

**MODELLING SPATIOTEMPORAL SURVIVAL PATTERNS AND  
SURVIVAL ANALYSIS OF HIV-TB CO-INFECTED PATIENTS IN  
SELECTED COUNTIES IN KENYA**

**BY**

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## DECLARATION

### Declaration by Candidate

This thesis is my own work and has not been previously presented for an award in this or any other learning institution. No part of this thesis may be replicated without prior consent of the author and/or Moi University.

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## **DEDICATION**

To Almighty God for the guidance, strength, power of the mind, protection, and good health to complete the research work.

To my supervisors on their intellectual guidance needed in my research work.

To my wife, Mrs. Linet Bitutu, To my sons, Newton, Laprussian and Annan for their patience, Love and Support throughout the thesis process

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## ABSTRACT

The illnesses tuberculosis (TB) and the human immunodeficiency virus/acquired immune deficiencies syndrome (HIV/AIDS), which result in approximately 10 million illnesses and 1.45 million fatalities each year, account for a sizeable share of the global burden. HIV survival rates are decreased by co-infection with TB because it is more difficult to manage and treat HIV. The objective of the project was to mimic in a few Kenyan counties the spatial-temporal survival dynamics of patients who also had TB and HIV infections. The study's specific objectives included comparing the survival rates of patients receiving ART and TB treatment in a few Kenyan counties with those receiving ART alone, analyzing geographic variations in associated patient deaths, demonstrating the spatial-temporal the distributions of HIV/TB fatalities, and using a Bayesian model to look into regional/county demographic factors associated with survival rates in a few Kenyan counties. A retrospective collaborative research methodology was used in the project. The patients who received co-therapy for TB and ART maintenance at medical hospital through January 1, 2015, and December 31, 2019, comprised the target population. This information was compiled using the National AIDS & STIs Control Program (NASCOP) database, which contains all the records of patients from the chosen Kenyan counties that had associated with HIV and TB. The Kaplan-Meier estimator was used to calculate the survival function. A Cox Proportional Hazard Regression Analysis was fitted in a multivariate analysis to assess subject survival trends and the influence of covariates on survival time. The fit of the data to the Cox proportionate hazard regression model is given by the log component likelihood function. The hazard ratios for every covariate data, under consideration were tested for statistical significance using the Log-rank, Score, and Wald tests. A Bayesian model was created to display the temporal and spatial variance in mortality hazard by County in Kenya. STATA 14.2 and Bayes 3.0.2 were used for the analysis. The results showed that 2,555 (7.9%) of the HIV and TB patients in Kenya reported passing away five years after starting ART. The mean duration of event incidence for the category receiving both ART and treatment for TB was 4 years, according to the mean surviving time for the resultant (dead) cases of 4 years. The study's log-rank test showed a p-value of 0.00, indicating that the two curves were statistically independent from one another. The p-value of 0.000, which was lower than the value of the p-value at the 5% significance threshold, demonstrates this. The probabilistic survival of those with HIV and TB mutual infection is thus impacted by ART and TB treatment. More persons with TB and HIV illnesses survived more time when they obtained both ART and antibiotics for TB compared to when they only received ART up until about the 750th day. Between 2015 and 2019, the study also discovered geographical disparities in the mortality rate for HIV-TB patients. The study also found that over a five-year period, the frequency of TB and HIV mortality varied in the selected Counties. The study discovered that ART and TB therapies, marital status, gender, WHO diagnostic stage, age, weight, and institution of residence are the key factors influencing HIV-TB patients' survival rates. Starting medicine later in the course of the medical condition may have less of an effect on lowering TB/HIV than targeted therapies in the initial few weeks and months after ART began. HIV-rationality. As a result, the use of ART and TB treatments, as well as demographic variables and geographic determinants, each have a statistically noteworthy impact on the life expectancy of HIV/TB infected as well individuals. The study urges the MoH to give preference to the use underlying ART and TB medication, the assessment of demographic traits, and spatial variables in order to increase survival

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## ACRONYMS AND ABBREVIATIONS

AFT:	Accelerated Failure Time Model
AIDs:	Acquired Immunodeficiency Syndrome
ART:	Antiretroviral Therapy
ATT:	Anti-Tuberculosis Treatment
CPT:	Cotrimoxazole Preventive Therapy
DIC:	Defiance Information
DOT:	Directly-Observed Treatment
EEA:	European Economic Area
EMR:	Electronic Medical Records
ESDA:	Exploratory Spatial Data Analysis
EU:	European Union
GIS:	Geographic Information System
HIV:	Human Immunodeficiency Virus
HMIS:	Health Management Information System
HR:	Hazard Ratio
INLA:	Integrated Nested Laplace Approach
IREC:	Institutional Research Ethics Committee
K-M:	Kaplan-Meier
LISA:	Local Indicators of Spatial Associations
MDR-TB:	Multi-Drug Resistant Tuberculosis
MOH:	Ministry of Health
NASCOP:	National AIDS & STIs Control Program
NTLD-P:	National Tuberculosis Leprosy & Lung Disease Program
PEPFAR:	President's Emergency Plan for AIDS Relief

PLWHA:	People Living With HIV/AIDS
PR:	Probability Ratio
SNNP: SSA:	Southern Nations, Nationalities, and People Sub-Saharan Africa
TB:	Tuberculosis
TIBU:	Tuberculosis Information from Basic Unit
UNAIDS:	United Nations Programme on HIV/AIDS
WHO:	World Health Organization

## DEFINITIONS

**HIV/TB Confection:** This occurs when a person has both latent or active TB disease as well as HIV infection.

**Human Immunodeficiency Virus:** Due to the virus's attack on immune system cells, a person is more susceptible to contracting further illnesses and infections.

**Prevalence:** The proportion of a particular population with specific characteristics over a specified period.

**Spatial Patterns:** These are geographic observations representing the occurrence of a disease and its characteristics across different locations.

**Temporal distribution:** This refers to the occurrence of a disease across time in a specific location.

**Tuberculosis:** This is a contagious infection caused by bacteria (*Mycobacterium tuberculosis*) that is transmitted the lungs most frequently when contracted from breathing in tiny droplets from an infected person's cough or sneeze.

## **CHAPTER ONE**

### **INTRODUCTION**

#### **1.1 Background of the Study**

According to a WHO (2019) report, the Human Immunodeficiency Virus (HIV) has proven to be a significant obstacle in the fight against TB over the years. Since the early 1980s, when HIV first emerged, tuberculosis and AIDS have been the two main causes of mortality among people with HIV. According to Hayibor, Bando & Kenu (2020), one-third of the 36.9 million PLWHA worldwide were co-infected with TB in 2019. Of the over 10 million people with active TB in 2019, 9% were HIV positive. Additionally, roughly one-third of AIDS-related deaths in 2018 were brought on by TB.

By starting early ART, detecting TB, and starting treatment, HIV/TB partnership initiatives were created by the World Health Organization (2019) to improve the various systems for delivering comprehensive HIV and TB services and lessen the burden of TB in individuals living with HIV.

Although the Kenyan government and non-governmental groups have put numerous efforts in place to decrease the incidence of HIV/AIDS and TB, the infection still cause a sizable portion of the country's fatalities (Otiende, Achia & Mwambi, 2020).

According to studies (Dhungana, Sharma, Khadga & Verma, 2013), early ART introduction during TB treatment improves patient survival, lowering HIV-TB co-infection prevalence. This research aims to identify the patterns in patient survival within this target demographic.

### **1.1.1 Co-infections with the human immunodeficiency virus (HIV) and tuberculosis (TB).**

HIV is a virus that weakens the body's defenses against infection. Due to the body's reduced immunity, the degradation of the immune system makes the body vulnerable to various opportunistic illnesses. AIDS, a deadly disease of an HIV-positive patient, has no known cure yet. Other dermatological conditions like acne and tuberculosis are examples of opportunistic infections. In addition, TB is a treatable and preventable, it is caused by bacteria and interferes with lung cells. In this context, a co-infection occurs when an HIV patient contracts TB as an opportunistic infection due to weakened body defenses. According to a 2019 WHO report, HIV- positive people are 20 to 30 times more likely than HIV-negative people to get active TB. A diagnosis of active TB in HIV-positive people represents the transition from HIV to AIDS.

### **1.1.2 Spatial Temporal Patterns**

Describing observations of medical conditions (in this case, HIV-TB prevalence) as well as their regional variation and geographic distribution are considered to be spatial patterns, according to Sankey (2017). The study will be able to better understand how or whether local factors, such as ecological, demographic, genetic, and socioeconomic factors, influence co-infection survival patterns, the use of ART, and the care and treatment of TB. The condition's chronological component is the distribution of an event throughout a specific time period and season, such as the co-infection of HIV and TB. Therefore, a spatial-temporal study of HIV/TB concurrent infections allows for the evaluation of events like disease and death along space and time at a specific location and time frame.

### **1.1.3 Survival Analysis**

The "survival analysis" branch of statistics looks at how long an event, such as a living being dying or a machine breaking down, is likely to happen. The deaths following the application of ART and the beginning of TB care will be the event of interest in HIV-TB co-infection.

### **1.2 Statement of the Problem**

HIV contributes greatly to the TB pandemic in different countries worldwide (Mabuza & Shumba, 2018). In addition, in high HIV prevalence regions, tuberculosis is one of the reasons of mortality and morbidity within prevalence HIV patients. The HIV infection rate in Kenya in 2019 stands at 4.7% (ages 15-49); hence, it is assumed that one of the nations with a high infection rates of HIV prevalence around the globe (UNAIDS, 2018). Together with Mozambique, Uganda, and Tanzania, Kenya has the third-largest pandemic of HIV in the world as of 2018 with around 1.6 million HIV-positive individuals (Nduba, 2019). Kenya is also ranked 10th globally out of 22 nations with a high TB burden. According to the Centers for Disease Control, TB had a probable prevalence of 558/100,000 in 2018, up from 233/100,000 in 2015, and a fatality rate of 50/100,000 in that same year.

HIV and TB interact, with TB raising the mortality rate in HIV patients and HIV increasing the incidence of TB. Several programs in Kenya have been geared towards reducing HIV/TB-related deaths. For instance, through PEPFAR, the CDC Kenya has collaborated with numerous parties including Kenya MOH and local partners, to promote and expand HIV and TB prevention and control initiatives (Centers for Disease Control, 2018). In addition, Kenya has NTLD-P and NASCOP responsible for monitoring and managing TB and HIV/AIDs, respectively.



Mortality of co-infected TB/HIV patients in the country remains high despite several efforts to contain the disease. As such modeling of the spatial and temporal distribution of the mortality of HIV/TB co-infected patients for different parts of the country will play a key role in developing strategies focusing on specific regions and risk factors associated with mortality and survival rate.

### **1.3 Objectives of the Study**

#### **1.3.1 General Objective**

To model spatiotemporal survival Patterns of HIV-TB co-infected patients in selected counties in Kenya and Regional /county demographic factors associated with Mortality trends.

#### **1.3.2 Specific Objectives**

Specific objectives are to:

- i. Determine the survival rates of patients receiving ART plus TB treatment and those receiving ART alone in selected counties Kenya.
- ii. Analyze spatial variations of deaths of HIV-TB co-infected patients (individuals with HIV and tuberculosis infections).
- iii. Model temporal distribution of HIV and TB deaths in selected counties in Kenya.
- iv. Determine regional/county demographic factors associated with survival trends.

### **1.4 Significance of the Study**

HIV and TB contribute considerably to mortality and morbidity in Kenya. The two diseases also considerably impact the labor productivity of the patients. In addition, HIV and TB have high treatment and non-treatment costs that individuals and the government often bear. This negatively affects the achievement of Vision 2030, the Big

Four Agenda, and the United Nations Sustainable Development Goals. In addition, to deliver scalable integrated health care, particularly for important groups, finance for the HIV response continues to be a serious barrier that has to be addressed. In Kenya, approximately 75 percent of national HIV and TB response programs are externally funded. However, the country cannot continue depending on external funds only. Hence, more financing strategies must be developed to ensure sustainable financing of HIV/TB co-infection programs. Further, young people require targeted interventions, improved monitoring, and reporting.

To the Ministry of Health in Kenya, the research gave data on the current status of HIV and TB mortality in Kenya, which in line contributes to the overall mission and vision of Kenya Health policy 2014 to 2030, the Vision 2030, and NTLD-P.

Health 2019 – 2023 focuses on reducing HIV and TB death rates in Kenya. This goal requires a paradigm change from the sector of health directed on a multiple-sectoral strategy for the TB and HIV prevention and care, including County-based organizations. As such, the study provides information on most affected Counties in terms of HIV/TB co-infection rate and the mortality rate.

To the NTLD-P, National AIDS & STIs Control Program, and HIV/TB program financiers such as the PEPFAR, the research will give data that will be essential on the impact of their programs on the survival of HIV and TB patients that can be used in the review of current strategies, formulation of new strategies and in making informed decisions on resource allocation to various programs.

### **1.5 Study Limitations**

Limitations of the study included accessing data without necessary authorizations and time to obtain the authorizations and missing data due to some patients who dropped out of the study.

## **CHAPTER TWO**

### **LITERATURE REVIEW**

#### **2.1 Introduction**

This chapter outlines the reading list for a study of the research on the survival rates and regional and temporal prevalence of a combination of viruses with HIV and TB. After giving a general review of TB and HIV co-infection, it is discussed the comprehensive therapy for HIV and TB mutual infection, indicators of risk for TB/HIV mutual infection, the survival rates of patients on ART and therapy for TB, and the regional distribution of death among individuals with both HIV and TB co-infection.

#### **2.2 HIV Infections**

HIV focuses on the immune system's weaknesses and reduces a person's resistance to numerous infections such as cancers that those with strong body immunity have the ability to combat. People with the disease progressively lose their immunological function as the virus destroys and affects body cells. The CD4 cell count is widely put in practice to check immune uses. Based on the person, developing AIDS, which is the most severe stage of HIV infection, may consume many years to stabilize. When some tumors, infections, or other serious long-term clinical indications occur, AIDS is present.

The indicators of HIV infection depend with infection stage. Although the first few months following HIV infection are usually when people are most contagious, a lot people do not get to understand that they have the disease until later. Others might develop flu-like symptoms including a high temperature, throat redness, or headache during the first few weeks after contracting the illness. As the virus steadily impairs the immune system, they may also experience additional signs and symptoms like as swollen lymph nodes, weight loss, a high body temperature, vomiting, and cough.

People run the danger of getting potentially fatal illnesses like Kaposi's sarcoma and lymphomas, severe bacterial infections, cryptococcal meningitis (CM), and tuberculosis (TB) in the absence of medical care.

Blood, which is breast milk, semen, and secretions from the genitals are among the fluids produced from body of people with the infection that can transmit HIV. A mother who has HIV infection bears the risk of transmitting the viral infection to her unborn child during pregnancy and delivery. Hugging, kissing each other, grasping hands, or exchanging greetings with someone else, as well as typical daily activities like them, do not spread disease. Remember that HIV-positive individuals who are receiving antiretroviral medication (ART) and having their viral loads decreased do not transfer the virus to their sexual partners. Antiretroviral therapy (ART) must therefore be started as soon as possible, and patients must get support to complete it in order to increase their health and stop HIV transmission.

Antiretroviral (ARV) medication combinations can be used in HIV treatment plans. As it is currently practiced, antiretroviral therapy (ART) lessens viral replication while allowing a patient's immune system to recover, strengthen, and regain its ability to combat diseases such as HIV, infections that are opportunistic, some types of cancer, and other kinds of infections. Despite of medical condition, WHO has advocated since 2016 for the administration of lifespan ART for every HIV-positive people, including kids, teenagers, adults, pregnant women, and nursing mothers. The 189 countries have already adopted this proposal by June 2022, giving medication to 99% of the HIV-positive population globally. Along with the cure, WHO supports providing ART as quickly as possible to all HIV-positive people, not exempting those who are ready to start medication the very day as they receive their diagnosis. 97 nations that had confirmed their endorsement of this plan by June 2022 declared that it had been

executed on a national level. The HIV approach still struggles with advanced HIV illness. Patients who frequently seek or re-seek medical care are more likely to develop opportunistic infections due to advanced immune suppression. In order to decrease illness and death, WHO is assisting governments with ensuring the use of the advance HIV disease package of care.

In China, Guoping, Li, Chunqing, and Stephanie (2017) assessed the effect of HIV/AIDS on children and families. This research combined qualitative and quantitative methods in a mixed technique. In Anhui, China, focus groups with local schoolteachers, village leaders, people with HIV/AIDS, and also those who care for HIV-positive children were held. One hundred fifty-four family members of HIV-positive children underwent in-person interviews. According to the study, families affected had annual incomes per person that were significantly below the province average by HIV/AIDS. HIV had an impact on the wealth and interaction of families. How well they did in school provided evidence of how HIV affected youngsters were affected. Children's nutrition and health were also impacted.

Eilami, Nazari, Dousti, Sayehmiri, and Ghasemi (2018) assessed HIV/AIDS-related risk components of FSW between 2010 and 2017. Researchers carefully examined PubMed, Embase, and Scopus to locate English-language papers that discussed the infection of virus and the conditions that form risks of FSW. The 37 publications were chosen for this meta-analysis because they were the most pertinent and high-quality studies. To review full texts, any cross-sectional, group, or descriptive studies examining the association between a risk factor or collection of various risk factors, as well as the virus rate of transmission, were considered. According to the study, FSWs have a significant transmission rate of HIV infection. The research discovered that because of the high frequency and daily sexual relationships with various partners, FSW

may be a major group in HIV/AIDS transmission. Furthermore, the prevalence of intravenous drug usage among FSWs and the use of condoms infrequently highlight these groups' role in the transmission of HIV/AIDS more than ever.

In Kuwait, Alhasawi et al. (2019) assessed senior secondary school students' knowledge, awareness, and attitudes about HIV/AIDS. Moreover, cross-sectional research measuring students' attitudes and knowledge concerning HIV/AIDS was carried out on a sample of 346 students in eight randomly chosen secondary schools throughout three. The respondents were given the questionnaires to fill out. While the study's participants were cognizant of the nature and process of HIV/AIDS distribution, they needed more information to prevent stigmatizing and discrimination against those who were affected.

Research by Gifford, Cunningham, Heslin, and Andersen (2017) examined how HIV-positive patients acquire experimental therapies and participate in research. A sample of 2864 people who represented the 231,400 persons with HIV infection and getting care throughout the contiguous US were questioned separately between 1996 and 1998. The study found that non-Hispanic Whites and non-Hispanic Blacks were much less likely to participate in clinical trials. Compared to individuals with fee-for-service insurance, those receiving care from private healthcare providers significantly less likely to participate in clinical trials. Women were not disadvantaged in research studies and were just as probable to receive experimental medicines. The study found that the capacity of people with HIV to become involved in research trials and get experimental medicines depended on their racial or cultural background and the type of health insurance they had. Hernandez-Romieu et al., (2019) conducted a study to examine whether, from 2009 to 2010, HIV-infected people had a greater prevalence of diabetes than the general population. The study included data from the National Health and

Nutrition Examination Survey, encompassing 5604 people from the general population, and the Medical Monitoring Project, which included 8610 people with HIV. The study also examined and compared the weighted prevalence of diabetic mellitus (DM) in two populations and variables related to DM in HIV-positive individuals. These analyses were done using fit logistic regression models. According to the study, one in ten HIV-positive adults receiving medical attention developed DM. Although DM risk among HIV-infected persons is increased by obesity, comparisons to the general population indicate that DM in HIV-infected individuals may occur earlier in life and without obesity.

In 2016, Mohammadnezhad et al. conducted a systematic review of the literature on the prevalence, etiology, and risk factors for HIV/AIDS in Pacific countries. The Cochrane Library Guidelines were utilized in this systematic review study to search, gather, and analyze HIV/AIDS-related resources. To analyze the data, data extraction forms and summary statistics were produced. Ethnicity and gender were the most common characteristics in community-based studies, as opposed to age and ethnicity in educational institutions research and age for hospital-based research. The greatest risk associated with HIV were substance abuse, an excessive amount of sexual collaborators, and unsafe contact.

In two metropolitan hospitals in Ghana, Ogyiri, Lartey, and Ojewale (2022), we conducted a retrospective cohort research to examine whether HIV infection influences TB treatment results and period to death. The study examined the medical records of TB patients who received care in two metropolitan hospitals in the Accra Metropolitan Area between January 2013 and December 2015. The relationship between HIV infection and TB treatment results was assessed using a modified Poisson regression analysis. The study found that co-infected participants were taking up relatively



minimal ART. Therefore, steps should be taken to increase ART coverage for people with HIV/TB co-infection to aid in lowering the death rate.

Asante and Oti-Boadi (2018) examined undergraduate students' knowledge of HIV/AIDS and how Ghanaian HIV prevention programs could utilize it. A cross-sectional study involving 324 chosen students in a tertiary institution within Accra, Ghana, was carried out utilizing structured questionnaires. The study revealed that students in Ghanaian tertiary institutions are aware of HIV/AIDS, have used electronic and print media as their sources of information about the disease (especially television and the internet), and most have not taken HIV tests. However, some are aware that counseling and testing services are accessible.

Kimera, Vindevogel, Reynaert, Justice, Rubaihayo, and De Maeyer (2020) investigated how stigma associated with HIV affects young people living with the disease in Western Uganda. To learn more about HIV-related stigma lived experiences in 11 Youth Living with HIV/AIDS (YLWHA) (15–19 years old) who had been purposefully chosen from a peer support group held at a hospital, photovoice was used. Transcripts of group interviews, notes, and images were examined through phenomenological hermeneutic analysis. Participants' photographs and accounts frequently featured encounters with externalized, internalized, and anticipated stigmas and the consequences that followed. According to the report, the stigma associated with HIV for youth living with HIV/AIDS includes being devalued, afraid, encountering injustices, feeling lonely, and having no hope for the future. The study found that HIV-related stigmas were prevalent in homes and schools, which are supposed to be safe spaces for children, and in other socio-ecological domains.

In Tanzania, Chambuso, Shadrack, Lidenge, Mwakibete, and Medeiros (2018) have examined the effect of HIV/AIDS on Cervical Cancer. The Morogoro Regional Referral Hospital examined 536 women using visual examination techniques over three years. The women were divided into various groups based on HIV status for the comparative retrospective analysis. The research found that virus has a highly adequate relationship and great effect on the growth of cervical precancerous lesions in HIV infected women; nevertheless, its clear engagement in development to invasive cervical cancer, more so in this era of highly active ART, is questionable. According to the research, HIV incidence decreased across all age categories and marginally skewed toward older ages. Women aged 15 to 24 and males aged 20 to 29 have a disproportionate number of new HIV infections, encouraging targeted prevention in these populations.

Risher, Cori, Reniers, Marston, Calvert, and Crampin (2021) assessed HIV age patterns in southern and eastern Africa. In a joint assessment of the ALPHA network, the study employed the model of Bayesian was used to rebuild age-specific HIV prevalence from repeated data of people's HIV serostatus and survival obtained among population HIV cohorts in rural Malawi, South Africa, Tanzania, Uganda, and Zimbabwe. The study evaluated the mean age at diagnosis and the percentage of new infections by age using estimated incidence and prevalence estimates for 2000–17, standardized to study population distribution. According to the study, HIV incidence decreased across all age categories and marginally skewed toward older ages. Men and women between 20 and 29 years have disproportionately more new HIV infections, which supports targeted prevention in these age groups.

In Uganda, Ruzagira et al., (2021) assessed HIV incidence and prevalence in the HIV vaccine readiness cohort based in rural Communities. An HIV seroprevalence survey

based on house-to-house was conducted from February to July 2004 among consenting persons aged 18 and 60. Interviews, counseling, and requests for blood samples for HIV testing were made of the participants. The participants in the study were then enrolled in two-year HIV sero-incidence research. Every three months, patients received medical assessments, HIV testing and counseling, and sample collection for lab analysis. Data on sexual risk behavior was gathered every six months. The study discovered high HIV prevalence although a low incidence of HIV, which means that a vaccination efficacy study in the community may not be possible due to the huge sample size of the study that would be necessary.

Rehima, Zenebe, Mamo, and Shaka (2019) examined the factors that affect HIV infection in children delivered from women participating in a southern Ethiopian program to prevent mother-to-child transmission of HIV. To prevent mother-to-child transmission (PMTCT), 27 health facilities in Southern Ethiopia were used in a multicenter facility-based mismatched case-control study. The study collected data from 290 mother-child pairs of 58 cases and 232 controls. Cases included children born by mothers participating in the PMTCT program who had tested positive for HIV by DNA PCR or antibody at below or equal to 24 months of age. According to the study, infants born to women who lived in rural areas and delivered at home had low partner engagement in PMTCT, were aware of HIV status during recent pregnancy, had poor adherence to ART, and had a higher risk of developing MTCT. Additionally, mixed-fed children enrolled on ARV prophylaxis late and did not receive cotrimoxazole therapy had an increased risk of contracting HIV from their mothers using PMTCT.

The research involved two parallel, longitudinal studies based on the community conducted in the South African cities of Vulindlela and Greater Edendale. The 2014 survey included 9812 respondents from 11 289 houses, and the 2015 survey had 10 236

respondents from 12 247 households. The study randomly chose census enumeration areas using a multistage cluster sampling technique. Randomly chosen families in every census enumerator area were allowed to choose one age-eligible (15–49 years old) study participant per willing household. Each willing subject was given a standardized questionnaire to gather data. According to the study, HIV incidence has dramatically decreased among young women (aged 15 to 19). Still, it has decreased a little or remained stable among men and women in other age groups. Antiretroviral therapy, viral suppression, HIV-positive status knowledge, and medical male circumcision all witnessed an increase simultaneously.

Dzah, Tarkang, and Lutala (2019) used a descriptive, cross-sectional design to examine senior high school (SHS) students' knowledge, practices, and attitudes linked with HIV/AIDS. Data were gathered in August 2017 from a stratified sample of 294 seniors chosen from 3 selected high schools using a validated self-administered questionnaire. Participants exhibited negative views toward PLHIV, lacked adequate knowledge of HIV/AIDS, and engaged in risky behaviors that could have put them at risk for HIV transmission.

A study by AMREF (2020) assessed how HIV/AIDS influences universities and the host communities, as well as the reactions and management gaps in the epidemic that might be utilized to improve and broaden national and regional interventions. A total of 3942 students from six universities in Kenya, including four from the Lake Victoria Basin, made up the study's representative sample. Significant knowledge was seen among students in the universities examined, although it is unclear whether this has any bearing on risky behavior. Unprotected sex, numerous sexual partners, sex for favors, intergenerational sex, sex with lecturers, mobility and sexual assault, anal sex, the influence of alcohol and drugs, decrease in primary abstinence with increment in the

year of study, and also infection with other STI's, among other risky behaviors among students that can provide the engine that compels the spread of HIV in the university. The survey also found that condom usage, abstinence, and availability of HIV information via university-level courses as a common unit, and also HIV testing, were recognized as important interventions associated with HIV and AIDS prevention in universities across the country.

Yang, Li, and Subramanian (2021) evaluated young women in middle- and low-income countries' HIV/AIDS knowledge and its relationship to socioeconomic differences from 2003 to 2018. This cross-sectional analysis examined data about HIV/AIDS awareness from 51 LMICs from 2003 to 2018 from nationally representative health and demographic surveys. The total data set included 282,757 female students. The study investigated socioeconomic inequalities and changes in knowledge for 40 LMICs with several surveys available. Survey data analysis occurred between December 1, 2019, and July 31, 2020. Among young women, less than one-third reported having an accurate understanding of HIV/AIDS, and the survey indicated low levels and wide disparities in this knowledge.

Musyoki, Kellogg, Geibel, and Muraguri (2019) examined the frequency of HIV, STDs, and risky behaviors among Kenyan FSWs in Nairobi. A respondent-driven sample survey was used for the investigation. Participants had to be 18 years old and have sold sex at least once in the previous three months to be eligible—FSWs who provided consent filled out a questionnaire and had tests for HIV and other STIs. The log-binomial regression analysis determined the parameters significantly linked to HIV infection. The analysis included 596 eligible respondents. The study determined that using a male condom as a form of contraception, using a condom inconsistently with paying customers, and being older were all independently related to undiagnosed HIV

infection—low rates of STI prevalence, including Chlamydia, gonorrhea, and syphilis. The study suggested high HIV prevalence among FSWs within Nairobi.

In Kenya, Waruru, Wamicwe, Mwangi, and Achia (2021) conducted a study to assess the newly diagnosed HIV Positives. Between 2015 and 2016, the study examined facility-level HTS data. Moran's Index (Moran's I) was used to identify hotspots of recently diagnosed HIV-positive results to evaluate the local and global spatial autocorrelation of recently HIV-positive tests. The study found that whereas counties with high HIV burdens include clusters of locations with a large number of recently HIV-infected people, most of these clusters were also found in counties with low HIV burdens. Geospatial analysis and mapping simplify ascertaining and defining localized outbreak trends in spatially distributed pandemics. As a result, refocus and prioritize HTS methods to extend HTS where it is most necessary and achieve the "first 90" targets.

### **2.3 TB Infections**

In a nation with low TB incidence, Nina, Martinsen, and Jensen (2022) conducted cohort research on the long-term effects of latent infection. The study comprised socially disadvantaged individuals who had received an LTBI diagnosis while taking part in TB screening in high-risk settings in three significant Danish cities (Aalborg, Aarhus, and Esbjerg) between 2010 and 2020. Through local databases of screening findings, study participants were contacted. The study discovered that those with LTBI who are socially excluded have greater rates of TB development. Even though TB failed to manifest in the first two years after TPT, the administration of TPT did not decrease the prevalence of TB overall significantly.

Song, Zhao, Zhang, Liu, and Zhu (2021) examined COVID-19 and TB Coinfection in CHINA. A comprehensive search of related literature was carried out using PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and 2 Chinese databases for publications released up until December 18, 2020. Additionally, a review of COVID-19 case reports and case series was created, highlighting the clinical characteristics and variations between patients who are still alive and those who have passed away. Utilizing GRADEpro, the effectiveness of the outcome was evaluated. The study found that among COVID-19 instances, there may be some signs of a worse prognosis. There is a clear indication that COVID-TB patients have a higher mortality or serious illness rate than COVID-19 individuals. Regular TB testing may be suggested among suspected or confirmed COVID-19 infections in countries with a high TB burden. Corbett, DPhil, and Walker (2018) carried out an assessment of the Global Trends and the HIV Epidemic concerning the Growing Burden of TB. The study examined information from reports of TB cases, cohort treatment results, examinations of MTB infection, and incidence of HIV in TB patients and other subgroups. The Joint UN Programme on HIV/AIDS (UNAIDS) has databases that contain country-specific estimations of the incidence of HIV infection among people aged 15 to 49 (referred to as adult HIV prevalence henceforth). The study found that the HIV epidemic is accelerating the spread of TB even though disproportionately few infections are caused by HIV-positive people individually. This happens because HIV and TB patients are less likely to experience positive smear tests than patients without HIV. Because their disease progresses more quickly than patients without HIV, their infectiousness lasts only relatively short.

Javed and Mahmood (2018) investigated the disparities in hematological profiles of patients with PTB co-infected with metabolic disorders and chronic infectious diseases.

In central Punjab, Pakistan, this study involved 366 patients, including PTB patients and those with diabetes, myocardial infarction (MI), hepatitis C virus infection (HCV), and HIV infection. Ninety-five healthy people were also added as a standard control group. PTB, diabetes, MI, HCV infection, and HIV infection were tested for in each participant in the study. To establish MTB infection at the molecular level, polymerase chain reaction (PCR) was used. The study discovered a significant rise in PTB patients with HCV, HIV, diabetes, or MI. This finding implies that co-morbidities should be investigated to rule out PTB co-infection with metabolic and infectious illnesses before beginning anti-TB drug therapy.

Annan, Stockbridge, Dolly, Eun-Young, and Miller (2021) conducted cross-sectional research on latent TB infection, insurance coverage, and typical healthcare sources among non-US citizens in the US. Using data from the 2011–2012 National Health and Nutrition Examination Survey (NHANES) on 1793 sampled individuals, indicators for LTBI were combined with self-reported health insurance and typical sources of care for non-US citizens. Both physical assessment and interviews were used to gather data. The survey undertaken with laboratory measurements and questions related to TB, the 2011–2012 NHANES dataset, was used for this research.

Using a cross-sectional research design, Kabiri, Agamba, Awuffor Darkwa, and Larweh (2022) examined factors influencing TB Case Detection in Ghana. The study focused on 138 tuberculosis patients who were receiving therapy. Due to the availability of participants at the various treatment facilities, the non-probability sampling approach (also known as the easy sample technique) was used to research the TB patients. Participants were questioned using a structured questionnaire. The survey found that understanding of TB was above average. However, variables, including stigma, poor accessibility, and a lack of treatments, impact the district's ability to discover TB cases.



Ongol (2022) examined the factors related to Tuberculosis infection among patients at Lira Region Referral Hospital, Uganda. Secondary data from the Biostatistics Department, District Health Offices in Lira, was used in the analysis. The study revealed that the factors associated with tuberculosis infection were attributed to demographic, socioeconomic, clinical, and healthcare risk factors as provided by the study. The study found that body weight was a significant risk factor related to the infection, hand contact was also significantly associated with TB infection, alcohol use had a significant relationship with the infection, HIV status was another risk factor significantly associated with TB infection, and finally, diabetes level had a significant association with the infection. Nonetheless, sex and education level were not significantly associated with TB infection.

Wademan, Mainga, Gondwe, and Shanaube (2021) conceptualized tuberculosis recurrence among patients in South Africa and Zambia using a cross-sectional qualitative research design. Data was collected using semi-structured interviews with 28 South Africa and Zambia community members from October 2018 to March 2019. After finding them in clinic registries, the Pop ART intervention staff referred individuals who had TB symptoms. According to the study, patients with TB blame dirt for their exposure to TB transmission and infection. In these areas, "dirt/dirtiness" is a warning to moralized behavior and an indicator of their socio- environmental situations. The study found that following their initial TB episode, most individuals could get a quick diagnosis. This results from their practical experience with healthcare systems and biological responsiveness to TB symptoms and signs. However, their biological sensitivity and experience with healthcare institutions were not enough to stop the psychological, social, economic, and physical effects of widespread TB.

Anzats et al., (2019) evaluated the risk factors for death in TB patients at Kinshasa General Provincial Reference Hospital. In this cross-sectional investigation, which took place between January and November 2018, TB patients' medical records were examined. The Fischer formula was used to compute the sample size. This led to the selection of and consultation with 144 files. Data were gathered using a pre-made, anonymous, standardized questionnaire. A sample of 40 files was used to test and validate this questionnaire. The primary risk factors for mortality were clinical TB combined with poor compliance and substantial immunosuppression, followed by diagnosing TB patients without anti-tuberculin prophylaxis.

In Kenya's congested university dorms, Maina, Willetts, and Ngari (2021) examined the prevalence of tuberculosis infection among young people. Between January 2016 and December 2017, cross-sectional research with an active contact case-seeking technique was conducted among students getting care at Kilifi County Hospital. Students enrolled in university, living in residence halls or off-campus hostels, or with close social connections to index cases made up the study population. The study period's index patient was a fellow student with a TB diagnosis. Using GeneXpert, contacts were then traced and evaluated for TB. According to the study, there was a significant rate of TB spread among college learners who interacted with index patients. Being in the same bed as the index patient was the one single factor strongly linked to TB infection. There was no evidence linking TB infection to any other demographic or clinical condition.

Kimani et al (2021) evaluated the factors impacting TB treatment discontinuation and treatment results of individuals within Kiambu County from 2016 to 2019. The study examined data for medication outcomes acquired from TB tracking forms linked with patients' TB Information Basic Unit (TIBU). This study comprised 292 individuals in

total. The research revealed that treatment disruption is prevalent in males, those aged 25 to 34 years, and people who live in the Githunguri and Kiambaa sub-counties. According to the study, relocation and a lack of information were the main causes of treatment disruptions. Patients undergoing an intensive treatment period were more likely to experience treatment interruptions.

Kroidl, Ahmed, and Horn (2020) researched the TB disease activity in HIV and Mycobacterium tuberculosis infection patients. The research was done from January 1, 2013, to August 31, 2018. In this investigation, the Expert RIF/MTB diagnostic test was used in eleven clinics throughout Kenya, Uganda, Nigeria, and Tanzania to screen patients living with HIV for active TB. The study found that, in most instances, the development of active TB began 6–12 months before clinical signs, and the presence of bacilli in the sputum led to a diagnosis. Blood biomarkers may help with early TB identification, enhance clinical results, and stop the spread of MTB.

Putra and Toonsiri (2019) examined the elements contributing to tuberculosis treatment success. The integrative review of Whitemore and Knafl was applied. Four electronic databases were used to search for literature between 2002 and 2017: EBSCO, PubMed, Science Direct, and Google Scholar. Only 28 articles—out of a total of 146—were chosen for inclusion based on the topic's inclusion criteria. According to the study, several important elements contribute to successful TB treatment, like family support, socioeconomic status, assistance from doctors and nurses, accessibility to health services, knowledge, social stigma, and psychological stress.

Using a cross-sectional research methodology, Gitau (2019) conducted a study to ascertain the incidence of latent TB infection in fifth-year medical students at the University of Nairobi, Kenya. At Kenyatta National Hospital, Kenya, final-year

undergraduate medical students participated in the study from September to November 2013. Three hundred ten medical students in their final year of school made up the target population. Consecutive sampling was done to select the sample size. One hundred eighty-one medical students in their last year of study were questioned using a standard questionnaire and subjected to QFT-Gold testing. The study indicated that medical students in their last year at the national referral hospital had a significant LTBI prevalence.

#### **2.4 HIV and TB Co-Infection**

The diagnosis of active TB in HIV-positive individuals suggests that the infection is developing into AIDS, according to Otiende, Achia, and Mwambi (2020). Approximately 10 million people in 2019 had active TB, and 9% additionally had HIV. According to Hayibor, Bandoh, and Kenu (2020), TB is also present in around a third of the 36.9 million people living with HIV and AIDS worldwide. Sub-Saharan Africa, where 70% of all people living with HIV/TB co-infection reside, is the area most severely impacted.

In order to improve the mechanisms for providing integrated TB and HIV services, reduce the burden of TB in people living with HIV, start receiving antiretroviral medication early (the "Three I's for HIV/TB"), and reduce the burden of HIV in patients with suspected and confirmed TB, the World Health Organization (2019) has established HIV/TB collaborative activities. Increased case discovery, isoniazid preventative medication, and preventing infections for TB are the three I's for HIV/TB. Additionally, the UNAIDS set a goal that by 2020, through a number of programs, 90% of people with HIV will be aware of their status, 90% of people with HIV will get sustained antiretroviral medication, and 90% of people who are receiving antiretroviral therapy will have viral suppression.

TB is a disease common among people with weakened immunity, like HIV-positive individuals, and hence, TB and HIV are related strongly (Mabuza & Shumba, 2018). According to Abdullahi, Ngari, Sanga, Katana, and Willetts (2019), about 50 percent of patients with both HIV and TB infections are fatal during treatment, with the majority of deaths occurring within two months of TB diagnosis. In addition, around 60% of the projected global HIV-related TB cases are not being detected or treated, and TB was the cause of almost one-third of all AIDS-related fatalities in 2018 (UNAIDS, 2018). One of the top health objectives in poor nations, including Kenya, is preventing and controlling opportunistic infections, such as HIV/AIDS, TB, and other diseases. People without HIV who have low CD4 counts are far more vulnerable to active TB infection (when TB infection leads to illness). Still, healthy individuals may not get sick from latent TB infection (when a person has TB but shows no symptoms). As a result, it is believed that those who live with HIV have a higher risk of having active TB than those who do not (Wei, Wei- Sheng & Ming-Qin, 2016). Low CD4 count HIV-positive individuals are considerably more likely than HIV-negative individuals to get TB infection (Tesfaye et al, 2018). Nevertheless, early detection and efficient treatment are crucial to stop TB-related mortality.

Globally, TB surpassed HIV in 2014 as the largest infectious disease killer, a concerning development for a generally curable and treatable condition. In 2017, 1.3 million persons died from TB, while 300,000 HIV-positive individuals also succumbed. It continues to be the main reason people with HIV die (Mabuza & Shumba, 2018). Globally, 11% of HIV/TB co-infected persons died while undergoing treatment in 2017, over three times the rate of other TB patients (4%). TB-related deaths among HIV-positive individuals decreased by 100,000 between 2015 and 2017, primarily

because of the quick uptake of antiretroviral HIV treatment. This indicates that progress has been made in lowering these fatalities.

The Political Declaration on Ending AIDS (2016) by the United Nations sets a target of reducing TB-related deaths among HIV-positive people by 75 percent by 2020 (UNAIDS, 2018). Additionally, all UN and WHO member nations have committed to eradicating tuberculosis as a public health issue by 2030. To accomplish this, the incidence of active TB must decrease by 80%, and TB mortality must decrease by 90% from 2015 levels (Centers for Disease Control, 2018). The fight against TB is still far from over, and there are still significant gaps in TB prevention, diagnosis, and treatment. If progress slows, 35 million people will die from the disease, and over one billion people will contract TB in the next 20 years (Dhungana et al., 2013). UNAIDS has urged nations to integrate HIV and TB care by ensuring HIV prevention and treatment programs include frequent TB screening, preventative therapy, and early treatment. Together with WHO, UNAIDS has made this request for immediate action.

In a cross-sectional study, Jha et al. (2008) examined TB/HIV co-infection status among recently diagnosed TB Patients. The study population was among 300 newly infected TB patients in health facilities in Nepal. The authors argued that the estimation of the ratio of HIV cases to TB cases can serve as a caution for a country's transmission of TB caused by HIV. The study population was 300 recently diagnosed TB cases tested for HIV. Out of 300 new cases of TB, 4.7 percent of patients had HIV and, hence, an HIV/TB co-infection rate of 4.7%. The problem of TB-HIV co-infection in 2008 seemed small, but it has grown to an alarming rate of 12%, and hence, collaborative planning and practices to handle current co-infected persons must be addressed by TB and AIDS programs.

In addition, Dhungana et al. (2013) conducted a surveillance of TB among persons infected with HIV in three diverse Nepal regions, which include the Shree Siddhanath Science Campus, Regional Tuberculosis Centre, and Tribhuvan University Teaching hospital. The researcher used a cross-sectional study method, and primary data was obtained using a pre-structured questionnaire. In addition, a Sputum specimen was collected from HIV/AIDS patients to investigate tuberculosis by culture and microscopy. Out of all the 394 HIV infection individuals, 8.1% had tuberculosis.

Alemu, Wubie, and Dilnessa (2021) assessed the frequency of co-infection with HIV and TB and any related variables among patients diagnosed with TB. TB patients in the Comprehensive Specialized Hospital in Debre Markos from 2012 to 2016 were included in the research. SPSS version 22 was utilized in data analysis. Logistic regression was performed to ascertain the relationships between independent and outcome variables. In the previous two years, co- infection of HIV and TB has declined in the study area. The kind of TB was correlated with TB/HIV co-infection. No correlation existed between TB/HIV co-infection and sex, age, location, or TB category. The present integrated TB/HIV prevention strategy in Ethiopia has shown assurance in lowering rates of HIV/TB co-infection.

Pimpin et al. (2017) conducted a systematic review (EEA) to estimate HIV-TB infection prevalence in the European Economic Area and European Union (EU). Researches that gathered information in 1996 and later, irrespective of the particular year that data collection began, were used to extract information on the HIV infection burden in TB patients and risk factors for HIV- TB co-infection in EEA/EU. According to the study, compared to central EU/EEA countries, infection levels in Western and Eastern countries were greater and showed rising tendencies over time. Additionally,

males, young adults, homeless, foreign-born, injecting drug users, and convicts were at a higher risk of contracting TB and HIV.

At Goa Tertiary Care Hospital, Parrikar, Lawande, and Cacodcar (2020) researched HIV-TB co-infection and its factors. The control group comprised an equivalent number of HIV-infected patients but not TB-positive. It was diagnosed in the same period as the study group, which included 342 cases of co-infected HIV-TB patients over 15 years. Some factors were compared, including age, gender, occupation, educational level, HIV transmission method, addictions, CD4 levels, etc. According to the study, the state's greater frequency of HIV-TB co-infection justifies upgrading TB-HIV control efforts and maintaining a high level of alert for early detection. Co-infection was linked to male gender, lower CD4 levels, alcohol intake, poorer educational attainment, and semiskilled occupation. These sociodemographic characteristics will aid in directing control methods to focus on the high-risk groups and reduce disease severity and treatment outcomes. Increased default and mortality rates call for stronger and more effective TB-HIV control program operations. The study found that the state may have a considerably higher prevalence of coinfection due to migration and tourism.

In India, Bariha, Pujari, Kullu, and Thakur (2018) conducted prospective research on tuberculosis co-infection in HIV-positive individuals in Burla, VIMSAR, Sambalpur, and Odisha. This research was conducted to learn more about the epidemiology and clinical characteristics of co-infection with HIV and TB. All 269 HIV-TB co-infection adult patients who visited the hospital for a year participated in this prospective research. The clinical parameters were examined after a thorough clinical examination and detailed history. According to the study, the working class is more impacted than the rest of the population by extra-pulmonary TB. Compared to other kinds of TB, TB



Meningitis and Disseminated TB have poor prognoses. Early suspected diagnosis of TB and early beginning of ATT by HIV patients dramatically reduce morbidity and mortality. During TB diagnosis, a low CD4 count is related to greater mortality.

According to socioeconomic status, Subba and Rimal (2017) evaluated the co-infection of HIV and TB and the accessibility to medical treatments. Four HIV care and prevention facilities run by various non-governmental organizations (NGOs) in Nepal were the subject of cross-sectional research. Fifty-one samples from the target population were chosen randomly among those who agreed to the interview. Data were gathered using a pre-tested semi-structured questionnaire. HIV/TB co-infection was relatively common in wealthy and low-income families in the research area. By restricting their access to HIV services and information like CD4 and viral load testing, the underprivileged and productive age groups suffered an additional disadvantage.

Using a systematic review of published articles in Ethiopia, Teweldemedhin, Asres, and Gebreyesus (2018) examined TB- HIV co-infection. An electronic search was carried out in databases like Google Scholar, Hinari, Cochrane library, Embase, and PubMed to obtain articles on HIV-TB co-infection. From selected articles, TBHIV co-infection prevalence was between 6% and 52.1%.

In a systematic literature review, Mohammed, Assefa, and Mengistie (2018) studied the prevalence of extra-pulmonary TB among PLWHA in SSA. Published articles on EPTB among PLWHA were obtained from Google Scholar and PubMed. The results indicated that among PLWHA, the prevalence of EPTB ranged between 6.4% and 36.8%. As such, it was considered important that healthcare professionals emphasize extra-pulmonary TB testing, particularly when screening for TB among PLWHA. Among Congolese children, Mukuku et al (2019) studied Tuberculosis and HIV co-infection.

The research utilized a cross-sectional study design and targeted children below 15 years. The study discovered that the prevalence of TB/HIV co- infection was 20.95%. HIV-infected children had a greater mortality rate for TB infections (47.73%) than HIV-uninfected children (17.02%).

In a study in Nigeria on TB and the immunological profile of HIV/TB co-infected persons, Musa et al., (2015). The research covered ten years and used 345 HIV treatment-naïve persons as the target population. The study found that 13.62% of the TB patients were HIV positive. Comparing those with HIV infection alone to people with TB/HIV coinfection shows that the time to first- line ART regimen failure is statistically significantly shorter.

Despite the significance of offering HIV/TB Co-Infection Care as a way of dealing with both TB and HIV, studies show that these services were lacking in Africa countries. For instance, in cross- sectional research of health facilities, Kaboru et al. (2013) examined HIV/TB Co-infection care in medical facilities conflict-influenced settings in DRC. Results indicated that HIV care was less accessible than TB care (9% vs. 61% of facilities). Only 29% of the health facilities offered different services to numerous co-infected persons. Moreover, HIV/TB coinfection rates were undetermined in 82 percent of health amenities.

Ojiezeh, Adefosoye, and Ogundipe (2016) conducted retrospective research on pulmonary TB and HIV co-infection patients showing up for the National Leprosy and TB Control Programme, Owo Center, in Nigeria. Using pre-made case record forms, 342 additional cases were found. The researchers retrieved crucial data on demographics, social history, medical history, laboratory findings, treatment accessibility, and death records. According to the study, TB occurs frequently and has

a low cure rate. The comparatively low cure rate for TB infection may indicate that drug-resistant forms of the disease have emerged in the community under study. Due to the development of more virulent, multi-drug resistance strains, non-adherence to the prescribed medication regimen may not be unrelated to the resurgence of TB, which may as well explain why the cure rate is poor. Living conditions and unhygienic treatment of pulmonary exudates by infected individuals may also be at fault. Living in poorly constructed, unplanned environments and being overcrowded in most homes may contribute to the persistence of this long-lasting sickness in society.

In Ethiopia, Tesfaye (2018) examined HIV/TB co-infection prevalence and related factors. Major databases like Pub Med, CINAHL, Google Scholar, Online Africa Journals, and Google were thoroughly examined using search criteria to undertake this systematic review and meta-analysis. The authors gathered the required data using a uniform data-gathering procedure. According to this research, the prevalence of TB/HIV co-infection is rising and needs urgent attention. Advanced WHO stage and low CD4 count are key factors in both infections.

Using a cross-sectional study design, Belay, Bjune, and Abebe (2018) assessed the prevalence of HIV, tuberculosis, and TB-HIV co-infection among PTB suspects in major pastoralist areas in northeast Ethiopia. Three hundred twenty-five suspected pulmonary TB cases from five healthcare facilities were involved in the research. For each subject, three sputum samples were taken. Ziehl-Neelsen staining was used to test the sputum samples for the existence of acid-fast bacilli, and the remaining samples were cultured. HIV testing and participant interviews both took place. The study found that, despite the high overall frequency of TB-HIV co-infection in the current sample, HIV infection rates among ethnic Afar were significantly lower among both suspects

and TB patients. According to the findings, there is presumably a low HIV infection prevalence among Afar pastoralists.

Deribew, Tesfaye, Hailmichael, and Negussu (2019) examined the effect of TB/HIV co-infection on people's standard of living. Cross-sectional research was conducted in a few hospitals in the Ethiopian region of Oromiya. 467 HIV patients and 124 HIV and TB co-infected patients made up the study population. Through in-person interviews, professional nurses gathered information on quality of life (QoL). Compared to HIV-infected individuals without active TB, the study found that TB/HIV co-infected individuals had inferior quality of life across the board. Most QoL disciplines were strongly correlated, having financial sources as well as support from the family. Patients with co-infections were likely to have poor physical health if they had depression compared to patients without depression. A low quality of life in the psychological realm was linked to self-stigma.

Mukuku et al. (2019) studied the co-infection of Congolese children with HIV and tuberculosis. The research utilized cross-sectional research of teenagers under fifteen years who received TB treatment between 2013 and 2015. Data on clinical, paraclinical, and outcome variables were gathered in 22 DOTS in Lubumbashi, Zambia. HIV-infected TB children who died and those who survived were compared statistically. According to the study, HIV-positive children had a greater mortality rate than those who were not. Moreover, deaths during anti-TB medication were linked to under-5-year-old age, poor nutritional condition, and negative acid-fast bacilli tests.

Lemos, Feijão, Gir, and Galvão (2018) assessed the QoL among patients with HIV/TB co-infection. Fortaleza, Brazil, a specialized outpatient clinic, conducted qualitative and quantitative research on 34 co-infected patients from 2009 to 2010. A 42-item

quality of life measure called HAT-QoL was utilized for data collection, along with open-ended questions to gauge the changes the illness brings about. The study found that most individuals had pulmonary tuberculosis, were men, and had low levels of education. The quality of life suffered concerning money, sexuality, and secrecy. The co-infection that inflicts changes on daily living that highlight and worsen living standards was also established. Co-infection alters the patients' lives while receiving adequate treatment; health-promoting activities can reduce these effects.

Shah, Ewetola, Etheredge, and Maluantesa (2021) assessed the risk factors for TB/HIV Coinfection and its effects on Patient Outcomes in DRC. Data obtained from 49,460 patients undergoing ART from 241 HIV/AIDS clinics in Kinshasa and Haut-Katanga were used in this quantitative study. The study's design was quantitative, retrospective, and observational. The researchers used logistic regression and chi-square analysis. This investigation of a fairly large patient population revealed that in 241 clinics that shared data for this particular research, 3.6 percent of patients receiving antiretroviral medication had TB/HIV coinfection. The likelihood of inverse outcomes was significantly increased by TB/HIV coinfection (death, loss to follow-up, and no viral load suppression).

In North Central Nigeria, Hassan, Olukolade, and Ogbuji1 (2016) evaluated the TB Treatment Outcome of TB/HIV Co-Infection. In Benue and the Federal Capital Territory (FCT) of Nigeria, eight service providers of Directly Observed Treatment Short (DOTS) courses and Anti-Retroviral Therapy (ART) participated in retrospective research using secondary data. The time frame under consideration lasted from January 2010 to December 2013. The study found that HIV-negative patients had better treatment outcomes than HIV-positive patients and that the patient's CD4 count is the most likely predictable factor contributing to this. This suggests that TB/HIV co-

infection was a serious public health issue in Benue State and the Federal Capital Territory (FCT).

In South Sudan, Sube, Seriano, Jaja, and Gore (2019) examined HIV and TB co-infection. The variables for this retrospective analysis were gathered from records at the HIV clinic at Juba Teaching Hospital. The study gathered information about the patients' age, sex, residence area, and HIV and HIV/TB status from January 2011 to December 2013. If one of the factors was not present, a case was disregarded. Thus, only 2,547 of the 2,577 patient records evaluated were considered. Data sheets were used to gather the information, which was checked and entered into SPSS Version 20. According to the study, HIV/TB is a serious and difficult health issue in this young country. Males are more prone than females to co-infect, with individuals aged 25 to 34 having the highest prevalence of co-infection.

In Western Ethiopia, Melkamu, Dessie, and Seyoum (2018) examined TB Infection determinants among mature HIV Positives going for Clinical Care. Moreover, two public health institutions participated in this case-control study. A Case-control research with no matches was conducted between December 26, 2011, and February 29, 2012. HIV positives with TB infections made up 123 cases, while 246 of the controls did not have TB infections. The study discovered that advanced WHO HIV/AIDS clinical staging and being divorced or widowed were determining factors related to HIV/TB co-infection. Other risks were not going to formal schooling, being underweight, having a diabetic mellitus history, and being underweight. A different kitchen demonstrated a protective task. The study found that while these factors are amenable to institutional and individual-level interventions, others, including education and nutrition, require societal-level integration.

In Aurangabad, Maharashtra, Warkari, Nakel, Mahajan, and Adchitre (2017) have conducted cross-sectional research on treatment outcomes of TB among HIV co-infected patients. A descriptive cross-sectional research design only gathered information on patients' TB-HIV status once HIV-co-infected and registered patients at city TB centers were recognized. 87 HIV-TB co-infected individuals out of all patients diagnosed with Tuberculosis were chosen for this research work. A Retrospective research of all accessible secondary data of diagnosed TB-HIV coinfecting cases listed at the Tuberculosis Centre, Aurangabad city, in one calendar year and who had completed TB treatment. Universal purposive sampling was used. The researcher found that relatively few patients were cured of TB. One of the causes could be HIV patients' immunosuppression, which makes them susceptible to developing active TB and hastening its progression.

Kenya is ranked among the world's third worst TB-affected countries, with about 169,000 patients diagnosed with the disease in 2018 (UNAIDS, 2018). Kenya is also one of the countries with the highest prevalence of HIV globally. According to Otiende, Achia, and Mwambi (2020), the prevalence of HIV in Kenya in 2018 was 4.7 percent. The country has one of the highest rates of co-infection in the world (30%), which implies that 3 in every ten patients with tuberculosis are also HIV positive. Compared to the UNAIDS 90 90 90 targets, In terms of lowering co-infections with HIV and TB, Kenya is currently underperforming. Only 73% of HIV patients were suppressed by the virus in 2019; nevertheless, 89% of Kenyans living with HIV were aware of their condition, 68% were receiving treatment, and 89% were aware of their status (Otiende, Achia, & Mwambi, 2020). Although the Kenyan government and non-governmental groups have implemented a number of methods to lower HIV/AIDS and tuberculosis (TB) occurrence, the two diseases continue to be a major cause of death in the nation.

In order to understand how the two diseases are related to one another and how they affect the outcomes of patients receiving co-therapy for TB and HIV, it is necessary to model the death rate of HIV/TB co-infection and use time-to-event data. Because the outcome significance (in this case, death) is the probability that the event will come to pass and when the event is likely to occur, time-to-event data is distinctive. Using a cross-sectional study design, Nyamogoba, Mbuthia, Mining, and Waiyaki (2012) investigated HIV association with TB and non-tuberculosis mycobacteria in western Kenya. According to the findings, 76% of the 346 TB cases were HIV positive whereas 41.8% were HIV negative yet nonetheless had TB. The prevalence ratio of HIV-TB co-infection in women to men was 1.35. The average rate of TB-HIV co-infection in Nyando Sub-County was reported to be 69.80% by Achieng (2016) in a study on the parameters relating to TB treatment results in HIV/TB co-infected and TB-only patients.

Cherono (2018) evaluated the patients attending the TB Clinic at the Kericho County Hospital in Kenya who were co-infected with HIV and MTB and had their immune systems. Patients with mono-infection from tuberculosis and the typical standard references were used as controls. Demographic information about the patients was gathered using questionnaires, including age, occupation, sex, and marital status. Blood samples were taken at the beginning of TB therapy and after anti-TB medications had ended. The number of CD4+ T cells was measured using a FACS Caliber flow cytometer. After six months, the viral load levels were collected from the hospital patient's records. According to the study, many TB-HIV coinfecting persons were married females between 18 and 74 who had only completed primary school. Most casual workers with poor wages were primarily afflicted with pulmonary tuberculosis. After completing TB therapy, the study discovered that individuals who were HIV and



TB co-infected experienced greater improvement in CD4+ T cell counts than those who were only infected with TB. After TB chemotherapy, viral load numbers considerably decreased due to decreased HIV virus replication, which had been quickened by M. tuberculosis.

Otiende, Achia, and Mwambi (2019) examined the probability of TB-HIV co-infection. Additionally, the study examined data from the Kenyan national TB control program's seven- year analysis of case notification information for cases of tuberculosis and tuberculosis with HIV in 47 counties (2012–2018). Six models with various time-space formulations were tested to find the best match model. The authors then mapped the posterior marginal from the best-fit model to analyze spatial patterns and temporal trends of co-infection risk. According to the report, 194,129 of the 608,312 TB case notifications overall also had HIV. Females had a higher rate of TB-HIV co-infection compared to males. Adults aged 35 to 44 and 45 to 54 comprise a sizeable portion of the co-infected population.

## **2.5 Integrated Therapy for HIV and TB co-infection**

For patients with TB who are HIV-infected, integrated therapy is essential. HIV and TB must both be treated at the same time. During the initial stages of TB treatment, HIV-infected patients experience a significant rate of TB-related mortality. Additionally, data from systematic reviews and randomized clinical trials have demonstrated that starting ART early improves the survival of HIV-infected individuals with TB (Sinai, Cleghorn & Kinkel, 2018). The two diseases must be managed more skillfully to increase patients' survival and quality of life at this crucial time. The WHO recommends starting ART during this time (Herce et al. 2018). However, the start of ART is frequently postponed for several reasons, including patient features, drug toxicity overlap, patient or physician anxiety, and local HIV and TB program

restrictions. Patients sent from TB to HIV in separate clinics are more likely to experience delays in starting ART (Elsadig 2020). HIV- infected individuals with TB who are delayed in starting ART are more likely to die, especially if they have extremely low CD4 cell counts.

Single facilities, like integrated HIV/TB care centers, and a single healthcare clinician who treats both diseases are the essential components of effective care integration models for HIV and TB (Meda et al., 2013). The benefits include quicker introduction of ART for HIV-infected patients with TB, comprehensive patient evaluation, and effective therapy when patients experience negative drug side effects. It is also easier to establish, sustain, and train healthcare professionals using this approach in environments with limited resources. Integrated care for HIV and TB has effectively addressed issues, including losing patients to follow-up during the referral process between HIV and TB clinics, burdening patients with greater travel expenditures, and spending more time in clinics (Negussie, Debalke & Belachew, 2018). Social support and adherence- improving interventions can further enhance this strategy. The same team of healthcare professionals delivering HIV and TB integrated therapy may produce superior clinical results and better use of scarce resources.

Meta-analysis and systematic review were undertaken by Abay, Reda, Deribe, and Biadgilign (2019) to evaluate the impact of early ART commencement (within 2 and 4 weeks of TB treatment) on some treatment results among HIV/TB coinfecting patients. PubMed, Google Scholar, Embase, Medscape, Science Direct, and Cochrane Library databases were thoroughly searched for clinical studies. Before the final date of the search, clinical trials that were published in any particular language were included. The Cochrane Library's standards were used to evaluate the studies' quality. A heterogeneity test was performed to evaluate the differences in research results. The study supported

the idea that early ART initiation lowers overall mortality. However, the significant incidence of TB-IRIS and deaths linked to it were also confirmed by this research.

Worodria et al. (2018) assessed the impact of mortality within a routine health context on the recent WHO recommendations for ART in TB-HIV co-infected persons. The efficiency of delayed versus early ART on death in TB-HIV co-infected patients with CD4 cell counts of 100 cells/l or below was studied in the study, which compared two cohorts prior (2008 to 2010) and after (2012-2013) a policy amendment on ART scheduling after TB. In addition, to balance the research arms, the study utilized negative probability censoring-weighted Cox models on baseline characteristics and produced mortality hazard ratios. According to the study, early ART in persons with HIV-TB co-infection was not linked to a lower mortality risk when receiving routine medical care. Both groups' risk of death rose in the presence of asymptomatic cryptococcal antigenemia.

In Singapore, Teng, Chua, and Lai (2021) conducted research intending to determine the prevalence and features of HIV-TB co-infected patients. The National University Hospital (NUH), a quaternary care facility, and the National Centre for Infectious Diseases, the country's HIV center, provided retrospective data spanning 11 years. Results show that between December 2005 and December 2016, 48 out of 819 HIV patients and 272 out of 3,196 HIV patients, respectively, who were treated at NUH and TTSH, had TB diagnoses. The study found that HIV- positive patients are not being tested for latent TB, and HIV-TB patients with low CD4 counts wait longer to start ART.

Yan, Chen, Wu, Fu, Zhang, and Li (2015) compared early against delayed ART for HIV and TB Co-Infected Patients. International Clinical Trials Registry Platform,

EMBASE, and PubMed were all used in the study's systematic search for pertinent articles. In the course of TB treatment, the study compared early ART commencement (within four weeks of the start of anti-TB treatment) versus late ART beginning (after eight, although not beyond twelve weeks after the beginning of anti-TB treatment). A meta-analysis of six RCTs involving 2272 individuals was analyzed. The study found that early initiation of ART significantly lowers all-cause death in patients with HIV-positive TB occurrence rate ratio when compared to delayed ART introduction, even while there is a higher risk for IRD. Furthermore, there was no evidence that early ART beginning was linked to a higher likelihood of grade 3 and 4 drug-associated side events.

Chelkeba, Fekadu, and Mekonne (2020) assessed the influence of time of starting integrated ART in the treatment of HIV/TB co-infection patients. Randomized clinical trials (RCTs) contrasting early and late antiretroviral treatment (ART) were included. Electronic databases in PubMed, Science Direct, and EMBASE were searched. 4 425 people in the 8 RCTs were part of this meta- analysis. In contrast to late ART commencement, the study discovered that early ART was connected to overall mortality. Early ART resulted in conclusive evidence of increased TB-IRIS incidence and TB-IRIS-linked mortality in HIV/TB co-infected patients. However, the timing of the start of ART was not linked to Grade 3 or 4 adverse events, reaching a reduced viral load, or developing a new AIDS-defining disease.

In Indonesia, Maemun, Mariana, Rusli, Mahkota, and Purnama (2020) conducted a study intending to assess the early beginning of ARV Therapy among TB–HIV coinfection Patients. Two hundred seventy-five patients who had TB and HIV coinfection and were ARV-naive participated in this retrospective cohort study between January 2011 and May 2014. Two hundred forty-eight patients made up the study

sample and were split into two groups: those who started taking ART early during their TB treatment (124 patients) and those who started taking it later (124 patients). The study found that ART commencement's influence is crucial in an intensive period of anti-TB treatment (2-8 weeks) to increase survival among the group with TB and HIV coinfection.

Manosuthi, Wiboonchutikul, and Sungkanuparph (2016) examined integrated therapy for HIV and TB. A randomized clinical trial showed that antiretroviral therapy (ART) that is started early on enhances survival in HIV-TB patients. Patients sent from TB to different HIV clinics frequently delay starting ART, which may be linked to a higher death risk. A successful concept involves treating patients for HIV and TB simultaneously in a single facility with a single healthcare professional. HIV-positive individuals should undergo TB therapy using at least the same programs and for the same length of time as HIV-negative patients. The currently accepted standard of care for drug-susceptible TB is a two-month initial intensive phase with isoniazid, pyrazinamide, ethambutol, and rifampin, followed by a four-month continuation phase of isoniazid and rifampin. ART should be started regardless of CD4 cell level in all HIV-infected TB patients. The ideal time to begin antituberculous therapy (ART) is within the first eight weeks after beginning treatment and within the first two weeks for patients with CD4 cell counts under 50 cells/mm<sup>3</sup>. In areas with low resources, non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART continues to be the first-line treatment for HIV-infected individuals with TB.

In a before-after quasi-experimental research in Lusaka, Zambia, Herce, Morse, Luhanga, and Reid (2018) they examined the inclusion of HIV care and treatment tuberculosis clinics. The findings showed that patients with HIV-associated TB in Lusaka, Zambia, had greater linkage to HIV care, rates of early ART initiation, and

success with TB treatment when HIV treatment and care services were integrated into regular TB clinics utilizing a one-stop shop paradigm.

Kerschberger, Hilderbrand, Boulle, Coetzee, and Goemaere (2017) assessed the influence of complete incorporation of HIV/TB therapy on time to initiating ART. 209 TB/HIV co-infected persons with CD4 count below 250 cells/l registered for TB treatment at just one key care clinic within a South African township from June 2008 to May 2009 had their TB registrations and clinical notes examined. The researcher evaluated the time between the start of TB treatment and the beginning of ART for the duration before and after the comprehensive, "one-stop shop" incorporation of HIV and TB care. Fifty-six person-years of observation were obtained from 188 patients (100 pre- and 88 post-integration) in the analysis. Full TB/HIV care incorporation is achievable. According to the study, it enhances the likelihood that co-infected patients will start ART while shortening the period to ART commencement by an average of 72 days. The results suggest reducing excess mortality and morbidity by scaling up comprehensive TB/HIV integration of service in locations with high TB/HIV prevalence.

To treat patients with HIV/TB co-infection, Chelke, Fekadu, and Tesfaye (2020) evaluated the impact of the timing of the start of antiretroviral medication. The study included randomized clinical trials (RCTs) contrasting early and late antiretroviral treatment (ART). 4 425 people in the 8 RCTs were part of this meta-analysis. The findings indicated that improving TB-IRIS and TB-IRIS-related mortality was linked to early ART initiation. Compared to late ART commencement, early ART was linked to overall mortality. The beginning of ART was unrelated to grade 3 or grade 4 adverse occasions, reaching a lower viral load or developing a new AIDS- defining disease.

Early ART resulted in conclusive evidence of enhanced TB-IRIS incidence and TB-IRIS-linked mortality in HIV/TB co-infected patients.

Kogieleum, Sanisha, and Abdool (2019) conducted a study to examine how to improve survival with TB & HIV treatment integration. The purpose aimed to reduce co-infection mortality by reviewing published literature regarding clinical trials and cohort studies on TB-HIV treatment integration techniques. Moreover, the study included studies released after 2009, when various treatment recommendations called for therapy integration. A total of 43 papers were found, of which 23 observational studies and nine clinical trials provided useful information on the integration of treatment of TB-HIV. The study showed that by beginning antiretroviral therapy quickly after starting TB treatment, the survival advantage of AIDS therapy in TB-infected patients could be enhanced among those with higher levels of immunosuppression. However, to lessen the incidence and severity of immune reconstitution illness and subsequent hospitalization, individuals with greater CD4+ cell counts must delay starting ART until eight weeks following TB treatment. By reducing the death rate in areas with high HIV/TB prevalence, operational issues in incorporating TB-HIV care can considerably positively impact patient outcomes.

In Ghana, Anku et al (2020) found some challenges in scaling up HIV-TB integrated service delivery. Data was obtained by interviewing 31 healthcare providers attached to TB-HIV service delivery. Staffing shortages in complex HIV-TB management, usage of public facilities under DOT protocols, inadequate infrastructure, ineffective communication between the two programs and hospital administrators, and funding limitations were some of the difficulties. In South Africa, Sinai, Cleghorn, and Kinkel (2018) they have conducted a study on enhancing the management of tuberculosis in patients with HIV by integrating HIV and TB services. The study used secondary data

covering July 2015 and February 2016. The findings indicated that 75.4% and 79.2% of the patients diagnosed with TB by HIV and TB providers had started treatment. HIV providers had a greater default rate (12.8% vs. 4.2%) than TB providers. Healthcare professionals and facility administrators viewed the intervention (integration of HIV-TB coinfection treatment) favorably but expressed concerns about the possibility of an additional workload, administrative challenges, and infection control.

In Cape Town, South Africa, Uyei et al. (2014) measured the extent of integrated HIV and TB service delivery. The focus of the study was 33 integrated clinics that covered services for both tuberculosis and HIV. The study found high variability within the group, implying that ART and TB co-location services are necessary, although inadequate for the incorporated delivery of services. Co-located services Clinics outperformed single clinic services on parameters relating to implementing combined TB/ART services. Additionally, the study discovered that almost all of the clinics in the sample that provided solely TB services had highly combined pre-ART services, which suggests that integrating services in many clinics is both feasible and well-liked by clinic staff. As co-infected individuals are already receiving care, TB clinics are effective locations to combine ART services because numerous HIV-interrelated services, like CD4 monitoring and testing, were strongly incorporated into clinics where various TB services were offered.

The data on the association regarding unified TB and HIV therapy and TB treatment outcomes, particularly successful treatment and all-cause death in TB/HIV coinfecting patients in SSA, were examined by Kadia, BTakah, Dimala, and Simms (2020). Additionally, a thorough examination of studies published between March 2004 and July 10, 2019 was completed. Seven internet databases, including the Medline database, Cochrane, and Embase, have been searched for observational, interventional, and



quantitative research on combined HIV/TB treatment. Utilizing the National Lung, Heart, evaluated Blood Institute's qualitative assessment procedures, two researchers independently reviewed the available studies, filtered the search results, and evaluated the eligible studies' overall quality. Although there is conflicting information regarding the effect of integrated TB/HIV therapy services affecting therapy results and deaths from all causes in TB/HIV in combination patients in SSA, the study asserts that the few high-quality studies that are currently available tend to support the efficacy of these services.

Kadia and Akem (2021) examined the constraints to and facilitators of ART uptake in SSA treatment programs for HIV and TB. A thorough analysis was done. Searches for appropriate quantitative, qualitative, and mixed-techniques research published from March 2004 to July 2019 were conducted across seven databases. Estimates of ART uptake that were pooled were obtained using a random-effects meta-analysis. In SSA, programs combining TB and HIV treatment typically do not attain high ART adoption; nevertheless, net enhancement in uptake was found following WHO released 2012 guidelines regarding cooperative HIV/TB activities.

In Ethiopia's urban primary healthcare facility, Haile, Zewdu, Klinkenberg, and Woldeyohannes (2018) they studied HIV and TB patients who are on ART and when it started. A retrospective cohort study was conducted using information from a regular program. All adult TB and HIV patients who registered at a sizable TB-HIV facility in Addis Abeba between September 2008 and August 2014 were included. Both descriptive as well as inference statistics were utilized to compile and analyze the data. Patients who were on ART prior to their TB diagnosis were excluded. Data sources included unit TB values and ART registers. The study found that commencing ART required a mean of 41 days after the commencement of TB treatment. All infected with

HIV TB patients must receive ART upon the most recent diagnosis as early ART initiation in TB treatment is a life-saving strategy through constant follow-up as well as training of health staff.

Burnett, Zawedde-Muyanja, Herman, and Weaver (2018) assessed the influence of TB/HIV Integration on HIV and TB indicators in Ugandan Rural Health Facilities. The study compared performance on ART initiation and TB treatment outcomes during integrated and non-integrated facility periods to examine the impact of integration. The patient served as the analytic unit for the logistic regression, which also took other intervention effects into account, adjusted for age and gender, and clustered patients by healthcare facility. The study discovered that receiving care in a facility that integrated TB/HIV therapy was linked to lower mortality. Still, there was no change in the percentage of patients beginning ART with successful TB treatment, lost to follow-up.

Uthman and Okwundu (2019) assessed the optimal timing of ART Initiation for HIV-Infected Adults with recently Diagnosed Pulmonary Tuberculosis. Data Sources included PubMed, EMBASE, conference abstracts, and Clinical Trials (January 1980 to May 2015). The study carried out randomized, controlled trials comparing deferred ART commencement with early ART initiation (1 to 4 weeks vs. 8 to 12 weeks following the start of TB treatment) (after TB treatment). The study discovered that, despite being linked with a 2-fold increased frequency of TB-IRIS, early ART increases survival in HIV-infected persons with recently diagnosed TB when CD4+ T-cell counts are below 0.050 10<sup>9</sup> cells/L.

In South Africa, Water, Fulcher, Cilliers, Meyer, and Wilson (2022) examined the connection between HIV infection and combined ART and the likelihood of a poor TB treatment result in a small-town district hospital in the Eastern Cape. The people who

were found to have TB at the district hospital from January 2017 to April 2020 were the subjects of this retrospective cohort study. The study included 711 persons over fifteen years old who reported having HIV and the results of their therapy. Unfavorable, down referral, and success were the three levels of a categorical outcome that were considered. The study showed that many patients had successful TB treatment outcomes. But compared to persons with untreated HIV, those without HIV had almost five times higher odds of success.

In northwest Tanzania, patients receiving rifampicin who also had TB and HIV were examined for sub-therapeutic drug levels by Gunda, Kalluvya, Kasang, Kidenya, Mpondo, and Klinker in 2017. Adult HIV patients receiving at least one month of ARV and TB co-treatment participated in a cross-sectional hospital study. Until the sample size was met, patients were repeatedly enrolled through standard HIV care and treatment facilities. STATA 12 software was used to gather and evaluate data. According to the study, adult HIV-positive individuals in Tanzania receiving ARV and anti-TB co-treatment had considerably high sub-therapeutic ARV plasma levels. These patients are highly susceptible to short-term insufficient virological suppression, the emergence of resistance, and long-term poor clinical outcomes.

Burke et al. (2021) researched to examine the optimum period to start integrated ART in persons with tuberculosis and HIV coinfection. Nine databases were searched for trials comparing the beginning of ART in persons with HIV and tuberculosis. The analysis covered publications made between the creation of the database and March 12, 2021. Additionally, the researcher stratified the analysis by CD4 count and contrasted ART in 2 weeks with ART from 2 to 8 weeks after TB therapy and ART within four weeks against ART more than four weeks after TB treatment. Nine experiments were discovered after the researcher reviewed 2468 abstracts. The study showed that among

persons with HIV and TB illness, early ART had no overall impact on mortality risk. Early initiation of ART for all patients with TB and HIV may be ideal for later ART for logistical and patient preference reasons.

Owiti et al. (2015) studied the uptake and outcomes of integrating HIV and TB services in rural Kenya. A prior-and-after cohort research design was selected by employing program data. The findings indicated that out of 501 HIV-infected TB persons, 71% were started on CPT and 39% on ART before initiating HIV-TB integrated care. Following the incorporation of services, 323 HIV-positive people were started on CPT and ART, respectively, in 98% and 61% of cases. In the pre-and post-integration phases, the median time to initiation of ART and CPT declined from 7 to 2 days and 42 to 34 days, respectively.

## **2.6 Factors Associated with TB/HIV Co-infection**

Different research conducted worldwide has highlighted factors related to HIV/TB Co-infection. In a population-based, retrospective cohort study, Rossetto et al (2019) examined the causes of death and hospitalization among people with TB and HIV co-infected in Porto Alegre, Brazil. The results indicated that hospitalization occurrence was related to  $\leq 7$  years of study, place of birth— health authority in the district, category of entry into the surveillance system just like in situations of reentry upon withdrawal, closure in surveillance as well as in therapy withdrawal, and multidrug-resistant tuberculosis. Death rates were correlated with age, years of education, place of birth, health authorities—and type of entry—cases of reentry after withdrawal and relapses—in the surveillance system. Among patients who have co-infections, hospitalizations, and fatalities occur often.

In a different study, Carvalho et al. (2008) indicated factors linked to HIV/TB co-infection in Brazilian reference hospitals and found that these factors include gender, age, and education levels. The study covered the period between 2004 and 2005 of medical records of 171 patients. The results indicated that most of the respondents were male among these co-infected patients. Moreover, patients over 40 and those with lower education levels experienced co-infection more frequently (less than eight years of schooling).

In the EU and EEA countries, factors related to co-infection with HIV and TB were examined by Pimpin, Drumright, and Kruijshaa (2011). To approximate the prevalence of TB-HIV infection, a systematic review was conducted (EEA). Comparing western and eastern nations to central EU/EEA nations, western and eastern nations reported higher infection rates and rising trends over time. Males, young adults, those from foreign countries, the homeless, injectable drug users, and inmates were at higher risk of contracting TB and HIV.

In a 2017 study, Cui, Lin, Nie, and Lan evaluated the risk elements for tuberculosis in HIV/AIDS patients. Between 2013 and 2015, surveillance research of 1 019 HIV-positive individuals getting treatment at 3 AIDS prevention and control departments was carried out. A surveillance survey was carried out using questionnaires to collect demographic, clinical, and behavioral features medical records reviews to gather information on HIV testing, most recent CD4+ T-cell count, therapeutic schedule, and ART status, and TB screening using the symptom screen. The study looked at the overall TB prevalence over two years. A 1:1 pair-matched case-control research of patients with recently active HIV-TB co-infection was done to examine risk factors related to active TB. Patients with HIV who did not have latent TB infection, active TB, or other lung-related diseases made up the control group. According to the

research, smoking, prolonged HIV infection, and absence of ART were active TB risk factors in patients with HIV/AIDS.

Winter, Stagg, and Smith (2018) conducted research to determine trends and factors related to HIV infection amongst TB patients during ART period. The retrospective research was conducted in Wales, Northern Ireland and England. The study analyzed data from a national HIV surveillance program to identify HIV status for all TB cases reported between 2000 and 2014. Additionally, relationships between HIV and clinical, demographic, and social characteristics were found using logistic regression. Data were then analyzed using Stata version 13.1. The study found that patients who overused medications, those with miliary or meningeal TB, and persons of black African origin from high-HIV prevalence nations had the highest rates of HIV infection.

Farias, Couto, Pingarilho, and Fronteira (2021) carried out a study to investigate the prevalence of HIV, TB, HIV and HIV-TB co-infection among immigrants who resided in Lisbon, Portugal, metropolitan region and used NGO services. Quantitative, cross-sectional, and descriptive pilot research was conducted. Employees of an NGO in a metropolitan region applied an anonymous, structured questionnaire created especially for the study to a purposive sample of one hundred immigrants receiving health services. The immigrants studied shared several characteristics, including being unemployed, having low income and lower education level, using illicit drugs frequently, and smoking tobacco regularly. These traits highlight social and economic drawbacks that may affect the risk of contracting TB/HIV.

A study by Darraj, Abdulhaq, and Yassin (2021) examined tuberculosis among HIV-positive patients in the Jazan region in southwest Saudi Arabia. Cross-sectional research was performed among HIV-positive people who visited the major referral

hospital within the Jazan Region between 2017 and 2019. Moreover, the study evaluated the subjects' viral load, CD4+ lymphocyte count, and TB status. In addition, a systematic questionnaire was used to gather their demographic and medical data. The study indicated that participants aged 18 to 30 had the highest proportion of TB-positive People with HIV/AIDS (PLWHA). Moreover, male gender, past medical history, PMH of other RTIs CD4+ lymphocyte count of  $<200$  cells/mm<sup>3</sup>, and viral load of  $\geq 1 \times 10^3$  copies/mL were TB significant risk factors among studied PLWHA.

In northeast Ethiopia, a region dominated by pastoralists, Belay, Bjune, and Abebe (2017) evaluated the prevalence of HIV, tuberculosis, and TB-HIV co-infection among pulmonary tuberculosis suspects. The cross-sectional research design included three hundred twenty-five pulmonary TB suspects from five healthcare facilities. For each subject, three sputum samples were obtained. Ziehl-Neelsen staining was employed to test sputum samples for acid-fast bacilli, and the remaining samples were cultured. HIV testing and participant interviews both took place. The study found that ethnic Afars had HIV infection rates in TB patients and suspects despite the high overall incidence of HIV/TB co-infection in the present research. According to findings, there is presumably a low HIV infection prevalence amongst Afar pastoralists.

In Southern Ethiopia's Arba Minch General Hospital, Mama, Manilal, Tesfa, Mohammed, and Erbo (2018) examined the prevalence of PTB and related factors among HIV-positive individuals visiting the ART clinic. Cross-sectional research was conducted, and a sample size calculation formula for estimating the single population proportion was used to calculate the sample size. Using a systematic random selection technique, the respondents took an average of 70 HIV patients who visited an ART clinic daily. A standardized questionnaire that had already been evaluated was utilized to evaluate the related factors. Sputum samples were taken, stained with acid-fast, and

inspected under the microscope. SPSS Version 20 was deployed to analyze data. According to the findings, smoking, a low CD4 count, and a history of tuberculosis were all potential risk factors.

In a hospital-based retrospective study, Mitku et al. (2016) studied the factors that influence TB/HIV co-infection in HIV-positive patients in Ethiopia's Amhara region and discovered that factors like marital status, baseline CD4 count, WHO clinical staging, smoking status, taking alcohol, as well as home ownership influence HIV/TB co-infection in HIV-positives adult. The key determinants for TB/HIV co-infection were identified to be severe clinical illness, smoking, and alcohol use.

In Ethiopia, Fite et al. (2019) examined HIV and TB Co-infection as well as related factors among HIV-reactive persons using 373 patients who were selected by employing simple random sampling. The authors found that educational status, World Health Organization clinical stage, drug dependency, and baseline CD4 count were determinants of co-infection. Hence, counseling, regular monitoring of pharmaceutical medication adherence, and health education regarding lifestyle adjustment are advocated.

In another study in southern Ethiopia, Negussie, Debalke, and Belachew (2018) they used a facility-based retrospective study to assess factors related to HIV-Tuberculosis coinfection among PLWHA going to ART clinics. The results revealed that PLWHA's at WHO clinical phase 3, CD4 level of 200 to 500 cells/mm<sup>3</sup> and < 200 cells/mm<sup>3</sup> at ART initiation, and who didn't take INH prophylaxis were related to HIV-TB co-infection. As such, the authors argued that In addition to strengthening INH preventative efforts to lower TB incidence, quick and sensitive diagnostic approaches must be used to identify co-infections early.



Using a Case-Control Study design, Hatoluf, Berhanu, and Yadeta (2013) examined the TB Infection determinants among HIV-positive adults going for clinical care within Western Ethiopia. Results indicated that being widowed/divorced, not having a formal education, being underweight, having a diabetic mellitus history, and being in advanced WHO HIV/AIDS clinical staging were determinant factors related to TB/HIV co-infection. In South Africa, Shamu et al (2019) studied knowledge regarding related factors of TB as well as HIV/TB co-infection in young people in selected districts. The population was women and men aged between 18 and 24 years.

In the Shegaw Motta district hospital, Fenta, Demeke, Bitew, Kebede, and Hailu (2020) assessed the prevalence, related factors, and determinants of TB co-morbidity of HIV seropositive persons. Between February and April 2019, 326 HIV-positive individuals participated in a cross-sectional study. The respondents were chosen using the systematic random selection method. Data were then entered into SPSS version 20.0 for analysis. According to the study, TB is highly prevalent among people who are HIV seropositive. Alcohol consumption, WHO clinical phase, BMI, and functional status were all predictors of HIV-TB co-infections.

Zeru (2021) conducted research on the prevalence as well as HIV-TB co-infection contributing factors among HIV patients. Patients at the Hiwot Fana hospital who tested positive for HIV between December 2014 and 2018 were the subject of a retrospective analysis. The study subjects were chosen using straightforward random sampling. Data were examined using SPSS and STATA. Logistic regressions with one and two variables were used. According to the study, there is a significant frequency of TB among HIV patients, and it is forecasted by factors including marital status, education level, weight as well as WHO clinical phase III.

Among HIV patients receiving ART at Jimma University, Desalegn (2017) assessed the prevalence of tuberculosis co-infection and related elements. From March to April 2016, institution-based cross-sectional research was carried out at the ART clinic of Jimma University Specialized Teaching Hospital (JUSTH). Each participant in the study was subjected to a convenient sampling method for data collection. Skilled data gatherers gathered data. Data were gathered using a standardized questionnaire based on interviews. SPSS version 20 and Microsoft Office Excel for Windows 2008 were used for the statistical analysis. To evaluate the association between study variables, bivariate and multivariate logistic regressions were performed. The study discovered that HIV patients had a significant prevalence of TB infection. HIV and TB co-infection was linked to high age groups, CD4 counts below 200 cells/mm<sup>3</sup>, not taking ART frequently, and a history of consuming alcohol and smoking cigarettes.

In Burkina Faso, Meda et al. (2013) observed TB infection risk factors among patients with HIV/AIDS. The findings indicated that among PLWHAs, TB risk factors include urban setting, lack of education, TB history, a large number of people living in the household, male gender, present or past history of pulmonary asthma, and poor geographical access to care. In addition, Elsadig (2020) studied the related factors of HIV/TB Coinfection in Kassala State, Eastern Sudan, using a cross-sectional design. The results indicated that the age group most influenced by HIV/TB was 21 to 30 years. Males comprised 75% of the cases, making them the most affected group.

In government health facilities in northeast Ethiopia, Ahmed, Mekonnen, Shiferaw, and Belayneh (2017) evaluated the prevalence of TB and its determinants among those with HIV/AIDS. In north-east Ethiopia, 451 HIV/AIDS-infected adults registered in government health institutions' HIV care clinics were the subject of 5-year retrospective cohort research between May and June 2015. From July 1, 2010, to May

2015, 451 newly recruited, fully informed HIV-positive persons in the adult HIV care clinic were monitored. In comparison to the following years, TB incidence among individuals with HIV/AIDS was greater in the first three years. The factors of the occurrence of TB were shown to include prior TB disease, low BMI, no IPT, and hemoglobin levels, advanced WHO clinical stages, and bedridden status.

In Ethiopia, TB/HIV co-infection prevalence and its contributing factors were evaluated by Tesfaye et al. (2018). Major databases like Pub Med, CINAHL, Online Africa Journals, and Google were thoroughly searched using search criteria to conduct this systematic review and meta-analysis. Moreover, STATA version 11 was employed for analysis. The authors obtained the required data using a uniform data extraction procedure. The researcher assessed statistical heterogeneity between researches by employing Cochran's Q test and I<sup>2</sup> statistic. The pooled effect size was calculated as prevalence, and odds ratios were used to calculate relationships. The results showed that HIV/TB co-infection prevalence is rising and needs attention. Advanced WHO stage and low CD4 count are key components to double infection.

In Southwest Ethiopia, HIV and tuberculosis co-infected individuals had their rates of delayed presentation for HIV care evaluated by Gese sew, Tsehaineh, and Massa (2018). Between August and October 2013, records from the ART clinic at Jimma Hospital, located in Addis Ababa, Ethiopia, were used in a retrospective observational cohort research. Data was extracted using a data extraction checklist from the database. The data analysis used logistic regression mode. The researcher found that HIV/TB co-infected persons made up three out of five late presentations for HIV care. According to the study, higher proportions of delayed presentation were visible in tobacco smokers, bedridden patients, and those living in single rooms.

In Northern Tanzania, Mollel et al. (2019) evaluated incidence rates for TB among HIV-positive patients. This retrospective cohort analysis includes information regularly gathered from patients who attended CTCs in Kilimanjaro, Arusha, and Tanga districts from 2012 to 2017. The participants were all patients (over 15) who tested positive for HIV and visited one of the 489 CTCs. Hospitals, health clinics, and dispensaries were listed as categories for public and private CTCs. The study discovered that better TB diagnosis due to a national effort was the reason for greater TB incidence. The poor state of nutrition, not receiving ART treatment, and low CD4 counts were linked to a greater TB prevalence among HIV-positive persons going for CTCs.

A study by Magomere and Obwoye (2018) evaluated clinical parameters influencing the development of TB among people with HIV after the start of ART in Bungoma and Webuye hospitals within Bungoma County. There were 156 cases and 156 controls that made up the study population. Additionally, case-control research was done at two public hospitals from January 2017 to April 2017. Adults with HIV who acquired TB after starting ART were the cases, whereas adults with HIV who did not get TB after starting ART were the controls. Information was gathered using a standardized questionnaire that an interviewer presented. The findings of this study indicate that, after controlling for potential confounders, not taking isoniazid, having WHO clinical phase III/IV, and having interrupted ART were all independent predictors of increased risk of TB in PLWH following ART commencement. After starting ART, quitting smoking reduced PLWH's risk of contracting TB. The risk of TB among HIV patients was decreased by expanding access to isoniazid preventive medication.

Achieng (2016) investigated the factors influencing the effectiveness of TB treatment in TB-HIV co-infection patients and those with TB alone in Nyando Sub-County. Using a descriptive research design, the results indicated that factors that increased the risk of

co-infection include male sex, age, and urban areas. Factors related to treatment success (treatment and cured completely) were female sex, residing in a rural area, having pulmonary TB, being HIV negative, and being on ART.

### **2.6.1 Demographic Factors Associated with TB/HIV Co-infection**

In Mombasa County, Kenya, Yonge (2017) evaluated the epidemiology of HIV TB co-infection, clinical manifestations, and effects on immunohaematological parameters. AFB was detected in the sputum of 500 suspected tuberculosis patients and then cultured on solid and liquid media. Using the BACTEC MGIT 960 incubator, a drug susceptibility test was conducted. Human immunodeficiency virus testing was done on blood samples from tuberculosis suspects. Sysmex Kx-2 and CD4+T cells were used to perform the complete blood count, which was then analyzed using a FACS count flow cytometer. The medical and demographic information of the tuberculosis suspects was gathered using a questionnaire. The study revealed that tuberculosis prevalence was higher in females compared to males. The majority of TB cases had between 25- 34 years of age.

Using cross-sectional data from SSA, Aliyu (2018) investigated demography and the co- epidemics of HIV and TB. In this cross-sectional research, participants were drawn from 2 TB clinics within the Nigerian state of Kaduna: Barau Dikko Hospital (BDH) and National Leprosy and TB Training Center. Suspected cases who visited the facilities for the first time with symptoms indicative of TB and an undetermined HIV status were included. Participants submitted written informed consent and had to be 18 or older. In the clinic, a spot sputum sample under observation was taken from each patient, and their HIV status was ascertained. A sequential testing strategy was used to examine samples obtained from 1603 probable cases of pulmonary TB who gave informed agreement. In inconclusive samples, HIV was tested using 2 HIV fast tests

and then retested using a third assay. According to the study, those who had both TB and HIV were more likely to be female, younger, and unmarried.

A study by Melkamu, Seyoum, and Dessie (2018) evaluated the factors that influence the development of TB/HIV coinfection in adult HIV-positive patients receiving clinical care at two public health institutions in Nekemte, western Ethiopia. A Case-control research with no matches was conducted between December 26, 2011, and February 29, 2012. HIV positives with TB infections made up 123 cases, while 246 of the controls did not have TB infections. The data was gathered using a pre-tested structured questionnaire. The method used to acquire the data was face-to-face interviewing. Data on other clinical features were taken from each patient's file. The study discovered that among adult HIV positives, TB co-infection is related to age, marital status, body mass index, WHO clinical staging, and having a history of diabetes mellitus.

In Shashamene Town, Oromia Region, South Ethiopia, Gisso, Hordofa, and Ormag (2022) evaluated the prevalence of PTB and related elements in HIV-positive persons visiting government-owned hospitals. An analysis of cross-sectional data was carried out between November 2020 and February 2021. Blood was taken to count CD4 using a BD FACSPresto analyzer, and a sputum sample was taken for analysis using the Expert RIF/MTB assay. Data were gathered using semi-structured questionnaires. In this study, persons with HIV/AIDS who visited public hospitals had a relatively high overall frequency of pulmonary tuberculosis. Age between 50 and 64, female gender, and WHO stages (III and IV) were factors strongly linked to TB infection prevalence.

In the Amhara area, Ethiopia, Mitku, Dessie, Muluneh, and Workie (2018) investigated the prevalence and contributing elements of HIV/TB co-infection among HIV-positive

individuals. HIV-positive adult patients who attended HIV clinics from 2006 to 2014 were subjects of retrospective research carried out in hospitals. To choose the 572 patients, a stratified random sampling technique was used. ART clinic nurses were chosen to gather data between January 2013 and January 2014. To gather information, a structured questionnaire was used. The study looked at patient cards, lab request forms, follow-up forms, ART forms, and follow-up forms. The study found associations between TB/HIV co-infection among adult HIV positives and functional capacity, WHO clinical staging, marital status, baseline CD4 count, drinking alcohol, smoking status, and home ownership. The key predictors for HIV/TB co-infection were discovered to be advanced clinical illness, smoking, and alcohol usage.

In Ethiopia, Fite, Chichiabellu, Demissie, and Hanfore (2019) determined HIV and TB Co-infection and demographic-related factors among patients with reactive HIV. The selection process involved 373 patients and basic random sampling. Cross-sectional research was undertaken in the health facility at WSUTRH. A review of the literature led to the adaptation of a structured questionnaire. An interview and assessment of medical records were done. According to the study, co-infection was significantly predicted by educational level, drug use, WHO clinical stage, and baseline CD4 count.

In Argentina, Zerbini, Greco, Estrada, and Cisneros (2017) conducted a study to investigate the demographic factors related to HIV/TB Co-infection in adults from six provinces. A Historical - case-control research was conducted. All patients over 18 with a clinical or bacteriological diagnosis of TB who received treatment between January 1, 2012, and June 30, 2013, were included in the research. Surveys were conducted on sociodemographic, clinical, and bacteriological factors. Two hundred eighty-one controls and 157 cases data were gathered. Patients whose deaths were reported to the TB Control Program were treated as cases, while those whose effective treatment

outcomes were reported within a similar period were treated as controls. Poor TB treatment adherence, males who identify as indigenous, and age were linked to demographic factors linked with TB/HIV co-infection.

In Eastern Nepal, Jha, Yadav, Pokharel, Niraula, Bhattacharya, and Nagesh (2012) conducted a study to evaluate the sociodemographic aspects related to TB and HIV/AIDS as well as the prevalence of PTB among HIV positives visiting HIV clinics. Cross-sectional prospective research was conducted among HIV-positive people attending several VCT and HIV clinics in the eastern Nepali districts of Sunsari Morang and Jhapa. A face-to-face interview was conducted to gather a sputum sample. Moreover, with the support of a pretested questionnaire, data on associated socio-demographic factors and risk-taking behavior were gathered from PLHA. Using SPSS 15.0, univariate and bivariate analyses were carried out. According to the study, PTB prevalence is relatively high among PLHA who visit VCT and HIV clinics. Moreover, PTB strongly correlates with advancing age, residence, and risk-taking behavior.

Arun, Tejaswi, and Ranganath (2016) examined the sociodemographic profile of persons co-infected with HIV and TB and its relationship to the success of TB therapy in a South Indian metropolis. From 2010 to 2011, longitudinal observational research was conducted by interview method with a questionnaire on HIV-TB co-infected patients who received Directly Observed Treatment Short-course (DOTS) from five Tuberculosis Units within the Bangalore Municipality area that were randomly selected. Males and middle-aged persons were more likely to co-infect with HIV and TB, although none of these sociodemographic characteristics significantly correlated with TB treatment success.



In a hospital in Imo State, Nigeria, Obidiegwu, Chineke, Adogu, and Ubajaka (2020) evaluated the sociodemographic characteristics that affect TB/HIV co-infection in patients following a brief course of directly observed treatment. The DOTS center in Umuguma was the subject of this descriptive, cross-sectional epidemiological study that examined demographic characteristics as predictors of HIV/TB co-infection over a five-year period (January 2013–December 2017). The target group was made up of 2240 patients treated between 2013 and 2017 at the General Hospital Umuguma DOTS center in Owerri's west LGA, ranging in age from 2 to 80. Regarding demographic data, it entailed checking the DOTS registration for TB and HIV co-infection. Study subjects included all 2,240 patients recorded in hospitals' DOTS registers between January 2013 and December 2017. According to the study, age, sex, marital status, and geography all to some extent predict HIV co-infection in TB patients. Co-infection was anticipated in urban areas, among women, those in the 31–40 age range, and by being single and female.

In Northwest Ethiopia, Alemu, Wubie, and Dilnessa (2021) they assessed TB and HIV Co- Infection and demographic-related factors at Inclusive Specialized Hospital in Debre Markos. The TB patients participated in retrospective cross-sectional research. One hundred eighty patients who had full records in the DOTS clinic's log book between 2012 and 2016 made up the sample. Moreover, TB patients with complete data collected during the research period were included in the sample. Using a data extraction sheet, information was gathered by reviewing each TB patient profile in the registry log book. SPSS version 22 was utilized in analyzing data. Logistic regression was performed to ascertain the relationships between independent and outcome variables. The study discovered an insignificant association between TB/HIV co-infection and sex, age, residence, or TB category.

In South Ethiopia, Fekadu, Teshome, and Alemu (2019) assessed prevalence and Tuberculosis demographic factors among HIV-positive patients. Retrospective evaluation and analysis of patient medical records were used in this research. Variables were recorded, and 499 HIV/AIDS patient cards were evaluated. HIV and TB are the most impacted patients. In terms of the prevalence of tuberculosis, there were statistically significant disparities between males and females, with males being more afflicted. Additionally, there was a positive correlation between being single and wealthy.

Using a descriptive cross-sectional research design, Mumbe, Nzioki, Mutai, and Ndiritu (2020) examined the sociodemographic elements affecting treatment compliance in Kenya's Mwingi East Sub-County. A semi-structured questionnaire was used to gather the quantitative data. To find TB patients to participate in the study, clustered random sampling was used. To analyze data, SPSS version 20 was used. There was the use of descriptive and inferential statistics (regression analysis). According to the results, TB patients had relatively high adherence rates to medicine intake for the condition. Age was the only sociodemographic variable that was discovered to have a significant impact on treatment compliance for tuberculosis.

Feleke, Adane, Demelash, and Gelaye (2020) assessed the prevalence of co-infection with TB and HIV among patients who attended a TB clinic at Comprehensive Specialized Hospital in Debre Tabor in North-Central Ethiopia over five years (May 2015–April 2020) and demographic characteristics. The 298 tuberculosis patients registered for treatment from May 2015 to April 2020 were the subjects of the institution-based quantitative retrospective cross-sectional study. To choose the record data, a simple random sampling technique was utilized. Data was gathered using a pre-

tested Checklist. SPSS version 20 was employed for analysis. To decrease HIV/TB co-infection, it is important to focus on the type of TB, age, place of living, and weight.

Otiende, Achia, and Mwambi (2019) assessed the demographic elements of co-TB/co-HIV infection. The study looked at data on TB and HIV-TB case notifications from Kenya's national TB control program that was combined for 47 counties for seven years (2012 to 2018). The study analyzed the probability of TB-HIV co-infection by employing the INLA paradigm. To find the best match model, six models with various time-space formulations were tested. According to the study, men were less likely than women to co-infect with TB and HIV. Adults between the ages of 35 and 44 and 45 to 54 made up a significant portion of the co-infection.

### **2.6.2 Socio-Economic Factors Associated with TB/HIV Co-infection**

Brunello et al. (2021) carried out a study to find places where co-infection with HIV and TB is more likely to take place. By georeferencing new HIV/TB cases reported in Ribeiro Preto, Southeast Brazil, in 2006, ecological descriptive research was carried out. Based on examining the key characteristics from the 2000 Demographic Census, city sectors were divided into three socioeconomic categories: lower, upper, and average levels (education level, income, and percentage of families with five or more residents). The study found that pulmonary TB was the most common and that a higher percentage of economically active male adults had TB/HIV co-infection. The occurrences were higher in regions with lower and average socioeconomic levels than those with higher socioeconomic levels.

In Khartoum, Awadalla, El-Samani, Soghaier, and Makki (2019) assessed social and economic factors associated with the development of Tuberculosis Among HIV-Infected Patients in 2010. After making a list of all the patients getting care, the cases

(HIV-TB co-infection persons) and controls (HIV persons) were chosen from 6 voluntary counseling and testing/ART treatment clinics using simple random sampling (SRS). PTB or extra-pulmonary TB patients, as well as prevalent or incident TB, met inclusion criteria. The study excluded patients under the age of 15. To boost the study's power, two controls were chosen. Ninety-seven cases, as well as 194 controls, were enrolled in the research after being screened for exclusion and inclusion criteria.

Patient registries, structured questionnaires, and records of screening outcomes were all used to gather data. The survey revealed that there were no formal jobs and no formal education. TB history, CD4 count of below 200 cells/l, and advanced clinical stages are risk factors for acquiring TB in HIV patients.

In Ethiopia, Alene et al. (2019) conducted research with the aim of investigating socio-economic factors associated with HIV and TB co-infection. Between June 2015 and June 2017, an ecological analysis was conducted using HIV and TB data from all Ethiopia regions via HMIS. Using a Bayesian methodology, different spatial binomial regression models were created for the prevalence of HIV amidst TB patients and TB prevalence among people with HIV, with and without spatial components. TB/HIV co-infection prevalence was highly correlated with the availability of health care, closeness to global borders, and demographic characteristics such as adult literacy and low wealth.

Cutrim, Medeiros, and Costa (2021) conducted a study to identify factors related to Tuberculosis/HIV coinfection. Moreover, The State of Maranhão's capital, So Lus, was the site of the researcher's spatial examination of TB/HIV cases. The analysis of cross-sectional research of confirmed incidences of HIV/TB coinfection was used in this research. Using Poisson regression, the factors connected to the co-infection with HIV

and tuberculosis were analyzed. Local and global Moran indices, as well as spatial lag regression, were used to conduct the spatial analysis. The study showed a positive correlation between population density and income and TB/HIV coinfection.

Olagunju, Odukoya, Olagunju, and Balogun (2018) evaluated the socio-economic factors related to HIV/TB Co-infection among Nigerians with TB. This was a multi-center cross-sectional research with 440 participants drawn from 40 DOTS centers using a multi-stage sampling method. To gather data on the respondents' sociodemographic and medical characteristics, interviews were conducted using a questionnaire. Moreover, a questionnaire was deployed to obtain data. The study found that employment status, educational status, and monthly income were correlated with TB Co-infection.

In Goa, Parrikar, Lawande, and Cacodcar (2020), they have researched HIV-TB Co-infection and its determining factor at Tertiary Care Hospitals. The control group was made up of an equal number of HIV patients who were not TB positive and were diagnosed during the same period as the study group, which included 342 cases of co-infected HIV-TB patients over 15 years. A chi-square test was performed to determine statistical significance, and percentages and proportions were calculated using SPSS 14.0. The prevalence of coinfection was higher in semiskilled employees and those with education levels up to secondary school, all of which were determined to be significant. The statistical significance of drinking, low CD4 levels, and comorbid illnesses, including anemia, were also discovered.

Aliyu and Magaji (2020) conducted research to establish prevalence and social demographic factors related to HIV-TB Co-Infection among Tuberculosis Patients Treated in 2014- 2017 at Specialist Hospital in Sokoto State, Nigeria. The hospital-

based retrospective study was conducted. The study comprised all registered TB patients who commenced TB treatment for the past four years (January 1, 2014 – December 31, 2017). The main data sources for this investigation were the hospital patient folders and the TB treatment registration. Data was obtained retrospectively by health professionals by employing a structured checklist. HIV- TB co-infection was moderately high, and it was associated with no formal education, previously treated TB cases, and unsuccessful treatment outcomes.

Vandana et al. (2016) examined the prevalence and socioeconomic factors influencing tuberculosis in HIV-positive patients in South India and receiving antiretroviral medication in a clinic. The ART center conducted this research from June 1, 2012 to May 31, 2013. The study comprised HIV-positive participants over 15 who had been receiving antiretroviral medication (ART) for more than six months. Purposive sampling with nonprobability was used. Moreover, data was gathered using a predesigned semi-structured questionnaire. The study revealed that demographic factors like living in rural areas, living in overcrowded houses, and consumption of alcohol were found with a higher proportion of TB.

Between January 2012 and December 2017, Nzuzi et al. (2021) examined the social and economic aspects that may have contributed to the rise in the percentage of HIV-positive TB patients at Baobab and Kiamvu TB Screening and Treatment Health Center (TSTHC) in Nzanza HZ, Matadi. This study examined 187 TB and HIV-positive patients and 187 TB patients who tested negative for HIV between 2012 and 2017. In addition to logistic regression, the study also used the homogeneity test and Pearson's Khi square test. According to the study, drinking alcohol and having extra-pulmonary tuberculosis were linked to higher rates of TB/HIV co-infection. Moreover, HIV-positive TB persons had higher daily income than HIV-negative people.

Jiamsakul, Lee, and Nguyen (2018) assessed socio-economic Statuses and Risk of Tuberculosis. This was a Case-Control research of HIV-infected Patients in Asia. According to sex, age, and CD4 cell count, TB-positive HIV-positive infections were compared to HIV-positive-TB- negative controls. A socioeconomic survey with 23 questions was sent out, including topics like education level, employment status, housing, and drug use. Conditional logistic regression analysis was utilized to examine socioeconomic risk variables for tuberculosis. The study discovered that increased TB risk in Asia is linked to poorer socioeconomic levels. The study found that not having a university education level was the greatest risk factor for TB. Additionally, living in the same place of origin and frequently burning wood or coal inside were weakly linked to TB diagnoses.

In a case-control study conducted in the Nepalese district, Mishra, Hansen, Sabroe, and Kafle (2019) they have investigated socioeconomic level and compliance with tuberculosis treatment. Face-to-face interviews using a questionnaire were used to gather the data. There were 100 controls and 50 cases in the study sample. Unemployment (odds ratio, low annual income, low occupation status, and travel expenses to TB treatment center) were all significantly linked to the probability of non-adherence to TB treatment.

Farias, Couto, Pingarilho, and Fronteira (2021) conducted cross-sectional, community-based descriptive research to assess socioeconomic factors associated with Tuberculosis and HIV co- infection among immigrants who resided in the Lisbon metropolitan area and utilized NGO services. Employees of the NGO applied an anonymous, structured questionnaire created especially for the study to a purposive sample of one hundred immigrants receiving health services there. The study discovered that regular illicit drug use, unemployment, low income and education, and

smoking tobacco regularly were all socioeconomic characteristics linked to co-infection with TB and HIV.

In Madhya Pradesh, India, Jyothi, Rao, Sharma, and Muniyandi (2017) they have assessed economic factors associated with pulmonary tuberculosis among the Saharia tribe within the Gwalior district. Saharias in the Madhya Pradesh district of Gwalior participated in a prevalence survey. 12,123 people were surveyed, and they served as the cases and controls in the current research. The survey comprised all cases and controls that tested positive for bacilli and had a 1:5 ratio. The trained health professionals gathered information from the participants and the controls using a semi-structured, pre-tested and pre-coded questionnaire. The study found that Malnutrition and low family income were related to an enhanced risk of PTB.

Prado and Maciel (2017) examined the socioeconomic traits linked to poor tuberculosis treatment results in Brazilian patients with TB and HIV. TB treatment outcomes were used to identify and classify TB-HIV patients reported from 2001 to 2011 in the Brazilian information system. Polytomous regression analysis was used in the research to model treatment outcomes as a patient's socioeconomic factors and TB clinical features' function. The study found that the use of alcohol, homelessness, low levels of education, and non-white race were the main causes of poor TB treatment results in TB-HIV co-infected patients.

Megersa (2018) conducted a study to assess the socioeconomic causes of TB co-infection in HIV/AIDS patients receiving antiretroviral therapy (ART) in one of Ethiopia's public health facilities. An observational, analytical, case-control, and quantitative investigation involving 367 randomly chosen individuals with HIV and AIDS, 92 of whom also had TB, was carried out. Utilizing a self-structured



questionnaire, data was gathered. In this study, characteristics that were independently linked with active TB among HIV and Aids patients using ART included educational status, waste disposal system, monthly income, awareness of tuberculosis prevention, and history of substance exposure.

### **2.6.3 Health Facilities Factors Associated with TB/HIV Co-infection**

Mitku, Dessie, Muluneh, and Workie (2016) examined the frequency and contributing elements of TB/HIV co-infection among HIV-positive individuals in Ethiopia's Amhara region. 571 participants tested positive for HIV. One hundred fifty-eight of them tested positive for pulmonary TB. Significant risk factors for tuberculosis in PLWHIV were lower baseline CD4 count 200 cells/l, alcoholic patients, and ambulatory patients at the start of ART. Moreover, patients who were not smokers, those in WHO clinical phases I and II, and those who owned their own homes significantly reduced their chance of contracting tuberculosis. The frequency of TB/HIV co-infection in persons receiving ART was moderately high. The existence of risk factors, as well as having an advanced clinical status, were discovered to be the best predictors of co-infection. The study suggested that health offices must establish TB/HIV co-infection units and that healthcare professionals should exercise caution while treating patients with severe illnesses.

Shah, Ewetola, and Etheredge (2021) assessed the risk factors for HIV/TB coinfection and its effects on patient outcomes. The study was done in DRC at 241 clinics. DRC hosted 241 clinics where the study was done. This study compared patients with and without TB/HIV coinfection regarding variance in coinfection rates and chances of adverse outcomes. Data from 49,460 patients undergoing ART from 241 HIV/AIDS clinics in Haut-Katanga and Kinshasa were used in this quantitative research. The study used chi-square as well as logistic regression analysis. According to the study,

considerably more patients with HIV/TB coinfection were new patients who lived in an urban or semi-rural health zone in Kinshasa province. The study demonstrated that, after adjusting for clinical factors, co-infection with TB and HIV increased the chances of death.

A study by Adejumo, Olusoji and Otesanya (2017) assessed factors related with HIV/TB Co- Infection among Drug Sensitive TB Patients Managed by Nigerian health facility. From January 1 to December 31, 2014, treatment records for patients visited at a secondary referral hospital were retrospectively reviewed. According to the study, extra-pulmonary TB cases and patients who had already undergone treatment had a higher likelihood of having HIV/TB co-infection than PTB cases and new patients, respectively. Patients who had unsuccessful treatment results had a reduced chance of TB/HIV co-infection than patients who had successful treatment. Additionally, the odds of suffering from HIV/TB co-infection were greater among patients with more than 40 years compared to patients below 25 years,

In Sichuan, China, Yang, Chen and Li, (2022) assessed the treatment outcome of Tuberculosis and health facilities related factors among MTB/HIV Co-infected Patients. All MTB/HIV co- infected patients registered and diagnosed in TB designated hospitals as well as health institutions in Sichuan from 1 January 2016 to 31 December 2020 were the subject of a cross- sectional study. Information on patients' clinical, social support, and demographic characteristics was gathered from their electronic medical records. By using Fisher's exact as well as Pearson's chi-square tests, the study determined the proportions of the various components and treatment results. According to the study, the WHO aim was not met for the overall success rate of TB therapy. Additionally, in predefined TB hospitals within Sichuan Province, MTB/HIV co-infected patients over 60 years old, being a returned or relapse treatment after default

case, having TB sputum smear positive, having EPTB infection, and getting treatment from city-level medical institute were related with unsuccessful TB treatment outcomes.

In Ethiopia, Fite, Chichiabellu, Demissie and Hanfor (2019) assessed HIV and TB Co-infection and health facilities related factors among HIV reactive patients. Study population consisted of a sample of patients going for ART clinic throughout data collection process who met the inclusion criteria. The population was made up of all HIV positive patients who attended ART clinic at WSUTRH. The study comprised HIV/AIDS patients with 18 years. In order to calculate the sample size, a single population percentage was used. A review of the literature led to the adaptation of a structured questionnaire. The study discovered that rigorous monitoring of pharmaceutical medication adherence, counseling, and health education regarding lifestyle change were important predictors of co-infection.

In Lusaka, Zambia, Nanzaluka and Chibuye (2016) conducted a research to examine the factors related with TB Mortality in health facilities. In three purposefully chosen public health institutions in Lusaka—a first-level hospital, an urban clinic, and a periurban clinic—a cross-sectional research was carried out. The World Health Organization's (WHO) 2013 criteria and reporting system for TB were used in the research, and TB mortality was regarded as any TB patient who passed away for any reason while receiving TB treatment. For TB cases receiving treatment in 2016, the study extracted data from treatment registrations. Data were analyzed using multivariable logistic regression in the study. The lack of a TB diagnostic facility in the hospitals that were chosen for the study led to higher-than-expected TB mortality rates compared to the national target.

Mollel, Maokola and Todd (2019) assessed TB prevalence among HIV-positive individuals in northern Tanzania. This retrospective cohort analysis employed information that was regularly gathered from CTCs in 3 northern Tanzanian areas. The participants in this research were all patients (over the age of 15) who tested positive for HIV and visited one of the 489 CTCs in Kilimanjaro, Arusha and Tanga districts between January 1, 2012, and December 31, 2017. The ratio of TB cases that began taking anti-TB drugs to the number of person-years of follow-up was used to calculate TB incidence. The study found an enhanced risk of TB incidence in hospitals than health facilities of lower level.

Zenbaba, Sahiledengle, Tesaw and Bonsa (2022) carried out a study to assess the health facilities associated factors with HIV infection amidst TB patients in selected public hospitals within Bale Zone, located in Southeast Ethiopia. A 5-year retrospective analysis of TB individuals registered at 2 public hospitals in Bale Zone's direct observation therapy short-course strategy (DOTS) clinic was done. The study included complete socio-demographic as well as treatment outcomes data on all categories of TB patients who were registered between 2013 and 2019 and followed up in the TB clinics at Goba referral as well as Robe general hospitals. Using a data extraction checklist, information was taken from a registry of TB cases treated using DOTS between July 2013 and June 2018. The study found that TB patient category, TB screening equipment and duration of medication as related factors of HIV infection prevalence amidst TB patients.

Lin (2016) examined the health facility parameters linked to poor treatment outcomes for tuberculosis among people with HIV in Yangon, Myanmar's antiretroviral treatment program. 958 people over the age of 15 who were registered in significant ART program with comprehensive care were included in the retrospective cohort analysis.

Between January 2012 and December 2014, the study was conducted. The study included every person who had both an HIV and TB diagnosis. Univariate and multivariate logistic regression were employed to analyze data. According to the research, 654 of 958 patients had successful treatment outcomes, whilst 186 patients lost their lives, 88 were lost to follow-up, and 30 experienced treatment failure during the course of the 12-month study period. The patients who did not undergo ART and who did not have their CD4 cell levels checked tended to experience the worst outcomes. Low CD4 cell count at TB diagnosis and patients who did not get antiretroviral therapy during antituberculosis treatment were statistically significant predictors for poor treatment outcomes for TB. The study also showed that a shortage of HIV/TB care professionals and institutional commitment to TB screening measures hampered early detection of both infections and early ART introduction during ATT.

A study by Narh-Bana, SKawonga and Odopey (2022) examined the factors affecting the execution of TB screening among PLHIV in certain Ghanaian HIV clinics. This was a qualitative research carried out in three districts of Ghana from May 6 to May 31, 2019. Seventeen in-depth interviews with HIV care providers were done as part of the study, including eight focus group talks with 65 respondents including two regional, six district, and nine institution TB/HIV coordinators. The design of interview guides, data collection, and analysis were all directed by the Consolidated Framework for Implementation Research (CFIR). All comments were verbatim digitally audio-recorded, transcribed, and coded using the Framework Approach. The study discovered lack of implementers' commitment to TB screening and inadequate facility infrastructure for screening activities.

In Kenya, Langat and Callahan (2021) assessed the factors associated with late presentation for services related to Early Infant HIV Diagnosis (EID). The study

gathered routinely data obtained from 1,346 health institutions supported by the President's Emergency Plan for AIDS Relief (PEPFAR) from October 2016 to September 2018 on all HIV-infected newborns having a positive polymerase chain reaction (PCR) test. The study discovered that the absence of maternal antiretroviral medication was related to late presentation for Early Infant HIV Diagnosis (EID) services (ART). Early infant diagnosis services must be improved, maternal pre-pregnancy HIV diagnosis rates must be increased, timely antenatal care must be provided, early infant diagnosis services must be provided, mothers who seroconvert while pregnant or nursing must be identified early, and outpatient and inpatient HIV screening must be increased. By implementing national PMTCT guidelines, early referral from the community and access to healthcare institutions should be improved.

### **2.7 Survival of Patients ART and TB Treatment**

Ji, Liang and Shen (2018) carried out retrospective cohort research in China on HIV positive patients' mortality with PTB using KaplanMeier method. The results indicated that overall death was 15.92 percent during median 27-month follow-up. Moreover, risk factors, involving more than 60 years old, complication with bacterial pneumonia, diagnosis delay, CD4+ T cell count below 50/mm<sup>3</sup> and pulmonary atelectasis, may perhaps independently aid to minimal survival. In persons who had not started cART before beginning anti-TB therapy, it was discovered that starting cART later (over eight weeks after beginning anti-TB therapy) boosted the mortality rate, whilst starting cART within 4 and 8 weeks of beginning anti-TB therapy was linked to fewest deaths (0/14).

Zenner, Abubakar and Conti (2015) examined the influence of TB on HIV infected peoples' survival in England, Northern Ireland and Wales. The study population was persons aged above 15 years who had been diagnosed with HIV between 2000 and 2008. The results indicated that patients with HIV and TB co-infection accounted for

79% of mortality in the year after HIV diagnosis and 18 percent of 1880 deaths during follow-up. Increased all-cause mortality was substantially correlated with TB co-infection. Similar findings were revealed by an analysis of AIDS-associated survival. Improved latent and active TB case-finding among HIV patients, as well as HIV testing among TB patients, are essential for ensuring proper and prompt treatment induction for both diseases. This is demonstrated by the unexpectedly high mortality in HIV-TB patients in a population with good ART accessibility and healthcare access.

In addition, Keet (2019) indicated that even after successful TB treatment, tuberculosis increases the mortality risk in HIV-infected individuals. People with HIV and TB diagnoses were the study's target population, and descriptive research design was used to conduct the investigation. About 10% of the 1,051 patients with TB who received an anti-TB and HIV prescription during their initial visit had passed away after 5 years, as opposed to less than 6% of those without TB. In contrast to individuals who had not had TB at the beginning of the study, over 19% of the respondents who had been co-infected with HIV and TB at their initial clinic visit had passed away after 10 years.

In Brazil, Swaminathan (2017) examined standard anti-TB treatment regimens using cross-sectional research design. He argues that cure rates with standard anti-TB therapy regimens average 86 percent, but that HIV-positive patients experience worse outcomes than uninfected ones. Even while the majority of HIV-infected patients react to anti-tuberculosis treatment (ATT) successfully at first, there is a high chance of contracting additional opportunistic infections and recurrent TB, which increases mortality. ART should be started as soon as possible to improve these patients' long-term outcomes and lower death.

Myanmar et al. (2019) calculated survival rates at initiation of ART by employing K-M method. The study adopted a retrospective follow-up study design covering 3598 co-infected patients. The results indicated that patients with TB and HIV co-infection had survival rates of 82.0 percent at 5 years and 58.1% percent at 10 years. Within ten years of starting ART, two out of every five TB-HIV patients passed away. Those receiving second-line ART and patients who are bedridden should be given more attention by current HIV treatment and prevention programs. Cox regression analysis was used to demonstrate that HIV co-infection significantly influences TB patients' survival rate, with death rate being 20.7 times higher than that of TB infected patients alone, according to Roshanaei et al (2014) study of survival rates of HIV and TB co-infected persons in Iran.

In Mahalapye, Botswana, Tshitenge, Ogunbanjo and Citeya (2018) conducted a mortality review of patients with HIV and TB co-infection using cross-sectional research design. The results indicated that majority of patients with HIV and TB infection were receiving antiretroviral therapy (ART) (81.63%) or had begun cotrimoxazole preventative therapy (CPT) (87.2 percent) while receiving anti-TB medication. 73 (13.6%) individuals with HIV and TB co-infection passed away prior to finishing anti-TB therapy. Two of the patients under ART for a minimum of three months prior to starting anti-TB treatment were among the three-quarters (74.4%) of patients who passed away before finishing anti-TB therapy. The majority (87.7%) of patients with TB and HIV co-infection started taking CPT before they passed away. This study proved that persons with HIV and TB co-infections had 13.6% TB death rate. In those who failed to take ART for the first three months and in those who did not start CPT for the second and fifth months, higher death rate was seen.



In a retrospective cohort study, Manosuthi et al (2006) studied survival rate among HIV/TB-co- infected persons with and without ART in Thailand. The results indicated that Survival rates among HIV/TB co-infected patients taking ART were 96.1%, 94.0%, and 87.7% after 1, 2 and 3 years following TB diagnosis, in comparison with 44.4%, 19.2%, and 9.3% among patients not getting ART, respectively. Isolated pulmonary TB, cervical tuberculosis lymphadenitis, isoniazid resistance, and multi-drug resistant tuberculosis were more prevalent in the ART group of patients (MDR-TB). According to the Cox proportion hazard model, multi-drug resistant TB and gastrointestinal TB were linked to increased death, while ART was linked to lower mortality. Antiretroviral therapy significantly lowers mortality in HIV/TB co-infected patients, and starting ART within six months after TB diagnosis is linked to improved survival, according to this study.

In retrospective cohort research, Azeez et al. (2019) studied the effects of TB treatment on individuals who also had co-infection with the HIV. HR of mortality for every variable at baseline and an estimation of the impact of risk variables among patients with TB were calculated using Cox proportional-hazards regression and log-linear model, respectively. The results showed that HIV co-infection was cause of death in 50 percent of TB/HIV patients. During extension care phase, risk of death was noticeably greater in patients with TB who were HIV-positive. Moreover, patients with TB and HIV who are receiving antiretroviral medication have a lower survival rate. HIV positive individuals have a much lower chance of surviving TB, and significant effects of age, weight, smoking, and alcohol have also been reported. According to Achieng (2016), treatment completion rates, cure rates, and success rates were all higher, with mortality, failure, and default rates being recorded as 10.33%, 1.24%, and 8.65% respectively.

Naidoo, Rampersad and Karim (2019) conducted a study with an aim of examining on how to improve survival with HIV and tuberculosis treatment integration. In order to lower co-infection mortality, the researcher analyzed existing literature regarding clinical trials as well as cohort researches on techniques for TB-HIV medication integration. Included were studies that had been released after 2009, when various treatment recommendations called for therapy integration. A total of 43 publications were found, of which 23 past studies and 9 clinical trials provided useful information on TB-HIV treatment integration. The study shown that by beginning antiretroviral treatment (ART) soon after commencement of TB medication, that is, in patients with CD4+ cell counts under 50 cells/l, the survival gain of AIDS therapy in TB patients which can be enhanced in patients. However, to lessen severity and incidence of immune reconstitution illness and subsequent hospitalization, individuals with greater CD4+ cell counts must delay starting ART until eight weeks following starting TB treatment.

In Thailand, Akksilp and Karnkawinpong (2017) evaluated ART during TB Treatment and Marked decline in HIV-Infected Patients Death Rate. The research was limited to TB patients in Ubon-ratchathani, Thailand, who were registered for TB treatment from 2003 through 2004 and who had laboratory confirmation of HIV infection. Patient outcomes were only documented up to the point at which TB treatment ended, which was typically six months following the start of treatment; no information regarding outcomes was documented after this point. Using multivariate analysis to account for CD4 count, smear status, co-trimoxazole use, and treatment facility, the study discovered a significant decrease in the risks of death for individuals getting ART before or during TB therapy. For HIV-infected TB patients, ART is linked to a significant drop in fatalities during TB treatment.

An investigation was conducted by Mutembo et al. (2016) to determine whether antiretroviral treatment increases survival in TB-HIV co-infected individuals with CD4+ T-cell counts greater than 350 cells/mm<sup>3</sup>. In retrospective cohort research, the researcher examined 337 HIV-TB co-infected individuals with baseline CD4+ T cell counts greater than 350 cells/mm<sup>3</sup> who were identified in the southern province of Zambia between 2006 and 2012. By comparing survival as per cART and accounting for differential loss to follow-up, the study calculated the impact of cART. According to the study, cART treatment decreased mortality for up to four years in patients with HIV-related TB and CD4+ T cells over 350 cells/mm<sup>3</sup> when compared to no cART, and it was also linked to greater care retention.

The survival of HIV-positive patients beginning antiretroviral therapy from 1996 to 2013 was analyzed by Lancet HIV (2017). Data from 18 HIV-1 cohorts in Europe and also North America were analyzed for the study. Patients having a minimum of a year of prospective follow-up who started using ART with three or more drugs during 1996 and 2010 and were older than 16 were eligible for this study. For the first year following the start of ART, as well as the second- and third-years following ART beginning in four calendar periods, the study calculated all-cause and cause-specific mortality hazard ratios (HRs), compensated (for age, sex, AIDS, risk category, CD4 cell count, and HIV-1 infection RNA at start of ART). The study discovered that, even in the late ART era, longevity during the first three-year period of ART is continuously increasing. The use of less harmful antiretroviral drugs, increased adherence, prophylactic interventions, and comorbidity management are probably responsible for this improvement.

Padayatchi, Karim, Naidoo and Grobler (2018) conducted a study to find out whether ART enhances survival in multi-drug resistant TB and HIV patients. 489 of the 642 individuals who were involved in the SAPIt (Beginning ART at 3 Points in TB

treatment) research, randomized controlled research of HIV/TB coinfecting individuals had their sputum culture as well as susceptibility for MTB tested. 23 patients were found to have MDR TB (at least isoniazid and rifampin resistance). Patients who were randomized to get ART within 4 to 12 weeks of starting TB therapy (combined integrated treatment arm) had their clinical results at 18 months of follow-up than patients who started ART after finishing tuberculosis treatment (sequential treatment arm). Despite a late diagnosis and a delayed start to the proper MDR TB treatment, the study indicated that early ART starting in TB individuals with MDR TB decreased death. The death rate declines seen with early beginning of ART in all other HIV-TB co-infected persons are supplemented by this survival benefit.

The effect of ART on mortality in HIV-positive people receiving tuberculosis treatment was evaluated by Odone et al. in 2017. An organized literature review as well as meta-analysis were undertaken for the study. Through manual reference searches, electronic database searches, conference books, expert consultation, and manual reference searches, researches published between 1996 and 2013, were located. Individuals getting ART either before or during TB therapy were encompassed in study population. The researcher discovered that beginning ART prior or even during TB therapy lowers probability of death in clinical settings.

Atey and Girma (2020) carried out a study to determine whether early ART initiation is better than later ART initiation in HIV/TB Co-infected Patients. Retrospective cohort analysis on 77 as well as 105 patients who began ART early and recently was carried out in Ayder Comprehensive Specialized Hospital as well as Mekelle Referral Hospital. An independent samples t-test was performed to compare the means of continuous variables between two cohorts, and Kaplan-Meier and life-table analyses were employed to compare survival curves. In the research settings, it was discovered that

TB/HIV co-infected persons who started an ART regimen within 2 weeks of starting TB treatment and who had CD4 count of less than 250 cells/ul had better survival results compared to those who started ART later. Additionally, patients with bedridden functional status had higher death rate than those with working or ambulatory functional status, as well as patients who were female.

A research by Abay et al., (2017) examined impact of early antiretroviral therapy beginning with patients with co-infections for TB and HIV. The databases PubMed, Embase, Google Scholar, Science Direct, Medscape, and the Cochrane library were all thoroughly searched for clinical studies. Before the closing date of the search, clinical trials that were published in any language were included. The Cochrane Library's standards were used to evaluate the studies' quality. A heterogeneity test was performed to evaluate the differences in study results. The study offered unambiguous proof of the decrease in all-cause mortality as a result of early ART initiation.

Damtew, Mengistie and Alemayehu (2019) assessed the likelihood of adult HIV/Aids patients starting antiretroviral medication surviving and the factors that affect mortality in Somali Region located in Eastern Ethiopia. To determine survival and the causes of mortality among PLHIV on antiretroviral treatment, a retrospective cohort research was conducted. The study comprised 784 PLHIV commencing ART at Kharamara hospital from 2007 to 2011, who had more than years 15 years of age. Reviewing the pre-ART register, the ART intake form, the laboratory request, the monthly cohort form, and the follow-up form allowed for the collection of the data. In the Somali region of Ethiopia, patients using ART showed improved survival. The study found that advanced WHO stages patients, low CD4 counts, low Hgb levels, low BMI levels, and concurrent TB infections had a greater risk of death.

Diwakar, Raghavendra and Kuma (2020) examined regardless of CD4 count, ART for persons with human immunodeficiency virus has been shown to provide survival benefits. From June 2017 to June 2018, a prospective observational cohort research was done. Kaplan Meier estimates were used for the survival analysis. The range of opportunistic infections and their contribution to mortality causes were investigated. The study discovered that PLHIV clinical and also immunological recovery with increased CD4 counts as well as decreased opportunistic infections is facilitated by early ART initiation.

Burke, Rickman and Singh (2021) conducted a study to determine the optimum time to start antiretroviral therapy in people with TB and HIV coinfection. Nine databases were searched for trials comparing the introduction of ART in patients with HIV and TB earlier or later. Studies that were released between the database's launch and March 12, 2021, were included. Additionally, the researcher stratified the analysis by CD4 count and contrasted ART within two weeks with ART between 2 and 8 weeks after TB therapy, as well as ART within 4 weeks against ART beyond 4 weeks following TB treatment. The study found that among persons with HIV and TB illness, early ART had no overall impact on risk of mortality.

Stijnberg, Commiesie and Marín (2019) examined the factors related with death in co-infected persons with HIV and tuberculosis in Suriname. This researcher used data from national TB as well as HIV databases for the years 2010 to 2015 and was a retrospective cohort research. The Kaplan-Meier estimates and log-rank test were utilized to assess the likelihood that patients with TB as well as TB/HIV co-infection would survive. It was done using Cox proportional hazard model. The findings disclosed that, for HIV/TB co-infected patients, TB treatment reduces risk of death. Similar to this, HIV

therapy that is postponed or begun within 56 days has a lower risk of mortality, and Directly Observed Treatment further reduces the risk.

Saraceni, Durovni, Cavalcante and Cohn (2019) conducted a study to determine the THRio cohort, Rio de Janeiro, Brazil's HIV patients with tuberculosis who began treatment on HAART at the same time or later. 17,983 HIV-positive individuals in 29 public clinics were part of the THRio cohort. Between September 2003 and June 2008, patients who were HAART-unaware at the period of a recent TB diagnosis were included. Days from the TB diagnosis were used to measure survival. In the research, survival was compared between those who started HAART within sixty days of TB treatment (simultaneously - ST) and those who started HAART more than 60 days later or never started TB treatment (deferred – DT). The study found that the HAART administered at similar time with TB therapy was related with enhanced survival after TB diagnosis.

A study conducted in General Military Hospital (GMH) in Bombo army barracks by Acleo (2018) aimed at examining the factors related with the Uganda's HIV/TB positive service men survival on TB treatment. The laboratory and clinical case reports in patients' files at GMH from 2009 to 2011—sample size of 143 patients—were data's primary source. A time-to-event analysis based on Kaplan-Meier estimate, Log-rank Chi-square test, and the Cox-Proportional Hazard Model were used in the analysis. According to the study, individuals who get TB before beginning ART had a higher mortality rate and a higher probability of dying than those who acquire TB while using ART.

Weerawat and Wiroj (2019) conducted a study to investigate the best time to start antiretroviral therapy in HIV-infected patients from 4 to 12 weeks of TB treatment.

Additionally, patients with TB and HIV were randomly assigned to begin taking tenofovir, lamivudine, and efavirenz after 4 or 12 weeks of TB treatment. The main result was mortality from all causes within 1 year. According to the study, there is no survival benefit to starting ART right away for HIV-infected individuals with active TB compared to waiting 12 weeks.

Gopalan and Santhanakrishna (2018) conducted a study with an aim of comparing the effectiveness and security of antituberculosis drug regimens administered on a daily, part-daily, and intermittent basis for treatment of HIV-related pulmonary TB. The National Institute for Research in Tuberculosis in south India carried out this open-label, random clinical trial. Between September 14, 2009, and January 18, 2016, adults with HIV and newly diagnosed, culture-positive pulmonary TB were enrolled. In terms of effectiveness and the formation of rifampicin resistance, a daily anti-TB regimen outperformed a thrice-weekly treatment in individuals with pulmonary TB and were HIV-positive and receiving antiretroviral therapy.

Zhandybayeva, Truzyan and Shahumya (2020) assessed survival rate of HIV-treated individuals with tuberculosis in 2008–2018 cohort in Almaty, Kazakhstan. This retrospective cohort research used data from national registries to create a descriptive, Kaplan-Meier estimate, and Cox proportional hazards regression model for all persons in Almaty who were coinfecting with HIV and pulmonary TB between 2008 and 2018. The test and description of indicators predicting the chance of survival for TB treatment results was carried out. The study discovered that the CD4 count of HIV/TB co-infected individuals and effectiveness of TB treatment had a significant impact on how long they live.



Kimani et al., (2017) examined the survival rates of individuals in Kiambu County co-infected with TB and HIV. The researcher employed a retrospective cross-sectional design with data produced by the County-level Tuberculosis Information Basic Unit. Patients with TB and HIV co-infection who had been registered in Kiambu County between 2012 and 2016 on TIBU, Kenya's computerized platform for collecting data on TB patients, made up the study population. There were 1,189 people in the population who qualified for analysis. This included patients who had received initial diagnoses of HIV infection and TB. The study found that when ART was started 14 days following the start of TB treatment, the survival of those with recently confirmed HIV and TB co-infections improved.

### **2.8 Spatial Pattern of Deaths of People Infected With both HIV and TB**

In spatial statistics, spatial patterns are used to refer to statistical description of data across space (Sherman, 2010). It is also considered a statistical or quantitative description that allows modeling and exploration of distribution of data and its relationship either other spatial phenomenon (Sankey, 2017). In spatial epidemiology, spatial patterns refer to examination and description of diseases and their geographical variations of distribution (Cressie & Wikle, 2011). The geographical distribution puts into consideration environmental, demographic, genetic and socio-economic factors. Temporal Distribution, on the other hand, refers to distribution of events across time and seasons. In epidemiology, it refers to the distribution of disease or other events such as death over a specific duration of time and seasons (Finkenstadt, Held & Isham, 2006). Spatio-temporal analysis enables the estimation of events including disease and death across both space and time in a particular location and period of time.

In Iran, Ghanbarnejad et al (2015) studied spatial pattern of TB/HIV coinfection in South Iran. The aim was to describe the districts in Hormozgan Province with

considerable disease clustering and to explain the geographical distribution of TB/HIV co-infection using GIS and ESDA. The province of Hormozgan's health centers provided the information. ArcGIS 9.3 software was used to examine the evidence of local and global spatial clustering using Moran global and LISA. The location of TB/HIV cases was not random but rather grouped. Six districts were suggested to be categorized as "hot spots" using spatial clustering. Additionally, these areas have dense populations.

Krishnamoorthy, Majella, Rajaa and Bharathi (2021) assessed the geographic distribution and factors that influence HIV infection in Indian adults between the ages of 15 and 54. The National Family Health Survey-4 data was used in the study's secondary data analysis. Using the svyset command, the study took clustering and stratification into consideration while creating its sample plan. The study found that being separated/widowed/divorced, living in an urban area, being resident in North-Eastern, Southern or Western region, having history of many sexual partners, a suspected STI or self-reported TB were significantly in relation with HIV infection. The study found a positive spatial autocorrelation. The revealed that in India, HIV infection among individuals aged 15 to 54 is spatially concentrated, with the bulk of cases occurring in the southern and northern regions.

Corbett, Watt and Walker (2018) assessed the global trends and linkages between the HIV Epidemic and the rising tuberculosis burden. The study examined information from reports of TB cases, cohort treatment results, examinations of MTB infection, and the incidence of HIV in TB patients and other subgroups. The WHO, the Joint United Nations Programme on HIV/AIDS (UNAIDS), the US Census Bureau, and US Centers for Disease Control and Prevention (CDC) all have databases that have been used to compile the statistics. There were 8.3 million new cases of TB in 2000. The WHO

African Region had highest rates of tuberculosis incidence and a 6% annual increase in the number of cases. HIV infection was responsible for 9% of recent TB cases (15–49 years), but the percentage was substantially higher in the WHO African Region and other developed nations, most notably the United States. A total of 12% (226 000) of the estimated 1.8 million TB-related fatalities were caused by HIV. Of all adult AIDS deaths, tuberculosis accounted for 11% of the cases. Adults had a 0.36% frequency of *M. tuberculosis*-HIV coinfection (11 million people). In 8 African countries, the prevalence rates of infections were equal to or higher than 5%. There were 2 million coinfecting adults in South Africa alone.

Queiroz, Berra and Garcia (2018) examined the spatial distribution and temporal trend of tuberculosis-related death. Based on secondary mortality data, an ecological research was conducted. The study took TB-related deaths into account. The Local Empirical Bayesian Method was used to compute descriptive statistics and estimate and smooth gross mortality rates. In order to examine the temporal trend in TB mortality coefficients, Prais-Winsten's regression was applied. To examine the regional distribution of TB mortality, the kernel density method was employed. According to the report, tuberculosis caused 236 fatalities. Males, singles, and persons of mixed ethnicity had a disproportionate share of the burden of tuberculosis mortality, which had a mean age of death of 51 years. The East, West, and North health districts witnessed a concentration of TB deaths, and the research period found no change in the tuberculosis mortality coefficient.

In South of Iran, Qanbarnezhad, Roustazadeh and Alizadeh (2018) conducted a study with an aim of determining the spatial distribution of HIV and TB Co-infection. This ecological descriptive study was carried out in the Hormozgan province. Patients with various forms of TB and HIV positive residing in the area were eligible for this study.

New cases of co-infection TB / HIV municipal residents identified from March 2006 to February 2011 at the period of diagnosis of TB serology and HIV were selected for the study. Health facilities in the province of Hormozgan provided the information. ArcGIS 9.3 software was used to examine the evidence of local and global spatial clustering using Moran local and global indicators of spatial associations (LISA). In the province of Hormozgan, the spatial dissemination of TB/HIV cases was not random and was concentrated. Six districts were suggested to be "hot spots" by spatial grouping.

In Macapá and Amapá, Brazil, Giacomet and Santos (2021) evaluated temporal trend of tuberculosis incidence and its geographic dispersion. Environmental analysis of instances of tuberculosis reported in the SINAN Information System for Notifiable Diseases from 2001 to 2017. Additionally, the study classified the temporal trend of incidence using the Prais-Winsten test, and employed disrupted time series to spot variations in temporal trend prior and also after quick molecular test was implemented, as well as to confirm seasonality in the municipality. Scan statistics and case density were classified using the Kernel estimator to pinpoint high-risk locations for tuberculosis. The study found that although the incidence of tuberculosis had been declining over time, detection had increased following the introduction of RMT-TB, and the disease had a seasonal pattern. The distribution of cases was varied, with an inclination to concentrate in at-risk and vulnerable areas, demonstrating a pattern of illness inequality in the area.

Uthman, Yahaya, Ashfaq and Uthman (2019) conducted a study to investigate the trend analysis as well as sub-regional distribution of the number of HIV-positive and TB-dead in Africa. Multilevel Poisson growth curve models were used to examine time trends across 16-year research period from 1990 to 2005. The study looked for evidence of local and global spatial clustering using the Moran LISA. The researcher discovered

an increase in TB-HIV mortality recorded in Eastern, Southern, Middle and Western Africa. TB cases were not distributed randomly but rather in clusters. According to spatial clustering, six nations might be considered "hot spots," while thirteen countries were at an enhanced risk of HIV-TB mortality.

In Ceara, Brazil, Peres, Façanha, and Junior (2019) looked at spatial patterns of co-infection and TB/HIV. Between 2005 and 2014, patients in Ceará who were 15 years old and above and had tuberculosis made up the majority of the population. The Mortality Information System (SIM) and SINAN were used to gather data on diagnosis and fatalities related to tuberculosis from 2005 to 2014. A spatial analysis revealed that the health regions of Sobral, Fortaleza, Caucaia, Maracana, Cascavel, and Itapipoca were linked to the majority of municipalities with a high risk of TB. Two clusters of elevated risk for tuberculosis were found in spatial autocorrelation. The Macro regions of Health and Sobral Fortaleza depict the accumulation of municipalities with high danger for TB/HIV coinfection, and the municipalities of Tauá acid and Orós Jaguaribe showed a spatial relationship of two clusters discovered in the aforementioned macro regions.

Musenge and Vounatsou (2018) assessed the use of spatial analysis in understanding child HIV/TB mortality. Based on cross-sectional data gathered in 2004 from Agincourt sub-district located in rural northeast South Africa, the study performed a secondary data analysis. In total, 5,084 homes contributed to 54 of the 6,692 children from 1 to 5 years who died from HIV/TB, according to the report. The greatest effect on child TB/HIV mortality was caused by maternal death. In households with higher socioeconomic position and when the child was older, a protective effect was discovered. The regions with the highest rates of child HIV/TB death rate were those without any health facilities, according to spatial models.

Kibuuka, Mpofu, Neave and Manda (2021) conducted a study to look into the spatial epidemiology, distribution, and relationship between HIV prevalence and local poverty for TB mortality in South Africa in 2010. Methods: From 2005 to 2015, a total of 776,176 TB fatalities were examined. Global and local Moran's Indices (Moran's I) approaches were utilized to look into spatial and TB death rates local clustering. To determine how poverty and HIV affect TB death rates, geographical regression analysis was used. The results of this study showed a statistically significant decline in TB fatalities as well as an unbalanced distribution of TB fatalities among different regions and population categories.

In Ethiopia, Alene et al. (2019) looked at geographic patterns of co-infection with HIV and tuberculosis. The HMIS was utilized to collect TB and HIV data between June 2015 and June 2017. Moran's I statistic was used to evaluate spatial clustering. Using Bayesian methodology, different spatial binomial regression models were created. The findings showed that 7.34 percent of TB patients also had HIV; hotspots were found in Afar, Amhara and Gambela area districts, and coldspots were found in Oromiya district. In Oromia area, the TB prevalence among HIV-positive individuals ranged from 0.7 percent to 14.5%. Districts in the Gambela, Somali, Afar and Oromiya regions were found to have TB hotspots prevalence among PLWHA, while Amhara and Tigray regions had cold spots. Low adult literacy and, wealth index and closeness to various international borders were ecological-level variables linked to TB prevalence among HIV-positive persons.

Kefyalew et al., (2020) conducted a study with an aim of investigating the district-level geographical patterns of co-infection with TB and HIV in Ethiopia. Between June 2015 and June 2017, the study conducted ecological analysis using TB and HIV reported data from every region. The Getis-Ord statistic was used to evaluate spatial clustering. Using

a Bayesian methodology, different spatial binomial regression models were created for the prevalence of HIV among TB patients and prevalence of TB among people with HIV, with and without spatial components. The study provided proof that TB/HIV co-infection in Ethiopia cluster geographically.

He et al., (2022) assessed spatial HIV/AIDS burden patterns over time and space between 1990 and 2019. Information was taken from 2019 GBD Study. To measure change in trends at the national, regional and global levels, the estimated annual percentage change (EAPC) and age- standardized rate (ASR) were utilized. The analysis discovered a global decline in HIV/AIDS incidence, deaths, and DALYs over the previous 15 years, particularly in rates of mortality and DALYs. The number of HIV positive people worldwide is constantly rising, nevertheless. Notably, there has been a negative tendency in high-middle and high SDI locations.

In Namibia, Shipanga (2019) conducted spatial temporal assessment of survival among HIV and TB Co-Infected individuals in Erongo Region. A retrospective cohort research between 2003 and 2017 was conducted utilizing data from 3145 participants from all 16 health facilities in the Erongo Region of Namibia that provided ART and TB management. The study also evaluated the spatial as well as space-time clusters of HIV and TB Mortality using Bayesian Inference in STAR models. Of the 3145 patients, 1673 were still alive at the end of the research, whereas 424 defaulted on their treatment, 42 ceased receiving it, and 542 were relocated. Mortality was found to be greater in the Usakos district. As the WHO clinical stage increased, mortality got worse.

Additionally, global Moran's I demonstrated the hotspots and clustering of EAs in the Erongo Region. HIV-TB co-infected patients' deaths made up large percentage of the cohort's deaths.

In Uganda, Aturinde, Farnaghi, and Mansourian (2019) conducted spatial analysis of HIV/TB co-clustering. The study looked into the geographic clustering patterns of two diseases, both separately and together, using the world-wide Moran's index. The District Health Information Software 2 system, which is held and managed by the MOH, provided the HIV and TB case data for 2015 to 2017. The findings revealed that whereas TB and HIV are strongly associated (55- 76%), their spatial clustering patterns are rather dissimilar. Joint TB/HIV prevalence data exhibits recurrent hotspot clusters in areas near Lake Victoria and also in northern Uganda. The clusters may be related to, respectively, the existence of refugee and internally displaced person camps and high HIV prevalence amongst Lake Victoria's fishing community. Low HIV prevalence in areas with a culture of circumcision may help to explain the persistent cold spot seen within eastern Uganda and Kasese area.

Musenge, Vounatsou, and Kahn (2013) conducted research in South Africa on the application of spatial analysis to comprehend child HIV/TB mortality. The study employed cross-sectional data from the Agincourt sub-district in rural South Africa. In Kenya, Otiende, Achia, and Mwambi (2019) investigated spatiotemporal patterns of TB-HIV co-infection risk using Bayesian modeling. The study examined data from Kenyan national TB monitoring program's 7-year analysis of case notification information for cases of tuberculosis and tuberculosis with HIV in 47 counties (2012-2018). The researcher analyzed probability of HIV-TB co-infection using spatiotemporal poisson regression models within INLA paradigm. To find the best match model, six models with various space time formulations were tested. By drawing posterior marginal from best fit model, the study evaluated the spatial patterns and temporal trends of co-infection risk.



Otiende, Achia, and Mwambi (2019) investigated spatiotemporal patterns of TB-HIV co-infection risk using Bayesian modeling. The study examined data from Kenyan national TB control program's seven-year analysis of case notification information for cases of tuberculosis and tuberculosis with HIV in 47 counties (2012-2018). The researcher analyzed probability of HIV-TB co-infection by employing spatiotemporal poisson regression models in INLA paradigm. To find the best match model, six models with various space-time formulations were tested. The study used posterior marginal from best fit model to map temporal trends and geographic patterns of co-infection risk. Spatiotemporal model was the best at describing regional differences in TB-HIV co-infection, in accordance to comparisons of Bayesian DIC and effective number of parameters (pD).

In rural western Kenya, Sifuna, Oyieko and Ogutu (2018) carried out spatiotemporal analysis of HIV related mortality from 2011 to 2015. In order to determine if local aggregation of HIV-related mortality will become substantial over a 5-year period, the researchers used Enhanced Hot Spot Analysis. The results showed that hotspot analysis found 20.0 percent of the research region (72 km<sup>2</sup>) to be hotspots, while 4.2 percent was determined to be cold spots (15 km<sup>2</sup>).

Sherman (2010) claims that the Poisson distribution describes likelihood that specific number of events will happen within specific period of time or space, provided that they do so at a known constant mean rate and regardless of the interval between occurrences. There are four conditions of using Poisson distribution. An event can happen at any number of times throughout the course of a time period, which is the first requirement. Second, things happen on their own. In other words, if an event happens, it has no bearing on the likelihood that another one will happen at the same moment. Thirdly, probability of an event occurring is proportional to the length of period. The number of

occurrences in other prescribed time, such as area, distance, or volume, are likewise subject to the Poisson distribution. The study assumes that the count data has a Poisson distribution, and that the relative risks' log will be modeled. For example, in Kenya, Bayesian hierarchical modeling was utilized in Otiende, Achia, and Mwambi's (2020) research on combined spatiotemporal risk patterns for HIV and TB.

In Kenya, Muriithi (2018) conducted a spatial analysis to determine spatial distribution patterns of notified teenage TB cases over three years (2013 to 2015). The study took place at diverse counties. This considered reported cases in 2013 to 2015 that ranged in age from 13 to 19. The National TB Program provided the data. In comparison to the generalized mixed model, the conditional autoregressive model was found to be the most effective. The findings demonstrated that the incidence of TB remained stable over time and that there was little sex-specific variation. The investigation also discovered an important county-level TB epidemic pattern.

Musika (2016) carried out a spatial visualization as well as analysis of TB infection in Kitui County. All TB cases that had been reported in all the 5 TBMU centers between January 2010 and December 2012 took part in this research. The total sample size was 500, with an average of 166 cases chosen from each year. Data was collected randomly from patients between January 2010 and December 2012. Data mainly comprised secondary data obtained from registers at the TBMU centers with the authority of the concerned stakeholders and as per the policy of the Ministry of Public health & Sanitation. Primary data was also collected from respondents by conducting both face to face interviews and telephony. For display and analysis, the participants' and the facilities' actual addresses were transformed into GIS coordinates and then exported to ArcGIS/R-GIS. According to the report, TB is more prevalent in major cities, along major roads, and in highly populated areas. High mortality rates were observed in both

densely inhabited and sparsely serviced locations. There was a connection between the high death rate, HIV, and poor literacy rates, and it also demonstrated a connection between the prevalence of TB infection and HIV. Lack of criteria in the selection of TB diagnosis and treatment centers and related services was also demonstrated.

A spatial temporal analysis of patterns of pediatric tuberculosis was carried out by Kibet (2019). The Kenyan National Tuberculosis Control Program provided information on the pediatric cases that had been reported. After then, the cases were divided up by county. Thematic maps were then provided via visualization using the ArcGIS software, which assisted in identifying space- time inconsistencies. The study discovered that pediatric TB cases are generally trending upward. Additionally, smear positive cases of TB were least common in children and were connected with urban areas with high population. Over the course of the study, the study showed an escalating trend toward clustering. However, Kitui, Isiolo, and Meru counties were found to have high-high link with their neighbors, indicating clustering. The majority of the counties had an insignificant relation with their neighbors. While the counties nearby indicated a propensity to become hot places, Tharaka-Nithi and Machakos counties were designated as the hot spots for 2010. 2010 found the designation of Baringo, Uasin-Gishu, Nandi, Kisumu, and Kericho as cold spots. In 2011 there were no hot spot counties, but Isiolo and Meru did exhibit some signs of potential hot spots, whereas Baringo displayed signs of potential cold spots.

Woldeyohannes and Abera (2017) looked into the temporal and spatial distribution of tuberculosis over the world (TB). In order to conduct the literature review, a variety of sources, such as books, articles from scholarly and professional journals, and web-based resources, were identified and evaluated. Search engines were employed to locate data in bibliographic databases and on the web. The investigation discovered enough

proof that there was significant high-rate geographic and temporal TB clustering across study locations. In "TB Epidemic" and hyperendemic "hotspots" that are frequently characterized by overcrowding, HIV infection, unemployment, and other social variables, significant clustering of TB was observed. The general development indicators that varied geographically were connected with TB incidence trends. Another risk factor implicating differences in TB incidence among nations was people mobility.

Bastida, ATellez and Montes (2018) conducted a study with aim of identifying TB prevalence in the State of Mexico from 2006 to 2010 was examined using a GIS and the SCAN statistics tool. Using spatial and space-time analysis, nine significant clusters were found. According to the study, TB is focused in places adjacent to Mexico City rather than being spread randomly throughout the State of Mexico.

Otiende, Achia and Mwambi (2019) examined the spatial Bayesian modeling of patterns of TB- HIV co-infection risk in Kenya. Over a seven-year period (2012-2018), the national TB prevention and control program in Kenya gathered and analyzed case registration data on TB & TB-HIV for 47 counties. The study analyzed geographical patterns of coinfection risk by mapping the posterior boundary from the best fit model. The spatial map shows the relative risk plot in order to show the cumulative predicted values of the risk of TB-HIV a combination of viruses over a 7-year period (2012-2018) for each county. Twelve of the 47 counties, as indicated by values more than 1, had a high co-infection risk. These high-risk counties, the majority of which were found in western Kenya, were Siaya, Kisumu, Migori, and Busia counties, with Homabay County at the top of the list.

## **2.9 Temporal Distribution of People Infected With both HIV and TB**

In Northeast Brazil, Queiroz et al (2018) assessed temporal trend of mortality because of TB. In order to examine temporal trend of TB mortality coefficients, Prais-regression Winsten's was utilized. To examine the regional distribution of TB mortality, kernel density method was employed. Temporal trends in death showed that some regions have greater TB mortality rates therefore, to be given priority in TB public health initiatives. In Brazilian metropolis, Cavalin, Pellini and Lemos (2020) examined temporal distribution of TB-HIV co-infection. In this study, the trends of time of the disease were analyzed using Prais-Winsten regression. The results indicated that between the year 2007 and 2015, TB-HIV co-infection ranged between 10.5% and 13.7%, but there was a drop of 3.0 percent per year.

Dias, Rodrigues and Gomes (2022) studied the temporal epidemiology used to eradicate the HIV Epidemic in the major Brazilian Rainforest capital. In addition to applying spatial autocorrelation, Kernel density, scan statistics, and regression methods, autoregressive integrated moving-average models were used to examine the incidence rates according to time and according to location. Results: There were 6007 reports of new HIV/AIDS cases reported during the study period. The time series analysis of the incidence data showed that it stabilized from 2007 to October 2016, then fluctuated erratically till the end of December 2018. A seasonal pattern was seen between 2019 and 2022. The central and transitional regions were where the high-high incidence clusters were located. In the central region, there has been an increase in the number of newly reported cases.

Umata, Yermosa, and Dufera (2022) used Bayesian parametric modeling at Jimma Medical Center to model the time to a combination of viruses of HIV/AIDS individuals who had tuberculosis. Retrospective cohort data on 421 patients with HIV/AIDS at the

Jimma Medical Center in Ethiopia were provided. These patients were tracked from January of 2016 to December 2020 until an identification of continuing tuberculosis was made or until the trial's conclusion. The model that best suited the data was found to be the Probability log-logistic advanced timing of failure model. With a progression factor of 0.2842, patients in urban regions had shorter TB concurrent infections free survival times compared to people in rural areas. In addition, people who smoked and/or drank alcohol had shorter survival periods from co- tuberculosis compared with those who did not. Patients with a low BMI, severe WHO clinical stages (Stage III and IV), a reduced functional level, and considerable anemia had a shorter survival time from co-infection with tuberculosis.

Using Bayesian modeling, Otiende, Achia, and Mwambi (2019) looked at the temporal trends of the risk of TB-HIV a combination of viruses in Kenya. The national TB prevention and control project in Kenya collected and analyzed case reporting data regarding TB as well as TB-HIV for 47 counties over the course of seven years (2012–2018). By exhibiting the posterior boundaries using the best fit model, the study evaluated the temporal patterns of the infection risk. The co-infection risk trend exhibits an initial gradual fall between 2012 and 2016, followed by a notable spike in 2017 and a minor decline in 2018. In 2016 (0.9), the danger was at its lowest, whereas in 2012 (1.07), it was at its highest.

In China, women aged 15 or older were the subjects of Chen, Guo, and Qin's (2018) study on the seasonality of newly discovered HIV/AIDS cases. From 2010 to 2016, data on newly diagnosed HIV/AIDS cases among Chinese women aged 15 or older were gathered. In 2010 and 2016, the number of newly diagnosed HIV/AIDS cases among women aged 15 or older increased yearly from 16 603 to 26 196. The temporal trajectories of hot areas varied by demographics, with the epidemic trending towards

western boundary and southern coastal areas among women aged 15 to 49 while expanding northward out of the southwestern regions among elderly women aged 50 and over among senior ladies 50 years of age and older.

He, Ou, Yu, and Li (2019) examined the trends in the incidence of HIV/AIDS through time in several regions from 1990 to 2019. The 2019 Worldwide Cost of Disease (GBD) Survey was used to compile the data. Age-standardized rate (ASR) and estimated annual percent change (EAPC) were used to gauge the shift in tendencies at the global, regional, and national levels. The incidence, mortality, and DALY incidences of HIV/AIDS have all decreased during the past 15 years, especially the mortality and DALY rates. The number of people living with HIV/AIDS worldwide is constantly rising, nevertheless. It is important to note that places with medium- middle and high SDI showed a negative trend. To combat these alarming trends, HIV/AIDS prevention and control still need to be reinforced.

## **CHAPTER THREE**

### **RESEARCH METHODOLOGY**

#### **3.1 Introduction**

The stages along with the methods employed in this investigation are presented in this chapter. It addresses the research design, the intended audience, the data collection methods, the study's variables, and the description and specification of the model.

#### **3.2 Study Design**

The study adopted retrospective cohort study design to investigate the survival of individuals who had co- infections with HIV and TB. The target population included all patients visiting medical centers in a few Kenyan counties throughout January 1, 2015, and the last day of 2019, who were receiving complementary therapies for TB combined ART maintenance. The study cohort consisted of all 32281 individuals diagnosed with TB and HIV co-infections from the National AIDS & STIs Control Program (NAS COP) database.

#### **3.3 Data**

The study made use of the additional information collected through the NAS COP program information base. For routine case-based surveillance and report guidelines for HIV and TB, Kenya's Ministry of Health utilizes NAS COP and NLTP, respectively. NAS COP offers an Integrated Electronic Medical Records (EMR) Information Warehouse (IDWH) for Kenyan healthcare facilities that contains information about HIV/AIDS. Medical facilities in Kenya are required to monthly update existing EMR databases in IDWH. NLTP serves as the host for the Tuberculosis The data from Basic Unit (TIBU), a case-based tracking system with real-time reporting capabilities. Since its establishment in 2012, TIBU has made warnings for TB patients instant and extremely timely, facilitating the creation of reporting with ease. All medical facilities



in Kenya, public as well as private, are required to enter data concerning tuberculosis patients to the TIBU system. The NLTP and NASCOP program use the same regions' health facilities. In this research, individual patient information that was available in the NASCOP databases at the beginning of gathering data for this investigation and had been obtained throughout a five-year period between the first day of 2015 and 31 December 2019 was used. NASCOP secondary databases were gathered for the study utilizing a data extraction tool. The research used zoning criteria to arrive at the selected (sample) counties of study in Kenya. Treatment compliance was measured by the patient's consumption of the prescribed medications at the proper dosage and timing.

The study also checked on the monitored data regarding the risk of progression from latent to active TB. Patients' attendance at ART clinics and TB sub-clinics was recorded. Data on treatment outcomes also calculated the degree of adherence. Missing data was handled by use of multiple and regression imputation.

### **3.4 Inclusion and Exclusion Criteria**

The study enrolled adults who were HIV and TB co-infected and older than 15 years. The counties were supposed to be the locations where the patients received their treatments and drugs. Patients had to be receiving treatment between January 1, 2015, and December 31, 2019. Following the start of ART and TB therapy, patients who transferred to medical institutions outside the considered counties were lost to the study's follow-up. Patients who died while they were still being studied had their data treated as right censored.

### **3.5 Data Abstraction**

To protect the study participants' privacy and confidentiality, the NASCOP data was de-identified and given special ART and TB therapy random numbers before being shared.

### **3.6 Variable for the Study**

The outcome variable considered was the time to death' for those co-infected patients who were already enrolled in the trial (2015-2019) during the study period. However, for co-infected patients who were lost during follow-up, the time of death was censored. Age, sex, CD4 counts remaining under care, marital status, patient status, weight, WHO clinical stage, and facility level were the independent factors that were considered for the distinct survival, spatial, and space-time modeling.

### **3.7 Models Specification**

#### **3.7.1 Kaplan Meier curves**

A Kaplan-Meier curve, which represents a probability of survival function  $S(t)$  against survival time  $t$ , is typically used to represent the survivor function. If the subject made it to the cut-off date of December 31, 2019, the data is censored in the categories of Alive, lost to follow-up, or default if the patient could not be located. Right censoring was used in this study, which means that individuals were no longer being watched before they passed away, but they were still all at least being watched for a while, allowing for the collection of some data regarding each subject's survival. The most popular non-parametric approach for calculating the survival function  $S(t)$ , which is the likelihood that a subject survives longer than time  $t$ , is the Kaplan-Meier (K-M) method (Kaplan & Meier, 1958). This approach makes use of data from both participants who have personally experienced an event and subjects who have been appropriate censored.

A Kaplan-Meier curve represents a probability of survival function  $S(t)$  against survival time  $t$ , is typically used to represent the survivor function. If the subject made it to the cut-off date of December 31, 2019, the data is censored in the categories of Alive, lost to follow-up, or default if the patient could not be located. Right censoring was used in this study, which means that individuals were no longer being watched before they passed away, but they were still all at least being watched for a while, allowing for the collection of some data regarding each subject is selected randomly and separately from a larger population.

- Subjects enrolled both early in the data collection process and during it had identical survival odds.
- The filtering and survival times differ from one another.
- The deaths happened at the times mentioned.

The chances of survival for censored subjects are the same as those for uncensored subjects. Vertical drops show the times an event (in this case, death) was noticed. Summary statistics that can be derived from this survival curve include the survival probability at a specific period, the median survival time, the mean survival time, and various quartiles (Rich, Neely, Paniello & Voelker, 2010). Occasionally, it can be interesting to find out if subjects from one county say, Bungoma County survive differently than those from another, like Kiambu County. Visual comparisons of the survival curves or statistical tests can be used to do this type of comparison.

### **3.8 The Log-rank test**

The approach used to statistically compare the total the separation in the survival curves is known as the log-rank test (Goel, Khanna, & Kishore, 2010). By definition, a log-rank test measures the significance of a chi-square difference between the distributions

of two or more KM curves using a large sample. According to Etikan, Abubakar, and Alkassim (2017), this (log- rank) statistic uses the observed vs projected number of cells over subcategories of outcomes, just as many other statistics used in other types of chi-square tests. Each ordered decomposition time for the whole set of data under consideration defines the categories for the log-rank measurement. tests utilizing the log-rank statistic against the alternative hypothesis that at least some survival function differs from the others for some time periods, and the null hypothesis that the survival curves for all groups are alike at all time points. 2014's (Bland & Altman).

In other terms, the log-rank statistic evaluates the following for  $g$  groups:

$H_0$ : There are no variations in the survival curves.

$H_1$ : Among the survival curves, at least one is distinct from the others.

The log-rank statistics is given by:

$$\chi^2 = \sum_{i=0}^N \left( \frac{O_i - E_i}{E_i} \right)^2$$

$N$  is the number of groups,  $O_i$  is the actual number of deaths in every group, and  $E_i$  is the expected number of deaths in each group  $i$ , under the null hypothesis that there is no variance among survival across the groups.  $O_i$  and  $E_i$  are calculated for each occurrence of an event. The log-rank test is based on the same fundamental premise as the K-M test, and under the assumption  $H_0$ , the log-rank number has  $n - 1$  degrees of freedom, in which  $n$  is the total quantity of groups being compared.

### 3.9 Bayesian Model

Bayesian hierarchical approach was used to estimate the temporal and spatial parameters of HIV and TB jointly and individually. The approach modeled for the two diseases with co-epidemic overlap and hence it will account for the joint space-time

interaction. The study went on to use the Poisson distribution to represent the likelihood that a specific number of events will occur in a fixed period of time or space, provided that these events occur at a known constant mean rate regardless of the interval since the previous occurrence. It is crucial to understand that a Poisson distribution has requirements that must be met. An event can happen any number of times throughout the course of a time period, which is the first requirement. Second, things happen on their own. In other words, the occurrence of one event has no influence on the possibility that another will take place simultaneously. Thirdly, the likelihood that an occurrence will occur is influenced by the total length about the time period. The Poisson distribution will also be used to calculate how many events will occur at different intervals, such as those for distance, area or volume. The study consequently assumed that the number of counts had a distribution that was similar to Poisson, and the main emphasis of the modeling was the log of the corresponding risk.

The first step was defining the model that was used within Hierarchical Bayesian Framework, this involved selecting a probability distribution for the observed data. For counties in the year  $t$ , the study modelled cases  $y_{dst}$  for the disease  $d$ , where  $d=1$  if HIV and  $d=2$  if TB as;

$$y_{dst} \sim \text{Poisson}(\mu_{dst}) = \rho_{dst} E_{dst}$$

The mean  $\mu_{dst}$  is defined in terms of the unknown relative risk  $\rho_{dst}$  and the expected number of cases  $E_{dst}$  in every County on yearly basis. Statistical consideration for the population  $N_s$  was the average pooled County population estimates, that is  $N_s = \frac{P_s}{T}$ , where  $P$  is the estimated population in Counties, which are being considered to the population risk of disease  $d$  and  $T$  is the number of years, which depended on the availability of dat. The crude rate was calculated as  $R_{dst} = \frac{\sum Y_{dst}}{P_{dst}}$  where  $\sum Y_{dst}$  is the

number of disease  $d$  and estimated population for Counties in the year  $t$ . the crude rate was then multiplied by the standard population  $N_s$  to obtain the expected number of cases for disease  $d$  for Counties in the year  $t$  as; In case the study may require the linear predictor of the unknown relative risk will be on the logarithmic scale,  $\eta_{dst} = \log(\rho_{dst})$  which is the recommended invertible link function for the Poisson family of distributions. The variation of the cases around the unknown relative risk  $\rho_{dst}$  for HIV and Tb respectively as follows;

$$Y_{1st} \sim Pois(\rho_{1st} E_{1st}) \eta_{1st} = \alpha_1 + \lambda_s + \xi_t k + \beta_{1s} + y_{1t} + v_{st}$$

$$Y_{2st} \sim Pois(\rho_{2st} E_{2st}) \eta_{2st} = \alpha_2 + \frac{\lambda_s}{\delta} + \frac{\xi_t}{k} + \beta_{2s} + y_{2t} + v_{st}$$

The linear predictor was defined by using the following terms; the shared spatial effect, ( $\lambda = \{\lambda_s\}_{s=1,2,\dots,s}$ ) the disease-specific spatial effect ( $\beta = \{\beta_{ds}\}_{d=1,2:s=1,2,\dots,T}$ ) the shared time trend ( $\xi = \{\xi_t\}_{t=1,2,\dots,T}$ ) the disease-specific time trend ( $\gamma = \{\gamma_{dt}\}_{d=1,2:t=1,2,\dots,T}$ ) and the space-time interaction term ( $v = \{v_{st}\}_{s=1,\dots,S:t=1,\dots,T}$ ). The notation  $\alpha_d$ ,  $\lambda_s$ ,  $\xi_t$  captured disease specific intercept, space and time main effects respectively whereas  $\gamma_{dt}$  and  $\beta_{ds}$  be disease-space interactions of order 2 respectively. The common term for risk of TB in comparison to HIV is given by the coefficient's delta and k, which represent the geographical and temporal scaling parameters. Although the overall comparative risk level for both diseases is the same, there may be differences in the size of the area- and time-specific relative risks, necessitating the use of scaling parameters. Scaling settings weigh the shared component's contribution to the cumulative relative risk to enable various risk cascades for each condition.

The study applied symmetric formulation to both the shared and disease-specific random effects, which implies that, and captured the common spatial and temporal

patterns. The terms, and allowed departures from the shared patterns for the different diseases. The space-time interaction term, provided additional flexibility towards the identification of varying patterns. The study assumed that the shared random effects were the structured effects and the disease-specific random effects were the unstructured effects.

### **3.10 Multivariable Survival Model**

Univariate studies are helpful in establishing if a covariate has an impact on survival and are best suited for descriptive purposes. These include the K-M curves and the log-rank test. They are especially helpful when the variables being predicted are segmented and do not integrate seamlessly with continuous predictors. They make it impossible for us to understand how other model-included aspects affect a group's ability to survive. The study used the Cox Proportional Hazards model to determine how different factors affected survival. Age, sex, weight (kg), relationship status, CD4 cells, function, and WHO clinical stage were all measured at the start of the treatment regimen and taken into consideration as confounders in this study. The Cox Proportional Hazard model is often used in multivariate survival data analysis to assess the effect of a group of factors on the length of survival (Khanal, Sreenivas, & Achar-ya, 2017). It also deals with data that has been censored, continuous and categorical parameters, and variables that change over time, all of which may have an impact on survival (Kraisangka & Druzdela, 2018). There are various ways to introduce fragility.

### **3.11 Cox Proportional Hazard model**

Let  $x_1, x_2, \dots, x_p$  be the value of  $p$  covariate  $X_1, X_2, \dots, X_p$ . The hazard function is given as;

$$h(t, X) = h_0(t) \exp \left( \sum_{i=1}^p \beta_i X_i \right)$$

Where  $\beta_i$ 's  $h_0(t)$  represents the baseline hazard value at that time, and are regression coefficients. It is crucial to confirm that the covariates meet the proportionality assumption given that the model of Cox regression depends on the hazards remaining proportional, or on the impact of a given covariate data, remaining constant across time (Etikan, Abubakar, & Alkassim, 2017). In this study, hazard proportionality where factors are expected not to change over time was assumed. The hazard ratio, abbreviated HR, provides a measurement of the impact of the provided factors on survival time. The hazard ratio given the two subgroups is defined as follows for a class of variables with two levels,  $X = 1$  and  $X = 0$ ;

$$HR = \frac{h(t|X = 1)}{h(t|X = 0)} = \exp(\beta)$$

Where  $HR = 1$ , suggests that people in the two categories have an equal chance of experiencing the event; when  $HR > 1$ , it suggests people in the first category ( $X=1$ ) have a high chance of experiencing the event; and when  $HR < 1$ , people in the second level ( $X=0$ ) have a high chance of experiencing the event. The global test can be used to determine whether the hazard is or is not proportionate to all of the covariates. If this assumption is broken, the Cox regression model, are necessary. The hazard for this study's variables were proportionate.

### 3.11.1 The Stratified Cox regression model

According to Goel, Khanna, and Kishore (2010), the stratified Cox regression model modifies the original Cox regression model by stratifying covariates that do not adhere to the proportional hazard's assumption. The model includes covariates that are



presumed to satisfy the proportional hazards assumption but excludes stratified covariates (Cressie & Wikle, 2011).

If  $p$  covariates meet the proportional risks assumption while  $k$  covariates do not, then the proportional hazards assumption is violated. The covariates that do not fulfill the proportional hazards assumption are designated by  $Z_1, Z_2, \dots, Z_k$ , and the covariates that do are denoted by  $X_1, X_2, \dots, X_p$ . A new variable is created from the  $z$  variables to create the stratified Cox regression model and is indicated by the symbol (\*). The total number of possibilities (strata) created after categorizing each of the stratification variables,  $z^*$ , has  $k^*$  categories. The notion of the stratified Cox regression model defines models with and without interactions (Sherman, 2010). The models are defined by: The stratified partial likelihood function is: Using the aforementioned format, you multiply the likelihoods after computing the likelihood for each stratum. Two different stratified Cox models can be constructed. One in which there is no connection, i.e., the values of for each subscript  $g$  in the framework are the same. The no interaction assumption states that there is no expectation that the stratified variables will interact with the model's  $X_s$ . Separate models are fitted for each stratum in an approach that allows for interaction.

For a non-interaction model, where the subscript  $g$  represents the strata and,

$$h_t(t, x) = h_{0g}(t) \exp[\beta_{1g}x_1 + \beta_{2g}x_2 + \dots + \beta_{pg}x_p], g = 1, 2, \dots, k$$
 for an interaction model.

Regression coefficients in the stratified Cox regression model do not change with strata. The model's no-interaction assumption refers to this feature. Different coefficients for each of the strata are derived if interaction is considered. The likelihood ratio test statistics is used to investigate the no-interaction hypothesis. The interaction and no-interaction models' log likelihood functions are employed for this

test statistics. The product terms in the interaction model set it apart from the no-interaction model. The product terms' coefficients being equal to zero is the null hypothesis. Under the null hypothesis, the likelihood ratio test statistic displays a Chi-square distribution with  $(k-1)$  degree of freedom.

## CHAPTER FOUR

### RESEARCH FINDINGS AND DISCUSSIONS

#### 4.1 Introduction

This chapter covers data analysis, results' representation,' interpretations as well as discussion of study findings as per study objectives. The first section presents socio-demographic information. Second section covers first objective on survival trends of patients on ART with TB treatment and on TB treatment only in selected counties in Kenya. The third section covers presentation of spatial variations of deaths of HIV-TB co-infected patients. The fourth section presents a model for temporal distribution of HIV and TB deaths in selected counties in Kenya. The fifth section presents regional/county demographic factors associated with survival trends. The study used a total of 32,281 cases distributed those selected counties in Kenya.

#### 4.2 Socio-Demographic Information

Participants' demographic data, which included their gender, marital status, and WHO Age, clinical phase, and initial weight during the study period. Their frequency obtained from the data in this study as is as shown in Table 4.1.

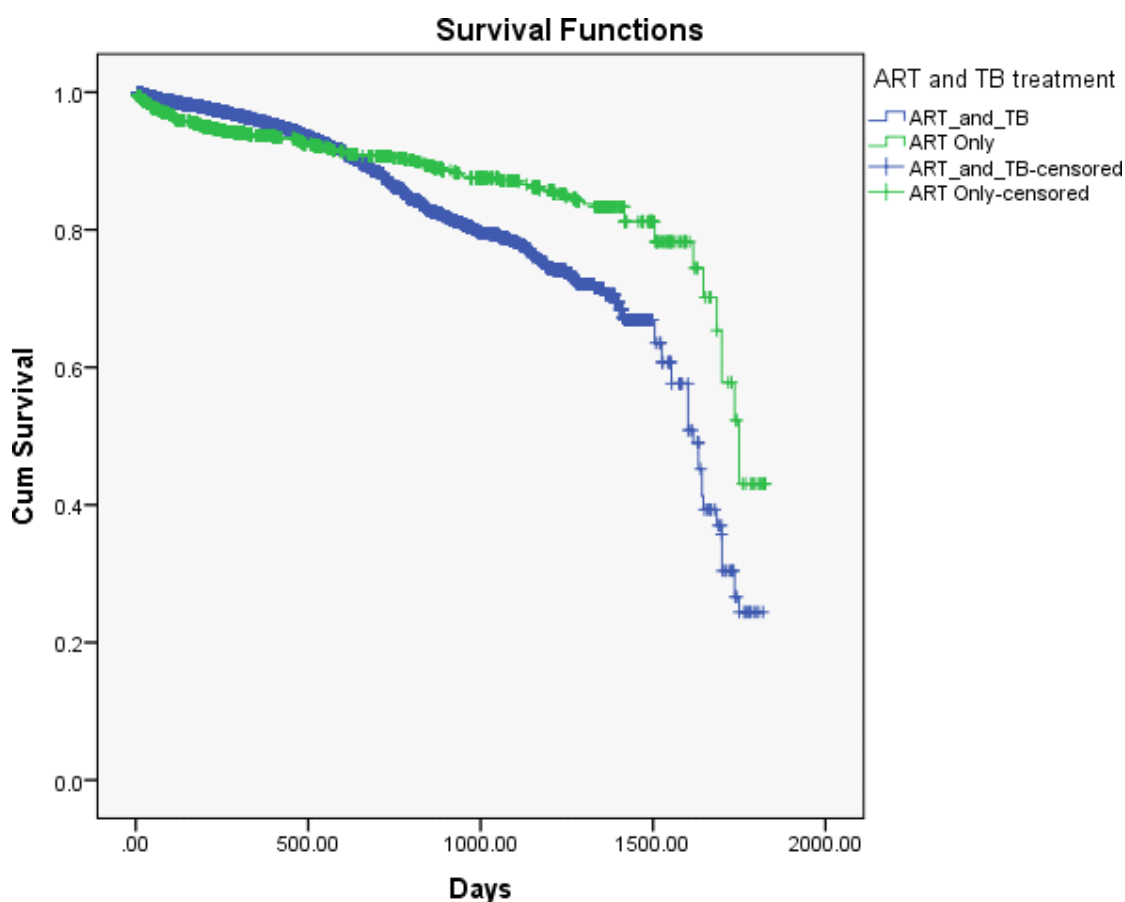
**Table 4.1: Socio Demographic Information**

	<b>Frequency (n=32281)</b>	<b>Percent</b>
<b>Gender</b>		
Male	14724	45.6
Female	17557	54.4
<b>Age</b>		
Mean $\pm$ SD	31.065 $\pm$ 13.0765	
Minimum; Maximum	1.0,80.0	
<b>Weight</b>		
Mean $\pm$ SD	66.2114 $\pm$ 20.99349	
Minimum; Maximum	3.00,130.00	
<b>Marital Status</b>	<b>Frequency</b>	<b>Percent</b>
Cohabiting	41	.1
Divorced	1208	3.7
Married Monogamous	7396	22.9
Married Polygamous	1216	3.8
Minor	2413	7.5
Separated	162	.5
Single	13665	42.3
Widowed	6180	19.1
<b>WHO stage</b>	<b>Frequency</b>	<b>Percent</b>
Stage one	14272	44.2
Stage two	10894	33.7
Stage three	4918	15.2
Stage four	2197	6.8

#### **4.3 Survival Trends of Patients on ART and TB Treatment, and On ART only**

Establishing survival trends between individuals receiving ART and TB treatment and those receiving only ART is the initial goal. In a few Kenyan counties, the Kaplan-Meier Estimate of Survivor Function is used to determine trends in patient survival when they are receiving ART together with TB treatment. Out of the 32281 individuals infected with both TB and HIV who participated in this trial in Kenya, 2,555 (7.9%) were able to participate and were reported deceased five years after starting ART and TB treatment. According to the Kaplan-Meier curve in Figure 4.1, those with HIV and TB who received both ART and TB therapy had longer survival times than those with

HIV and TB who were solely on ART and only made it to their 750th or so day. Following that, people receiving ART only outlived those not receiving ART and TB therapy. In order to treat active TB disease for six to twelve months, antibacterial medication combinations are recommended by the WHO. However, the drug-resistant disease therapy takes 20 to 30 months to complete. This demonstrates that everyone with an HIV and TB infection finishes their TB treatment in less than 900 days. As a result, no patients are anticipated to receive TB therapy after this time.



**Figure 4. 1: K-M survival Curve for patients on ART / TB Treatment and ART and Outcome**

The log rank test was used to determine the chi-square ( $\chi^2$ ) for each incidence time in each group, and the outcomes were then added. If the p-value is less than 0.05, there is typically a substantial difference in the time to incidents across independent groups. If the p-value is bigger than .05., the variations in time to event within multiple categories

is not significant. The log rank test found statistically significant differences between the two curves in this experiment. This is shown by the P-value of 0.000, that is not significant at all. This suggests that ART use and TB treatment both possess a statistically significant influence on the survival of people with HIV and TB co-infection.

#### 4.3.1 Means and Medians for Survival Time

With a 95% confidence level, the average time from event occurrence to death for the group receiving both ART and TB treatment was 1420 days. The mean survival time for the event (death) cases was 1420.328. Additionally, the event (death) cases' median survival time was 1617 days, meaning that more than half of the deaths occurred before 1617 days of therapy.

Additionally, the mean survival time for patients receiving solely ART was 1560.704, indicating that the average duration between the occurrence of the event (death) and that time was 1560 days. The summary of this is provided in table 4.2 below.

**Table 4.2: ART and TB treatment summary**

ART and TB treatment	Mean <sup>a</sup>				Median			
	Estimate	Std. Error	95% CI		Estimate	Std. Error	95% CI	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
ART and TB Treatment	1420.328	10.777	1399.206	1441.450	1617.000	18.454	1580.829	1653.171
ART Treatment Only	1560.704	15.606	1530.116	1591.291	1750.000	25.427	1700.163	1799.837
Overall	1458.906	8.975	1441.314	1476.498	1646.000	17.469	1611.760	1680.240

a. Estimation is limited to largest survival time if it is censored.

The Log rank Test was used to test if there was no difference in the probability of death at any time point in the ART treatment group and the ART/TB treatment group at a level of significance of 5%. The results are shown in table 4.3,

**Table 4.3: Log-rank test**

	<b>Chi-Square</b>	<b>Df</b>	<b>Sig.</b>
Log Rank (Mantel-Cox)	22.022	1	.000
Test of equality of survival distributions for various levels of ART and TB treatment. From the curves there was a significant statistical difference, ( $p < 0.00$ ) in survival distributions among the two groups.			

Findings indicated that the two curves, ART only curve and combination of medication curve, were statistically significantly different. This demonstrates that ART-only patients' survival was significantly worse than that of co-infected individuals who had both TB therapy and ART. In Kenya, 7.9% of patients with HIV and TB infection have been identified as dead in the five years following the start of ART. Ji, Liang, and Shen (2018) observed that the total mortality rate in China was 15.92% using the Kaplan Meier technique. Using the Kaplan Meier approach, Ji, Liang, and Shen (2018) found that the standard deviation of follow-up length in China was 27 months. In addition, according to Keet (2019), more than 10 percent of patients with TB who were also administered anti-TB and HIV drugs on their initial visit had passed away after 5 years, as opposed to less than 6% of patients without TB. The findings conform to Zenner, Abubakar and Conti (2015) discoveries that patients with HIV and TB co-infection accounted for 79% of mortality in the year after HIV diagnosis and 18 percent of the 1880 deaths during follow-up. The unexpectedly high mortality rate among HIV-TB patients in a population with easy access to healthcare and ART availability emphasizes the significance of improving the identification of active and latent TB cases among HIV patients as well as HIV testing among TB patients in order to ensure prompt and appropriate treatment commencement for both diseases. The findings are in line with Myanmar et al. (2019) findings that HIV co-infection significantly influences TB patients' survival rate, with death rate being 20.7 times higher than that of TB infected patients alone. The findings concur with Tshitenge, Ogunbanjo and Citeya (2018)

argument that persons with HIV and TB co-infections had 13.6% TB death rate. In those who failed to take ART for the first three months and in those who did not start CPT for the second and fifth months, higher death rate was seen.

The average length of the event (death) for the group receiving both ART and TB therapy was 1420 days, according to the mean duration of survival for the event (dead) cases, which was 1420.328 (range 1399.206-1441.450). Additionally, the median survival duration for event (death) individuals was 1617 days, indicating that the majority of fatalities occurred prior to the 1617-day mark following the start of treatment. The overall average time to mortality for event (dead) cases among patients receiving only ART was 1560.704 (range 1700–1799), indicating that the median deviation of the period of event manifestation (death) was 1560 days. Furthermore, the median survival time for the event (death) patients was 1750 days, indicating that the bulk of fatalities happened before 1617 days of therapy and that any survival after that period was due to factors other than the therapy itself. According to the findings, those having HIV and TB who were given ART survived longer than those who just received ART, at least up to roughly the 750th day.

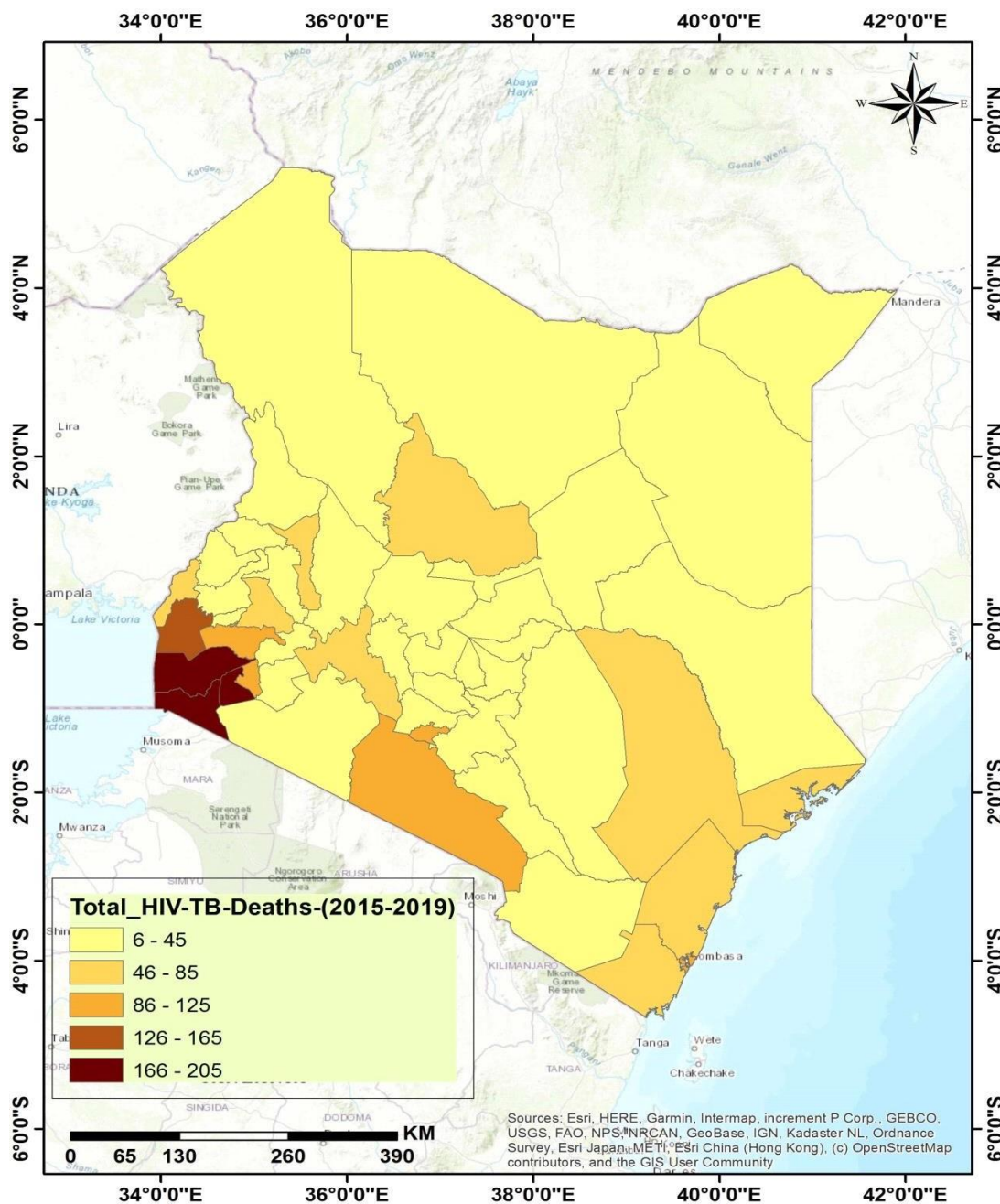
#### **4.4 Spatial variations of deaths of HIV-TB co-infected patients**

The Second objective in this study was to analyze spatial variations of patient deaths with HIV- TB co-infection. The study found HIV-TB patients' death rates varied across Counties as shown in the table 4.4.



**Table 4.4: Spatial variations of deaths of HIV-TB co-infected patients**

County	Number of deaths	% rate of deaths
Kisii	168	14,29
Migori	199	13.85
Homa Bay	188	13.4
Kajiado	185	12.9
Nakuru	174	12.10
Garissa	160	11.11
Siaya	130	9.0
Kisumu	121	8.0
Nairobi	97	6.0
Bungoma	23	1.6
Wajir	7	0.48
Marsabit	10	00.60
Mandera	6	0.40



**Figure 4.2: Spatial Distribution of HIV-TB Deaths**

Analysis of the regional variations in HIV-TB co-infected patients' (HIV and TB-infected individuals') mortality rates served as the study's secondary goal. Patients with HIV-TB mortality rates varied from region to county. Kisii County had among the highest rates of mortality, with 14.29% of all HIV-TB contracted individuals dying during a five-year period (143 deaths per 1000 people). Those three counties were followed by Migori County, which had an HIV-TB mortality rate of 13.85%, Homa

Bay County, which had an HIV-TB mortality rate of 13.47%, and Kajiado County, which had an HIV-TB mortality rate of 12.97%. These results support the contention made by Aturinde, Farnaghi, and Mansourian (2019) that hotspot clusters of combined TB/HIV prevalence exist in northern Uganda and the Lake Victoria region.

Further, Nakuru County had a HIV-TB patients' death rate of 12.10% and Garissa County had a HIV-TB patients' death rate of 11.11%. However, Migori County had the highest HIV-TB patients' deaths (199), followed by Homa Bay County (188), Kisii County (168), Siaya County (130), Kisumu (121) and Nairobi (97). Mandera County had the lowest number of HIV-TB patients' deaths (6), followed Wajir County (7), Garissa County (8), Marsabit County (10) and Bungoma County (23). These results supported the claim made by Ghanbarnejad et al. (2015) that HIV/TB spatial distribution was not random but was clustered. Six districts were suggested to be categorized as "hot spots" using spatial clustering. Additionally, these areas have large populations. Peres, Façanha, and Junior (2019) observed that spatial analysis revealed a concentration of Municipalities at High TB Risk in the Health Regions of Fortaleza, Sobral, Caucaia, Cascavel, Maracana, and Itapipoca. In addition, Giacomet and Santos (2021) observed that although the incidence of tuberculosis had been declining over time, detection had increased following the introduction of RMT-TB, and the disease had a seasonal pattern. In showing spatial distribution of HIV/TB deaths, Uthman, Yahaya, Ashfaq and Uthman (2019) observed that six nations might be considered "hot spots," while thirteen countries were at an enhanced risk of HIV-TB mortality. According to Kibuuka, Mpofu, Neave and Manda (2021), there is a statistically significant decline in TB fatalities as well as an unbalanced distribution of TB fatalities among different regions and population categories. Musika (2016) observed that HIV/TB co-infection is more prevalent in major cities, along major roads, and in highly

populated areas. High mortality rates were observed in both densely inhabited and sparsely serviced locations. There was a connection between the high death rate, HIV, and poor literacy rates, and it also demonstrated a connection between the prevalence of TB infection and HIV. From this study that agrees that spatial distribution was not random but clustered and high mortality rates was observed in densely populated, ministry of health is advised to so much concentrate their efforts in earlier diagnosis and initiating ART and TB treatment.

#### **4.5 Temporal Distribution of HIV and TB deaths in Counties**

The modeling of the time course of HIV and TB fatalities in a few Kenyan counties is shown in this section. In the Counties, the distribution of TB and HIV mortality changed over the course of the five years. There were 1077 HIV-related and TB-related fatalities worldwide in 2015. This number fell to 921 deaths from TB and HIV in 2016, then to 391 in 2017 and 106 in 2018. The findings also revealed that 60 people died from TB and HIV in the counties in 2019.

Highest number of HIV and TB Deaths was in first quarter of year one at 400 cases. However, this figure decreased in the second quarter of the year to 252, 217 in the third quarter and 208 in the fourth quarter. The first quarter of the second year had a low TB and HIV Deaths at 190, which increased 252 in second quarter, before decreasing to 232 to TB and HIV deaths and increasing to 247 in fourth quarter of second year.

Comparing the first year and the second year, number of TB and HIV Deaths decreased considerably and in the first quarter it decreased to 166 in the first quarter. In the second quarter it decreased to 129, before decreasing again to 70 in third year and 26 in fourth quarter. In the fourth year, number of deaths was 49 in the first quarter, before decreasing to 28 in the second quarter, 13 in the third quarter and 16 in the fourth

quarter. In the fifth year, the first quarter, the number of TB and HIV Deaths was 12, which slightly increased to 20 in the second quarter, remained constant in the third quarter and decreased to 8 TB and HIV Deaths in the fourth quarter. The distribution of HIV and TB deaths in the first year was the highest in Kwale County with between 30 and 36 TB and HIV deaths, the figure in Kwale County remained with the same range in the same year, but decreased to the third year and the fourth year. In the first year, Vihiga County followed Kwale County in terms of the number HIV-TB deaths between 23 and 29. In the second year, the number of TB and HIV deaths was the highest in Nakuru County between 30 and 36. In addition, the number of TB and HIV deaths in Samburu County, West Pokot County, Laikipia County, Kitui County and Nandi County increased considerably in the second year as compared to the second year.

In the third year, Homa Bay County had the highest number of TB and HIV deaths, followed by Siaya and Migori, Kwale, Kilifi, Nakuru and West Pokot Counties. The number of TB and HIV deaths remained low across the years in Turkana County, Mandera County and Wajir County. In Marsabit and Isiolo Counties, the number of TB and HIV deaths was moderate in Year one and Year two but decreased in Year three and Year four. In first and second year, number of TB and HIV deaths in Kilifi County was between 15 and 22 cases, but increased to between 29 and 57 cases in Year three and Year Four. In the fourth year, Migori County had the highest number of TB and HIV deaths, followed by Nairobi County, Kisumu County, Kiambu County, Muranga County, Kirinyaga County and Kilifi County. Majority of the The proportion of HIV and TB mortality in the chosen Counties fluctuated during the five years, according to the results. The results support the claim made by Queiroz et al. (2018) that certain localities have higher rates of TB death than others and, as a result, should receive

priority in public health interventions for the disease. In the chosen countries, there were 1077 total TB and HIV deaths in 2015. In 2016, there were 921 fatalities from TB and HIV. The following years saw further declines of 391 and 106. The results also showed number of HIV and TB deaths in 47 counties in 2019 was 60. Highest number of HIV and TB Deaths was in first quarter of year one at 400 cases. However, this figure decreased in the second quarter of the year to 252, 217 in the third quarter and 208 in the fourth quarter. The first quarter of the second year had a low TB and HIV Deaths at 190, which increased 252 in second quarter, before decreasing to 232 to TB and HIV deaths and increasing to 247 in fourth quarter of second year.

Compared the first year and the second year, number of TB and HIV Deaths decreased considerably and in the first quarter it decreased to 166 in the first quarter. In the second quarter it decreased to 129, before decreasing again to 70 in third year and 26 in the fourth quarter. In fourth year, number of deaths was 49 in the first quarter, before decreasing to 28 in the second quarter, 13 in the third quarter and 16 in the fourth quarter. In the fifth year, the first quarter, the number of TB and HIV Deaths was 12, which slightly increased to 20 in the second quarter, remained constant in the third quarter and decreased to 8 HIV and TB Deaths in fourth quarter.

The distribution of HIV and TB deaths in the first year was the highest in Kwale County with between 30 and 36 TB and HIV deaths, the figure in Kwale County remained with the same range in the same year, but decreased to the third year and the fourth year. In the first year, Vihiga County followed Kwale County in terms of the number HIV-TB deaths between 23 and 29. In the second year, number of TB and HIV deaths was the highest in Nakuru County between 30 and 36. In addition, the number of TB and HIV deaths in Samburu County, West Pokot County, Laikipia County, Kitui County and

Nandi County increased considerably in the second year as compared to the second year.

In third year, Hima Bay County had the highest number of TB and HIV deaths, followed by Siaya and Migori, Kwale, Kilifi, Nakuru and West Pokot Counties. The number of TB and HIV deaths remained low across the years in Turkana County, Mandera County and Wajir County. In Marsabit and Isiolo Counties, the number of TB and HIV deaths was moderate in Year one and Year two but decreased in Year three and Year four. In first and second year, number of TB and HIV deaths in Kilifi County was between 15 and 22 cases, but increased to between 29 and 57 cases in Year three and Year Four. In the fourth year, Migori County had the highest number of TB and HIV deaths, followed by Nairobi County, Kisumu County, Kiambu County, Muranga County, Kirinyaga County and Kilifi County. Majority of the Counties had less than 17 TB and HIV deaths in the fourth year.

Counties had less than 17 TB and HIV deaths in the fourth year.





#### 4.6 Regional/county Demographic Factors Associated with Survival Trends.

This section will examine regional/county demographic factors related with survival trends, which is objective number four in our study.

**Table 4.5: Regional/county Demographic Factors Associated with Survival Trends**

-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
541344.801	520.583	33	0.00	530.038	33	.000	530.038	33	.000
a. Beginning Block Number 1. Method = Enter									

Regression coefficients forecast the hazard for terminal event (HIV-TB confections) as a covariates' function in the model. Moreover, positive coefficient implies positive nexus between covariate and hazard for terminal event (in this case, HIV-TB confections). This implies that higher covariate values are related with less survival tome (until terminal event). Additionally, negative coefficient means negative correlation between covariate and hazard for terminal event. Greater values on covariate are related with longer survival period.

The gender of the participants was coded as 1=Male and 2=female. The significant positive coefficient ( $\beta=0.033$ , p-value=0.021) indicates that the female gender is more likely to experience the event (HIV-TB confections) than the male gender. The results also show that marital status has a significant effect on HIV-TB confections (p-value=0.000). The marital status of the participants was coded as 1=Cohabiting, divorced=2, Married Monogamous=3, Married Polygamous=4, Minor=5, Separated=6, Single=7 and Widowed=8. From the results, the married polygamous ( $\beta=-0.109$ , p.value=0.000), minors ( $\beta=-0.261$ , p.value=0.000), separated ( $\beta=-0.349$ , p.value=0.000), singles ( $\beta=-0.191$ , p.value=0.024) and widowed ( $\beta=-0.063$ , p.value

=0.002) compared to those who were married monogamously, married polygamously, cohabiting, or divorced, were more likely to get HIV-TB infections.

HIV-TB confections were significantly impacted by the WHO clinical stage (p-value = 0.000). When compared to individuals in stages three ( $\beta=-0.071$ , p.value=0.006), two ( $\beta=-0.074$ , p.value=0.010), and one ( $\beta=-0.074$ , p.value=0.010), people in stage four were more likely to experience HIV-TB confections ( $\beta=-0.052$ , p.value =0.045). This suggests that the likelihood of HIV-TB confections occurring rises when the WHO clinical stage deteriorates.

The findings indicate that the facility level had a significant influence on HIV-TB confections (p.value =0.000). Individuals in level four facilities were more likely to experience the HIV-TB confections ( $\beta=-0.290$ , p.value =0.000) as compared to other facilities. This was followed by level five facilities ( $\beta=-0.213$ , p.value =0.000) and level two facilities ( $\beta=-0.137$ , p.value=0.000). The patients age at the start of ART was statistically and significant related with HIV-TB confections (p-value=0.000). However, latest weight of patients had no significant influence on HIV-TB confections.

The results indicated that weight had a statistically significant effect on HIV-TB confections (p- value=0.000). The weight of the participants was coded as 1=below 10 kilograms, 2=11-20 Kilograms, 3=21-30 Kilograms, 4=31-40 Kilograms, 5=41-50 Kilograms, 6=51-60 Kilograms, 7=61-70 Kilograms, 8=71-80 Kilograms, 9=81-90 Kilograms, 10=91-100 Kilograms and 11=above 100 Kilograms. Individuals with between 11 and 20 kilograms ( $\beta=-5.171$ , p- value=0.000) followed by 21 to 30 kilograms ( $\beta=2.604$ , p-value=0.000) were likely to experienced death. In addition, individuals with 71 to 80 kilograms were less likely to experience death ( $\beta=-2.210$ , p-

value=0.000), 81 to 90 kilograms ( $\beta=-1.727$ , p-value=0.000), followed by 91 to 100 years ( $\beta=-1.979$ , p-value=0.000) and above 100 years ( $\beta=-1.781$ , p-value=0.000).

The findings showed that age bracket of the participants had significant effect on HIV-TB confections and deaths (p-value=0.000). The age of the participants was coded as 1=1 to 10 Years, 2=11 to 20 Years, 3=21 to 30 Years, 4=31 to 40 Years, 5=41 to 50 Years, 6=51 to 60 Years, 7=61 to 70 Years and 8=71 to 80 Years. The results show that individuals aged between 11 and 20 years were less likely to experience death as compared to those aged between 1 and 10 years ( $\beta=-6.886$ , p-value=0.000). These were followed by those aged between 31 and 40 years ( $\beta=-2.532$ , p-value=0.000), 61 and 70 years ( $\beta=-2.053$ , p-value=0.000) and 51 and 60 years ( $\beta=-1.810$ , p-value=0.000).

Table 4.6: Cox Regression Results

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
<b>Gender</b>	<b>.033</b>	<b>.014</b>	<b>5.366</b>	<b>1</b>	<b>.021</b>	<b>1.034</b>	<b>1.005</b>	<b>1.063</b>
<b>Marital Status</b>			<b>97.441</b>	<b>7</b>	<b>.000</b>			
Marital Status (1)	.009	.162	.003	1	.957	1.009	.735	1.385
Marital Status (2)	.019	.034	.309	1	.578	1.019	.953	1.090
Marital Status (3)	-.109	.020	28.802	1	.000	.897	.862	.933
Marital Status (4)	-.261	.035	57.117	1	.000	.770	.719	.824
Marital Status (5)	-.349	.070	24.887	1	.000	.705	.615	.809
Marital Status (6)	-.191	.085	5.065	1	.024	.826	.699	.976
Marital Status (7)	-.063	.020	10.008	1	.002	.939	.903	.976
<b>WHO Stage</b>			<b>9.017</b>	<b>3</b>	<b>.029</b>			
WHO Stage (1)	-.052	.026	4.037	1	.045	.949	.902	.999
WHO Stage (2)	-.071	.026	7.471	1	.006	.931	.885	.980
WHO Stage (3)	-.074	.029	6.584	1	.010	.929	.878	.983
<b>Facility Level</b>			<b>145.592</b>	<b>3</b>	<b>.000</b>			
Facility Level (1)	-.137	.027	26.108	1	.000	.872	.828	.919
Facility Level (2)	-.290	.028	107.290	1	.000	.748	.708	.790
Facility Level (3)	-.213	.027	64.364	1	.000	.808	.767	.852
<b>Weight</b>			<b>1625.271</b>	<b>10</b>	<b>.000</b>			
Weight (1)	5.171	.677	58.333	1	.000	176.143	46.723	664.046
Weight (2)	2.604	.673	14.973	1	.000	13.517	3.615	50.545
Weight (3)	-9.890	69.254	.020	1	.886	.000	.000	4.508
Weight (4)	.208	.094	4.894	1	.027	1.231	1.024	1.480
Weight (5)	-1.231	.077	253.835	1	.000	.292	.251	.340
Weight (6)	-1.253	.064	379.048	1	.000	.286	.252	.324
Weight (7)	-2.210	.085	678.925	1	.000	.110	.093	.130
Weight (8)	-1.727	.088	388.972	1	.000	.178	.150	.211
Weight (9)	-1.979	.091	469.108	1	.000	.138	.115	.165
Weight (10)	-1.781	.078	520.717	1	.000	.168	.145	.196
<b>Age</b>			<b>737.379</b>	<b>7</b>	<b>.000</b>			
Age (1)	-6.886	.698	97.208	1	.000	.001	.000	.004
Age (2)	-15.137	38.261	.157	1	.692	.000	.000	984.000
Age (3)	-2.532	.197	165.684	1	.000	.079	.054	.117
Age (4)	-1.704	.194	77.369	1	.000	.182	.124	.266
Age (5)	-2.053	.198	107.467	1	.000	.128	.087	.189
Age (6)	-1.810	.206	77.464	1	.000	.164	.109	.245
Age (7)	-.542	.202	7.213	1	.007	.582	.392	.864

#### 4.6.1 K-M Curves demonstrating how demographic Factors are Associated with Survival Trends

##### Marital Status

In Figure 4.2, the separated and married polygamous had low survival rates throughout the period, according to the Kaplan-Meier curve for marital status and outcome. Minors had a modest chance of surviving, whereas singles and monogamous couples had a high chance. The cohabiting individuals' survival rates were high for the first 1.5 years, but thereafter they started to deteriorate.

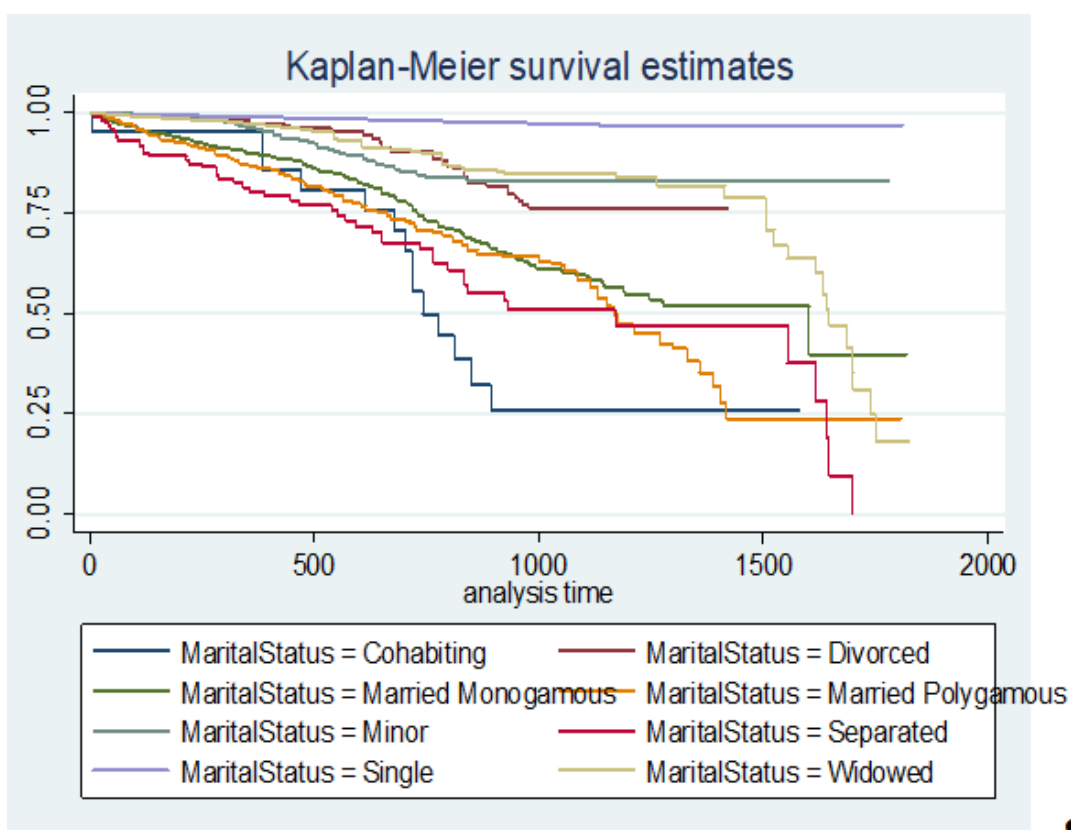
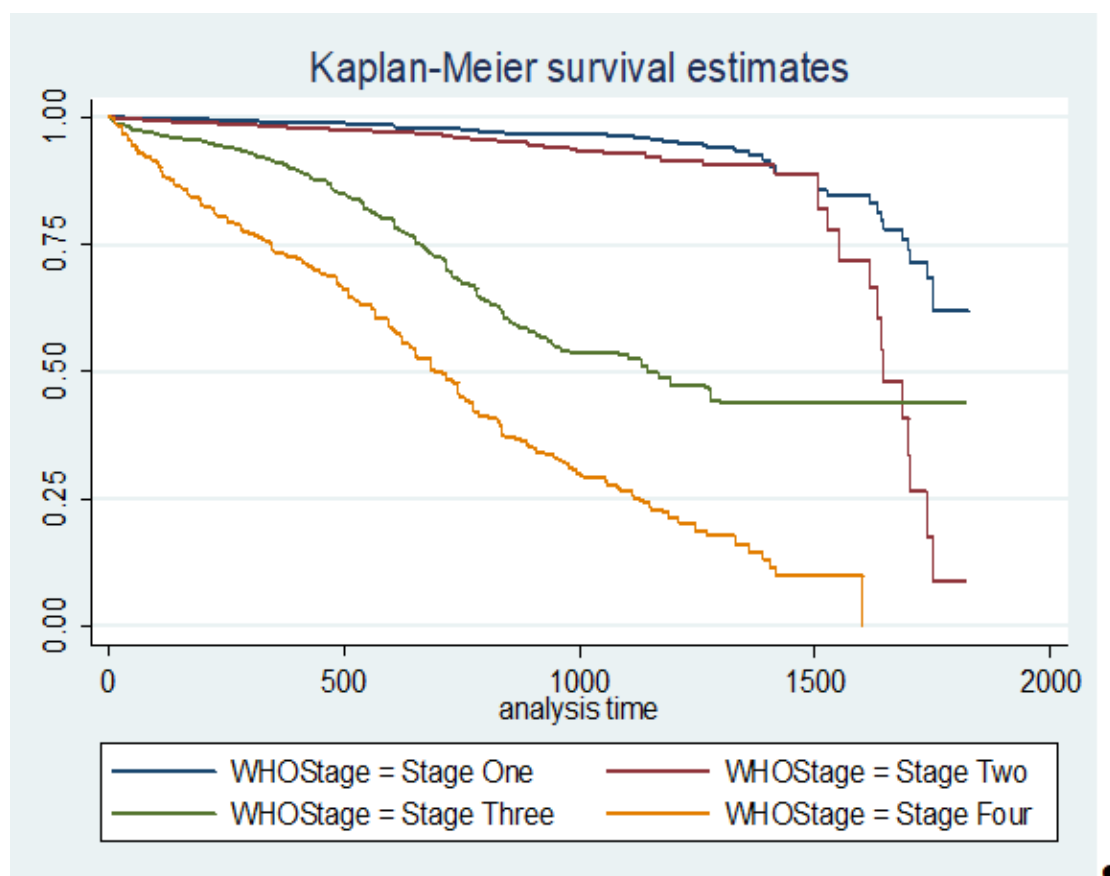


Figure 4.4: K-M Curve for Marital Status and Outcome

### WHO Clinical stage

According to Figure 4.5, patients in WHO clinical stages one, two, and three had the highest percentages of survival. The WHO medical stage four patients' survival rates were the lowest.



**Figure 4.5: Kaplan- Meier Curve for WHO Stage and Outcome**

### Facility Level.

According to the findings, as depicted in Figure 4.6, lowest survival rates were seen in level 3 institutions, subsequent to level 2 and level 5 clinics. In level 4 institutions, the lowest likelihood of survival was seen for those who also had TB and HIV.

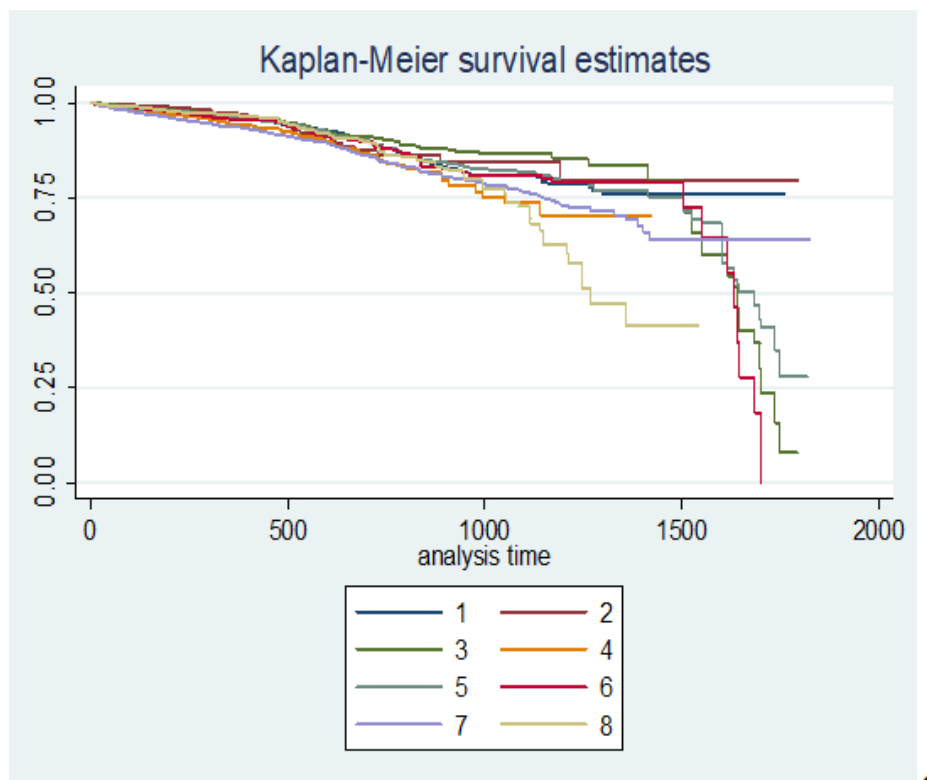
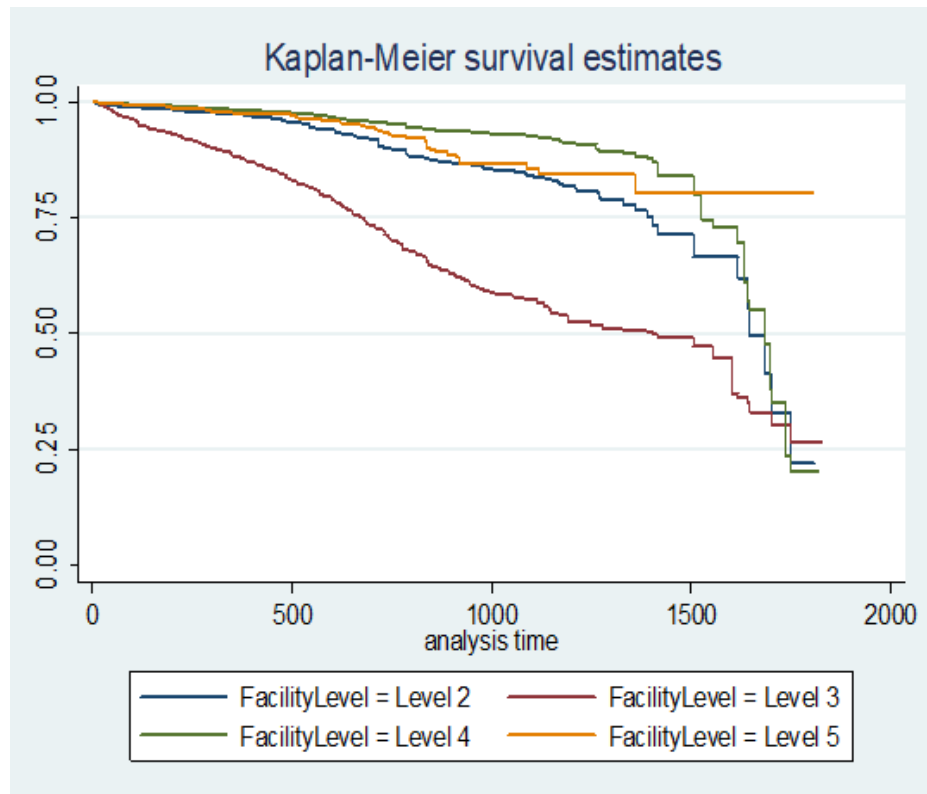


Figure 4.6: Survival estimates

The investigation determined that the participants' gender had a major impact on HIV-TB survival rates. In particular, the study discovered that women are more likely than men to experience the event (HIV-TB confections). These findings are contrary to Carvalho et al. (2008) observation that among these co-infected patients, most of the respondents were male. Also, the findings are contrary to Pimpin, Drumright and Kruijshaa (2011) findings that groups at greater risk of HIV and TB deaths were male as compared to females. In addition, male gender was a risk factor associated with TB related deaths among HIV/AIDS patients in Burkina Faso. According to Muriithi (2018), in a study on incidence of TB, the results showed that there was little sex-specific variation.

The findings also demonstrate that marital status significantly affects HIV-TB survival rates. Compared to cohabiting, divorced, married monogamous, and married polygamous people, minors, separated, singles, and widowed people were more likely to encounter HIV-TB fatalities earlier in life. The findings concur with Mitku et al. (2016) findings that factors associated with TB/HIV deaths in Amhara region of Ethiopia include marital status. According to Hatoluf, Berhanu and Yadeta (2013), being divorced/widowed was a determinant related with TB-HIV death.

Deaths from HIV-TB had a substantial impact on the WHO clinical stage. Those in the fourth level are more inclined to die from HIV and TB than those in stages three, two, and one of the WHO's stages. This suggests that the likelihood of HIV-TB deaths occurring increases when WHO clinical stage deteriorates. The findings conform to Mitku et al (2016) findings that WHO clinical staging was related to HIV/TB deaths along HIV positive adult. Also, Fite et al. (2019) observed that WHO clinical stage was a significant predictor of death. The results also agree with Myanmar et al. (2019) argument that those receiving second-line ART and patients who are bedridden should



be given more attention by current HIV treatment and prevention programs. The findings also agree with Damtew, Mengistie and Alemayehu (2019) argument that WHO stages patients, low CD4 counts, low Hgb levels, low BMI levels, and concurrent TB infections had a greater risk of death.

The findings indicate that the facility level had a significant influence on HIV-TB deaths. Comparatively to other institutions, those in level four hospitals were far more likely to die from HIV-TB. Level five centers and level two facilities came next. Musenge and Vounatsou (2018) found that using geographic models, the regions with the greatest rates of juvenile HIV/TB death rates were ones without any health facilities.

The patients' age at the start of ART was statistically and significant associated with HIV-TB deaths. These findings conform to Rossetto et al. (2019) observation death was related with age of HIV/TB co-infected persons within Porto Alegre, Brazil. Further, Shamu et al (2019) observed that knowledge pertaining to related factors of TB and HIV/TB deaths on young people in South Africa. Krishnamoorthy, Majella, Rajaa and Bharathi (2021) observed that in India, HIV deaths among individuals aged 15 to 54 is spatially concentrated, with the bulk of cases occurring in the southern and northern regions.

Also, the findings indicated that weight had a significant influence on HIV-TB deaths. Hatoluf, Berhanu and Yadeta (2013) observed that being underweight was a determinant associated with TB/HIV deaths.

## CHAPTER FIVE

### CONCLUSIONS AND RECOMMENDATIONS.

#### 5.1 Introduction

The chapter covers conclusions and recommendations for policy and practice as well as recommendations for further research.

#### 5.2 Conclusions and Discussions

##### 5.2.1 Conclusions

The study's findings suggest that the usage of ART and TB condition statistically affect the survival of patients who are infected with both TB and HIV. Up to roughly the 750th day, individuals with HIV and TB who received both ART and TB therapy outlived people with HIV and TB who received only ART. Following that, those receiving ART alone outlived those receiving ART and TB treatment by a longer margin. TB therapy often lasts up to 900 days, therefore after that time patients stop using TB medications.

The study concludes that the mortality rates for HIV-TB patients between 2015 and 2019 differed from county to county. HIV and TB did not vary uniformly across different geographic contexts in the research area, indicating a non-probabilistic distribution. Kisii County had the greatest number of HIV-TB patient death rates, accounting for 14.29% of all HIV-TB patients during the five-year period. Migori County was next, with a 13.85% HIV-TB patient mortality rate, followed by Homa Bay County with a 13.47% HIV-TB individuals death rate, and Kajiado County was fourth, with a 12.97% HIV-TB individuals death rate. Six HIV-TB patient fatalities occurred in Mandera County, followed by seven in Wajir, eight in Garissa, ten in Marsabit, and twenty-three in Bungoma.

According to the study's findings, the distribution of HIV and TB mortality within the chosen Counties changed over the course of five years. The overall counts of TB and HIV fatalities in the chosen countries was 1077 in 2015; this figure fell to 921 in 2016, then to 391 in 2017, 106 in 2018, and 60 in 2019.

The study found that the basic demographic information, WHO clinical stage, and position of hospitals in the region provides the primary demographic characteristics that significantly affect HIV-TB fatalities. The event (HIV-TB confections) is more likely to occur in females than in males. Additionally, HIV-TB deaths were more common among married polygamous people than among cohabiting, divorced, married monogamous, and married polygamous people as well as minors, separated, singles, and widows. Additionally, people in stage four were more likely than those in stages three, two, and one of the WHO to experience HIV-TB related mortality. This guides that the likelihood of TB and HIV mortality occurring rises when the WHO clinical stage deteriorates. Additionally, compared to other facilities, level four hospitals had a higher rate of HIV-TB fatalities among its residents. Level five facilities and level two facilities were next. The findings showed that age had a big impact on HIV and TB fatalities. Additionally, the results showed that weight significantly influenced HIV and TB-related fatalities.

### **5.2.2 Recommendations**

- The study established that the combination of medicine as well as TB cure influenced the survival of people infected with both TB and HIV. In those selected Kenya. Further still, initiation of ART and TB treatment and earlier at diagnosis improves the rate at which patients survives. The study therefore advises that the MOH should put more emphasis on earlier diagnosis and the

combination of ART and TB treatment so as to improve survival rates among individuals with HIV-TB confections.

- The study found that HIV-TB deaths varied from one County to another. Different counties in Kenya are characterized by varying levels of income, different income generating activities and varying levels of healthcare services' availability and accessibility. This study therefore recommends that the ministry of health should develop a new programme to monitor HIV-TB mortality rates together with County characteristics so as to develop strategies to improve rates of survival for people in each county who have HIV and TB co-infections. The report also advises MOH to maintain its attention on TB and HIV related deaths in the high-risk areas through the concerned organizations such as NASCOP. Low TB and HIV survival rates were in Kisii, Homa Bay, and Migori, which were considered to be hotspots. To ensure that there is an increase in survival rates among TB among patients with HIV, there is need for targeted intervention in these areas.
- The study found out that the distribution of HIV and TB mortality within the selected counties changed over the course of five years. This research therefore recommends to the MOH from time to time monitor the trends and associate the trends with specific interventions guiding the trends to support those that are improving survival rates
- The study found that marital status as one of the demographic factors has an influence on the rate of survival of and HIV and TB affected individuals. This project recommends that the MOH concerned that they should develop strategies targeting married polygamous, minors, separated, singles and widowed individuals. In addition, the study found that WHO clinical stage had

a significant influence on the rates of HIV and TB survival individuals. This paper recommends that more emphasis should be put on Individuals who were in stage four and stage three so as to ensure that they adhere to combine HIV-TB therapy and increase their survival rates. The study further recommends that level four and five facilities should increase emphasis on HIV-TB confected patients by improving service delivery so as to increase their survival rates. The results show that age bracket had sufficient evidence to prove influence on survival rates. This paper recommends that strategies should focus mainly on the very young individuals (1-20 years) and the old individuals (51-70 years) so as to increase their survival rates.

Given that study focused on influence of demographic factors influencing HIV-TB deaths, which included gender, marital status, WHO stage, facility level, age at ART start and latest weight. The study did not thoroughly address additional characteristics that are associated with TB and HIV mortality, such as TB type, travel time to a health institution, socioeconomic status, as well as viral suppression in HIV and TB patients. The study therefore recommends other factors that may influence HIV-TB deaths including the patients' level of education, income level, occupation, area of residence, access of health care, wealth index and adult literacy among others should be researched on. In addition, there should be further studies on risk factors related with HIV and TB deaths in hotspot areas in Kenya including Homa Bay, Kisii and Migori.

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**APPENDICES****Appendix 1: List of County Governments in Kenya**

1. Mombasa
2. Kwale
3. Kilifi
4. Tana River
5. Lamu
6. Taita–Taveta
7. Garissa
8. Wajir
9. Mandera
10. Marsabit
11. Isiolo
12. Meru
13. Tharaka-Nithi
14. Embu
15. Kitui
16. Machakos
17. Makueni
18. Nyandarua
19. Nyeri
20. Kirinyaga
21. Murang'a
22. Kiambu
23. Turkana
24. West Pokot
25. Samburu
26. Trans-Nzoia
27. Uasin Gishu
28. Elgeyo-Marakwet
29. Nandi
30. Baringo
31. Laikipia
32. Nakuru
33. Narok
34. Kajiado
35. Kericho
36. Bomet
37. Kakamega
38. Vihiga
39. Bungoma
40. Busia
41. Siaya
42. Kisumu
43. Homa Bay
44. Migori
45. Kisii
46. Nyamira
47. Nairobi (County)



## Appendix 2: Research Authorisation letter



An ISO 9001:2015 Certified Hospital



### MOI TEACHING AND REFERRAL HOSPITAL

Telephone : (+254)053-2033471/2/3/4  
 Mobile: 722-201277/0722-209795/0734-600461/0734-683361  
 Fax: 053-2061749  
 Email: [ceo@mtrh.go.ke](mailto:ceo@mtrh.go.ke)/[directorsofficemtrh@gmail.com](mailto:directorsofficemtrh@gmail.com)

Nandi Road  
 P.O. Box 3 – 30100  
 ELDORET, KENYA

Ref: ELD/MTRH/R&F/10/2/V.2/2010

15<sup>th</sup> December, 2021


Benard Onserio Okemwa,  
 Moi University,  
 School of Science and Aerospace,  
 P.O. Box 3900-30100,  
 ELDORET- KENYA.

#### MODELLING SPATIOTEMPORAL SURVIVAL PATTERNS OF HIV-TB CO-INFECTED PATIENTS IN SELECTED COUNTIES IN KENYA

You have been authorised to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) and its satellites sites. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff, patients and study participants seen at MTRH.

- 1 The study shall be under Moi Teaching and Referral Hospital regulation.
- 2 A copy of MTRH/MU-IREC approval shall be a prerequisite to conducting the study.
- 3 Studies intending to export human bio-specimens must provide a permit from MOH at the recommendation of NACOSTI for each shipment.
- 4 No data collection will be allowed without an approved consent form(s) to participants unless waiver of written consent has been granted by MTRH/MU-IREC.
- 5 Take note that **data** collected must be treated with due confidentiality and anonymity.

The continued permission to conduct research shall only be sustained subject to fulfilling all the requirements stated above.

*for* 

DR. WILSON K. ARUASA, *MBS, EBS*  
 CHIEF EXECUTIVE OFFICER  
 MOI TEACHING AND REFERRAL HOSPITAL

c.c. - Senior Director, Clinical Services  
 - Director of Nursing Services  
 - HOD, HRISM



*All correspondence should be addressed to the Chief Executive Officer*

*Visit our Website: [www.mtrh.go.ke](http://www.mtrh.go.ke)*

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### Appendix 3: NACOSTI Research License

NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Ref No: 135752 Date of Issue: 31/January/2022

#### RESEARCH LICENSE

This is to Certify that Mr.. BENARD ONSERIO OKEMWA of Moi University, has been licensed to conduct research in Homabay, Kakamega, Kisii, Kisumu, Uasin-Gishu on the topic: MODELLING SPATIOTEMPORAL SURVIVAL PATTERNS OF HIV-TB CO-INFECTED PATIENTS IN SELECTED COUNTIES IN KENYA for the period ending: 31/January/2023.

License No: NACOSTI/P/22/15288 135752

Applicant Identification Number Director General NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

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The Grant of Research Licenses is Guided by the Science, Technology and Innovation (Research Licensing) Regulations, 2014 CONDITIONS

The License is valid for the proposed research, location and specified period

The License any rights thereunder are non-transferable

The Licensee shall inform the relevant County Director of Education, County Commissioner and County Governor before commencement of the research

Excavation, filming and collection of specimens are subject to further necessary clearance from relevant Government Agencies

The License does not give authority to transfer research materials

NACOSTI may monitor and evaluate the licensed research project

The Licensee shall submit one hard copy and upload a soft copy of their final report (thesis) within one year of completion of the research

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**Appendix 4: Authorisation letter from NASCOP**

Mr. Benard Onserio Okemwa  
Moi University  
School of Science and Aerospace  
P O Box 3900 – 30100  
NAIROBI  
Mobile: 07258087461  
Email: okemwabenardo@gmail.com  
bokemwa@nita.go.ke

**RE: PERMISSION TO ACCESS/SHARE HIV/TB CO-INFECTED****PATIENTS INDIVIDUAL LEVEL DATA**

This is in reference to your letter dated 11<sup>th</sup> March 2022, requesting for permission to access/share HIV/TB co-infection individual level data for a research study titled, **“modelling spatiotemporal survival patterns of HIV – TB co-infected patients in selected counties in Kenya”, in counties of Homa Bay, Kakamega, Kisumu, Kisii and Uasin Gishu.**

The purpose of this letter is therefore to inform you that this office has no objection to this request and therefore invite you to sign a data signing agreement to enable us share the data for the intended research as per the attached protocol.

Dr. Rose Wafula  
HEAD NASCOP  
INTERNATIONAL AIDS & STI, CONTROL PROGRAMME (NACOP)