UNIVERSITY OF NAIROBI

TIME TO TREATMENT OUTCOME AND ASSOCIATED FACTORS AMONG TUBERCULOSIS PATIENTS: AN APPLICATION OF COX REGRESSION MODEL.

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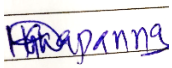
DECLARATION

I, the undersigned, hereby declare that this project is my original work and has not been presented to any other institution of higher learning other than the University of Nairobi.

Signature  Date **9/9/2022**

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DEDICATION

This study is dedicated to my late mother, Mama Amina Waqoh, for her unwavering support towards my education before her demise.

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LIST OF ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immune-Deficiency Syndrome
EPTB	Extra Pulmonary Tuberculosis
HIV	Human Immunodeficiency Virus
MDR TB	Multi-Drug Resistance Tuberculosis
NTLDP	National Tuberculosis, Leprosy and Lung Diseases program
PTB	Pulmonary Tuberculosis
TB	Tuberculosis
W.H.O	World Health Organization
NASCOP	National AIDS and STI Control Program.

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DEFINITIONS OF OPERATIONAL TERMS

i. TUBERCULOSIS

Tuberculosis is an infectious disease caused by a bacillus belonging to a group of bacteria called *Mycobacterium tuberculosis complex*. From this group of bacteria, the leading causative agent is *Mycobacterium* tuberculosis. It is transmitted through coughing, laughing, talking, spitting, and sneezing (Bloom, et al., 2017).

ii. COX REGRESSION MODEL

Cox regression is a regression model used for investigating the association between the survival time of patients and one or more predictor variables. It is a semi-parametric technique used in survival analysis, and its baseline function must be positive.

The linear function of a set of K fixed covariates that are exponentiated, as shown below.

$h(t) = h(t)e^{(\beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k)}$

iii. SURVIVAL FUNCTION

Survival function refers to the probability of surviving longer than time t.

ABSTRACT

Background: Tuberculosis is among the leading causes of morbidity in the world. According to the World Health Organization (WHO), TB is ranked ninth leading cause of death worldwide and the leading cause of a single infectious agent, ranking above HIV/AIDS. Over 25% of TB deaths occur in the African Region. Kenya is one of the 30 high burden countries that together account for more than 80% of the world's TB cases. This study aims to find out whether treatment outcome of TB patients at Isiolo TB Center is dependent/associated on/with the study variables

Objective: This study was conducted to investigate risk factors associated with: treatment outcome and time to recovery/death of Tuberculosis (TB) patients, using the Cox regression model. The study variables were socio-demographic factors (age and gender), treatment regimen type and HIV status of the patients.

Methodology: The study population was the cohort of TB patients enrolled at the Isiolo TB center for the period 2018-2019. The research data were gotten from the record (registers) of patients at the Isiolo County Referral Hospital in Isiolo County, with a sample size of two hundred and twenty eight (228), obtained using a systematic sampling technique. The data collected was cleaned in Excel and imported to R where analysis was done. Cox Regression Model was fitted to the data to determine the effects of socio-demographic factors on the treatment outcome of the TB patients. The analysis was also used to evaluate the relationship between treatment regimen type and the recovery time and time to death and also to assess the effects of HIV status on the time to recovery or death.

Results: A total of 228 patients were included in the study. Male (138) and female (90). The Cox Regression analysis was done in two parts: when the event of interest=”Cured” and when the event of interest=”Dead”. The covariates age and regiment type were associated with the treatment outcome time though partially. HIV status had influence on the time to recovery and time to death of the TB patients. While gender of the patients had no influence on treatment outcome time.

Conclusion: Socio-demographic factor age influences TB treatment outcome according to this study. For example, being young increased patient’s chance of cure from TB. Treatment regimen type affects the treatment outcome of the patients as those who were on 1st line treatment regimen type had more chance of cure as compared to those on the special line treatment. HIV positive patients had poor survivorship as compared to those who were negative.

Keywords: Tuberculosis (TB), socio-demographic factors, treatment type, HIV, Cox Regression, Survival function, Hazard Ratios.

CHAPTER ONE

1 INTRODUCTION

1.1 Background of the Study

Tuberculosis is an infectious and chronic disease. It is caused a bacterium referred to as *Mycobacterium tuberculosis* (Mtb). The probability of TB affecting every parts of the body can be high, but lung's infection accounts for around 80% of the total infections/cases. The transmission of the bacteria is through infectious aerosolized droplet nuclei generated by coughing, laughing, talking, sneezing, and singing (Bloom, et al., 2017).

The National TB, Leprosy, and Lung diseases Program (NTLDP), ranks TB as the fourth-leading cause of death in Kenya. In 2016, Kenya conducted a national TB prevalence survey, the first survey since independence. The main aim of the survey was to find out challenges existed in delivering TB treatment and testing, to provide an accurate estimation of Kenya's TB burden and identify gaps in TB detection by the national TB control program. The survey was also meant to inform the government on how effectively put in place TB control measures. The outcome of the survey showed that prevalence stood at 426 per 100,000 people with age group 25-34 years most affected and women age 65 years and above most affected (Enos, et al., 2018). According to Ethiopia's Ministry of Health TB, Leprosy, and HIV prevention program manual 2nd edition, TB patients are said to have factors such as disease-specific, personal and treatment-related that can affect the outcome of treatment adversely. Identification of these factors will help in providing better care to the patients so as to have improved health outcomes (Ali, Mavundla, Fantu, & Awoke, 2016).

Kenya's ministry of Health recently launched two policies to guide in ending TB in the country. They include Free Regimen and Latent TB Infections and the Latent TB Infections. The policies seek to address the treatment of the MDR-TB in line with the WHO's guidelines with the aim of

improving the treatment outcome by changing TB situation among people living with HIV, contacts of TB patients and high-risk populations through treatment of latent TB. Kenya's strategic goal is to get rid of TB by 2030.

In-order to decrease morbidity and mortality from TB disease in patients infected with HIV, early detection of TB followed by prompt initiation of the treatment with potent anti-TB drug regimens is advised. This approach is critically important for the prevention of TB transmission in the community. (WHO, 2010).

In as much as TB can be cured, its treatment and diagnosis continue to be a matter of major concern globally especially with the rise in the Multi-Drug Resistant (MDR) TB (Seung, Keshavjee, & Rich, 2015). Our study area is classified as part of Arid and Semi-Arid Kenya. In such an area, the lifestyle is nomadic with little/limited access to social amenities like schools, hospitals, etc. The prevalence of TB and other infectious diseases can be high, mainly due to the communal lifestyle practiced and the limited access to medical care. And little work has been done to understand the etiology of Tuberculosis and the associated risk factors that may influence the outcome of the treatment in the areas of arid and semi-arid parts of Kenya.

1.2 Problem Statement

Tuberculosis is among the top ten leading reasons for death worldwide and it is from a singular infectious causative agent. And Africa reports around 25% of the TB cases worldwide (Bloom, et al., 2017).

Despite having made positive steps in the fight against this disease, Kenya still has some gaps to fill in its battle against TB. In the annual report of NTLDP 2018, Kenya reported the surveillance system missed 36% of the TB cases. Also, there are research and literature gaps in the analysis of

the survivorship of the TB patients taking into consideration the underlying risk factors that can affect the treatment outcome of the TB patients.

1.3 Study Justification

According to the NTLDP annual report of 2018, 36% of the TB cases in Kenya were missed by the country's surveillance system. Isiolo County, our study site, being one of the hard to reach areas, is not fairly covered by the TB surveillance system. In-fact Isiolo is among the three counties missed by the TB Prevalence Survey of 2016; the first survey in post-independence Kenya.

It is also worth noting that the TB situation in the county is high (350/100,000) when compared to the national case (217/100,000), hence the choice of the county as a study site for the present study.

Also, the derived its motivation from the fact that 36% of the TB cases are missed by health's surveillance system, which is fairly high and aimed to study the risk factors associated with TB treatment outcome of the TB patients in Isiolo County.

1.4 Research Questions

The following were the questions that the study aimed to answer: -

1. What socio-demographic factors influence time to recovery and time to death among TB patients?
2. Does type of treatment regimen influences time to recovery and time to death among TB patients?
3. Does HIV status influences time to recovery and time to death among TB patients?

1.5 General Objective

To study the risk factors associated with the treatment outcome of TB patients using the Cox Regression model.

1.5.1 Specific Objectives

i. To determine the socio-demographic factors that influence time to recovery and time to death among TB patients.

ii. To evaluate if type of treatment influences time to recovery and time to death among TB patients.

iii. To assess whether HIV status influences time to recovery and time to death among TB patients.

CHAPTER TWO

2 LITERATURE REVIEW

2.1 Introduction

Tuberculosis is among the top ten leading causes of death globally, and it is from a singular infectious causative agent. In 2016 alone, two million and five hundred thousand people got diseased with TB in Africa, which accounted for a quarter of the TB cases worldwide then (World Health Organization (WHO), 2020). It is also worthy to note that about 25% of TB mortality occurs in African Region as Multidrug-Resistant TB (MDR-TB) remains a public health crisis and a health security threat. By the year 2018, estimates indicated that there were 451,551 new cases with resistance to rifampicin (the most effective first-line drug) in the African region (WHO, 2018).

2.2 Literature Gaps

Africa, home to 11% of the world's population, has a not proportionate case of tuberculosis as it reported 25% of the total global TB cases. An increase in the incidence of Tuberculosis cases in Africa is associated with the spread of HIV/AIDS cases, which is the single most crucial factor contributing to the incidence of the disease (WHO, 2010). Specifically, Sub-Saharan Africa experienced an upsurge of TB cases from mid of the 1980s (Corbett, et al., 2003). According Narain, *et al*., (2014), these countries are low-income countries where poverty and HIV have combined and propagated the transmission of TB. In as much as it was challenging to accurately measure, much of the recorded cases may have reflected the real change of the Tuberculosis in the community.

TB treatment default is a challenge in combating TB. According to a study on treatment default among pulmonary tuberculosis patients at an urban slum in South-Eastern Nigeria (Akinola, A. F.,et at (2009),it was established that there was high default rate on treatment where majority of patients defaulted during the continuation phase.The main reason for default according to the study was early relief from sysmptoms,poverty and drug-related issues.This default led to the transfer of patients to a second line/different treatment regimen.However,this study did not talk about the difference in treatment outcome for the defaulters and those who continued on the 1st line treatment.

HIV and TB are the most prevalent communicable diseases of public concerns.In Sub-Saharan Africa,an estimate of about 30% of HIV persons are also infected with TB.A study on the treatment outcome in HIV co-infected TB patients in Ethiopia (Ali, S. A, et al 2016) established that out of the total 575 patients enrolled in the study,360(62.6%) were HIV negative while 169(29.4%) were HIV positive,where,the treatment success rate among the co-infected patients is lower when compared to the negative person.However,the study recommended the need to look further into the cure rate and time to recovery and also the effects of co-infection on the mortality of the TB patients.

In low-and middle-income countries like Kenya, control of TB requires action on social determinant of Tuberculosis as well as investments in strengthening systems for diagnosis and treatment (Hargreaves, J. R, et al ,2011).Accelarated focus to addressing social determinants of TB has been stimulated within and without the TB sectors..According to Hargreaves, J. R, et

al(2011),creation of awareness on the other areas of health like HIV/AIDS, besides TB, is of great importance as there exists disparity in contracting TB influenced by the socio-economic factors.This awareness will play a key role in minimising risks and creating treatment access especially in pastrolist communities.

Access to the health services for the TB patients can be a challenge among the pastrol communities because of access to heath services centers.A grounded theory study carried out in Pokot County on health seeking pathway and factors leading to delays in tuberculosis diagnosis(Grace W.M et at,2018) established that cultural practices and believes of pastoral communities influence health seeking behavior.There are certain social factors that mostly influence health seeking and treatment behavior among patients especially the pastoral communities.Age,especially the young age, affects the health seeking behavior of individuals.(Rahmat H et al,2014).

There is a complex relationship between culture, health-related beliefs and health behavior. Attitudes towards beliefs on social network of health and personal experiences interacted and influenced health-seeking behavior. Several authors agree that the human element in TB control has often been overlooked (Liefooghe, *et al*., 1997). If more consideration could be given to the human health culture, TB control would improve significantly (Hargreaves, et al., 2011). One of the significant causes of morbidity and death in Kenya is Tuberculosis. It majorly affects the productive age of 15-44 years, though all age groups can be affected (Mbithi, et al., 2014).
Pastoralist communities in Kenya lack the required knowledge and perceptions about TB as most of the individuals historically thought that TB is a severe disease that is hard to diagnose and treat. They also believe that TB is a hereditary disease that is meant for certain people. Also, most of the

patients do self-medication instead of seeking specialized treatment due to the long distance to health facilities (Mbuthia, Olungah, & Ondicho, 2018) and irrespective of the outcome.

Reviews in the literature reveal that there was not much done on the risk factors associated with the TB outcome using Cox regression Model, especially in the Northern Kenya. This study was formulated to address this gap in the literature.

Modeling data using Cox Proportional hazard is a common method in anlysis of time to event data (Borucka, J. (2014).Modeling data using this model is based on some restrictive assumptions like the proportionality of the hazards.This proportionality reduces effects of confounding and interactions that might be experienced when modeling in other mathematical models.According to Collet, D. (1994),survival analysis is the best technique for studies involving an end-point or occurrence of some events of interest. Involves time origin which marks the start of recruitment into the study or diagnosis of a condition and treatment commencement.The end-point of interests can be fatal(death) or non-fatal like ease of pain and symptoms. Collet, D. (1994),argued that survival analysis has special features like censoring that takes care of those individuals who are lost to follow up or drop out of the study.This feature helps in ensuring that that missing data gap is minimised.

2.3 Tuberculosis (TB) Etiology, Transmission mode, history of infections

Tuberculosis is an infectious and chronic disease caused by a group of bacteria called *Mycobacterium tuberculosis complex*. From this group of bacteria, the leading causative agent is Mycobacterium tuberculosis (Bloom, et al., 2017).

Other agents include;

- *Mycobacterium bovis* (transmitted through contaminated milk and milk products).
- *Mycobacterium africanum* (Bloom, et al., 2017).

The disease is transmitted from an infected person to the healthy one through aerosolized droplets of nuclei. These droplets can be generated through coughing, talking, laughing, spitting and sneezing, etc. by an infected case (World Health Organization (WHO), 2020).

To be infected with TB, someone must be exposed to a TB case (WHO). Infection is defined as a condition where a person has TB bacteria in the body. This exposure depends on certain risk factors such as the following:

- population density
- Poverty
- Overcrowding
- Infectious TB incidence in a population
- Disease Infectiousness duration average
- Age
- Malnutrition
- Sex etc.

According to DLTLD, TB has two clinical forms, and they include TB outside the lung, which is called Extra-Pulmonary TB (EPTB) and TB in the lungs, also known as pulmonary TB (PTB). Pulmonary TB can further be classified as smear-positive and negative PTB. Extra Pulmonary TB is a TB that affects other organs of the body outside of the Lungs (Corbett, et al., 2003).

According to reports, a quarter of the world's population has latent TB, meaning presence of disease yet to manifest itself (World Health Organization (WHO), 2020).

2.4 TB Situation in Isiolo County

Isiolo County TB Services are provided in 19 diagnostic and 24 treatment sites according to the annual NTLD report of 2018.at the time of this study, the TB cases in the county stood at 549 cases

yielding a notification rate of 350/100,000. This is high when compared with the national case of 217/100,000. Of the reported cases, 77% came from Isiolo Central, 16% from Garba-Tulla sub-County and 7% from the Merti Sub-County

At the time of this study, in terms of treatment outcomes, the County's Treatment Success Rate (TSR) for new smear positive cases was 85.2%, which was below the national average of 88%. The table 2.1 illustrates TB Service Delivery (Isiolo County against National one) while Table 2.2 is about TB cases notification. Tables 2.2 and 2.3 show the relationships between TB/HIV and TB-Malnutrition respectively (Isiolo County TB Center, 2019).

Table 2.1

TB Service Delivery (Isiolo County against National)

Service Delivery	Isiolo	National
TB Diagnostic Sites/100,000	12	5
Treatment sites/100,000	15	7
Number of TB diagnostic sites	19	2079
Number of TB treatment sites	24	2995

According to the Annual NTLD annual report of 2018, a 5-year trend analysis of the TB cases notification in Isiolo County was as given in the table 2.2

It is worthy to note that, there was a steady increase of the New Bacteriologically confirmed TB cases in the county for the period 2014 to 2017 with a slight drop in the trend in 2018.For the new clinically diagnosed cases, the trend increased steadily for the period 2016-2018.

Table 2.2

DSTB Cases notified for the period 2014-2018

TYPES OF TB	2018	2017	2016	2015	2014
New Bacteriologically confirmed	264	284	270	217	192
New Clinically diagnosed	377	177	107	119	203
Previously Treated	66	14	24	25	41
Extra-pulmonary	49	147	126	183	146
TB among Children (all forms)	87	73	64	83	75

The TB/HIV Co-Infection rate in the county for the period 2014-2018 was as given in the table 2.3. The trend shows that there was a slight drop in the co-infections rate from 2015-2018.Probably this is attributable to the government's efforts/policy of 90-90-90 HIV treatment strategy.

Table 2.3

TBHIV Care Cascade among DSTB (All forms), (%), 2014-2018

TBHIV Indicator	2014	2015	2016	2017	2018
HIV Testing	97.5	90.2	95	89.5	96.2
TB/HIV co-infection rate	25.2	25.3	21.2	14.7	18.1
ART Uptake	97.2	97.1	100	98.9	98.5

Table 2.4

Nutrition Status among the DSTB (all forms) %, 2014-2018

TBHIV Indicator	2014	2015	2016	2017	2018
Proportion malnourished	51.2	48.7	55.4	51.6	36.3
Proportion on food support	43.2	45	48.9	41.9	41.4
ART Uptake	97.2	97.1	100	98.9	98.5

2.5 The Conceptual Framework

This study aimed to examine association between the certain perceived risk factors and the outcome of TB patients by using the Cox regression model (Borucka, 2014). The primary choice of this topic was because of the research gap in this specific area. The study utilized secondary data to try and achieve its objective, and since all the events have already taken place, retrospective cohort study methodology was applied.

The independent study variables were the survival time of TB patients measured in months while the independent variables, which are also called covariates in survival analysis, included: treatment type and HIV Status.

CHAPTER THREE

3 METHODOLOGY

3.1 Study Area

The study area was in Isiolo County. Isiolo is located in the Upper Eastern part of the former Eastern province and is about 285 kilometers to the North of Nairobi. The county covers 25,336.1 square kilometers of land. It has three sub-counties: Garba-Tulla, Merti and Isiolo Central. The county has total population of 268,002(Male=139,510 and female=128,483) (KNBS, 2019). The key health indicators are Neonatal disorders 7.1% Malaria & HIV prevalence of 3.8% and the doctor to population ratio is 1:143,000. Life expectancy stands at 57.6 years. The main economic activity is pastoralism. In terms of health services; the county has one County Teaching and Referral Hospital and one sub-county hospital and several health centers and dispensaries.

3.2 The Study Design

We used a retrospective cohort study design because all the events and exposure have already occurred. The 2018-2019 cohort register of the TB patients were used in this study.

3.3 Study population

Our study population was the Cohort of TB patients in Isiolo County during the year 2018-2019 that was traced by the health surveillance system and put on active TB treatment during the period.

3.4 Case Definition

Patients who exhibited signs, symptoms and radiological findings consistent with active Tuberculosis at any health site within the county.

3.5 Inclusion and exclusion criteria

Only patients above 15 years, and the bacteriologically confirmed cases were included in the study. Those who lost to follow up, Transfer Outs and those with unknown HIV status (declined to be tested) were censored.

3.6 Sample Size Determination and Sampling Strategy

Besides the study purpose and the size of the population, three criteria were specified for the sample size determination (Israel, 1992). These are:

- Precision Level.
- Confidence level.
- Variation in degree/attributes being measured.

We assumed our precision level to be 0.05, confidence level to be 95% and degree of variability 5%, and our population size was known.

Now applying Yamane (1967:86) formula, our sample size was obtained as follows: -

$n=N/(1+N(e)^2)$

N=530(Total number of TB patients during the study period, 2018-19)

e=0.05

$n=530/ (1+530(.05)^2) =228$

=228

3.7 The Study Variables

Dependent variable: Our response variable was the time to death/recovery of the TB patients measured in months. The time period was 24 months.

Independent variables: The covariates/the predictors in the study, and included:

- Socio-demographic factors (age in years coded as young=2 for between 15-40 years, and those above 40 years=1.Gender of the respondents coded as male=1 and female=2)
- Type of treatment: this the regimen type/drugs administered to the patient at the time of diagnosis. It consisted of Intensive Phase Treatment (regimens: 2RHZE/4RH and 2SRHZE/5RHE)) coded as 1, and special patient regimen (referred to as other in the record) for those patients who reacted to the 1st line treatment regimen, coded as 2 for ease of analysis.
- HIV Status**:** Is the HIV status of the respondents at the time of diagnosis. It was coded into two categories which are: “Negative=2,”Positive”=1

3.8 The Study Model

The Cox PH regression model is used to explore the effects of several covariates simultaneously on a right-censored, time-to-event outcome.

For k covariates; the model is of the form:

$$h(t) = h_0(t)e^{(}\beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_k X_k)$$

or

$$\ln[h(t)] = \ln[h_0(t)] + \beta_1 X_1 + \beta_2 X_2 + .. + \beta_k X_k$$

Where

h(t)= hazard rate of time to recovery or time to death

$h_0(t)$ = baseline hazard

X_1 , X_2,…,X_k are covariates

$\beta_1, \beta_2, \ldots\ldots, \beta_k$ are coefficients representing the effect of each prognostic factor

The proportional hazard assumption can be checked using Goodness of fit test based on Schoenfeld residuals. A non-significant result (preferably p-value > 0.10) suggests that the proportional hazard assumption holds, whereas a significant result (p-value < 0.05) implies that the covariate does not satisfy the assumption. This statistical test is carried out for each covariate. Additionally, the test performs a global test for the model as a whole. A non-significant result (p-value > 0.10) implies that the model is okay to be treated as proportional hazard model.

In the case where PH assumption is violated; Stratified Cox regression model may be applied. Alternatively, interaction terms between functions of time and covariates that violate the assumption maybe included in the model.

3.9 Data Collection Procedures

This study used secondary data to answer the research questions. The data were obtained from TB clinic registers at the Isiolo County Referral Hospital. Appropriate set criteria of secondary data collection were followed to ensure research viability and reliability. Reliability of the source data, quality, depth, as well as adequacy of the data, among others, were properly checked

In addition, the researcher reviewed the patients' cards, registers, and information sheets and collected the relevant data.

3.10 Data Processing and Analysis Procedure

Data compilation and cleaning were done in MS Excel. After which it was exported into R version 3.6.0 for coding and analysis.

The demographic characteristics of the respondents in terms of gender, age, HIV status, and nutritional status were given in table with brief explanations/discussions.

Secondly, Cox proportional-hazard models was fitted to investigate the association between the survival time of the patients and the covariates.

Study variables were analyzed for all the objective under the two events of interest i.e 'Cured' and 'Death'. The results were then presented in tables for each of the events; for the three variables.

For each model, the proportionality of the hazards was tested and the output presented in one table.

3.11 Minimization of Errors and Biases

Systematic sampling technique usage minimized sampling biases and data collection error because since registers were the data source, the first item was collected using the Simple Random Sampling method after which the subsequent items were selected systematically using the sampling fraction until all sample items were collected.

Coding was also done appropriately to eliminate data analysis errors.

3.12 Ethical Consideration

This study adhered to the research ethics in the following ways:

- The researcher signed a concept letter with the County TB coordinator committing to use the data only for the research purpose.
- The data collected for the study was treated with utmost confidentiality and was not exposed to a third party.
- Following the guideline laid down by the university on data collection/analysis to avoid errors and plagiarism.

3.13 Study Limitations

The study used secondary data. Due to the movement restriction as a result of the COVID-19 pandemic, physical contacts/discussions like Focused Group Discussion with health care givers were limited. However, the researcher made sure that adequate quality control of the data collected was done to ensure a quality outcome.

CHAPTER FOUR

4 RESULTS

4.1 Descriptive Statistics

4.1.1 Demographic Characteristics of the Respondents

Three hundred and twelve TB patients at the Isiolo County TB center were included in the study. Table 4.1 shows the descriptive statistics of the participants.

A large proportion (60.53%, n=138) of the study respondents were males while (39.47%, n=90) were female. 81.14 %,(n=185) of the patients were HIV negative, (18.86%, n=43) were HIV positive. A greater percentage of TB patients at Isiolo Hospital, who participated in the study, are HIV negative.

As illustrated in table 4.1, at the point of admission, 56.14 %,(n=128) of the respondents, who were TB clients at Isiolo TB center were severely malnourished, 41.67%, (n=95) were Normal weight while 2.19%, (n=5) obese.

Further, on treatment status of the patients, 78.07% (n=178) of the respondents were cured of TB, 3.07%(n=7) completed Treatment(TC),13.16%(n=30) Died(D) of TB, 1.75%, (n=4) Lost to Follow up (LTFU), (3.95%, n=9) did not Complete the treatment (NC) .Two hundred and one (201, 88.16%) of the patients were put on the 1st line treatment regimen while 11.84 %(n=27) were administered the patient narrowed regimen after they showed resistance to the 1st line treatment regimen.

Table 4.1

Demographic characteristics of the respondents

Variable	Frequency	Percentage
HIV Status of the respondents		
Negative	185	81.14
Positive	43	18.86
Treatment outcome of the respondents		
Cured(C)	178	78.07
Treatment Completed(TC)	7	3.07
Died(D)	30	13.16
Lost To Follow Up(LTFU)	4	1.75
Not Completed(NC)	9	3.95
Nutritional Status of the respondents		
Severe	128	56.14
Normal	95	41.67
Obesed	5	2.19
Gender of the respondents		
Male	138	60.53
Female	90	39.47
Treatment Regimen administered at diagnosis		
1^{st} line standard treatment regimen	207	88.16
Patient narrowed regimen-after resistance to 1^{st} line	27	11.84

4.2 Cox Proportional Hazard Model Analysis

From the cox analysis, at 5% level of significance, socio-demographic factors (age and gender) and the treatment regimen type have partial effects on the treatment outcome. HIV Status of the patients had full effects on the TB treatment outcome.

4.2.1 Effects of socio-demographic factors on the TB Treatment Outcome

This is done for the two events of interest i.e 'Cured' and 'Dead', where models were fitted for each event to compare effects.

When the event of interest is 'cured': Adjusting for gender, treatment type and HIV status, there was a significant association between age and time to recovery. The rate of recovery among patients aged below 40 years is 1.67 times higher than those equal to or above 40 years (AHR= 1.67; 95% CI: 1.23 -2.27). Overall, the model is significant

When the event of interest is death: Adjusting for gender, treatment type and HIV Status; there was no significant association between time to death and age. The risk of death among those aged 40 years and above is not significantly different from those who are 40 years or below (AHR= 1.81,95% CI : 0.85-3.88) and p-value= 0.13).

Gender effects on the treatment outcome was not significant. When the event of interest is 'Cured': Adjusting for age, treatment type and HIV status, there was not a significant association between gender and time to recovery (p-value= 0.89) and 95% CI includes 1(HR= 0.88; 95% CI: 0.72-1.33).

When the event of interest is 'death': Adjusting for age group, treatment type and HIV status, there was no significant association between gender and time to death. The risk of death among female

was not significantly different from that of male (AHR= 1.37; 95% CI: 0.64 -2.92) and p-value=0.41.

4.2.2 To evaluate if the type of Treatment Regimen influences the time to recovery and time to death among TB patients

From table 4.2 Treatment type administered to the patients had influence on time to recovery under the event of interest 'cured'. A patient who was administered special treatment regimen had difference in recovery time from an individual who was under 1st line treatment regimen by 61 %.(AHR=0.39, 95% CI: 0.17- 0.93).Under the event of interest death, there was no significant difference in time to death for those patients on the 1st line regimen and those on the special treatment regimen. (AHR=0.60; 95% CI: 0.74 -3.77),after adjusting for the other variables.

4.2.3 To assess whether HIV status influences time to recovery and time to death among TB patients

While adjusting for gender, age and the treatment regimen type; there was a significant influence of HIV Status of a patient on the time to recovery and time to death of a TB patient.

When the event of interest is 'cured', adjusting for age, gender and regimen type, a TB patient who is HIV negative is 4.16 times more likely to get cured from TB as compared to a HIV positive TB patient. (AHR=4.16, 95% CI: 2.07-8.39).

When the event of interest is 'death', a TB patient who is HIV negative was 97% less likely to die of TB when compared to an HIV positive TB patient (AHR=0.04, 95% CI: 0.01 -0.12)

Table 4.2

Effects of socio-demographic factors, treatment type and HIV on TB treatment outcome

Variable	Estimate	Coefficient Standard error	HR	HR(95% CI)		P-Value
When the event of interest ='cured'						
Gender	-0.02	0.17	0.98	0.72	1.33	0.89
Age-group	0.51	0.16	1.67	1.23	2.27	0.00 ***
Regimen	-0.92	0.43	0.39	0.17	0.93	0.03 *
HIV Status	1.43	0.36	4.16	2.07	8.39	6.66e-05 ***
When Event of interest ='death'						
Gender	0.32	0.39	1.37	0.64	2.92	0.41
Age-group	0.60	0.39	1.81	0.85	3.88	0.13
Regimen	0.51	1.67	0.60	0.74	3.77	0.22
HIV Status	-3.28	0.57	0.03	0.01	0.12	9.26e-09 ***

4.2.4 Checking for the proportional hazard assumptions

For the Cox Regression Models fitted, proportional hazard assumptions were checked using the Chi-square goodness of fit under the both events of interest.

From table 4.4 the GlOBAL P-values for both models were insignificant at 5% Level of Significance. Therefore the assumptions of proportionality of hazards were not violated.

Table 4.3

Proportionality of the Hazard Test

Variable	**Chisq**	**Df**	**P-Value**
When the event of interest='cured'			
Gender	0.57	1	0.45
Age-group	1.23	1	0.27
Regimen	3.39	1	0.07
HIV Status	0.46	1	0.49
GLOBAL	6.85	4	0.14
When Event of interest ='death'			
Gender	0.19	1	0.66
Age-group	1.60	1	0.21
Regimen	0.75	1	0.39
HIV Status	2.97	1	0.08
GLOBAL	5.80	4	0.21

CHAPTER FIVE

5.0 DISCUSSION

Among the 312 TB patients sampled, 60.53% were male while 39.47% were female, portraying that males were the most affected population by TB in the county. This finding is consistent with the National TB, Leprosy, and Lung Disease Program annual report which showed that 66% of all the national cases of TB were men (*NTLDP, 2020*). In terms of treatment adherence, 78.07% of the respondents got cured, 3.07% respondents completed their treatment (TC) but may still have TB, 1.75% Lost to Follow Up (LTFU) and 3.95% of the patients did not Complete the treatment while 13.36% of the respondents died (D) as 11.84% are transferred to the 4th Line treatment after they showed resistance (MT4) during the study period. In summary, individuals who got cured(C) and those who completed their treatment (TC) accounted for 81.14%. This shows good treatment adherence and is almost in agreement with the national adherence rate of 85 %,(*NTLDP*, 2019). Individuals who got cured accounted for 78.07% while deaths accounted for 13.36%, which indicates that overall, there is good survivorship for TB patients in the county.

According to the study findings, 18.86% of TB patients were co-infected with HIV&TB. This is lower when compared to the national co-infection rate of 25 % according to the National TB, Leprosy, and Lung Diseases Program annual report (*NTLDP*, 2020). Therefore, Isiolo County's co-infection rate is lower when compared to the national one.

In the study, malnutrition seems a major challenge to the control of TB in the county as 56.14% of the patients were severely malnourished at the time of diagnosis. This is high when compared to the national malnutrition rate (40%) in the NTLDP report of 2020 when this study was carried out.

5.1 Effects of Socio-demographic factors on the TB Treatment Outcome

The study fitted two models to investigate the effects under the two events of interest (‘cured’ and ‘dead’) for comparison purposes. The outcome showed that both age and gender is significantly but partially associated with both of the events. Young age is positively associated with getting 'cured' of TB. For instance, under the event 'cured', being young (<-40yrs) increased the cure rate by 67%.

Comparatively, for the event of interest: 'death', the study showed that there is no significant difference in time to recovery & time to death and the age of the patient. These findings are consistent with the results of a previous study on age-stratified Tuberculosis treatment outcomes in Zimbabwe, whose findings exhibited favorable outcomes in TB treatments outcome for young age (Nchube et al., 2017), where its key findings revealed that cure from TB increased proportionately with the young age of the patients. This according to (Nchube et al, 2017), may be related to immunosuppressant comorbidities or other old age-related diseases.

According to the current study, gender of the patients has no effects on the treatment outcome. From the study, there is no significant association between gender and cure from TB (P-value=0.8980), see table 4.2, and also, there was no association between gender and treatment outcome in terms of time to death from TB as indicated in table 4.2. Being female has equal chances of hazard to being male. The finding of the current study is consistent with those of a previous study on gender differences in tuberculosis treatment outcomes carried out in South Africa (Murphy et al., 2018),which established that there were no statistically significant differences in TB treatment outcomes between men and women.

5.2 Effects of type of Treatment Regimen on the recovery and death time

Effective treatment is an important pillar in control TB. Presently WHO recommends RH2ES(consisting of Rifampicin, Isoniazide, Pyrazinamide, Ethabutal, Streptomicin) as the first line treatment regimen for susceptible TB for two months intensive and four months continuation. And for the susceptible TB of bones and brain, two months of intensive phase followed by ten months of continuation. Those who showed resistance to the first line were administered patient narrowed regimen (*WHO*).In Kenya, these guidelines are under implementation since 2017.

In the present study, 88.16% of the patients were on the 1st line treatment regimen while those who showed resistance and transferred to the patient narrowed regimen accounted for 11.84% which shows that 1st line treatment resistance is low. This means there is a low 1st line resistance rate and patients without proof resistance were treated for 6 months continuously.

Good number of patients did not show resistance to the 1st line treatment category. Also it is good to note that those who resisted and transferred to the special regimen did experience lower cure rate by 60.3%. This is consistent with the findings of a study on Comparison of first-line tuberculosis treatment outcomes between previously treated and new patients: a retrospective study in Machakos subcounty, Kenya (Ndambuki et at, 2021), which showed patients who were previously treated and experienced resistance have poor cure rate as compared to new ones or those who did not show resistance.

5.3 HIV status influences on time to recovery and time to death of TB Patients.

During the study period, Isiolo county HIV prevalence rate was 4.2 %(NASCOP, 2019) while co-infection rate was 18.86 % as shown in table 2.3.

It is important to know the HIV status of a TB patient because HIV weakens the immune system and this makes latent TB to progress to TB disease. WHO recommends initiation of ART treatment within eight weeks of starting anti-TB treatment to avoid increased risk of mortality (Ismail I, Bulgiba, 2013).

According to the current study an HIV negative patient is 4.16 times more likely to get cured of TB as compared to a positive patient. This finding agrees with the findings of a study on impacts of HIV on Tuberculosis treatment outcomes carried out in Southern Ethiopia (Aleyu et al, 2020), which established that HIV-positive patients on TB treatment had poor survivorship as compared to a HIV negative person.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSIONS

The objectives of this study were to investigate the association between TB treatment outcome and the age, gender, Regimen type and HIV status of TB patients.

According to the findings, socio-demographic covariate age affects the outcome of TB treatment. Old age is associated with poor survivorship while young age is associated with good cure rates.

On gender, being male or female has no influence on the treatment outcome and time to recovery or time to death.

For the treatment regimen type, a patient put on special treatment regimen has difference in survivorship when compared to a patient on the 1st line standard treatment regimen.

HIV positive patient has a lower time to recovery and is likely to die of TB when compared to a patient who is HIV negative.

6.2 RECOMMENDATION

Based on the findings of the current study, the following recommendations are made:

- Older persons need better adapted TB management & handling and highly sensitive diagnostic tools.
- This study used only three variables to make the above conclusions but there can be many other social and economic factors that may influence the outcome of TB treatment. We recommend that further studies be carried out with more variables involved.
- Although those who lost to follow up and those who did not complete treatment account for only 1.75%,It is recommended that health caregivers and the County Health

Management Team give routine health promotions/ health education & counsel to the patients geared towards ensuring treatment adherence and completion so as to achieve 100% adherence.

- Further, health experts can use the findings in the formulation & improvement of TB treatment policy. It is specifically useful to the Isiolo county health caregivers and decision-makers who are involved in the management of TB patients.
- We also recommend nutritional assessment, routine counseling, and close follow-up & management of TB patients by healthcare workers for favorable treatment outcomes.
- The outcome of the study will be useful to academia (for future reference); the study contributes to the existing stream of literature on TB treatment.
- Further research on factors affecting TB treatment outcome using primary research data is recommended.

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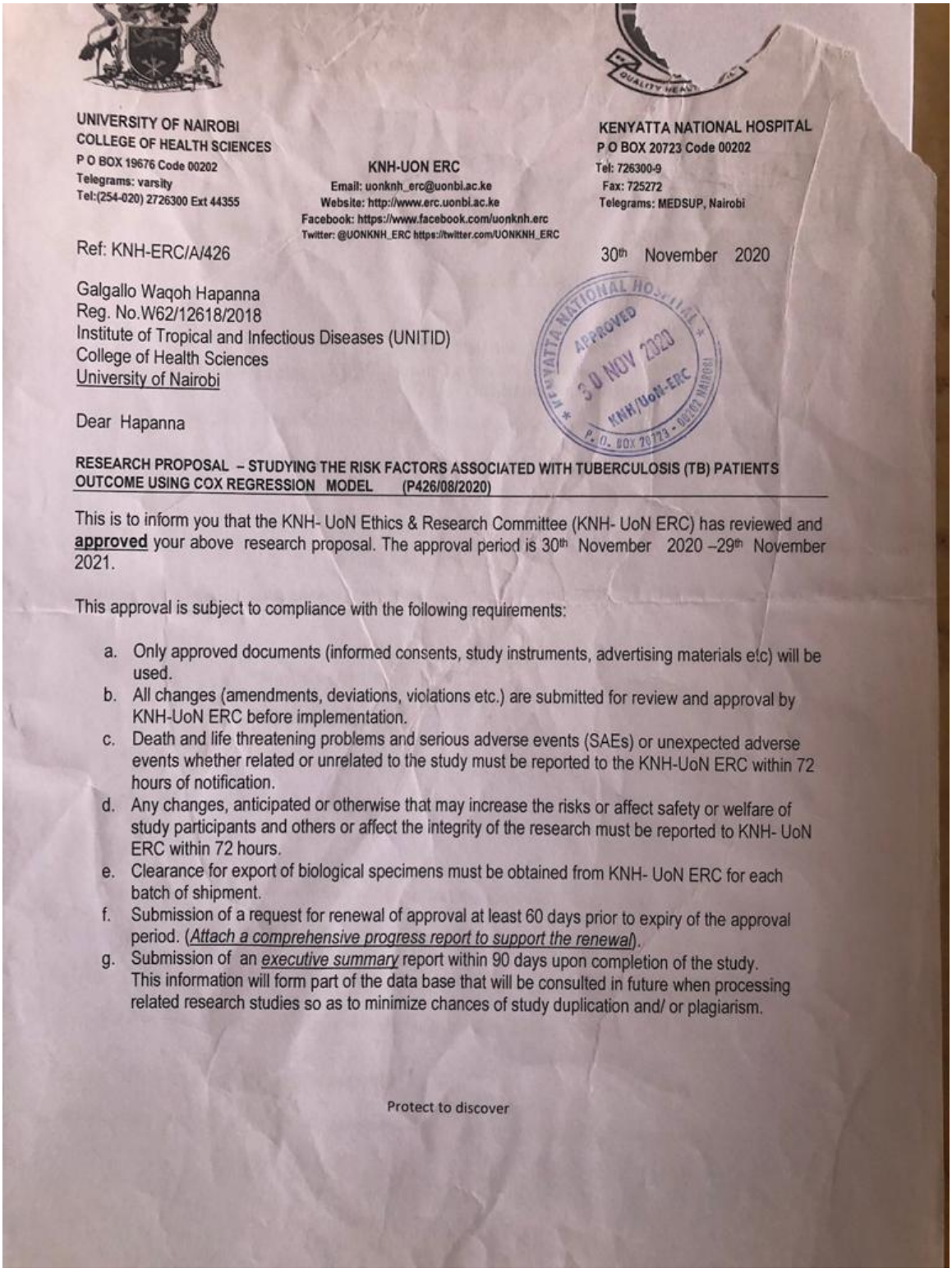
Appendices

Appendix A



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APPROVED 30 NOV 2020 KNH/UoN-ERC

Dear Hapanna

RESEARCH PROPOSAL – STUDYING THE RISK FACTORS ASSOCIATED WITH TUBERCULOSIS (TB) PATIENTS OUTCOME USING COX REGRESSION MODEL (P426/08/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 30th November 2020 –29th November 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

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The

Yours sincerely,

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