications. The timely distribution aligns with promptly informing policy and practice and ensuring that the research findings contribute to evidence-based decision-making. The study’s findings were communicated to a broad audience, including policymakers, healthcare professionals, academics, and the general public. The PI actively participated in conferences, presenting the research findings to encourage discussion and knowledge exchange. These oral presentations allowed stakeholders to engage with the research team, ask questions, and discuss the practical implications of the results. In addition to oral presentations, a written report was made available. The study’s materials were stored in the Moi University School of Public Health repository, ensuring access to both soft and hard copies. This collection is a valuable resource for students, researchers, and policymakers, contributing to the broader academic discourse on tuberculosis and drug resistance. The research team also prepared a manuscript based on the study’s findings for publication in scholarly journals. This peer-reviewed publication ensures that the research has undergone thorough evaluation, adding to the body of scholarly literature

and extending its impact to a global audience of scholars, healthcare professionals, and policymakers.

3.9 Ethical Considerations

The Moi University Institutional Research and Ethics Committee (IREC) No. 0004313 (Appendix 5) approved the study to ensure adherence to ethical guidelines. Subsequently, a study permit was obtained from NACOSTI (NACOSTI/P/23/23112) (Appendix 5) and the Nairobi City County Health Services Research Ethics Committee (NCCG/DHS/REC/288) (Appendix 6).

To protect participants' rights and privacy, informed written consent was obtained from each eligible study participant. The consent process provided thorough information about the research, benefits, potential risks, objectives, and procedures, allowing participants to make an informed decision about their participation.

Confidentiality measures were implemented by assigning unique codes instead of using patient names as identifiers for each consenting participant. This approach maintained anonymity and protected the privacy of individuals involved in the study. Additionally, data collected during the survey was securely stored on password-protected computers, safeguarding participant information.

CHAPTER FOUR

4.0 RESULTS

4.1 Demographic Characteristics of Study Patients

The study had 216 participants, 72 of whom were identified as cases and 144 as controls.

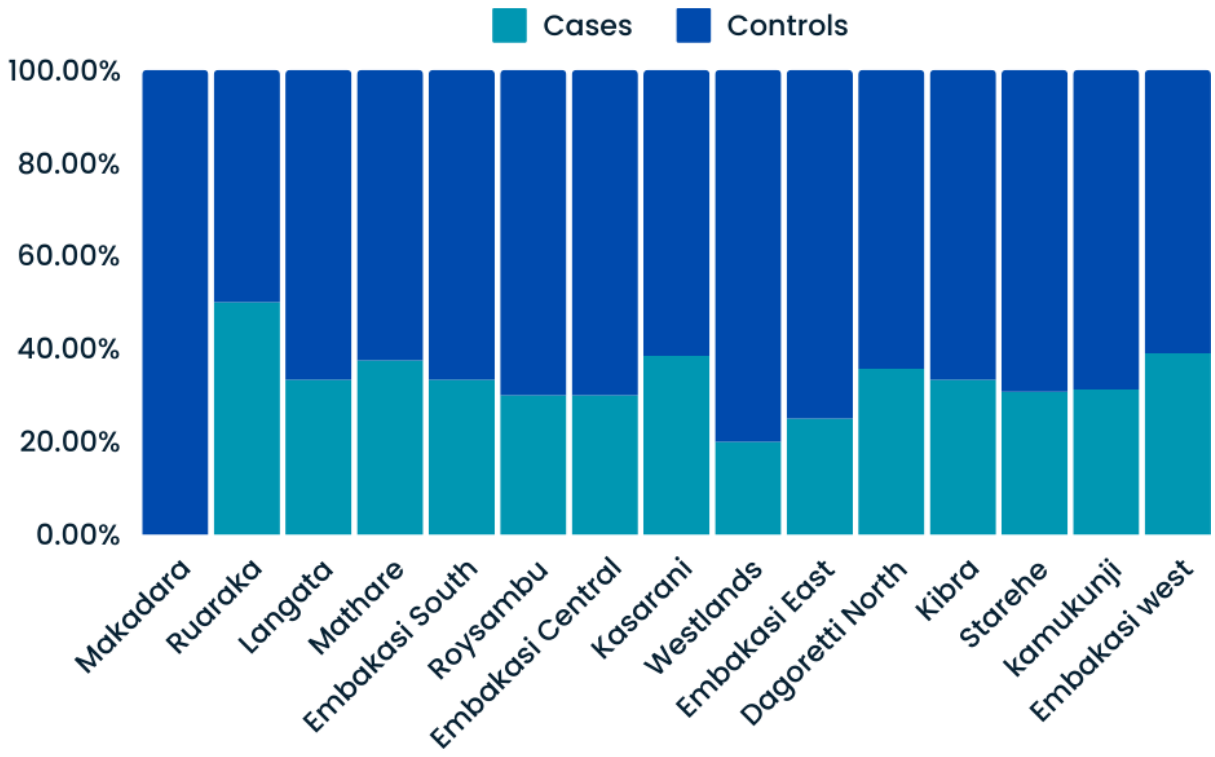

Figure 3: Distribution of RRTB (cases) and DSTB (controls) by Sub County, Nairobi 2023

The below graph shows the distribution of cases and controls across various levels of health facilities. In level 2 and level 3 facilities, there was a relatively balanced representation of cases and controls. Level 4 facilities had a lower number of cases compared to controls. Level 5 facilities had a balanced distribution of cases and controls, while level 6 facilities had a small number of patients but a balanced distribution. This results from referral cases and controls from high-level facilities to lower-level facilities for ease of access, patient follow-up and overall management. The

proportion of cases and controls varied across different levels of health facilities, indicating differences in the concentration of cases and controls (Figure four).

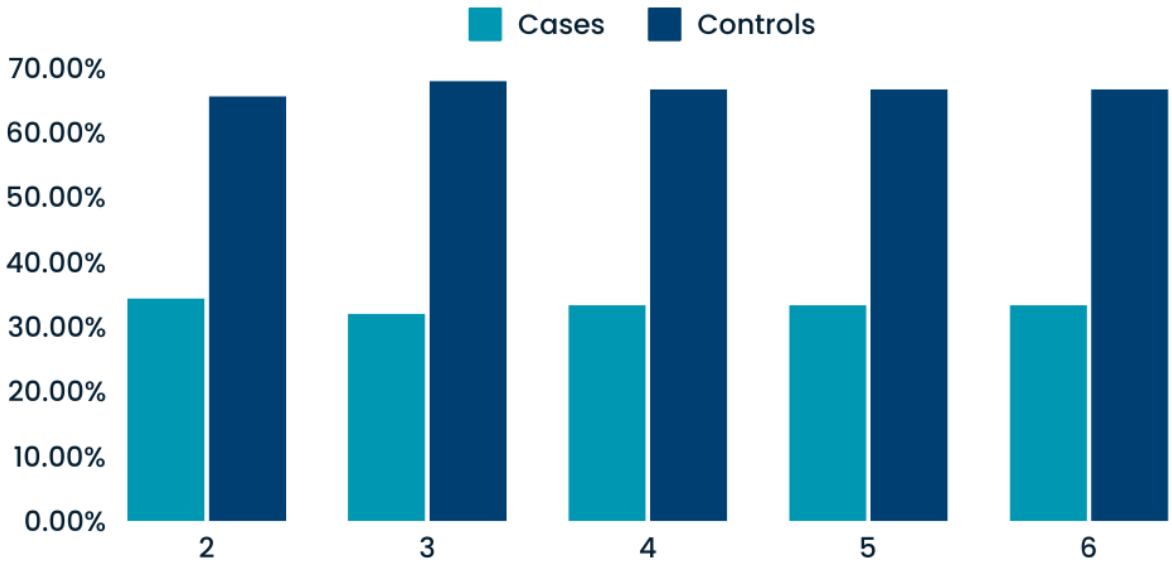

Figure 4: Distribution of Cases and Controls by Hospital Level in Nairobi County, 2023

The data from this study show that public hospitals had the highest number of patients overall, with a larger proportion of cases and controls compared to other types of hospital ownership. Public facilities are funded by the Ministry of Health (MOH) and thus offer free services. It is worth noting that faith-based organizations and NGOs also have a considerable number of patients, albeit smaller than public hospitals. Private hospitals had the lowest number of patients among the categories mentioned (Figure five).

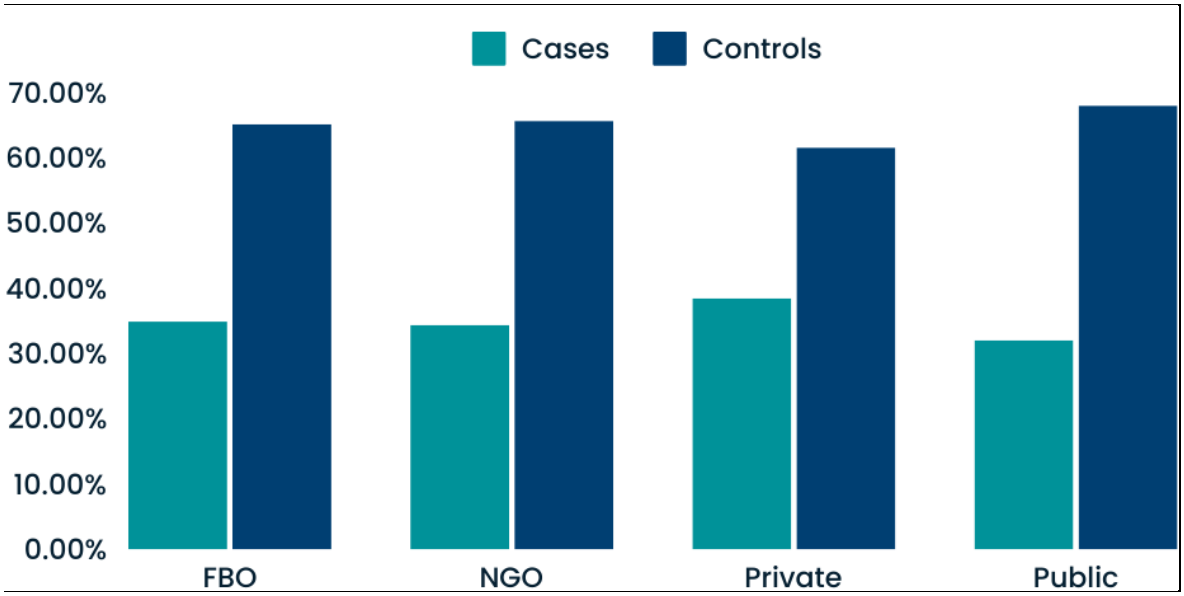

Figure 5: Distribution of Cases and Controls per Hospital Ownership Type

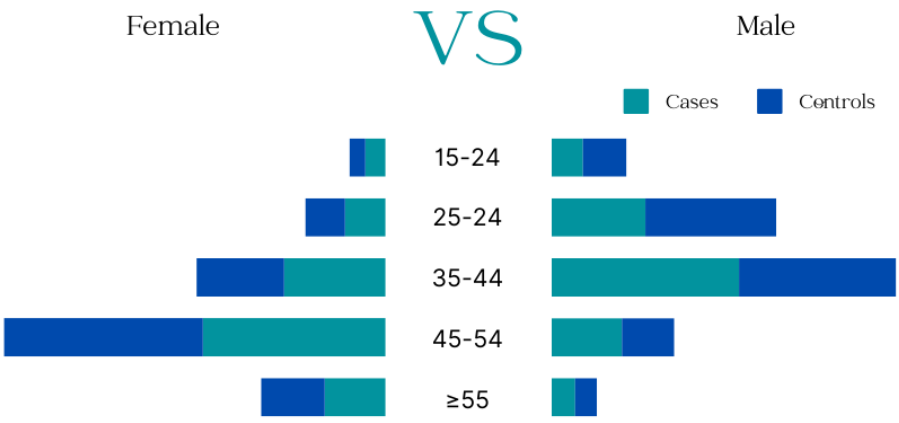

Figure 6: Age and Sex distribution of Cases and Controls

4.2 Demographic Characteristics of MDRTB Cases as well as Controls

In the research, the average distance travelled to healthcare facilities for services is 6.2 km for cases and 3.7km for controls, with a p-value of <0.001. Similarly, the average duration of time taken to reach the facilities was 25.5 minutes for cases and 23.2 minutes for controls; this indicates that the cases travel longer distances and spend more time accessing the services (Table three).

The average age of the cases was 37.7, slightly higher than the average age of the controls, which was 35.9. (Table three). The analysis of age distribution between cases and controls showed no statistically significant difference. Among the cases, 20(28%) were between 30 years or below, while 52(72%) were above 30 years old. Among the controls, 38(26%) were 30 years of age or below, while 106(74%) were above 30 years old (Table 2). The p-value of 0.828 showed that the alteration in age distribution within cases and controls is not statistically significant. The odds ratio (COR) of 0.932 suggests slightly lower odds of being a case for individuals aged 30 years or older than those below 30 years. However, the confidence interval (95% CI: 0.494 to 1.759) includes 1, indicating no significant association (table three).

The analysis of gender distribution between cases and controls showed no statistically significant difference. Among the cases, 28% were female, while 72% were male. Among the controls, 35% were female, while 65% were male. The p-value of 0.261 portrays that the distinction in gender distribution between cases and controls is not statistically significant. The odds ratio (COR) of 1.426 suggests slightly higher odds of being a case for males than females. However, the confidence interval (95% CI: 0.768 to 2.647) includes 1, indicating no significant association (table three).

The analysis of marital status between cases and controls showed no statistically significant variance. Among the incidents, 14% and the 10% controls were divorced with a p –p-value of 0.270, confidence interval (95% CI: -3.004 0.639); among the cases, 28% and 50% controls were married with a p-value of 0.899 confidence interval (95% CI: -2.048 1.374), among the cases 54% and 34% were Single with a p-value 0.158 with a confidence interval (95% CI((-3.087 0.293) which includes 1, indicating no significant association while for cases 3% and 6% of controls were cohabiting (table three).

The analysis of the level of education between cases and controls showed no statistically significant difference. Among the incidents, 47% and 50% of controls had attained secondary level education with a p-value of 0.445 with a confidence interval (95% CI: 0.776 1.358), which includes 1, thus no significant association. Among the cases, 17% and 20% of controls had attained tertiary education with a p-value of 0.369 with a confidence interval (95% CI: 0.938 1.227). In comparison, 36% of cases and 30% of controls had attained primary-level education (table three).

The analysis of religious practice among cases and controls showed no statistically significant difference. Among the cases, 18% and 8% controls were Muslims with a p-value of 0.110 and a confidence interval (95% CI: -1.807 0.178). In contrast, among the protestants who were the majority in this study, 51% were cases and 59% controls with a p-value of 0.578 with a confidence interval (95% CI: -0.505 0.880). Catholics comprised 25% of cases and 24% of controls (Table Three).

Furthermore, the employment status analysis showed no statistically significant variance based on employment status. Among the 29% of cases and 17% of controls had no form of employment with a p-value of 0.267 and confidence interval (95% CI:

-1.285 0.350), among cases, 17% and 17% controls were on salaried employment with a p-value of 0.901 and confidence interval (95% CI: -8.37 0.970), among the cases 28% and 38% controls self-employed with a p-value of 0.337 and confidence interval (95% CI: -0.395 1.146), among the cases 1% and 6% controls were students who were in learning institutions with a p-value of 0.302 as well as confidence interval (95% CI: -0.714 4.134), among the cases 25% and 26% controls were on casual employment (table three).

The analysis of distance to health facilities showed no statistically significant difference. Of individuals who travelled more than five kilometres to health facilities, 36% were cases, and 28% were controlled with a p-value of 0.211 and a confidence interval (95% CI: 0.372 1.244). In comparison, 64% of cases and 72% of controls travelled more than five kilometres (Table three).

Table 1: Distribution of Cases and Controls by Facility

	Facility	Case	Control
1	Babadogo (EDARP)	1	2
2	Bahati MSF Clinic	0	1
3	Baraka Dispensary (Nairobi) - Main	1	1
4	Blue House (AHF) Dispensary	2	8
5	Dandora (EDARP) Clinic	2	1
6	Dandora II Health Centre	3	4
7	Edarp Donholm Clinic	1	1
8	Edarp Komarock Health Centre	3	7
9	EDARP Njiru Clinic	2	4
10	Edarp Soweto Health Centre	0	2
11	Githogoro Runda Baptist Clinic	1	2
12	Huruma Lions Dispensary	3	5
13	Iom Wellness Clinic	4	5
14	Kahawa West Health Centre	3	7
15	Kangemi Health Centre	0	2
16	Karen Health Centre	1	2
17	Kayole Soweto Dispensary	1	3
18	Kibera Community Health Centre - AMREF	1	4
19	Kibera D.O. Dispensary	2	4
20	Mama Lucy Kibaki Hospital	9	18
21	Menelik Chest Clinic	1	1
22	Moi Air Base Hospital	0	2

23	Mukuru Health Centre	2	4
24	Nairobi Hospital	1	2
25	Nairobi Remand Prison Health Centre	4	8
26	Ngara Health Centre (City Council of Nairobi)	2	4
27	Pumwani Majengo Dispensary	1	1
28	Reuben Mukuru Health Centre	1	2
29	Riruta Health Centre	3	6
30	Shauri Moyo Clinic	1	2
31	Silanga (MSF Belgium) Dispensary	1	0
32	SOS Dispensary	1	2
33	South B Police Band Dispensary	1	4
34	St Barkita Dispensary Utawala	2	4
35	St Marys Mission Hospital	1	2
36	St Vincent Catholic Clinic	1	2
37	St Veronica EDARP	1	2
38	The Mater Hospital Mukuru	1	2
39	Uhuru Camp Dispensary (O.P. et al.)	2	4
40	Umoja Health Centre	3	3
41	Uzima Dispensary	1	0
42	Westlands Health Centre	1	4

Table 2: Demographic Factors Associated with RRTB, Nairobi, Kenya

Variable	Cases N=72 (%)	Controls N=144(%)
Age		
15-24	7 (6%)	18 (5%)
25-34	21 (10%)	55 (13%)
35-44	29 (29%)	47 (38%)
45-54	11 (40%)	17 (33%)
≥55	4 (15%)	7 (12%)
Gender		
Female	20 (28%)	51 (35%)
Male	52 (72%)	93 (65%)
Marital status		
Cohabiting	2 (3%)	8 (6%)
Divorced	10 (14%)	15 (10%)
Married	20 (28%)	72 (50%)
Single	39 (54%)	49 (34%)
Widowed	1 (1%)	
Level of education		
Primary	26 (36%)	43 (30%)
Secondary	34 (47%)	72 (50%)
Tertiary	12 (17%)	29 (20%)
Religion		
Catholic	18 (25%0	34 (24%)
Muslims	13 (18%)	11 (8%)
Protestant	37 (51%)	85 (59%)
Other	4 (6%)	14 (10%)

Current Employment		
Casual Employment	18 (25%)	34 (24%)
Not Employed	21 (29%)	25 (17%)
Salaried Employment	12 (17%)	24 (17%)
Self Employed	20 (28%)	55 (38%)
Student	1 (1%)	8 (6%)
Employment prior illness		
Casual Employment	18 (25%)	38 (26%)
Salaried Employment	18 (25%)	22 (15%)
Self Employed	16 (22%)	24 (17%)
Not Employed	19 (26%)	54 (38%)
Student	1 (1%)	8 (6%)
Changed Employment		
No	56(78%)	135(94%)
Yes	16(22%)	9 (6%)
Level of Health Facility		
2	32 (44%)	61 (42%)
3	2 (35%)	53 (37%)
4	5 (7%)	10 (7%)
5	9 (13%)	18 (13%)
6	1 (1%)	2 (1%)

Table 3: Bivariate analysis of the Demographic features, Nairobi, Kenya

Variable	Cases N=72(%)	Controls N=144(%)	P value	COR (95% CI) *LL - *UL
Mean distance (Km) travelled to Hospital (SD)	6.18 (7.93)	3.69 (4.21)	**<0.001***	-
Mean duration (minutes) travelled to Hospital (SD)	25.5(15.2)	23.2(13.49)	**<0.002***	-
Mean Age (Years) (SD)	37.74 (11)	35.93 (10.17)	**<0.001***	-
Age				
15-24	7 (6%)	18 (5%)	0.372	
25-34	21 (10%)	55 (13%)	0.617	
35-44	29 (29%)	47 (38%)	0.552	
45-54	11 (40%)	17 (33%)	0.909	
≥55	4 (15%)	7 (12%)	0.866	
Gender				
Male	52 (72%)	93 (65%)	0.261	1.426(0.768 2.647)
Female	20(28%)	51(35%)		1.00
Marital status				
Divorced	10 (14%)	15 (10%)	0.270	0.375(-3.004 0.639)
Married	20 (28%)	72 (50%)	0.899	0.9(-2.048 1.374)
Single	39 (54%)	49 (34%)	0.158	0.314(-3.087 0.293)
Cohabiting	2(3%)	8(6%)		1.00
Level of education				
Secondary	34 (47%)	72 (50%)	0.445	1.026(0.776 1.358)
Tertiary	12 (17%)	29 (20%)	0.369	1.072(0.938 1.227)

Primary	26(36%)	43(30%)		1.00
Religion				
Muslims	13 (18%)	11 (8%)	0.110	0.448(-1.807 0.178)
Protestant	37 (51%)	85 (59%)	0.578	1.216(-0.505 0.880)
(Other)	4 (6%)	14 (10%)	0.419	1.10 (0.875 1.379)
Catholic	18 (25%)	34 (24%)		1.00
Current Employment				
Not Employed	21 (29%)	25 (17%)	0.267	0.579(-1.285 0.350)
Salaried Employment	12 (17%)	24 (17%)	0.901	0.711(-0.837 0.970)
Self Employed	20 (28%)	55 (38%)	0.337	1.346(-0.395 1.146)
Student	1 (1%)	8 (6%)	0.302	2.842 (-0.714 4.134)
Casual	18(25%)	38(26%)		1.00
Employment prior illness				
Salaried	18 (25%)	22 (15%)	0.428	1.059 (-1.192 0.507)
Self Employed	16 (22%)	24 (17%)	0.447	1.456(-0.479 1.068)
Not Employed	19 (26%)	54 (38%)	0.201	0.630(-1.393 0.290)
Student	1 (1%)	8 (6%)	0.350	3.176(-0.822 4.021)
Casual Employment	18 (25%)	38 (26%)		
Distance to facility				
>5	26 (36%)	40 (28%)	0.211	0.680(0.372 1.244)
<5	46 (64%)	104 (72%)		1.00

Notes: *Variables that indicated a significant relationship during a bivariate assessment at p-value <0.05. T-test is used for numerical variables, and Yates corrected chi square test is used for categorical data. **Note that Lower limit = LL, upper limit = UP.**

4.3 Behavioral and Socio-Economic Factors Associated with RRTB

The prevalence of individuals with a smoking history was significantly higher among the cases 20 (28%) compared to the controls 22 (15%). The p-value of 0.031 indicates a statistically significant difference in the prevalence of smoking history between the two groups. Additionally, 14(70%) cases and 15(68%) controls had smoked for more than five years, while 2(10%) cases and 2(9%) controls had smoked for 3-5 years, and 4(20%) cases and 5(23%) controls smoked for less than 2 years. Among those who

were smoking, 4 (6%) cases and 5 (3%) controls were still smoking. On average, both cases and controls smoked eight sticks per day. In contrast, there was no significant difference in the proportion of cases and controls who lived with smokers. This suggests that smokers in the household do not have a statistically significant impact. Specifically, 9(38%) cases and 11(33%) controls lived with smokers for less than two years, 11(46%) cases and 15(45%) controls lived with smokers for more than five years, and 4(17%) cases and 7(21%) controls lived with smokers for 3-5 years (table four).

The prevalence of individuals with a history of alcohol intake was significant for the cases that had an eight per cent higher prevalence of alcohol intake; the difference compared to the controls did not reach statistical significance. The associated COR of 1.42 (95% CI: 0.778 to 2.592) suggests a minimal association between alcohol intake history and RRTB. Currently, 9 (13%) cases and 8 (6%) controls continue to consume alcohol. Among the participants, 9(35%) cases and 14(34%) controls consumed alcohol daily, 8(31%) cases and 8(20%) controls consumed alcohol occasionally, and 9(35%) cases and 16(39%) controls consumed alcohol weekly (table three).

The prevalence of people reported to be using recreational substances was 13(18%) cases and 22(15%) controls (Table four). The bivariate analysis examining the risk of having RRTB and taking recreational substances did not show statistical significance, with a p-value of 0.602 and a COR (95% CI) of 1.222 (0.576 to 2.594). Some of the recreational substances used by the participants included miraa, bhang, and shisha, with miraa being the most commonly used (table four).

In the study, the household size did not show statistical significance while examining the risk of having RRTB. In the cases, 61(85%) and controls, 126(88%) lived with four or more members per household. The bivariate analysis showed a p-value of 0.0573

and a COR (95% CI) of 1.262 (0.562 to 2.838) for members living in a household with four or more members (table four).

The type of houses a member was living in did not show statistical significance, and 24(33%) cases and 57(40%) controls were living in semi-permanent houses with a p-value 0.759 and a COR (95% CI) of 1.104(0.530 0.736), while 15(21%) cases and 16(11%) controls were living in temporary houses with a p-value 0.092 and a COR (95% CI) of 0.496 (0.119 1.524) (table four).

In the study, the number of houses with a single room was 98 (45%). The sum of rooms per house was established to be statically significant in relationship to the risk of having RRTB; those living in one-room houses for cases were 43(60%) and controls 55(38%) with a p-value of 0.003 and a COR (95% CI) of 2.399 (1.345 -4.280) (table four).

The number of houses having a single window was 99(46%). The number of windows in the house was statistically significant to the risk of having RRTB, with a p-value of 0.044 and a COR (95% CI) of 1.81(1.0 to 3.2). Specifically, 9 (13%) cases and 32(22%) controls kept their windows open for less than 2 hours, 44(61%) cases and 54(38%) controls kept their windows open for more than 5 hours, and 12(17%) cases and 35(24%) controls kept their windows open for 3-5 hours per day (table four).

In the study, a total of 27(13%) subjects had a history of imprisonment, which did not show statistical significance with the risk of having RRTB with a p–p-value of 0.144 and a COR (95% CI) 1.871(0.81 - 4.25). Specifically, for cases 12(17%) and 15 (10%), controls had a history of imprisonment (table four)

In the research, most cases and controls indicated that they had disclosed their tuberculosis (TB) status. Within the cases group, 58(81%) individuals disclosed their

TB status to their friends, whereas 8(11%) individuals disclosed it to their family. Among the controls, 120(83%) individuals disclosed it to their friends, and 15(10%) individuals disclosed it to their family. Participants who decided not to disclose their TB form mentioned stigma as the primary reason behind their choice 6(8%) controls and 9(6%) (table four)

The number of subjects who did not practice cough hygiene was 180(83%), specifically 66(92%) for cases and 114(79%) for controls. In bivariate analysis, those who did not practice cough hygiene had three times the odds of developing RRTB with a p-vale of 0.025 and a COR (95% CI) of 2.857 (1.107 to 7.318), which showed an association of statistical significance (Table four).

The amount of income a participant was earning showed statistical significance, where some subjects that had a monthly income of <kshs 5,000 were 82(38%) for the cases were 39(54%). Controls were 43(30%), while those who earned (kshs 5,000- 10,000) were 69(32%), specifically for cases 19(26%) and for controls 50(35%). Those who had a monthly income of >kshs 10,000 were 65(30%) specifically 14(19%) for cases and controls 51(35%).In bivariate analysis, those who had an income of (kshs 5,000-10,000) had three times the odds of developing RRTB with a p-vale of 0.001 and a COR (95% CI) of 3.304 (0.480 to 1.953) compared to those who were earning > kshs 10,000 with a p-vale of 0.013 and a COR (95% CI) of 2.387 (0.196 to 1.568) having twice the odds of developing RRTB (table fou

Variable	Cases N=72 (%)	Controls N=144 (%)	P-value	COR (95% CI) *LL - *UL
History of smoking				
Yes	20 (28%)	22 (15%)	**0.031**	**2.133(1.073 4.240) ***
No	52(72%)	122(85%)		1.00
Years of smoking				
Years of smoking (>5 years)	14 (70%)	15 (68%)	0.831	0.962(0.677 1.368)
Years of smoking (3-5 years)	2 (10%)	2 (9%)	0.844	0.946(0.543 1.646)
Years of smoking (<2 years)	4(20%)	5(23%)		1.00
Currently smoking				
Yes	4 (6%)	5 (3%)	0.830	0.850(0.193 3.740)
No	16(94%)	17(97%)		1.00
Lived with a smoker				
Yes	24 (33%)	33 (23%)	0.103	1.682 (0.90 3.143)
No	48(67%)	111(77%)		1.00
Living with a smoker				
Living with a smoker (>5 years)	11 (46%)	15 (45%)	0.848	1.027 (0.780 1.353)
Living with a smoker (3-5 Years)	4 (17%)	7 (21%)	0.627	1.09 (1.090 1.543)
Living with a smoker (<2 years)	9(38%)	11(33%)		1.00
History of alcohol intake				
Yes	26 (36%)	41 (28%)	0.254	1.420(0.778 2.592)
No	46(64%)	103(72%)		1.00
Currently taking alcohol				
Yes	9 (13%)	8 (6%)	0.171	2.184(0.714 6.678)
No	17(87%)	33(94%)		1.00
Frequency of taking alcohol				
Occasionally	8 (31%)	8 (20%)	0.480	0.897 (0.664 1.212)
Weekly	9 (35%)	16 (39%)	0.819	1.031 (0.790 1.348)
Daily	9(35%)	14(34%)		1.00
Recreational substance				
Yes	13 (18%)	22 (15%)	0.602	1.222(0.576 2.594)
No	59(72%	122(85%)		1.00
Household				
≥4	61 (85%)	126 (88%)	0.573	1.262 (0.562 2.838)
<4	11(15%)	18(12%)		1.00
Type of house				
Semi-permanent	24 (33%)	57 (40%)	0.759	1.104(0.530 0.736)
Temporary	15 (21%)	16 (11%)	0.092	0.496 (0.119 1.524)
Permanent	33(46%)	71(49%)		1.00
Rooms in the house				
1	43 (60%)	55 (38%)	**0.003**	**2.399(1.345 4.280) ***
≥2	29(40%)	89(62%)		1.00

Windows in the house				
1	40 (56%)	59 (41%)	0.044	1.81(1.0 3.19)
≥2	32(44%)			1.00
Duration of opening windows				
Duration of opening windows (>5 hours)	44 (61%)	54 (38%)	**0.008**	**0.795 (0.671 0.941) ***
Duration of opening windows (3-5 hours)	12 (17%)	35 (24%)	0.718	0.965 (0.795 1.172)
Duration of opening windows (<2 hours)	9(13%)	32(22%)		1.00
History of imprisonment				
Yes	12 (17%)	15 (10%)	0.144	1.871(0.81 4.25)
No	60(83%)	129(90%)		1.00
Practice cough hygiene				
No	66 (92%)	114 (79%)	0.025	2.857(1.10 7.318)
Yes	6(8%)	30(21%)		1.00
Monthly Income				
Monthly Income (5000 - 1000)	19 (26%)	50 (35%)	**0.001**	**3.304(0.480 1.953)** *
Monthly Income (>10000)	14 (19%)	51 (35%)	0.013	2.387(0.196 1.568)

Table 4: Bivariate analysis of the Behavioral and Socio-Economic related factors with RRTB in Nairobi, Kenya

Notes: *Variables which portrayed significant relationship during a bivariate assessment at p-value <0.05. T-test is used for numerical variables, and Yates corrected chi square test is used for categorical data. Note that Lower limit = LL, upper limit = UP.

4.4 Bivariate analysis of the clinical-related factors with RRTB

The number of individuals who had a previous episode of TB was 88 (41%). Among the Cases group, 66 individuals (92%) had undergone previous treatment, whereas, in the control group, only 22 individuals (15%) had received prior treatment. A comparison between the two groups reveals a strong association of acquiring RRTB if you had been previously treated for TB, with a p-value of less than 0.001. The odds ratio, with a 95% confidence interval of 61.000 (23.565 to 157.901), provides a range that encompasses the true odds ratio with 95% confidence. Within the Cases group, 30 individuals (45%) had more than one treatment episode, while 36 individuals (55%) had only one episode. In contrast, among the controls, 12 individuals (55%) had received only one treatment, while 10 individuals (45%) had received more than two treatments (table five).

The analysis of the data shows that among the Cases, a total of nine individuals, accounting for 12% of the group, reported skipping their prescribed TB drugs. On the other hand, within the control group, four individuals, making up 3% of the group, admitted to skipping their TB drugs. This comparison did not achieve a statistically significant difference in the prevalence of individuals who have skipped their TB drugs within the two groups, as evidenced by a p-value of 0.0508 (table five). For individuals who had received a BCG vaccine were 203 (94%) specifically for cases 67(93%) and controls 136 (94%).

In this study, individuals who had contact with known TB patients were 88(41%); among the cases group, 20(28%) had contact with a known TB patient, and a majority of contacts with known TB cases came from the control group with 46(32%) individuals. The bivariate analysis showed no statistically significant difference between the two comparison groups, with a p-value of 0.482 (table five).

In this study, individuals who were exposed to HIV were 43 (20%), where cases were 24(33%) and controls 19(13%). In the bivariate analysis, being HIV positive showed an increased three times odds of having RRTB with a p–p-value of 0.0007, portraying a statistically significant distinction between cases and controls, with COR (95% CI) 3.2895 (1.654 to 6.544) (table five).

Individuals in this study who had an admission to a hospital were 38(18%) for cases 21(29%) and controls 17(12%). In bivariate analysis, individuals who were admitted to the hospital had an increased three times odds of acquiring RRTB with a p-value of 0.002, indicating a statistically significant variance among the cases and controls, with a COR (95% CI) 3.0761(1.5014 to 6.3025) (table five).

The number of individuals who had experienced a chronic lung condition was 5(2%), specifically for cases 4(6%) and for controls 1(1%), which showed an increased eight times odds of contracting RRTB with the odds ratio of 8.412(0.923 to 76.701) at 95% confidence interval. This was not statistically significant, with a p-value of 0.059 (table five).

Interestingly, individuals under the Directly Observed Treatment (DOT) program showed a 2-fold increased likelihood of developing RRTB (crude odds ratio [COR] = 1.7; 95% confidence interval [CI]: (0.5542 - 5.2145) with a p-value of 0.3534. Additionally, 32 cases (84%) and six controls (75%) received instructions on how to

take TB medication. 87% of the cases had HCWs as their DOT providers, while 97% of the controls had household members as their DOT providers.

Our study assessed the nutritional status of both cases and controls. The number of individuals who were overweight was 12 (6%), specifically for cases 4(6%) and controls 8(6%), which were not statistically significant with no difference in odds ratio in comparison to those who had a normal nutritional status with an odds ratio of 1.026(0.776 to1.358) at 95% confidence interval with a p-value of 0.856. For the underweight individuals, 22(31%) were cases and 54(38%) for controls with an odds ratio of 1.072 (0.937 to 1.227) at a 95% confidence interval, which was not statistically significant with a p-value of 0.309 (table five).

Table 5: Bivariate analysis of the clinically connected factors with RRTB in Nairobi, Kenya

Variable	**Cases N=72**	**Controls N=144**	**P-value**	**COR (95% CI)**
	(%)	**(%)**		***LL - *UL**
Previous treatment				
Yes	66 (92%)	22 (15%)	**<0.001**	**61.00(23.5654 157.9009) ***
No	6 (8%)	122(85%)		1.00
Ever Skipped TB drugs				
Yes	9 (12%)	4 (3%)	0.0508	2.79 (0.9963 7.8459)
No	63 (88%)	140(97%)		1.00
BCG Vaccine				
Yes	67 (93%)	136 (94%)	0.686	0.7882(0.2483 2.5020)
No	5 (7%)	8 (6%)		1.00
Treatment supporter				
Yes	67 (93%)	111 (77%)	**0.006**	**3.9838 (1.4828 10.7028) ***
No	5 (7%)	33 (23%)		1.00
Contact with Known TB				
Yes	20 (28%)	46 (32%)	0.482	0.8194 (0.4393 1.5284)
No	52 (72%	98 (68%)		1.00
HIV Status				
Positive	24 (33%)	19 (13%)	**0.0007**	**3.2895(1.6536 6.5436) ***
Negative	48 (67%)	125 (87%)		1.00

Hospital admission				
Yes	21(29%)	17 (12%)	**0.002**	**3.0761(1.5014 6.3025) ***
No	51(72%)	127(88%)		1.00
Have chronic lung condition				
Yes	4 (6%)	1 (1%)	0.059	8.4118(0.9225 76.7011)
No	68 (84%)	143(99%)		1.00
Dots provider				
Yes	22 (33%)	5 (23%)	0.3534	1.7(0.5542 5.2145)
No	44 (67%)	17(77%)		1.00
Treatment interruption				
Yes	11 (17%)	4 (18%)	0.87	0.9(0.2548 3.1796)
No	55 (83%)	18 (82%)		1.00
Nutritional (Overweight)	4(6%)	8 (6%)	0.856	1.026(0.776 1.358)
Nutritional (Underweight)	22 (31%)	54 (38%)	0.309	1.072(0.937 1.227)
Nutritional (Normal weight)	46 (73%)	82 (56%)		1.000

Notes*Variables portrayed significant relationship during bivariate evaluation at p value <0.05. T-test is used for numerical variables, and Yates corrected chi square test is used for categorical data.

Note that Lower limit = LL, upper limit = UP.

4.5 Multivariate Analysis

A logistic regression model without any conditions was used for a multivariate evaluation. The variables identified as having a relationship with RRTB at a significant point of p-value ≤ 0.05 in the bivariate analysis were added to this model. The variables considered were as follows: cough hygiene, history of smoking, rooms, windows, HIV status, treatment supporter, previous TB treatment, hospital admission, treatment defaulters, living with a smoker, earnings per month, chronic lung condition, and comorbidity.

Individuals having a previous history of TB treatment were found to be significantly more prone to contracting RRTB, with a likelihood 69 times higher compared to those

without any prior TB treatment (adjusted odds ratio [AOR] = 69; 95% confidence interval [CI]: 27.490 - 211.215). Individuals with poor cough hygiene are approximately 5.3 times more likely to have RRTB than those practising proper cough hygiene. (Adjusted odds ratio [AOR] =5.265; 95% confidence interval [CI]: 1.625 18.764). Moreover, respondents who were infected with HIV had approximately three times greater chances of acquiring RRTB in comparison to participants without HIV infection (AOR = 3.326, 95% CI: 1.145 - 10.494).

All variables with p< 0.1 were entered into the model with the tabulated results.

Table 6: Step 1 Unconditional Logistic Regression Model

Variable	AOR	(95% CI)	Coefficient	S.E	Z-Statistics	P-value
Cough hygiene	3.940	(1.063 16.306)	-1.371	0.688	-1.992	0.046
History of smoking	1.562	(0.386 6.562)	0.446	0.718	0.620	0.535
Rooms	0.341	(0.037 2.351)	-1.075	1.066	-1.009	0.313
Windows	2.272	(0.345 20.028)	0.821	1.039	0.790	0.430
HIV Status	3.911	(0.356 50.350)	1.364	1.271	1.073	0.283
Treatment supporter	3.864	(0.906 19.703)	1.352	0.777	1.739	0.082
Previous TB treatment	53.972	(0.201 173.135)	3.988	0.543	7.350	>0.001
Hospital admission	2.944	(0.626 14.367)	1.080	0.794	1.359	0.174
Unable to take medication	**1.078**	**(0.197 7.698)**	**0.076**	**0.910**	**0.083**	**0.934**
lived with a smoker	**1.144**	**(0.291 4.418)**	**0.134**	**0.690**	**0.194**	**0.846**
Earnings per month	1.715	(0.526 5.700)	0.540	0.601	0.897	0.370
Chronic lung condition	1.518	(0.043 65.492)	0.417	1.906	0.219	0.827

Comorbidity	**0.999**	**(0.827 1.205)**	**-0.001**	**0.096**	**-0.012**	**0.990**

Due to their high p-values, the variables "Unable to take medication," "Comorbidity," and "lived with a smoker" were excluded from the analysis.

Table 7: Step 2 Unconditional Logistic Regression Model building process (continued)

Variable	AOR	(95% CI)	Coefficient	S.E	Z-Statistics	P-value
Cough hygiene	3.887	(1.063 15.855)	1.358	0.681	1.993	0.046
Smoked cigarettes	1.696	(0.556 5.429)	0.529	0.577	0.916	0.360
Rooms	0.328	(0.036 2.203)	-1.116	1.05	-1.063	0.288
Windows	2.341	(0.360 20.105)	0.851	1.029	0.827	0.409
HIV Status	4.163	(0.396 0.040)	1.426	1.239	1.151	0.250
Treatment supporter	3.908	(0.920 19.722)	1.363	0.774	1.762	0.078
Previous tb treatment	54.089	(2.035 171.910)	3.991	0.538	7.42	>0.001
Hospital admission	2.949	(0.632 14.357)	1.081	0.792	1.365	0.172
Earnings per month	**1.717**	**(0.530 5.660)**	**0.5401**	**0.598**	**0.905**	**0.366**
Chronic lung condition	**1.682**	**(0.050 56.434)**	**0.520**	**1.846**	**0.282**	**0.778**

Due to their high p-value, the variables "Earnings per month", and "Chronic lung condition" were excluded from the analysis.

Table 8: Step 3 Unconditional Logistic Regression Model building process (continued)

Variable	AOR	(95% CI)	Coefficient	S.E	Z-Statistics	P--value
Cough hygiene	4.335	(1.264 16.613)	1.467	0.650	2.256	0.024
Smoked cigarettes	**1.512**	**(0.508 4.682)**	**0.413**	**0.563**	**0.735**	**0.463**
Rooms	0.323	0.0401 2.081)	-1.130	1.016	-1.112	0.266
Windows	**2.154**	**(0.340 16.773)**	**0.768**	**1.002**	**0.766**	**0.444**
HIV Status	3.048	(0.968 10.349)	1.114	0.600	1.859	0.063
Treatment supporter	3.317	(0.902 13.864)	1.199	0.689	1.742	0.082
Previous tb treatment	58.589	(22.372 183.138)	4.071	0.530	7.682	>0.001
Hospital admission	3.176	(0.774 13.934)	1.156	0.734	1.575	0.115

Due to their high p-value, the variables "Number of Rooms", and "Hospital admission" were excluded from the analysis.

Table 9: Step 4 Unconditional Logistic Regression Model building process (continued)

Variable	AOR	(95% CI)	Coefficient	S.E	Z-Statistics	P-value
Cough hygiene	4.188	(1.245 15.574)	1.432	0.638	2.245	0.025
Rooms	**0.599**	**(0.238 1.503)**	**-0.513**	**0.466**	**-1.102**	**0.271**
HIV Status	2.902	(0.942 9.561)	1.065	0.586	1.816	0.069
Treatment supporter	3.126	(0.859 12.831)	1.140	0.681	1.674	0.094
Previous tb treatment	60.811	(23.414 188.165)	4.108	0.525	7.818	>0.001
Hospital admission	**2.982**	**(0.731 13.265)**	**1.093**	**0.739**	**1.479**	**0.139**

The variables "Number of Rooms" and "Hospital admission" were excluded from the analysis due to their high p-values.

Table 10: Step 5 Unconditional Logistic Regression Model building process (continued)

Variable	AOR	(95% CI)	Coefficient	S.E	Z-Statistics	P-value
Cough hygiene	5.190	(1.559 19.008)	1.647	0.631	2.61	0.009
HIV Status	3.268	(1.116 10.388)	1.184	0.564	2.098	0.036
Treatment supporter	3.352	(0.889 14.090)	**1.210**	**0.697**	**1.735**	**0.083**
Previous tb treatment	67.686	(26.404 206.068)	4.215	0.518	8.132	>0.001

The variables "Number of Rooms" and "Hospital admission" were excluded from the analysis due to their high p-values.

Table 11: Step 6 Unconditional Logistic Regression Model building process (continued)

Variable	AOR	(95% CI)	Coefficient	S.E	Z-Statistics	P-value
HIV Status	3.326	(1.145 10.494)	1.2017	0.561	2.144	0.032
Previous tb treatment	69.909	(27.490 211.215)	4.2472	0.514	8.26	>0.001
Cough hygiene	5.265	(1.625 18.764)	1.6611	0.617	2.692	0.007

Table 12: Final ''Best Fit'' model using unconditional logistic regression on variables related to RR-TB in Nairobi, Kenya

Variable	COR (95% CI)	AOR (95% CI)	Coefficient	P-value
Previous TB treatment	61.000 (23.5654 157.9009)	69.909(27.490 211.215)	4.2472	>0.001
Non-Cough hygiene	2.857 (1.10 7.318)	5.265(1.625 18.764)	-1.6611	0.007
HIV positive Status	3.2895 (1.6536-6.5436)	3.326 (1.145 10.494)	1.2017	0.032

COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval.

CHAPTER FIVE

5.1 DISCUSSION

An estimated 25% of the universal population is believed to have latent tuberculosis infection, indicating that they are infected with the bacteria but do not exhibit active symptoms. In 2022, an estimated 450,000 new incidents of Rifampicin-resistant tuberculosis were reported universally, representing a 3.1% increase compared to 2021. Kenya specifically recorded about 10,000 new incidents of RRTB in 2022, with a rate of 5.63 cases per 100,000 people. (KENYA TUBERCULOSIS ROADMAP OVERVIEW, FISCAL YEAR 2022, n.d., 2022)

The rise in RRTB cases can be attributed to a general increase in TB incidence from 2019 through 2022, which is believed to be influenced by the effect of the COVID-19 disease on TB discovery. (KENYA TUBERCULOSIS ROADMAP OVERVIEW, FISCAL YEAR 2022, n.d., 2022).The pandemic has had a detrimental effect on global TB targets, reversing the progress made in the years leading up to 2019. The reduced number of reported TB diagnoses in 2020 and 2021 due to the pandemic suggests that the cases of undiagnosed and untreated TB incidents may have increased.

This study conducted in Nairobi, Kenya, focused on recognizing the factors linked to RRTB to fill gaps in the study and then notify policy implementation for interventions that are most effective in addressing the issue. The findings of this research can lead to a better comprehension of RRTB in the local context as well as support the implementation of targeted strategies to combat the disease.

5.2 Demographic Characteristics Related to RRTB

The distance to a health organisation can significantly impact access to healthcare. Studies have shown that individuals close to healthcare facilities are more likely to seek timely and appropriate healthcare services than those living farther away. In this study, individuals farther away from the hospital may have an increased risk of RRTB. The cases had a significantly higher mean distance travelled to the hospital than the controls, with a p-value of ($p<0.001$). The recommended distance by a study done in Burkina Faso for individuals to gain access to primary health facilities is an average of five kilometers, which, on average, the cases travelled a longer distance compared to controls.(Oldenburg et al., 2021)

Formal education has long been identified as influential in shaping health-seeking behaviour. Various research has shown a positive correlation between higher levels of education and individuals' propensity to seek healthcare services. Educated individuals tend to possess greater health literacy, awareness of preventive measures, and an understanding of the importance of regular check-ups, leading to more proactive health-seeking behaviour. No significant correlations were found when examining the association between education and RRTB in this study.

Multicenter case-control research carried out in Pakistan revealed that male gender is a risk factor linked to RRTB (Atif et al.,, 2021). However, contrasting findings have been conveyed in other studies, where female gender was identified as a prognostic issue for RRTB (Josephine Amie Koroma et al.)and extensively drug-resistant TB (XDR-TB) (Oladimeji et al., 2023). Interestingly, there are also a few research articles that have shown no significant correlation between gender and drug-resistant TB (Demile et al., 2018). A cross-sectional study in Georgia also found that the female sex is a risk factor

for RRTB in the whole study population (AOR=1.58, 95% CI 1.02–2.32) (Lomtadze et al., 2009) . In this study, Males were at three times more risk of contracting RRTB. Conversely, our conclusions have no evidence of statistical significance. These discrepancies in results might be attributed to variations in study design and the characteristics of the study population. These varying results highlight the complexity of the connection between gender and drug-resistant forms of tuberculosis and emphasize the necessity for further research to explore and understand this association.

While there is no definitive evidence linking the number of rooms in a household to the development of RRTB, various research investigates the relationship between housing conditions and TB transmission, which can indirectly increase the risk of RRTB emergence. A systematic review and meta-analysis in sub–Saharan Africa on the impact of household crowding on the risk of tuberculosis transmission discovered that living in crowded conditions increased the risk of TB transmission by 2.2 times that of living in less crowded conditions (Seid et al., 2022). While not directly addressing RRTB, greater TB transmission in congested environments may increase the chance of drug-resistant strains arising if treatment adherence is poor. A population-based study in rural Vietnam on housing conditions and tuberculosis transmission discovered that residing in a house with fewer than four rooms was connected with an increased risk of TB infection. (Wrohan et al., 2022).

5.3 Behavioral and Socio-Economic factors associated with RRTB

Socioeconomic status has also been identified as a significant determinant of health-seeking behavior (Siddique Md,, 2016). The incidence of RRTB is significantly linked to various factors related to behavior and socioeconomic conditions. These factors include smoking history, the number of rooms and windows in the homes, cough

hygiene, and monthly income. Specific indicators such as income level and access to resources have consistently been linked to higher social status, which, in turn, has been linked to improved health-seeking behaviour. A study conducted on individuals with different income levels revealed that those with higher incomes had a lower likelihood of having RRTB. Additionally, the study found that 28% of the respondents had a history of smoking, and further analysis showed a statistically significant difference between the RRTB cases and controls, with a P-value of 0.031. The Odds Ratio of 2.133, along with a 95% confidence interval of 1.073 to 4.240, suggests that individuals with a smoking history have roughly twice the odds of developing RRTB (Kamau, T W;, 2021). However, despite its significance in the initial analysis, the history of smoking did not maintain its significance in the multivariate analysis. This finding aligns with a case-control study at St. Peters TB Specialized Hospital in Ethiopia (Workicho, A; Kassahun, W; Alemseged, F;, 2017). In separate research carried out in the state of Ceara, Brazil, smoking was identified to have a three times higher link to the acquisition of multidrug-resistant tuberculosis (RRTB) (Saifullah et al., 2021). Conversely, a study done in India cited that smoking was related to a lower risk of RR-TB (Ladha et al., 2022). These findings highlight the variability in the association between alcohol, smoking, and different forms of drug-resistant TB across different populations and geographical locations. Further research is needed to elucidate the underlying factors contributing to these varying associations.

This study did not find an association between the number of rooms in the household and RRTB. However, other studies have indicated that the number of rooms is associated with RRTB. Specifically, people living in households with only one room were found to have a five times higher risk of developing RRTB than individuals living in homes with more than one room.

Our study found no significant link between a history of imprisonment and RRTB, which aligns with related research conducted in Ethiopia (Assefa et al,, 2017). However, it is essential to note that prisoners have been a topic of discussion with tuberculosis. They often exhibit a considerably higher prevalence of TB compared to the overall population, primarily due to various factors, including mental diseases, substance abuse, and homelessness (Droznin et al., 2017). These factors, along with challenges like poor ventilation, overcrowding, and inadequate nutrition within prison settings, result in a higher risk of tuberculosis transmission and prevalence among prisoners (Droznin et al., 2017). In this study, the count of rooms in a household demonstrated statistical significance in the bivariate analysis, revealing an odds ratio of 2.399 (1.345, 4.280). Similarly, the count of windows in a household exhibited statistical significance, presenting an odds ratio of 1.81 (1.0, 3.19) during the bivariate analysis. However, it is noteworthy that in both cases, the number of windows and rooms, these variables did not retain statistical significance in the multivariate analysis.

A multicenter study in Southern Ethiopia found that persons living in homes with five to six family members had a higher risk of RRTB than those with fewer members. (Badgeba et al., 2022). In addition, a systematic review and meta-analysis on the influence of household crowding on the risk of tuberculosis transmission indicated a 2.2-fold greater risk of TB transmission in crowded households compared to less crowded ones. (Adigun & Singh, 2023). In this study, the number of people in a household was not statistically significant in the bivariate analysis.

In our study, we found that cough hygiene was significantly linked to multi-drug-resistant tuberculosis TB), with an adjusted odd ratio (AOR) of 5.265. The 95% confidence interval for the AOR ranges from 1.625 to 18.764, suggesting that

individuals practising proper cough hygiene had a 5.265 times higher likelihood of not having RRTB than those not practising proper cough hygiene.

5.4 Medical and Clinical History Factors Related to the RRTB

According to this study, there was no significant relationship between receiving the BCG vaccine and the risk of developing RRTB. (COR=0.788; 95%CI 0.248 to 2.502). This study showed a protective effect with a 32% reduced likelihood of developing RRTB. Moreover, an interesting observation from the study was that elderly individuals who lacked a vaccination scar appeared to be more susceptible to developing RRTB. It is worth noting that further investigation is necessary to elucidate the reasons behind this observation and explore potential risk factors related to RRTB development in the elderly. The absence of antecedent M. tuberculosis infection or sensitisation with environmental mycobacteria is related to increased efficacy of BCG against pulmonary tuberculosis and possibly miliary and meningeal tuberculosis (Mangtani et al., 2013)

In this study, those with positive HIV status were found to have a three-fold higher likelihood of developing RRTB (AOR=3.326; 95%CI 1.145-10.494). This finding aligns with a previous study conducted in Ethiopia, which reported a three-fold higher risk of developing RRTB among patients with positive HIV results (AOR= 3.1; 95%CI (1.02–9.40) (Workicho, A; Kassahun, W; Alemseged, F;, 2017). Another study by (Muluken Dessalegn et al.,, 2016). also supported this relationship, indicating that HIV infection was a significant risk factor for RRTB among HIV-positive patients (OR=2.5, 95%CI 1.2-5.2). A high HIV prevalence setting is also associated with high morbidity and RRTB, which increases the spread and rate of RRTB, contributing to high chances of the occurrence of an outbreak (Wells et al., 2012). According to a Mozambique report study, patients with advanced HIV disease and low CD4 cell count were at a

higher risk of RRTB (Chung-Delgado et al., 2011). However, a combination of numerous research and surveillance records has failed to demonstrate HIV as a risk factor for RRTB (Suchindran, Brouwer, & Van Rie, 2009). Regardless, other studies show that HIV is spurred by rifampicin resistance development (Li, Haoran, 2021). Patients with HIV and RRTB are prone to attacks by fatal diseases (Singh et al., 2020). The investigation also covered the impact of isoniazid on infected people with TB in Addis Ababa. The case-control research also covered 489 children infected with TB and HIV (Assefa et al., 2017). Prevalence of TB was recorded to have been established 69 months after the cessation of IPT. The results showed that 10.28% did not develop TB, while 17.14% developed the disease. Isoniazid reduced the possibility of TB development in HIV-infected babies. Tuberculosis prevalence fundamentally impacted TB-free in both groups and contrasted through the log-rank test.

Hong Kong's case-control study shows that RRTB patients received less direct observation treatment during the previous treatment (DOT). A report from British Colombia also showed that at a young age, Pulmonary TB (PTB) and reactivated TB also posed risk factors for RRTB. (Li, Haoran, 2021). The study in France found an association between MDR/RRTB to hospitalisation upon 24 hours' diagnosis and previous TB. (Guglielmetti,, 2018). A meta-analysis of 23 studies indicated that DOT was linked with a 66% lower probability of treatment failure than self-administered medication, indirectly lowering the likelihood of RRTB development. (Rekart et al., 2022). A study in Peru discovered that individuals enrolled in DOT had a considerably lower probability of getting RRTB than those receiving self-administered medication. (Yu et al., 2018). However, this study suggests that individuals on DOT during the previous treatment had higher chances of developing

RRTB. These findings suggest that there may be instances of inadequate monitoring by DOT providers, which could contribute to the higher risk of RRTB.

In this study's bivariate analysis, persons getting treatment support showed a statistically significant link with a p-value of 0.006 and a correlation effect of 3.9838 (1.4828, 10.7028). The data revealed that people who received treatment had a higher risk of getting RRTB. The correlation effect of 3.9838 revealed that those with treatment support were more likely to develop RRTB than those without. However, it is essential to highlight that these relationships were not statistically significant in the multivariate analysis. Multivariate analysis considers numerous variables simultaneously, allowing for a complete knowledge of the elements influencing the conclusion. The loss of statistical significance in the multivariate analysis may indicate that confounding variables influence the observed link between treatment support and RRTB. Kenya's healthcare system bears a significant strain, which is compounded by a variety of circumstances. The increased demand for healthcare resources and infrastructure may be partly linked to a greater emphasis on COVID-19 surveillance and response operations. The COVID-19 pandemic necessitated a rapid and robust reallocation of healthcare resources, staff, and facilities to address the grave issues posed by the novel coronavirus. With the increase in COVID-19 cases, healthcare facilities throughout Kenya were mobilised to prioritise pandemic-related services like testing, treatment, and quarantine measures. The diversion of healthcare staff, equipment, and financing to manage the impact of COVID-19 put a burden on the whole healthcare system.

RRTB affects about 20% of new TB patients and up to 80% of previously treated individuals (World Health Organization, 2020). Individuals who have previously had

TB therapy have an increased risk of developing RRTB than those who have not. This risk can be up to 14 times higher, according to research such as "Factors Associated with Multi-Drug-Resistant Tuberculosis among TB Patients in Selected Treatment Centers of Amhara Region: A Case-Control Study" (Getahun & Gebiyaw, 2021). A systematic review and meta-analysis focusing on strategies to reduce treatment default in drug-resistant tuberculosis revealed an interesting observation. While individuals under the DOT program were found to have lower rates of treatment default, those who had healthcare workers (HCWs) as their DOT providers were more likely to default treatment, especially in low-income countries. Due to work overload, the study indicates that HCWs in busy healthcare settings may have limited time to provide comprehensive patient support. Consequently, they may adopt a narrow interpretation of DOT, solely focusing on watching patients take their medication.

The most significant determinant of RRTB in this research was found to be a prior treatment for TB. This suggests that acquired drug resistance may be a consequence of non-compliance during previous treatment. Interestingly, a significant number of individuals in this study who had undergone previous TB treatment had a history of skipping their medication for an extended period, which could be connected to a higher risk of contracting RRTB. Previous literature consistently reports a significant association between a history of previous treatment and RRTB ; (Workicho, A; Kassahun, W; Alemseged, F;, 2017); (Muayad Aghali Merza et al., 2011). There is ongoing uncertainty among Health researchers regarding the functions of lung cavities in the development or progression of drug-resistant RRTB. On the one hand, a cavity can be seen as a potential cause of RRTB due to its ability to harbour a larger population of drug-resistant microorganisms. This offers a favourable setting for the rapid multiplication of these resistant mutants, facilitated by increased oxygenation and

protection provided by the thick walls of the cavity against anti-mycobacterial drugs. On the other hand, a cavity can also be viewed as a consequence of resistant illness resulting from a prolonged period of active sickness. This extended period of disease activity can contribute to further lung damage and the formation of cavities. The complex interplay between lung cavities and DR-TB necessitates further investigation to understand their relationship and implications for disease management fully. (Kritski et al.).

A systematic review and meta-analysis revealed a weak link between decreased Body Mass Index (BMI) and an increased risk of tuberculosis infection (T, Ishinda; S, Takeshi;, 2016). In this study, there was no statistically significant association between Body Mass Index and the occurrence of RRTB. Undernutrition, a form of malnutrition, has been linked to an elevated risk of developing RRTB due to its detrimental effect on the immune system. (Baluku et al., 2021). Poor nutritional status compromises immune function, making individuals more vulnerable to infection, including drug-resistant strains of Mycobacterium tuberculosis. Moreover, inadequate nutrition has been associated with unfavourable treatment outcomes, such as reduced treatment success rates, prolonged treatment durations, and increased mortality rates in RRTB cases. Additionally, malnutrition can impact the absorption, distribution, and metabolism of anti-TB drugs, potentially compromising their efficacy. Certain nutritional deficiencies or imbalances may alter drug metabolism, leading to suboptimal drug concentrations and impacting treatment outcomes.

5.5 Limitations of the study

5.5.1 Misclassification

The diagnosis of RRTB among the control group in this study was confirmed solely through sputum smear microscopy, a less sensitive method compared to culture and

drug susceptibility testing (DST). By excluding the application of more advanced testing techniques, there is a risk of misclassifying individuals within the control group who may have been affected by RRTB. This could lead to an underestimation of the true prevalence of RRTB among the controls and potentially affect the validity of the study's results.

Moreover, the Kenya Tuberculosis Roadmap Overview for Fiscal Year 2022 highlights a concerning issue in tuberculosis (TB) diagnosis and reporting. It reveals that a significant proportion, approximately 49 per cent, of estimated TB incidents in Kenya can remain undiagnosed or diagnosed but not disseminated to the National Tuberculosis Program (NTP). This suggests that the current study might have overlooked cases not officially reported to the NTP, potentially resulting in an incomplete representation of the TB burden. Consequently, the study's findings may not accurately reflect the true prevalence of TB and RRTB in the population, and there is a possibility of bias in the estimates.

Considering the factors, it is crucial to deduce the investigation’s report with caution and identify the possible limitations arising from the reliance on sputum smear microscopy for diagnosis and the potential underreporting of TB cases in the study population. Further research and more comprehensive diagnostic approaches, such as culture and DST, along with improved reporting systems, would be valuable for obtaining a more precise understanding of the actual burden of RRTB.

CHAPTER SIX

6.0 Conclusions and Recommendations

6.1 Information bias

Considering that the cases in this study have been treated several times for TB minus getting better, they may be more likely to recall past occasions compared to the controls. This increased recall potential stems from cases with a history of multiple TB treatments that have likely experienced more frequent and recent interactions with the healthcare system. These interactions may have involved discussions about their extensive medical history, diverse treatment regimens, and potential exposures to TB. Consequently, these cases might exhibit heightened awareness and enhanced recollection of past events, including relevant exposures or risk factors.

The rationale behind this heightened awareness is grounded in the assumption that individuals who have undergone multiple TB treatments would have received ongoing education and counselling during their interactions with the healthcare system. This guidance likely emphasised the importance of remembering and reporting pertinent information, aiding in the comprehensive assessment, treatment, and management of their condition.

In contrast, the majority of controls, having not undergone multiple TB treatments, may not have received the same level of medical attention or engaged in extensive discussions regarding their TB treatment history. Consequently, they may be less inclined to remember or recall past events, including potential exposures or risk factors related to TB.

This distinction in the level of medical attention and discussions about TB history between cases and controls underscores the importance of considering these factors in

the study design and analysis. It highlights the potential variability in the accuracy and completeness of the information gathered from cases and controls, emphasising the need for a nuanced approach when interpreting the data and drawing conclusions from the study findings.

6.2 Conclusions

1. In Nairobi, Kenya, the independent predictors for RRTB in this research were during tuberculosis treatment, Previous TB treatment, HIV-positive status and non-practice of cough hygiene.
2. Previous tuberculosis treatment was highly linked to RRTB in Nairobi.
3. A notable association exists between RRTB and a documented HIV-positive status, suggesting it is a risk factor.
4. Adhering to cough hygiene practices reduces the risk of contracting RRTB.

6.3 Recommendations

The results of this case-control research conducted in Nairobi can be inferred in other counties for RRTB control.

1. Enhanced Monitoring of TB Treatment: Strengthen follow-up and adherence support for patients undergoing TB treatment, particularly those with a history of previous TB treatment, to mitigate the risk of developing RRTB.
2. Integrated TB and HIV Care: Improve the integration of TB and HIV services by ensuring regular TB screening for HIV-positive patients and monitoring them closely for potential drug resistance.
3. Promotion of Cough Hygiene: Implement public health campaigns to promote cough hygiene practices, particularly among TB patients, as a preventive measure against RRTB.

4. Targeted Interventions for High-Risk Groups: Focus on tailored interventions for individuals with a history of TB treatment and HIV-positive status to reduce their risk of RRTB.
5. Policy Enhancement: Advocate for revising TB control programs to address the identified risk factors for RRTB, ensuring that they include guidelines for cough hygiene, integrated care, and patient follow-up.

References

Abyot Meaza et al. (2023). Prevalence of tuberculosis and associated factors among presumptive TB refugees residing in refugee camps in Ethiopia. *BMC Infectious Diseases*. doi:https://doi.org/10.1186/s12879-023-08469-5

Adigun, R., & Singh, R. (2023). Tuberculosis. *National Library of Medicine*. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK441916/

Akm Moniruzzaman. (2019). Risk factors for drug resistant TB in British Columbia. doi:https://doi.org/10.14288/1.0091623

Altare et al. (2021). From Insecurity to Health Service Delivery: Pathways and System Response Strategies in the Eastern Democratic Republic of the Congo. *Global Health: Science and Practice*. doi:https://doi.org/10.9745/GHSP-D-21-00107

American Lung Association. (2020). *Tuberculosis Symptoms and Diagnosis*. doi:https://www.lung.org/lung-health-diseases/lung-disease-lookup/tuberculosis/symptoms-diagnosis

Assefa et al,. (2017). Determinants of multidrug-resistant tuberculosis in Addis Ababa, Ethiopia. Infection and Drug Resistance. *National Library of Health*. doi:https://doi.org/10.2147/idr.s134369

Assefa et al. (2017). Determinants of multidrug-resistant tuberculosis in Addis Ababa, Ethiopia. *National Library of Medicine*. doi:https://doi.org/10.2147/idr.s134369

Atif et al.,. (2021). Frequency and Factors Associated With Adverse Events Among Multi-Drug Resistant Tuberculosis Patients in Pakistan: A Retrospective Study. *National Library of Medicine*. doi:https://doi.org/10.3389/fmed.2021.790718

A Comprehensive Study of Health Gaps and Needs in the Mandera Triangle The Cross-Border Health for Peace Programme. Retrieved from https://www.interpeace.org/wp-content/uploads/2022/03/2021-Cross-Border-Health-Policy-and-Practice-Report-Mandera_PRINT.pdf

Badgeba et al. (2022). Determinants of Multidrug-Resistant Mycobacterium tuberculosis Infection: A Multicenter Study from Southern Ethiopia. Infection and Drug Resistance. *National Institutes of Health*. doi:https://doi.org/10.2147/idr.s363628

Baluku et al. (2021). Undernutrition and Treatment Success in Drug-Resistant Tuberculosis in Uganda. Infection and Drug Resistance,. doi:https://doi.org/10.2147/IDR.S332148

Bayot, M L; Sharma, S;. (2018). *National Library of Medicine*. Retrieved from StatPearls: https://www.ncbi.nlm.nih.gov/books/NBK537121/

Boah et al. (2021). Self-reported gender differentials in the knowledge of tuberculosis transmission and curative possibility using national representative data in Ghana. *PLOS ONE*. doi:https://doi.org/10.1371/journal.pone.0254499

Bykov et al.,. (2022). Factors contributing to the high prevalence of multidrug-resistance/Rifampicin-resistance in patients with tuberculosis: an epidemiological cross sectional and qualitative study from Khabarovsk krai region of Russia. *National Library of Medicine*. doi:https://doi.org/10.1186/s12879-022-07598-7

Caviglia et al. (2021). Improving Access to Healthcare in Sierra Leone: The Role of the Newly Developed National Emergency Medical Service. *International Journal of Environmental Research and Public Health*. doi:https://doi.org/10.3390/ijerph18189546

CC Leung et al. (2015). Immigrants and tuberculosis in Hong Kong. *Hong Kong Medical Journal*. doi:DOI: 10.12809/hkmj144492

Centre for Health Solutions. (2020). *TB Annual Report (2020).* Retrieved from https://chskenya.org/tuberculosis-in-kenya/

Chakaya. (2018). *Current Practices in the Care of Drug Sensitive TB Patients.* Retrieved from https://www.tballiance.org/events/downloads/of4/presentations/Chakaya-Current-Practices.pdf

Chen et al. (2021). Tuberculosis-related stigma and its determinants in Dalian, Northeast China: a cross-sectional study. . *BMC Public Health*. doi:https://doi.org/10.1186/s12889-020-10055-2

Chida et al. (2018). Internal Medicine Residents' Knowledge and Practice of Pulmonary Tuberculosis Diagnosis. *Open Forum Infectious Diseases*. doi:https://doi.org/10.1093/ofid/ofy152

Chung-Delgado et al. (2011). *Factors Associated with Anti-Tuberculosis Medication Adverse Effects: A Case-Control Study in Lima, Peru.* PLoS ONE. doi:https://doi.org/10.1371/journal.pone.0027610

Cole, B. (2020). Essential Components of a Public Health Tuberculosis Prevention, Control, and Elimination Program: Recommendations of the Advisory Council for the Elimination of Tuberculosis and the National Tuberculosis Controllers Association. *CDC*. doi:https://doi.org/10.15585/mmwr.rr6907a1

Coleman et al. (2022). Mycobacterium tuberculosis Transmission in High-Incidence Settings—New Paradigms and Insights. *National Library of Medicine*. doi:https://doi.org/10.3390/pathogens11111228

Demile et al. (2018). Risk factors associated with multidrug-resistant tuberculosis (MDR-TB) in a tertiary armed force referral and teaching hospital, Ethiopia. *BMC Infectious Diseases,*. doi:https://doi.org/10.1186/s12879-018-3167-9

Diel, R; Nienhaus, A. (2023). Pathways of TB Transmission in Children—A Systematic Review of Molecular Epidemiological Studies. *International Journal of Environmental Research and Public Health*. doi:https://doi.org/10.3390/ijerph20031737

Directly Observed Therapy (DOT) for the Treatment of Tuberculosis. (2022, October). Retrieved from Minnesota Department of Health: https://www.health.state.mn.us/diseases/tb/lph/dot.html

DNTL*DP_Annual-Report-2020_Final.pdf*. (n.d.). Retrieved 3 September 2024, from https://www.nltp.co.ke/wp-content/uploads/2022/01/DNTLDP_Annual-Report-2020_Final.pdf

Droznin et al. (2017). Multidrug resistant tuberculosis in prisons located in former Soviet countries: A systematic review. *PLOS ONE*. doi:https://doi.org/10.1371/journal.pone.0174373

Espinal et al. (2019).

Falzm et al. (2023). The impact of the COVID-19 pandemic on the global tuberculosis epidemic. *Frontiers in Immunology*. doi:https://doi.org/10.3389/fimmu.2023.1234785

Falzon et al. (2011). WHO guidelines for the programmatic management of drug-resistant tuberculosis: 2011 update. *The European Respiratory Journal*. doi:https://doi.org/10.1183/09031936.00073611

Genet, C., Melese, A., & Worede, A. (n.d.). Effectiveness of directly observed treatment short course (DOTS) on treatment of tuberculosis patients in public health facilities of Debre Tabor Town, Ethiopia: retrospective study. *BMC Research Notes*. doi:https://doi.org/10.1186/s13104-019-4424-8

Getahun, Y. A., & Gebiyaw, W. T. (2021). Factors Associated with Multi-Drug Resistant Tuberculosis among TB Patients in Selected Treatment Centers of Amhara Region: A Case-Control Study. Ethiopian Journal of Health Sciences. *National Library of Medicine*. doi:https://doi.org/10.4314/ejhs.v31i1.4

Gill et al. (2022). New developments in tuberculosis diagnosis and treatment. *Breathe*. doi:https://doi.org/10.1183/20734735.0149-2021

Global Tuberculosis Report. (2021).

Guidelines-*on-the-Programmatic-Management-oF-Drug-Resistant-Tuberculosis-2021.pdf*. (n.d.). Retrieved 3 September 2024, from https://chskenya.org/wp-content/uploads/2022/04/Guidelines-on-the-Programmatic-Management-of-Drug-Resistant-Tuberculosis-2021.pdf

Guglielmetti,. (2018). Drug-resistant tuberculosis in France : epidemiology and management. *Hal.science*. Retrieved from https://theses.hal.science/tel-02448924

Humayun et al. (2022). Effect of gender on clinical presentation of tuberculosis (TB) and age-specific risk of TB, and TB-HIV coinfection. *Open Forum Infectious Diseases*. doi:https://doi.org/10.1093/ofid/ofac512

Hwang, S., & Actor, J. K. (2019). *ScienceDirect*. Retrieved from Academic Press: https://www.sciencedirect.com/science/article/abs/pii/B9780128138328000078

Jeremiah Chakaya et al. (2021). Global Tuberculosis Report 2020- – Reflections on the Global TB burden, treatment and prevention efforts. *National Library of Medicine*. doi:https://doi.org/10.1016/j.ijid.2021.02.107

Josephine Amie Koroma et al. (n.d.). Factors associated with unfavorable treatment outcomes among multidrug-resistant tuberculosis patients, Sierra Leone: a cross-sectional secondary data analysis. *BMC Infectious Diseases*. doi:https://doi.org/10.1186/s12879-024-09370-

Kamau, T W;. (2021). Determinants of Health Seeking Behavior Among Households With Chronic Non-communicable Diseases in Kenya. *Uonbi.ac.ke.* Retrieved from http://erepository.uonbi.ac.ke/handle/11295/160121

Kavindhran Venel ey al. (2021). Performance of GeneXpert MTB/RIF for Diagnosing Tuberculosis Among Symptomatic Household Contacts of Index Patients in South Africa. doi:Open Forum Infectious Diseases

Kenya Final Report 2018 - PHIA Project. (2018). *PHIA Project*. Retrieved from https://phia.icap.columbia.edu/kenya-final-report-2018/#:~:text=The%20Kenya%20Population%2Dbased%20HIV

Kenya Tuberculosis Roadmap Overview, Fiscal Year 2022, n.d. (2022). *Kenya Tuberculosis Roadmap Overview.* Retrieved from https://www.usaid.gov/sites/default/files/2022-12/Kenya-TBRM22.pdf

Kim et al. (2018). Mathematical model and intervention strategies for mitigating tuberculosis in the Philippines. *Journal of Theoretical Biology*. doi:https://doi.org/10.1016/j.jtbi.2018.01.026

Koch, A; Cox, H; Mizrahi, V. (2018). Drug-resistant tuberculosis: challenges and opportunities for diagnosis and treatment. (T. Egan , & D. Warner, Eds.) *Current Opinion in Pharmacology*. doi:https://doi.org/10.1016/j.coph.2018.05.013

Kritski et al. (n.d.). Retreatment Tuberculosis Cases: Factors Associated with Drug Resistance and Adverse Outcome. *National Library of Medicine*. doi:10.1378/chest.111.5.1162

Ladha et al. (2022). Determinants, risk factors and spatial analysis of multi-drug resistant pulmonary tuberculosis in Jodhpur, India. *Monaldi Archives for Chest Disease*. doi:https://doi.org/10.4081/monaldi.2022.2026

Lakhtakia. (2014). The Legacy of Robert Koch. *Sultan Qaboos University Medical Journal*. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3916274/

Law. (2018). Risk factors for multidrug-resistant tuberculosis in Hong Kong. *The Official Journal of the International Union against Tuberculosis and Lung Disease*. Retrieved from https://pubmed.ncbi.nlm.nih.gov/18713506/

Le Morvan, P. (2021). Ignorance, Knowledge, and Two Epistemic Intuitions. *Philosophia*. doi:https://doi.org/10.1007/s11406-021-00342-6

Leena Hussein Bajrai et al. (2022). Glycosylated Flavonoid Compounds as Potent CYP121 Inhibitors of Mycobacterium tuberculosis. *Biomolecules*. doi:https://doi.org/10.3390/biom12101356

Lee, J.-Y., Kwon, N., Goo, G., & Cho, S. (2022). Inadequate housing and pulmonary tuberculosis: A systematic review. *BMC Public Health*, *22*, 622. https://doi.org/10.1186/s12889-022-12879-6

Li et al. (2022). Factors associated with treatment outcomes of patients with drug-resistant tuberculosis in China: A retrospective study using competing risk. doi:https://doi.org/10.3389/fpubh.2022.906798

Li, Haoran. (2021). Investigating molecular clustering of Rv1747 in M. smegmatis (T). *University of British Columbia*. doi:https://dx.doi.org/10.14288/1.0400596

Lindmeier. C. (2022). *Tuberculosis deaths and disease increase during the COVID-19 pandemic*. Retrieved from Www.who.int.: https://www.who.int/news/item/27-10-2022-tuberculosis-deaths-and-disease-increase-during-the-covid-19-pandemic

Lomtadze et al. (2009). Prevalence and risk factors for multidrug-resistant tuberculosis in the Republic of Georgia: a population-based study. *The International Journal of Tuberculosis and Lung Disease : The Official Journal of the International Union against Tuberculosis and Lung Disease,*. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2645031/

Main causes of deaths in Kenya as of 2019. (n.d.). Retrieved from Statistica: https://www.statista.com/statistics/1221721/main-causes-of-deaths-in-kenya/

Mangtani et al. (2013). Protection by BCG Vaccine Against Tuberculosis: A Systematic Review of Randomized Controlled Trials. *National Library of Medicine*. doi:https://doi.org/10.1093/cid/cit790

Matakanye et al. (2021). Knowledge, Beliefs, and Perceptions of TB and Its Treatment amongst TB Patients in the Limpopo Province, South Africa. *International Journal of Environmental Research and Public Health*. doi:https://doi.org/10.3390/ijerph181910404

Mayo Clinic. (2023). *Tuberculosis - Symptoms and Causes*. Retrieved from Mayo Clinic: https://www.mayoclinic.org/diseases-conditions/tuberculosis/symptoms-causes/syc-20351250

Médecins Sans Frontières. (2018). *Msf.org*. Retrieved from https://api.scienceportal.msf.org/api/v1/blobs/8782

MedlinePlus. (n.d.). Retrieved from National Library of Medicine: https://medlineplus.gov/tuberculosis.html

Mehra et al. (2017). The association between alcohol, marijuana, illegal drug use and current use of E-cigarette among youth and young adults in Canada: results from Canadian Tobacco, Alcohol and Drugs Survey 2017. *BMC Public Health*. doi:https://doi.org/10.1186/s12889-019-7546-y

Menzies et al. (2020). Impact of Effective Global Tuberculosis Control on Health and Economic Outcomes in the United States. *American Journal of Respiratory and Critical Care Medicine*. doi:https://doi.org/10.1164/rccm.202003-0526oc

Ministry of Health Republic of Kenya Annual Report. (2020). *Ministry of Health Republic of Kenya Annual Report 2020.* Retrieved from https://www.nltp.co.ke/wp-content/uploads/2022/01/DNTLDP_Annual-Report-2020_Final.pdf

MOH. (2020).

Montenegro et al. (2019). Public Health, HIV Care and Prevention, Human Rights and Democracy at a Crossroad in Brazil. *AIDS and Behavior*. doi: https://doi.org/10.1007/s10461-019-02470-3

MSF. (2020, June). *MedlinePlus*. Retrieved from National Library of Medicine: https://medlineplus.gov/tuberculosis.html

Muayad Aghali Merza et al. (2011). Anti-tuberculosis drug resistance and associated risk factors in a tertiary level TB centre in Iran: a retrospective analysis. *The Journal of Infection in Developing Countries*. doi:https://doi.org/10.3855/jidc.1259

Muluken Dessalegn et al.,. (2016). Predictors of multidrug resistant tuberculosis among adult patients at Saint Peter Hospital Addis Ababa, Ethiopia. *PubMed*. doi:https://doi.org/10.11604/pamj.supp.2016.25.2.9203

Mutembo et al. (2019). Urban-rural disparities in treatment outcomes among recurrent TB cases in Southern Province, Zambia. *BMC Infectious Diseases*. doi:https://doi.org/10.1186/s12879-019-4709-5

Nayak, S., & Acharjya, B. (n.d.). Mantoux test and its interpretation. *Indian Dermatology Online Journal*. doi:https://doi.org/10.4103/2229-5178.93479

Okafor, Chika N.; Rewane, Ayesan ; Momodu, Ifeanyi I. (2023). Bacillus Calmette Guerin. *National Library of Medicine*. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK538185/#:

Oladimeji et al. (2023). Gender and Drug-Resistant Tuberculosis in Nigeria. *Tropical Medicine and Infectious Disease*. doi:https://doi.org/10.3390/tropicalmed8020104

Olowe et al. (2017). Epidemiological characteristics and clinical outcome of HIV-related tuberculosis in a population of TB patients in South-Western Nigeria.

European Journal of Microbiology and Immunology. doi:https://doi.org/10.1556/1886.2017.00003

Oldenburg, C. E., Sié, A., Ouattara, M., Bountogo, M., Boudo, V., Kouanda, I., Lebas, E., Brogdon, J. M., Lin, Y., Nyatigo, F., Arnold, B. F., Lietman, T. M., & for the Étude CHAT Study Group. (2021). Distance to primary care facilities and healthcare utilization for preschool children in rural northwestern Burkina Faso: Results from a surveillance cohort. *BMC Health Services Research*, *21*(1), 212. https://doi.org/10.1186/s12913-021-06226-5

Prasad et al. (2018). Multidrug-resistant tuberculosis/rifampicin-resistant tuberculosis: Principles of management. *Lung India*,. doi:https://doi.org/10.4103/lungindia.lungindia_98_17

Rekart et al. (2022). Family directly observed therapy for children with drug-resistant TB. *The International Journal of Tuberculosis and Lung Disease*. doi:https://doi.org/10.5588/ijtld.22.0168

Rendon et al. (2016). Classification of drugs to treat multidrug-resistant tuberculosis (MDR-TB): evidence and perspectives. *Journal of Thoracic Disease*. doi:https://doi.org/10.21037/jtd.2016.10.14

Robert Koch - Studies of tuberculosis and cholera. (n.d.). *Encyclopedia Britannica*. Retrieved from https://www.britannica.com/biography/Robert-Koch/Studies-of-tuberculosis-and-cholera

Robert Koch. (1890). Retrieved from https://books.google.co.ke/books?id=i8Q1AQAAMAAJ&printsec=frontcover#v=onepage&q&f=false

Saifullah et al. (2021). Evaluation of risk factors associated with the development of MDR- and XDR-TB in a tertiary care hospital: a retrospective cohort study. *Peer Journal*. doi:https://doi.org/10.7717/peerj.10826

Seid et al. (2022). Tuberculosis in household contacts of tuberculosis patients in sub-Saharan African countries: A systematic review and meta-analysis. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*. doi:https://doi.org/10.1016/j.jctube.2022.100337

Shahinda, S Alsayed; Hendra, Gunosewoyo;. (2023). *Tuberculosis: Pathogenesis, Current Treatment Regimens and New Drug Targets.* International Journal of Molecular Sciences. doi:https://doi.org/10.3390/ijms24065202

Siddique Md,. (2016). Socioeconomic Status & Health Seeking Behavior of Rural People: A Cross Sectional Study in Fatikchhari, Chittagong. . *MOJ Public Health*. doi:https://doi.org/10.15406/mojph.2016.04.00090

Singh et al. (2020). Drug-Resistant Tuberculosis and HIV Infection: Current Perspectives. HIV/AIDS. *Research and Palliative Care*. doi:https://doi.org/10.2147/hiv.s193059

Soedarsono et al. (2023). Characteristics of Previous Tuberculosis Treatment History in Patients with Treatment Failure and the Impact on Acquired Drug-Resistant Tuberculosis. *National Library of Medicine*. doi:https://doi.org/10.3390/antibiotics12030598

Soedarsono et al. (2023). Characteristics of Previous Tuberculosis Treatment History in Patients with Treatment Failure and the Impact on Acquired Drug-Resistant Tuberculosis. *National Library of Medicine*. doi:https://doi.org/10.3390/antibiotics12030598

Suchindran, S., Brouwer, E. S., & Van Rie, E. (2009). Is HIV Infection a Risk Factor for Multi-Drug Resistant Tuberculosis? A Systematic Review. *PLoS ONE*. doi:https://doi.org/10.1371/journal.pone.0005561

Sultana et al. (2021). HIV infection and multidrug resistant tuberculosis: a systematic review and meta-analysis. *BMC Infectious Diseases*. doi:https://doi.org/10.1186/s12879-020-05749-2

T, Ishinda; S, Takeshi;. (2016, Nov 3). Nrf2-ARE-Dependent Alterations in Zinc Transporter mRNA Expression in HepG2 Cells. *PLos One*. doi:10.1371/journal.pone.0166100.

(2019). *TB Stigma Measurement Guidance.* http://www.challengetb.org/. Retrieved from https://www.challengetb.org/publications/tools/ua/TB_Stigma_Measurement_Guidance.pdf

The Global MDT. (2007).

Tierney Dylan . (2018). *MSD Manual Professional Edition*. Retrieved from MSD Manuals: https://www.msdmanuals.com/professional/infectious-diseases/mycobacteria/tuberculosis-tb

Tiwari, D., & Martineau, A. R. (2023). Inflammation-mediated tissue damage in pulmonary tuberculosis and host-directed therapeutic strategies. *Seminars in Immunology*. doi:https://doi.org/10.1016/j.smim.2022.101672

Tortoli, E. (2006). *The new mycobacteria: an update. FEMS Immunology & Medical Microbiology.* doi:https://doi.org/10.1111/j.1574-

Total population of Kenya in 2019, by county. (n.d.). Retrieved from Statista: https://www.statista.com/statistics/1227219/most-populated-counties-of-kenya/

Van Den Hof et al. (2010). A systematic review on the role of gender in tuberculosis control. Retrieved from https://www.kncvtbc.org/uploaded/2015/09/Role_of_Gender_in_TB_Control.pdf

Waman et al. (2019). Mycobacterial genomics and structural bioinformatics: opportunities and challenges in drug discovery. *Emerging Microbes & Infections*. doi:https://doi.org/10.1080/22221751.2018.1561158

Wells et al. (2017).

WHO. (2015).

WHO. (2019).

WHO. (2020).

WHO. (2020). *Global tuberculosis report 2020.*

WHO. (2021). *TB guidelines*. Retrieved from Www.who.int.: https://www.who.int/publications/digital/global-tuberculosis-report-2021/featured-topics/tb-guidelines

Workicho, A; Kassahun, W; Alemseged, F;. (2017). Risk factors for multidrug-resistant tuberculosis among tuberculosis patients: A case-control study. Infection and Drug Resistance. doi:https://doi.org/10.2147/IDR.S126274

World Health Organization. (2008).

World Health Organization. (2014). *Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis.* Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK247427/

World Health Organization. (2018). *Global Tuberculosis Report 2018.* Retrieved from https://www.aidsdatahub.org/resource/global-tuberculosis-report-2018

World Health Organization. (2020). *Global tuberculosis report 2020.* Www.who.int. Retrieved from https://www.who.int/publications/i/item/9789240013131

World Health Organization. (2020). *Global tuberculosis report 2020.* Www.who.int. Retrieved from World Health Organization: https://www.who.int/publications/i/item/9789240013131

World Health Organization. (2022). *Medical doctors (per 10 000 population).* Retrieved from World Health Organization.: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/medical-doctors-(per-10-000-population)

World Health Organization. (2023). *Global Tuberculosis Report 2023.* Retrieved from https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023

World Health Organization. (2023). *TB incidence.* Retrieved from Www.who.int. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023/tb-disease-burden/1-1-tb-incidence

World Health Organization. (2023). *Tuberculosis.* Retrieved from https://www.who.int/news-room/fact-sheets/detail/tuberculosis

World Health Organization. (2024). *Tuberculosis*. Retrieved from World Health Organization: https://www.who.int/health-topics/tuberculosis#tab=tab_1

World Health Organization. (n.d.). *Www.who.int*. Retrieved from https://www.who.int/publications/i/item/WHO-HTM-TB-2015.19

Wrohan et al. (2022). Predictors of treatment outcomes among patients with multidrug-resistant tuberculosis in Vietnam: a retrospective cohort study. BMC Infectious Diseases. *National Library of Medicine*. doi:https://doi.org/10.1186/s12879-021-06992-x

Yu et al. (2018). Treatment Outcomes of Multidrug-Resistant Tuberculosis in Taiwan: Tackling Loss to Follow-up. *Clinical Infectious Diseases*. doi:https://doi.org/10.1093/cid/ciy066

Lee, J.-Y., Kwon, N., Goo, G., & Cho, S. (2022). Inadequate housing and pulmonary tuberculosis: A systematic review. *BMC Public Health*, *22*, 622. https://doi.org/10.1186/s12889-022-12879-6

Zimmer, A. J., Klinton, J. S., Oga-Omenka, C., Heitkamp, P., Nawina Nyirenda, C., Furin, J., & Pai, M. (2022). Tuberculosis in times of COVID-19. *Journal of Epidemiology and Community Health*, *76*(3), 310–316. https://doi.org/10.1136/jech-2021-217529

APPENDICES

Appendix 1: Consent Form

Hello, my name is _____ (doctor, clinical officer, or nurse's name), and I am a (doctor/clinical officer/nurse) working at this _____ (name) TB clinic.

You are being asked to take part in a study by **George Giathi Kamau** through FELTP to partially fulfil the degree of Master of Public Health of Moi University to assess the predictors as well as risk factors for the drug-resistant TB, including drug resistance tuberculosis (RRTB).

Why is this study being done?

Thanks to national as well as international efforts, many people have access to TB treatment all over Kenya. However, TB strains with the drug resistance (MDRTB) are a bit challenging to treat contrary to drug-susceptible ones and also threaten universal advancement toward the objectives put across by the End TB Strategy of the World Health Organization (WHO). Therefore, a vital requirement for the evidence-based policy recommendations on the predictors of MDRTB as well as the treatment and care of Individuals with the MDRTB founded on the latest as well as comprehensive evidence accessible. As such, the WHO consolidated directives on the drug-resistant tuberculosis treatment to accomplish the directive of the WHO to notify health professionals in the Member Nations on how to progress treatment as well as care for individuals with RRTB.

What is Multidrug resistant TB?

Multidrug-resistant TB (MDR TB) is triggered by the organisms resistant to at least isoniazid as well as rifampin, the two most potent TB drugs. These drugs are applied to treat all persons with Tuberculosis sickness.

How does drug resistance happen?

Resistance to anti-TB drugs takes place if the medicine are mismanaged. For instance if an individual fails to complete their entire course of dosage when healthcare physician recommend the wrong medicine, the wrong dose, the time for taking the

drugs, when the there is limited supply of medicine, or if the medicine are of poor quality.

Those at risk of contracting MDR TB?

Drug resistance is more popular in individuals who:

● fails to take their TB drugs often

● fails to complete their TB drugs as instructed by the care provider

● Contract TB illness again, after having taken TB drugs in past

● Come from regions of the globe where drug-resistant TB is more familiar

● spent quality time with an individual known to have drug-resistant TB illiness

What are the risks of taking part in the study?

There may be a few risks, including discomfort in producing the sputum. If problems occur at the site, the clinic staff will be available to offer treatment. Additionally, others may learn about your medical condition by participating in this study, despite our efforts to maintain all records confidentially.

What are the benefits of taking part in the study?

Your test result could help manage TB by determining the best treatment. Also, the survey will help estimate the rates of MDRTB in patients developing resistance to TB treatment in Kenya.

Do I have to take part in the study?

Your taking part in this survey is entirely voluntary. You can decide not to take part in the survey at all. You will still receive all the TB care and treatment services routinely provided according to national guidelines at this clinic whether you decide to take part.

Who can I talk to if I have any questions or concerns about this research study?

If you have questions about this survey or feel that you have been harmed due to the study, you may contact George Giathi Kamau Tel: +254721388092; Email address: georgegiathi@gmail.com.

If you have questions concerning your rights as a person taking part in a research study, don't hesitate to get in touch with the Secretary of The Moi Teaching & Referral Hospital / Moi University College of Health Sciences Institutional Research and Ethics Committee *(MTRH/MUIREC)*

How will my privacy be protected?

Your name, telephone number, or address will not be recorded in any forms or reports from this survey. The survey will only report group results. Your name will not be used. A code number will be used instead of your character. All collected information will be held confidential. You will be offered a copy of the consent form. As the research sponsor, FELTP may observe or audit research activities. The motive would be to ensure that the research is being conducted the way it is required to be. It would also ensure that your rights as well as health are safeguarded. Your private medical data will be reserved confidential; finally, you are free to ask any questions that you may have concerning the survey, or the procedure involved before we proceed.

Do you agree to take part in the survey?

□Yes □ No

Statement of Acceptance:

Certificate of Consent

I have gone through the above data, or it has been read to me. I have been asked to participate in the research above. I have had the chance to ask questions about it, and any questions I have asked have been answered to my gratification. I voluntarily consent to take part in this research.

Print Name of Participant	
Signature of Participant (or thumbprint of a participant if unable to sign)	
DD/MM/YYYY	

I have witnessed the correct reading of the consent form to the potential candidate, and the people has had the chance to ask questions. I confirm that the persons has given out their consent freely.

Signature of Witness	
DD/MM/YYYY	

Print Name/Title of Study Staff	
Signature of Study Staff	
DD/MM/YYYY	

Appendix 2: Questionnaire

Factors Associated with Multi-Drug Resistant Tuberculosis in Nairobi, 2022

1. General Information

Questionnaire number ☐

1. Status of patient

   ☐ Case ☐ Control

2. Date of interview DD / MM / YYYY _____ / _____ / _____

3. Interviewer Name_____

4. Health Facility details

   a) Name of Health Facility _____ Level 2, 3, 4, 5, 6

   ☐ Private ☐ Public ☐ Mission

   b) Name of Sub County_____

2. Personal details

1. Initials of patient _____ (*optional)*
2. Sex ☐ Male ☐ Female
3. Nationality _____
4. Date of birth dd / mm / yyyy ____/____/_____ Age in years_____

(***fill both & check for consistency***)

5. Religion

☐ Catholic ☐ Protestant ☐ Muslim ☐

None

Others specify_____

6. Marital status

☐ Single ☐ Married ☐ Cohabiting

☐ Separated ☐ Divorced ☐ Widowed

others specify_____

7. Level of education (highest level of formal education attempted or completed)

☐ None ☐ Primary ☐ Secondary ☐ Tertiary

Others specify_____

8. Current Employment

☐ Salaried employment ☐ Self-employed ☐ Not employed

☐ Casual employment ☐ Student

9. Have you changed your employment since the onset of your illness?

☐ Yes ☐, ***if no go to question 13***

10. If yes, what was your employment before your current illness

☐ Salaried employment ☐ Self-employed ☐ Casual employment

11. What means of Transport do you use to travel to the hospital for your treatment?

☐ On foot ☐ Motorcycle ☐ Private vehicle

☐ Bicycle ☐ Public transport

12. How long does it take to get to the health care facility from your residence?

_____(Minutes)_____(km)

3. Clinical information

Previous Medical history

1. When were you diagnosed to have the current episode of TB?

dd /mm/ yyyy ___ /____ /_____Duration of illness to the present date _____months

2. How was the TB diagnosed? (***check the TB register***)

☐ Bacteriologically confirmed ☐ Clinically diagnosed with an Xray ☐ Clinically diagnosed without an X-ray

(confirm from the TB facility register)

☐ New Bacteriologically confirmed PTB ☐ Relapse Bacteriologically confirmed PTB ☐

New Clinically diagnosed PTB ☐ Relapse Clinically diagnosed PTB ☐

Extrapulmonary TB ☐ Treatment Failure

3. What is your duration of TB treatment?

☐ 6 months ☐ 18-20 months Other specify_____

4. Was your TB treatment period changed from what you had been informed at the beginning of treatment?

☐ Yes ☐ No

If 'Yes' What were the reasons for the change_____

5. Were you, for any reason, during treatment for the current TB episode, unable to take your TB medicine?

☐ Yes ☐ No

If yes what were the reasons_____

If no, go to question 12

6. If yes in (8) above, for how long were you unable to take your medicine dates from dd/mm/yyyy_____/_____/_____ to _____/_____/_____ estimate the period

☐ less than one week ☐ 1 Week ☐ 2 weeks
☐ 3 weeks
☐ 4 Weeks ☐ 2 months ☐ 3 months
others specify_____

7. Did you continue taking the same medicines you had been carrying when you resumed treatment?

Yes ☐ No ☐

8. Was sputum sent to National TB Reference Laboratory for drug resistance testing?

Yes ☐ No ☐ ***if No go to question 13***

For those tested, what is the drug resistance pattern? (Check the District MDRTB register/ lab request forms)

Drug	Rifampicin	Isoniazid	Ethambutol	Streptomycin	
Sensitive					Not Available
Resistant					

Indicate if ☐ RRTB ☐ on RRTB ☐ XDR-TB

For Management of MDRTB are you on treatment? ☐ Yes No ☐

9. Were you admitted in the hospital at any time within two years before the onset of the current

Illness? ☐ Yes ☐ No

10. Did you come in contact with someone with TB or a chronic cough prior to the onset of the current illness?

☐ Yes ☐ No ☐ Don't Know

11. Have you ever received treatment TB Preventive Therapy(TPT) to protect you from developing TB Disease?

☐ Yes ☐ No Don't Know ☐

If yes for what reasons and how long? Reason _____duration _____months

12. Do you have diabetes?

☐ Yes ☐ No

13. Did you have any chronic lung condition prior to diagnosis of the TB?

☐ Yes ☐ No Don't Know ☐ If yes, what was the condition

☐ Asthma ☐ Other chronic lung condition

14. Were you tested for HIV during TB treatment?

☐ Yes ☐ No

If yes in 18 above, what were the results

☐ HIV+ ☐ HIV

15. If HIV positive are you on antiretroviral drugs

☐ Yes ☐ No

If on ART, when was it started relative to TB diagnosis? ☐ Before ☐ After

Indicate the difference in period of time_____

1. Have you ever been treated with anti-TB drugs before the current treatment?

☐ Yes ☐ No

If No, in 1 above, go to question 8

2. If yes, in 1 above, how many separate episodes of TB did you have _____

What were the dates, length of treatment and treatment outcomes of each of the episodes? **(ask the patient what they were told the treatment outcome was for each of the treatments)**

Date _____length of treatment _____

outcome_____

Date _____length treatment

_____outcome_____

Date _____length of treatment

_____outcome_____

3. Were you explained how to take the TB medicine during each TB treatment?

☐ Yes ☐ No

4. Were you, for any reason, unable to take TB medicine while undergoing any of the previous TB treatments?

☐ Yes ☐ No

5. If yes, for how long were you unable to take medicine?

Dates from dd /mm/ yyyy _____/_____/_____ to _____/_____/_____

☐ Less than I Week ☐ 1Week ☐ 2 weeks ☐ 3 weeks

☐ 4 Weeks ☐ 2 months ☐ 3 months

Other specify_____

6. Did you have someone observe you when taking your medicine during the previous episode of ordinary TB?

☐ Yes ☐ No

7. If yes in 6 above, how available was the person to observe you while taking treatment

☐ Daily ☐ Every 2 days ☐ Every 3 days ☐ Every 4 Days

☐ Every week ☐ Every 2 weeks ☐ Never Available

8. Did you receive the BCG (TB) vaccine during childhood or at any other time?

☐ Yes ☐ No Don't know

5. Behavioural and Social Economic Factors

1. Have you ever smoked cigarettes? ☐ Yes ☐ No ***If no, go to question 6***
2. If yes when did you commence (year) _____
3. Are you presently smoking? ☐ Yes ☐ No
   If not, when did you stop? Date dd/mm/yyyy_____/_____/_____
4. Duration of smoking? _____
5. How many sticks do you or were you smoking per day _____
6. Have you ever lived with someone who smokes? ☐ Yes ☐ No
   If yes for how long did you live with the person during his/ her active smoking_____
7. Any history of alcohol intake?

☐ Yes ☐ No If yes when did you start (Year/ month) _____

Are you currently taking alcohol? ☐ Yes ☐ No

If no when did you stop (Year/month) _____

Duration of alcohol intake_____

How frequent is or was the alcohol intake?

☐ Daily ☐ Weekly ☐ Monthly ☐ Occasionally

What type of alcohol were you or do you take? _____

How much were you/do you take per day glasses_____

8. Have you ever used any recreational substance (e.g. chewable tobacco, Miraa / Khat) ☐ Yes ☐ No

If yes, which one (specify)_____Is it current? Yes ☐ No ☐

9. Do you live with your family?

☐ Yes ☐ No

10. How many people do you live with_____?
11. What type of house do you live in?

☐ Temporary ☐ Semi-permanent house ☐ Permanent house

12. Who owns the house?

☐ Rental ☐ Personal ☐ Accommodated

If rental, how much rent do you pay per month? _____shillings

13. How many rooms are there in the house? _____

14. How many windows are in your room_____?

15. Do you open it/ them? ☐ Yes ☐ No

If yes, how many hours per day is a window open

☐ Less than an hour ☐ 1 hour ☐ 2 hours ☐ 6 hours

☐ 8 hours ☐ 10 hours ☐ 12 hours

☐ 24 hours others specify_____

16. Do you share the room with anyone else?

☐ Yes ☐ No ***(If no, go to question 18)***

17. If yes, in 16 or above, what is the age of those you share the house with?

Indicate their Age breakdown

1st ____2nd ____ 3rd _____4th _____ 5th ____6th ____7th ____8th ___9th ___ 10th_____

18. Have you ever been imprisoned or detained in police custody?

☐ Yes ☐ No

If yes, which one and how for how long? Prison/ custody_____ Duration weeks_____

19. Have you ever been in a situation where you did not have a house?

☐ Yes ☐ No

20. Have you ever stayed in a refugee camp or internally displaced persons camp?

☐ Yes ☐ No

If yes, which one and how for how long? Camp _____Duration _____Months

21. How many meals were you typically having per day before developing your current episode of TB

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 Others specify_____

22. Could you describe what you do while coughing?

_____

Decide if the patient practices cough hygiene

☐ Yes ☐ No

23. Have you disclosed the form of TB you have to anyone?

☐ Yes ☐ No

If yes, to whom have you disclosed? _____

If not, what are the reasons for nondisclosure?

_____

24. How much do you earn on average per month?

☐ >kshs 10,000 ☐ kshs (5,000 10,000) ☐ < kshs 5,000

25. What do you recommend to the TB control program regarding TB care? _

Appendix 3: Description of symbols used in the Fleiss formula for sample size

Description of Symbols in the Formula	Value
Z Score for the two-tailed test based on α level (z α/2)	1.96
Z - Score for the one-tailed test based on β level (z 1-β	0.80
The ratio of controls: cases (r)	1:2
The proportion of cases (Multi Drug Resistant TB) with HIV exposure (P_1)	50%
The proportion of controls (Drug sensitive TB) with HIV exposure (P_2)	29%
P_1	0.50
P_2	0.29
OR	2.4
Number of cases (n1) 65 + 10% for non-response	72
Number of controls (n2) 130 + 10% for non-response=	144
Total sample size (n1+ n2) 195+10% for non-response=	216

Appendix 4: Institutional Research Ethics (IREC)

MTRH/MU-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/341/2022
Approval Number: 0004313

15th December, 2022

George Giathi Kamau,
Moi University,
School of Public Health,
P.O. Box 4606-30100,
ELDORET- KENYA.

Dear Mr. Giathi,

PREDICTORS OF DRUG-RESISTANT TUBERCULOSIS AMONG INFECTED PATIENTS IN NAIROBI COUNTY

This is to inform you that ***MTRH/MU-IREC*** has reviewed and approved the above referenced research proposal. Your application approval number is ***FAN: 0004313.*** The approval period is **15th December, 2022- *14th* December, 2023.** This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, Material Transfer Agreements (MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***MTRH/MU-IREC.***
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***MTRH/MU-IREC*** within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***MTRH/MU-IREC*** within 72 hours.
v. Clearance for export of biological specimens must be obtained from ***MOH at the recommendation of NACOSTI*** for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***MTRH/ MU-IREC.***

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and other relevant clearances from study sites including a written approval from the CEO-MTRH which is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH) and its satellites sites.

Sincerely,

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
15 DEC 2022
APPROVED
P.O. Box 4606-30100 ELDORET

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOO

Appendix 5: IREC Amendments

MTRH/MU- INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference IREC/341/2022
Approval Number: 0004313

9th May, 2023

George Giathi Kamau,
Moi University,
School of Public Health,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Mr. Kamau,

RE: APPROVAL OF AMENDMENT

The Moi Teaching and Referral Hospital/Moi University College of Health Sciences- Institutional Research and Ethics Committee has reviewed the amendments made to your proposal titled:-

"Predictors of Drug-Resistant Tuberculosis among Infected Patients in Nairobi County".

We note that you are seeking to make an amendment as follows:-

- To change sample size from 148 cases and 148 controls: 296 to 72 cases and 144 controls: 216.

The amendment has been approved on 9th May, 2023 according to SOP's of MTRH/MU-IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
09 MAY 2023
APPROVED
P. O. Box 4606 - 30100 ELDORET

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH; Principal - CHS; Dean - SPH; Dean - SOD; Dean - SOM; Dean - SON

Appendix 6: NACOSTI

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Ref No: 514130

Date of Issue: 24/January/2023

RESEARCH LICENSE

This is to Certify that Mr.. George Gathi Kamau of Moi University, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act, 2013 (Rev.2014) in Nairobi on the topic: PREDICTORS OF DRUG-RESISTANT TUBERCULOSIS AMONG INFECTED PATIENTS IN NAIROBI COUNTY for the period ending : 24/January/2024.

License No: NACOSTI/P/23/23112

514130

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

See overleaf for conditions

Appendix 7: Nairobi County Ethical Approval

NAIROBI CITY COUNTY

Telephone 020 344194

Web: www.nairobi.go.ke

City Hall,
P. O. Box 30075-00100,
Nairobi,
KENYA.

COUNTY HEALTH SERVICES

REF: NCCG/DHS/REC/288 **DATE: 20th January 2023**

GEORGE KAMAU
MOI UNIVERSITY
ELDORET

Dear Mr. George,

RE: RESEARCH AUTHORIZATION

This is to inform you that the Nairobi City County – County Health Services Research Ethics Committee (REC) reviewed the documents on the study titled "Predictors of Drug Resistant Tuberculosis among Patients infected with Tuberculosis in Nairobi County."

I am pleased to inform you that you have been authorized to carry out the study in Nairobi County. The researcher will be required to adhere to the ethical code of conduct for health research in accordance to the Science Technology and Innovation Act, 2013 and the approval procedure and protocol for research for Nairobi.

On completion of the study, you will submit one hard copy and one copy in PDF of the research findings to the REC. In addition, you will disseminate recommendations of the research at a virtual meeting organized by the REC. By copy of this letter, all the Sub County Medical Officers of Health are to accord you the necessary assistance to carry out this research study.

Yours sincerely,

DR. ANDREW TORO
CHAIR - RESEARCH ETHICS COMMITTEE

Cc: Chief Officers – Medical Services, Health Facilities
County TB Coordinator
All the Sub County Medical Officers of Health

Appendix 8: Glossary

New case: A patient who has never been treated for TB or even taken anti-TB drugs for less than 28 days

Previously treated patients: have gotten 1 month or more of the anti-TB drugs previously. They are further categorized by the result of their most current course of treatment as follows:

i. **Relapse patients** formerly treated for TB, were confirmed treatment completed at the end of their most recent course of treatment, and are now diagnosed with a persistent episode of TB (either a true relapse or a new episode of TB caused by reinfection).
ii. **Treatment after failure**: Patients were previously treated for TB and whose treatment unsuccessful at the end of their most current course of treatment.
iii. **Treatment after loss to follow-up**: Patients have beforehand been treated for TB and were confirmed lost to follow-up at the end of their most current course of treatment. (These were previously known as treatment after default patients.) Other previously treated patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

Relapse: A patient who has undergone previous treatment for TB and has been declared cured or completed the full course of treatment but is now diagnosed with bacteriologically positive TB (confirmed through smear or culture).

Failure: A patient who is sputum-smear negative in the last month of treatment and on at least one previous occasion.

Cured: A patient who tests negative for sputum smear in the final month of treatment and has also tested negative on at least one prior occasion.

Return after default (RAD): A patient who restarts treatment and tests positive for bacteriological evidence of tuberculosis (TB) following a treatment interruption of 2 months or longer.

Treatment completed: A patient who has finished the prescribed treatment but does not meet the criteria for being classified as "cured" or "treatment failure."

Default: A patient whose treatment was discontinued for a consecutive period of two months or longer.

Transferred out: A patient who has been transferred to a different recording and reporting unit, and whose treatment outcome is not known or documented.

Appendix 9: Plagiarism Check

SR461

ISO 9001:2019 Certified Institution

THESIS WRITING COURSE

PLAGIARISM AWARENESS CERTIFICATE

This certificate is awarded to

George Giathi Kamau

FELTP/5435/21

In recognition for passing the University's plagiarism

Awareness test for Thesis: entitled: **PREDICTORS OF DRUG-RESISTANT TUBERCULOSIS AMONG INFECTED PATIENTS IN NAIROBI COUNTY with** similarity index of 3% and striving to maintain academic integrity.

Word count: 20139

Awarded by

Prof. Anne Syomwene Kisilu
CERM-ESA Project Leader
Date:
01/03/2024