UNIVERSITY FOR DEVELOPMENT STUDIES, TAMALE

SURVIVAL AND PROGNOSTIC FACTORS OF HIV/AIDS, TB AND CO-INFECTION IN PRU DISTRICT

BY

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DECLARATION

Student

I hereby declare that this thesis is the result of my own original work and that no part of it has been presented for another degree in this university or elsewhere.

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ABSTRACT

Survival analysis is a method for analysing the occurrence of a given event. This research seeks to evaluate the survival of HIV/AIDS, TB and co-infected patients and to identify the major prognostic factors that influence their survival. In this study, survival data for HIV/AIDS, TB and HIV/TB co-infection patients were obtained from St. Mathias Hospital in Yeji, Pru District of Brong Ahafo Region of Ghana. The data was fitted using both the Cox model and accelerated failure time model. The AFT (Gamma) was the best model for HIV/AIDS and HIV/TB co-infection survival data. However, the Cox proportional hazard model was best for the TB data based on the AIC and BIC values. The study revealed that none of the covariates significantly interact at 10% significance level. The diagnostic checks on the Cox-Snell residual plot of the gamma model shows that it has the best predictive power because it is closer to the bisector. Cox model revealed that the proportionality assumption was satisfied. The martingale residual plot of the continuous covariates indicate that for each of the covariates, the plot do not show trend and the resulting smoothed plots (LOESS) are approximately horizontal straight lines. This confirms that the martingale residual plots have a linear relationship with the survival time. Hence, the model is adequate. The HIV/TB co-infection patients experienced the worse survival rate. The study deduced that Weight significantly determines the patient's survival among all the three categories. Therefore health authorities should be very cautious and pay much attention to patients who weighed below the minimum weights.

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DEDICATION

This work is dedicated to my beloved mother Janet Akosua Yaka and father Nawumbeni Dabanyi.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ACRONYMS

3TC	Lamivudine
AFTM	Accelerated Failure Time Model
AIC	Akaike Information Criterion
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
AZT	Zidovudine
BIC	Bayesian Information Criterion
CBV	Combivir
CD4	Cluster of Differentiation Four
DOTS	Directly Observed Treatment Short-Course
EFV	Efavirenz
FANTA	Food and Nutrition Technical Assistance
GDHS	Ghana Demographic and Health Survey
GHS	Ghana Health Service
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
HRZ	Isoniazid Rifampicin Pyrazinamide
HRZE	Isoniazid Rifampicin Pyrazinamide Ethambotol
HRZES	Isoniazid Rifampicin Pyrazinamide Ethambotol Steptomymide
Kg	Kilogram
KM	Kaplan-Meier Estimator
LR	Likelihood Ratio

MLE	Maximum Likelihood Estimate/Estimator
MOH	Ministry of Health
NACP	National AIDS Control Programmes
NFHL	Nutrition for Healthy Living
NTP	National Tuberculosis Programme
NVP	Nevirapine
PH	Proportional Hazard
PLWHA	People Living with HIV/AIDS
TB	Tuberculosis
TR	Time Ratio
WHO	World Health Organization

CHAPTER ONE

INTRODUCTION

1.1 Background of the study

The complex relationship between Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) results in synergistic increases in their prevalence, morbidity, and mortality. The occurrence of both infections in the World is a great public health problem. The situation in Africa is not different. There is a looming threat of a pandemic emerging in Ghana as it has been in other African countries (GHS, 2006).

In an enlightened form, HIV is the virus that attacks and destroys the infection-fighting CD4 cells of the body's immune system. It is noteworthy that, loss of CD4 cells makes it very difficult for the immune system to fight infections. When the immune system is progressively damaged by HIV, the infected person becomes immune suppressed and is therefore exposed to other opportunistic infections, especially TB. The advanced form of HIV is called Acquired Immunodeficiency Syndrome (AIDS). HIV epidemic is one of the most destructive health crises of modern times destroying families and communities around the world. HIV is transmitted through the blood, semen, genital fluids, or breast milk of an infected person. Among the modes of transmission, unprotected sex or sharing drug injection equipment with an infected person, are the most common ways HIV spread (AIDS info facts sheet, 2012). Although tremendous researches have been conducted in the field of HIV/AIDS, there is no cure to it. However, there are steps one can take to delay the start of full blown AIDS and reduce it vulnerability. The

most promising advance made was the advent of potent combination of therapy in 1996. The antiretroviral therapy (ARV) drug's role is to prolong the life of the infected patient by slowing down wasting period by boosting the CD4 count in the immune system (Jackson, 2002).

On the other hand, TB is caused by the tubercle bacillus, Mycobacterium tuberculosis and spread through air (Friedland *et al.*, 2007). TB attacks the lungs, but sometimes affects other parts of the respiratory system. TB that affects the lung is called the pulmonary TB; otherwise it is called extra-pulmonary TB. There are two forms of TB; the latent TB and the TB disease. Latent TB infection is the inactive form; the TB germs in the body are sleeping and do not make a person sick. Others have strong immune system that quickly destroys the bacteria once they enter the body. A person with latent TB cannot spread it to unaffected persons. Without treatment, the latent TB infection can advance to TB disease (TB Facts, 2012). Generally, relatively small proportion of people infected with mycobacterium tuberculosis will develop TB disease, people who have much higher chances of developing the disease are those infected with HIV. TB cases are reported mostly among men than women, and affects adults in their productive ages. The burden of TB continues to increase due to poverty, population growth and HIV/AIDS (Tarimo, 2012). TB is the most common opportunistic infection complicating HIV infection especially in developing countries, and may occur at any stage in the course of immunodeficiency (Interagency Coalition on AIDS and Development, 2010).

HIV affects the immune system and increases the possibility of people acquiring new TB infections. It also promotes both the progression of latent

TB infection to active disease and a relapse of the disease in previously treated patients. TB is one of the leading causes of death for HIV infected people. HIV increases unfavorable drug reactions to treatment among TB patients. In addition, HIV infected people who have recovered from TB have an accelerated course of HIV disease and shortened survival compared with HIV infected people without a history of TB (WHO, 2004). People living with HIV (PLWH) are estimated to have between 12 to 20 times higher risk of developing TB disease compared to people living without HIV infection (Padmapriyadarsini *et al.,* 2011). It is also estimated that communities of higher HIV and TB rates have been rising severely even where effective TB control strategies are available. This underscored the need to improve TB control wherever HIV co-infection is common. The link between TB and HIV/AIDS may make people equate TB with HIV/AIDS. This may lead to increasing stigma and discrimination and delay TB patients in quest of health care and treatment (Refera, 2012).

HIV and TB pathogens potentiate each other accelerating the deterioration of immunological functions and resulting in premature death if untreated. Both TB and HIV have profound effects on the immune system as they are both capable of disarming the host's immune response through mechanisms that are not fully understood. Co-infection is the most powerful known risk factor for the progression of TB to active disease. HIV/TB co-infection significantly changes the original history of both diseases. This gives rise to different problems. One major problem associated with patients co-infected is intersecting both signs and symptoms between the diseases. The strange signs and symptoms of co-infection make the clinical diagnosis difficult in nearly all

cases. The fact that HIV/AIDS also makes the patient susceptible to other opportunistic infections with symptoms similar to TB are among the difficulties encountered in diagnosing TB in HIV patients. The other impact is that two different diseases with varying modes of diagnosis and treatment exist in a single patient. Both diseases involve the combination of different drugs. HIV/AIDS treatment is for life and a minimum of six month for TB (Pawlowski *et al.,* 2012).

Further, there has not been any efficient nationwide study on the prevalence of HIV/TB co-infection in Ghana. However, it is estimated that the influence of these diseases have been increasing such that in 1989 while about 14 percent of TB cases could be attributed to AIDS, by the year 2009 about 59 percent of the projected TB cases were attributed to the HIV/AIDS epidemic. Hospital studies have shown that the prevalence of HIV in TB patients is approximately 25-30 percent and that as many as 50 percent of patients with chronic cough could be HIV positive. Autopsies reports in Accra found that the proportion of TB deaths increased from 3.2 percent in 1987 to 1988 at the beginning of the HIV epidemic to 5.1 percent in 1997 to 1998. About 30 percent of PLWH at Korle-Bu Teaching hospital in 2007 were TB positive. TB accounts for 40-50 percent of HIV deaths in Ghana, while HIV is an important cause of medical deaths (GHS, 2007).

1.2 Problem Statement

TB is communicable and airborne disease. It is the second leading cause of death from a single infectious agent, after the HIV. About 8.6 million people fell ill with TB in 2012, as well as 1.1 million cases among PLWH. In 2012,

1.3 million people died from TB, together with 320 000 among people who were HIV positive. Women who died from TB in 2012 approaches 410,000 including 160,000 among women who were HIV positive. Out of the overall TB deaths among HIV positive people, 50 percent were among women. TB is one of the top killers of women of reproductive age an estimated 530 000 children became ill with TB and 74 000 children who were HIV negative died of TB in 2012 (WHO Global TB Report, 2013). About half of all adults in Ghana carry a latent TB infection, which is suppressed by a healthy immune system. When the immune system is weakened by HIV, it can no longer control the TB infection and overt TB disease can develop. In the year 2000, approximately 11,300 new cases of TB were reported in Ghana. The TB Control Programme estimates the true figure to be more than 30,000. In 1989, about 14 percent of the TB cases could be attributed to AIDS. In 1997 study conducted in the Komfo Anokye Teaching Hospital Kumasi, Ghana found that HIV prevalence among TB patients was 23 percent HIV/AIDS epidemic (HIV/AIDS in Ghana, 2001).

Survival analysis is one of the appropriate techniques to demonstrate life time events and to identify the major prognostic factors. This method is appropriate because it assesses survival and the prognostic factors of each patient on treatment.

1.3 Research Questions

This research will achieve its stated objectives if the following questions are duly answered.

i. What are the survival rates of the patients?

ii. What predictor variables significantly influence the survival of patients?

iii. What is the appropriate survival technique for this study?

1.4 General Objective

The main objective is to evaluate the survival of HIV/AIDS, TB and co-infected patients and to identify the major prognostic factors that influence survival.

1.5 The specific objectives

i. To evaluate the mortality rate of HIV/AIDS, TB and co-infection patients

ii. To examine the influence of prognostic factors on the survival of patients

iii. To fit an appropriate survival model for the study

1.6 Significance of the Study

The prevalence of HIV/AIDS, TB and co-infection among patients is high in African region. According to WHO report (2012), Ghana is among the forty-one countries with high HIV/TB burden. Ghana records 24 percent of her tested TB patients HIV positive. This high burden on the individual and the society lowers the productivity in the country.

This study will provide detailed knowledge about the prognostic factors and the most significant variables that have major impact on HIV, TB and HIV/TB co-infection patients and to identify the number of patients who died on treatment. It will be beneficial for policy makers and health workers to

institute effective measures to address the negative tendencies that these deadly diseases bring to the society. The study will be useful for further researches in the area of study.

CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

The literature carefully chosen and reviewed in this chapter is relevant to the study. The literature is grouped into four thematic areas; Historical review of survival analysis, the review of: HIV/AIDS, TB and HIV/TB co-infection.

2.1 Historical Review of Survival Analysis

The initial interest of survival analysis was death but now the scope has widened to include: time to the relapse of a disease, length of stay in a hospital, duration of a strike, money paid by health insurance, viral load measurements and time to finishing a thesis. Survival analysis is also used in the following studies: leukemia patients and time in remission, time to develop a heart disease for normal individuals, elderly population and time until death, and heart transplants and time until death products (Singh and Mukhopadhyay, 2011). The origin of survival analysis goes back to mortality tables from centuries ago. However, the new era of survival analysis emerged after the World War II. This was boosted as a result of the interest in the reliability of military equipment. This, resulted to the spread of private industry as customers became more demanding for safer and reliable products. As the usage of survival analysis grew in the field of clinical trials and medical researches, the parametric approach gave way for the nonparametric and semi parametric approaches. Survival analysis is suitable because medical intervention follow-up studies could start without all experimental units

enrolled at start of observation time and could end before all experimental units experience the event. Survival analysis is extremely imperative because some subjects will; withdraw, move too far away to follow, or die from some unrelated event. As such, censoring will enable researchers to analyse incomplete data (Smith and Smith, 2001). Censored data arises when we have information about individual survival time, but we do not know survival time exactly. Censoring is right censored, if it is known that the event of interest occurs sometime after the recorded follow-up period, left censoring occurs when the individual has experienced the event of interest prior to the start of the study, or interval censoring, where the only information is that the event occurs within some interval. Truncation schemes are left truncation, where only individuals who survive a sufficient time are included in the sample and right truncation, where only individuals who have experienced the event by a specified time are included in the sample (Klein and Moeschberger, 2003).

Furthermore, Chiang's (1960) expanded Kaplan and Meier's (1958) works aimed to deal with incomplete observations of survival data. Aalen's (1975) established mathematical theory of survival analysis based on the Martingale theory and Counting stochastic process. Aalen's work was not initially appreciated fully until the late 1980s. Fleming and Harrington (1991) and Andersen *et al.,* (1995) improved Aalen's work in 1975.

The development of statistical procedures and models for survival analysis improved marginally between 1970 and 1990 where survival analysis had established itself as an effective statistical method in biomedical research. Survival analysis became a dominant part of the standard biostatistics curriculum in medical schools, and now universally accepted for data analysis

in major medical fields. The Cox model was introduced by Cox, in 1972, for analysis of survival data with and without censoring, for identifying differences in survival due to treatment and prognostic factors in clinical trials. The Cox model is preferred over some statistical techniques including the logistic model because it ignores the survival time and censoring information. Given a Cox model and the coefficients, the baseline hazard function and the survival curves can be estimated (Singh and Mukhopadhyay, 2011).

2.2 Some Reviews on HIV/AIDS

Renier's *et al.,* (2006) modelled the life table estimates of adult HIV/AIDS mortality in Addis Ababa Ethiopia. Between 54.7% and 62.4% of adult deaths in Addis Ababa (age 20 to 64) were attributed to AIDS. The study revealed that the absolute number of AIDS deaths in men is higher than women.

McMahon *et al.,* (2011) modelled a prospective cohort study in poverty, hunger, education, and residential status impact survival in HIV. Their study examined data from 878 participants enrolled in NFHL studied from 1995 to 2005. The study took place at greater Boston Province in USA to investigate the effects of nutritional status of PLWH. The mortality rate was 23%, and median duration of follow up among the dead was 54.8 months. The study showed that age of the patients influence survival. The model deduced that patients with lower economic status are susceptible to death. Chi-square tests, Student's t-test, and Wilcoxon rank sum and Cox PH model were used.

Oduro and Aboagye-Sarfo (2011) researched into the modeling and control of HIV/AIDS propagation in the Ashanti Region of Ghana. Their study was carried out between 1982 and 2001 to assess the impact of the pandemic as well as the effectiveness of the existing control measures. Vector

Autoregressive time series analysis was employed to determine the discrete time linear autonomous models. The population dynamics of reported HIV/AIDS cases for females and males were found to be of second order, unstable, growing linearly in the mean but with a sinusoidal oscillation of period 4.2 years. The study revealed that condom use as a method of control has no significant impact on the disease.

Adams and Luguterah (2013) also studied the longitudinal analysis of change in CD4 cell counts of HIV patients on ARV in the Builsa District Hospital. Their study revealed that a patient's initial CD4 cell count significantly influence their present CD4 cell count. The duration of treatment was also significant. It was revealed that CD4 cell count increased in about 40 cells/mm^3in every 6 months. This according to them suggests that there is strong positive association between CD4 count and duration of treatment. The study was estimated using the linear mixed effects model.

2.3 Some Reviews on TB

Anyama *et al.*, (2007) modelled the challenge of re-treatment pulmonary TB at two teaching and referral hospitals in Uganda. Their analysis discovered that the prevalence of re-treatment pulmonary TB at Mbarara based on medical records was 30% and 21.3% from exit interviews. The corresponding estimates at Mulago hospital were 12% and 43.9%. Compared to the 18 to 26 year age category, the Prevalence Odd Ratio for a seven year increase in age was 1.54, while female patients were 0.39 times less likely to report re-treatment disease than males. A logistic regression was employed.

Pardeshi and Geeta (2009) worked on the survival analysis and risk factors for death in TB patients on DOTS. About 716 patients were registered at the TB unit. They recorded a survival rate at the end of the intensive phase of 96%, 93%, and 99% in the categories of I, II, III of DOTS respectively. There was no difference in the survival curves of male and female patients. Age groupings of 40 to 60 years and above 60 years were identified as significant risk factors. They employed Kaplan-Meier plot and log rank test to assess the survival pattern and Cox PH model.

Ponnuraja and Venkatesan (2010) studied survival models for exploring TB clinical trial data-an empirical comparison of PH model and AFT model. The data consists of 1236 TB patients admitted in randomised controlled clinical trial. They argued that the PH model displays significant lack of fit while the AFT model describes the data well.

Jakperik and Ozoje (2012) researched into the survival analysis of average recovery time of TB patients in Northern Region, Ghana. Their study was conducted on a retrospective moving cohort of sixty-one TB patients admitted into DOTS programme. Approximately 57.38% of the patients were males and 42.62% were females. New cases of TB were 88.52% and 11.48% relapse. Sixty-six (65.57) percent of the patients had Pulmonary TB, while 34.43% were diagnosed with extra Pulmonary TB. The study recorded 69% recovery and 31% treatment failures.

Jakperik and Kpakpo (2013) assessed the effects of prognostic factors in recovery of TB patients in the Upper West Region using Kaplan-Meier estimator and the logistic regression model. Out of the 400 patients they

studied over the period, 256 were males and 144 were females. It was also revealed that 62% of the respondents had pulmonary TB while 38% of the respondents had extra pulmonary TB. They recorded treatment success rate of 73.75% which was quite lower than the WHO target of 85%.

2.4 Some Reviews on Co-infection

Murcia *et al.*, (1996) evaluated the frequency of mycobacterium infection in an HIV positive population and its influence on medium term survival, along with clinical and epidemiological factors associated with co-infection. Several clinical specimens were studied for mycobacteria in a sample of 92 HIV positive patients at the San Juan de Dios teaching hospital in Bogota, Colombia, in 1996. Factors associated with infection were measured using a prevalence ratio at 95% confident interval. Logistic regression was used in the multivariable models. Eight percent (8%) of the patients had TB and 6% of them were found to be infected with atypical mycobacterium. Patients suffering from TB and stages III or IV HIV infection had a 16% survival rate.

Ngowi (2009) modelled HIV/AIDS and TB co-infection in rural Northern Tanzania. He sampled 440 patients, 102 health subjects for reference values, 105 newly diagnosed TB patients with unknown HIV status, and 233 PLWHA. The mean age for the PLWHA was (37.0 ± 10.2). The overall HIV/AIDS and TB co-infection prevalence was 10.1%.

Mohammed *et al.*, (2011) conducted a case control study in Jimma and Mettu Karl hospitals where the two hospitals serve as referral and treatment centers for HIV and TB in south-west Ethiopia from January to March, 2009. Their study population consisted of 162 cases and 647 controls. PLWHA who

developed active pulmonary TB and controls were PLWHA without active TB. The result reveals after adjustment for potential confounders an initial weight less than 18.5kg a CD4 cell count less than 200 cells/mm^3 a WHO clinical stage IV and not taking antiretroviral treatment were independently associated with the development of active TB in PLWHA. Multiple logistic regression was used.

Tarekegn (2011) conducted retrospective study in which a total of 632 patients, (316 in ART and pre- ART cohort) were followed for a median of 32.9 months in Pre-HAART and 35.4 months in HAART. The study was aimed to identify factors that increase the risk of TB in PLWHA. The result of the study indicated that WHO stage III or IV being bedridden and having hemoglobin level less than 10mg/dl were factors associated with increased risk of TB in PLWHA. Cox PH model was used.

Shaweno and Worku (2012) also employed a retrospective cohort study to compare the survival between HIV positive and HIV negative TB patients of 370 each, during an eight month DOTS period. They considered TB patients HIV status and follow up time until death was taken as an outcome. Cox PH regression model was used to determine the hazard ratio of death for each predictor. It had revealed that co-infected patients were less likely to survive.

Musenge *et al.*, (2013) modelled the contribution of spatial analysis to understanding HIV/TB mortality in children using the structural equation modeling approach. They used multiple logit regression model with and without spatial household random effects. Structural equation models were also used in modeling the complex relationships between multiple exposures

and the outcome of HIV/TB child mortality. A protective effect was found in households with better socio-economic status and older children. Spatial models disclosed that the areas which experienced the greatest child HIV/TB mortality were those without any health facility.

Chu *et al.*, (2013) studied the impact of TB on mortality among HIV patients on ART between 2000 and 2009 in Uganda using multiplicative Cox model. The percentages of death during follow-up were 10.47% and 6.38% for patients with and without TB, respectively. They discovered that HIV patients who had TB at the start of ART had an approximate 37% increased hazard of overall mortality relative to non TB patients.

Mor *et al.*, (2013) worked on the TB incidence in HIV/AIDS patients in Israel from 1983 to 2010. They used a retrospective cohort study based on the National HIV and TB Registries. PLWHA who developed TB were compared to those who did not using the Cox model and Log rank test. The cumulative TB incidence among PLWHA in 2010 was 586 times higher than in HIV negative individuals. It was also revealed that, time for HIV patient to develop TB was shorter among males than in females.

2.5 Conclusion

The chapter reviewed the literature that is relevant to the study. Review of the literature showed various techniques that researchers have employed in modelling HIV/AIDS, TB and HIV/TB co-infection survival data. However, among the various techniques reviewed the Cox Proportional Hazard model and the Accelerated Failure Model were used in this study.

CHAPTER THREE

RESEARCH METHODOLOGY

3.0 Introduction

This chapter deals with the data and survival techniques that were used to achieve the stated objectives of this study. The chapter is sub-divided into eight sections including; source of data, study variables, descriptive statistics, comparison of survivorship functions, regression models, model selection criteria, model development and model diagnostics.

3.1 Source of Data

The data for this study was obtained from St. Mathias Hospital in the Pru District of the Brong Ahafo Region of Ghana. This hospital serves as a referral center for different health centers in the District. The hospital has a unit for both ART and TB. The hospital started giving free ART services in 2008. Data was extracted from the patient folders, which have been adopted by the Ministry of Health, Ghana. The study considered all the patients on treatment with ages above five years. The study took place between 2008 and 2013 and the patient followed till the outcomes of either the event (treatment failure) or censored.

Pru District is one of the 27 districts in the Brong-Ahafo Region and it has Yeji as its administrative capital. It was originally curved out of the Atebubu-Amantin District in 2004 by an Act of Parliament through a Legislative Instrument and is the highest Administrative and Political authority within its

sphere of influence and jurisdiction. It is bordered to the north by East Gonja District in the Northern Region and to the south by Atebubu-Amantin and Nkoranza Districts. To the east, it shares boundaries with the Sene District and to the west with Kintampo South and Kintampo North Districts (http://pru.ghanadistricts.gov.gh/index.php).

3.2 Study Variables

3.2.1 Dependent Variable

The response or the experimental variable of this study is the survival time (months) from the day the patient begins ART and TB treatment till the day he/she dies or censor.

3.2.2 Explanatory Variables

They predict changes on the dependent variables. In this study the following predictors are considered: Age in years, Weight (kg), Disclosure to Sexual Partner (no, yes), Marital status (Single, Married, Divorce, Widowed), Drug Regimen, Religion (Christian, Islam, and Traditionalist), Gender (Male, Female), Type of TB (Pulmonary, Extra-pulmonary) and WHO Clinical Stages (I, II, III, and IV).

3.3 Descriptive Statistics

3.3.1 Survivor Function $S(t)$

This measures the probability that a patient survives from time origin to sometime beyond t. It describes the proportion of the patients surviving to or beyond a given time. The actual survival time of a patient t, is regarded as the

value of a random variable T, which takes any non-negative value. The different values that T can take have probability distribution with its underlying probability density function $f(t)$. The distribution function of T is given as:

$$F(t) = P(T < t) = \int_0^t f(u)\,du \qquad (3.1)$$

The survivor function $S(t)$ is the probability that survival time is greater or equal t. That is:

$$S(t) = P(T \geq t) = 1 - F(t) \qquad (3.2)$$

As t ranges from 0 to ∞ the survival function has the following properties, namely:

* it is non-increasing

* when $t = 0$, $S(t) = 1$. In other words, the probability of surviving past time 0 is sure.

* $t \rightarrow \infty$: $S(t) \rightarrow 0$. That is time goes to infinity, the survival curve approaches 0.

3.3.2 Hazard Function $h(t)$

This is used to express the instantaneous failure rate. The probability that a patient dies at time t, conditioned that the patient survived. Thus, the probability that the random variable associated with a patient's survival time, T lies between t and $t + \delta t$, conditional on T being greater than or equal to t, $P\{t \leq T < t + \varphi t \,/\, T \geq t\}$. This conditional probability is expressed as a probability per unit time by dividing the time interval by φt, to give a rate. The

hazard function $h(t)$ is the limiting value the quantity, as φt tends to zero (Collet, 2003).

$$h(t)=\lim_{\varphi t\to 0}\left\{\frac{P(t\le T<t+\varphi t/T\ge t)}{\varphi t}\right\} \tag{3.3}$$

The hazard function in (3.3) can be expressed in terms of the probability density function and the survivor function as,

$$h(t)=\frac{f(t)}{S(t)}=-\frac{d}{dt}\{\ln S(t)\} \tag{3.4}$$

The cumulative hazard function $H(t)$ is defined from (3.4) as,

$$H(t)=\int_0^t h(u)\,du=-\ln S(t) \tag{3.5}$$

3.3.3 Survivorship Function Estimation

In this study, we estimated the survivorship function using the life table method also known as the actuarial method. The study employed the Gehan's method (1969) where the mid-points of the interval was used to estimate the hazard and the density functions and the upper limit used to estimate the survival function.

$$\hat{S}_{(t_i)}=\prod_{j=1}^{i-1}(1-\hat{q}_j) \tag{3.6}$$

$$\hat{f}_{(t_{mi})}=\frac{\hat{S}_{(t_i)}-\hat{S}_{(t_{i-1})}}{b_i}=\frac{\hat{S}_{(t_i)}\hat{q}_{(i)}}{b_i} \tag{3.7}$$

$$\hat{h}_{(t_{mi})}=\frac{d_i}{b_i\left(n_i-\frac{1}{2}d_i\right)}=\frac{2\hat{q}_i}{b_i-\hat{p}_i} \tag{3.8}$$

in (3.6)-(3.8), t_{mi} is the mid-point of the i^{th} interval, d_i is the number of patients dying in the i^{th} interval, n_i is the number of patients exposed in the i^{th} interval, $q_i = (d_i / n_i)$ is the conditional probability of dying in the i^{th} interval, $\hat{p}_i = 1 - q_i$ is the conditional probability of dying in the i^{th} interval, b_i is the width of the i^{th} interval.

3.4 Comparing Survivorship Functions

Having obtained the description of the general survival experience, the survival and hazard functions, we proceeded to compare the survivorship experience of the subgroups of qualitative variables in the data. These groups are defined by the values of covariates which are related to survival times. For easy interpretation, it is desirable that we graph each group concerned. The Kaplan-Meier estimator is appropriate for such graphs. A graph that shows the pattern of one survivorship function lying above another means a group well-defined by the upper curve have a longer survival time than the group defined by the lower curve. The plot will be significant if an appropriate statistical test is used (Hosmer and Lemeshow, 1999).

3.4.1 Log Rank Test

The log rank test was used to compare the death rate between two distinct groups, conditional on the number at risk in the groups. This is a well-known and widely used test statistic. For k factor of groups, the log rank test hypothesis that;

H_0: All survival curves are the same,

H_1: *Not* all survival curves are the same.

Log rank test approximates a chi-square test which compares the observed number of failures to the expected number of failure under the hypothesis.

$$\chi^2 = \sum_{i=1}^{k} \frac{(O_i - E_i)^2}{E_i} \tag{3.9}$$

In (3.9), O_i and E_i are the observed and expected number of death respectively. k-1 is the degree of freedom with k being the number of groups. A large chi-squared value will lead to the rejection of the null hypothesis in favour of the alternative.

3.5 Regression Models for Survival Data

The data for each patient was collected to determine the relationship between the survival time and the covariates. This is to ensure the combination of the covariates that affects the hazard function. This will help obtain the estimates of the hazard function on the patients set of covariates.

3.5.1 The Cox Proportional Hazards Regression Model

The Cox model is used to determine the effects the predictor variables have on the survival time. This model is usually written in terms of the hazard model formula. It defines the hazard at time t for a patient and a number of explanatory variables represented by X. The variable X represents a collection of predictor variables that is modeled to predict the patient's hazard. This is defined by;

$$h(t, X) = h_0(t)\exp\left(\sum_{i=1}^{p} \beta_i X_i\right) \tag{3.10}$$

where, h_0 (t) is the baseline hazard function, X_i is the explanatory or the predictor variable and β_i is the regression coefficients.

Cox (1972) proposed a semi-parametric model making it more robust to produce results that will closely approximate to a correct parametric model.

3.5.2 Assumptions of the Cox proportional Hazard Model

i. The baseline hazard function h_0 (t) depends on time t, but not covariates X_i

ii. The hazard ratio $\exp\left(\sum_{i=1}^{p}\beta_i X_i\right)$ depends on the covariates X_i not on time.

iii. The covariates X_i are time independent.

Assumption (ii) and (iii) can be expressed mathematically in terms of the hazard ratio, the hazard for one patient divided by the hazard for another patient. The two patients compared can be differentiated by their explanatory variables, that is, the X's.

$$\hat{HR} = \frac{\hat{h}(t, X^*)}{\hat{h}(t, X)} = \frac{h_0(t)\exp\left(\sum_{i=1}^{p}\hat{\beta}_i X_i^*\right)}{h_0(t)\exp\left(\sum_{i=1}^{p}\hat{\beta}_i X_i\right)} \qquad (3.11)$$

$$\hat{HR} = \exp\left(\sum_{i=1}^{p}\hat{\beta}_i\left(X_i^* - X_i\right)\right) \qquad (3.12)$$

This apparently does not depend on time. This implies that the ratio of the hazard functions for two patients with different covariate values does not vary with time.

3.5.3 The Proportional Hazard Model Estimation

The unknown coefficients of the Cox PH model are estimated using the maximum likelihood. For the likelihood function to be applied to the survivorship function the Cox proportional data set are represented in three groups (t_i, φ_i, x_i), $i = 1, 2,...n$.

t_i is the survival time for i^{th} person, φ_i is an indicator of censoring for the i^{th} patient given by 1 for censored and 0 for death, x_i a vector of covariates for patient i^{th} $(x_{i1}, x_{i2},..., x_{ip})$

The full maximum likelihood is deduced as

$$L(B)=\prod_{i=1}^{n} h(t_i,x_i,\beta)^{\varphi i} S(t_i,x_i,\beta) \qquad (3.13)$$

Where $h(t_i,x_i,\beta)=h_0(t_i)\exp(\beta_i X_i)$ is individual hazard function for i, $S(t_i,x_i,\beta)=S_0(t_i)\exp(\beta_i X_i)$ is individual survivorship function for i.

The full model becomes

$$L(B)=\prod_{i=1}^{n}\left(h_0(t_i)\exp(\beta_i X_i)^{\varphi i} S_0(t_i)\exp(\beta_i X_i)\right) \qquad (3.14)$$

We maximize (3.13) with respect to the unknown parameters of interest to obtain the full maximum likelihood.

3.5.4 Partial Likelihood Function

Cox (1972) proposed the partial likelihood function that depends only on the parameter of interest. Thus, suppose that k of the survival time of the n patients are uncensored and distinct, and n-k are right censored. Consider

$t_{(1)} < t_2 < \cdots < t_{(k)}$, $R(t_i)$ as the risk set at time. $R(t_i)$ consist of all the persons whose survival time are at least t_i . For the particular failure at time t_i conditionally on the risk set $R(t_i)$ the probability that the failure is on the individual as observed is

$$\frac{h(t,x)}{\sum_{j\in R(t_i)} h(t,x)} = \frac{h_0(t)\exp(\beta_i x_i)}{\sum_{j\in R(t_i)} h_0(t)\exp(\beta_i x_j)} = \frac{\exp(\beta_i x_i)}{\sum_{j\in R(t_i)} \exp(\beta_i x_j)} \qquad (3.15)$$

This likelihood of the Cox PH model does not consider probabilities for all the patients on treatment.

$$L_p(\beta) = \prod_{i=1}^{m} \frac{\exp(\beta_i x_i)}{\sum \exp(\beta_i x_i)} \qquad (3.16)$$

Where the product is over m distinct ordered failure times and x_i denotes the value of the covariate for the patients with ordered survival time t_i. The log partial likelihood function is

$$L_p(\beta) = \sum_{i=1}^{m} \left[\beta_i x_i - \ln\left(\sum_{j\in R(t_i)} \exp(\beta_i x_j) \right) \right] \qquad (3.17)$$

The maximum partial likelihood (MPLE) can be obtained by differentiating (3.16) with respect to β_i setting the derivative to zero and solving the unknown parameters. This method is limited to only data sets that have no ties. Thus, there are no two or more variables with same survival time (Lee and Wang, 2003).

3.5.4.1 Efron's Approximation

The problem of tied data set that makes the partial likelihood function estimation impossible is possible when the Efron's method is used. This method is considered to give a better result.

Let D_j be the set of subjects who are observed dead at time t_i.

$$L_B(\beta)=\prod_{j=1}^{m}\frac{\prod_{i\in D_j}\exp\left(\hat{X}_i\beta\right)}{\prod_{k=1}^{D_j}\left[\sum_{l\in R_j}\exp\left(\hat{X}_l\beta\right)-\frac{k-1}{D_j}\sum_{l\in D_j}\exp\left(\hat{X}_l\beta\right)\right]} \tag{3.18}$$

The partial log of (3.18) is given as;

$$L_B(\beta)=\sum_i\left(\sum_{i\in D_j}\beta\hat{X}_i-\sum_{l=0}^{k-1}\left\{\log\left(\sum_{i:Y_i\geq t_j}\exp\left[\beta\hat{X}_i-\frac{1}{k}\sum_{i\in D_j}\exp\left(\beta\hat{X}_i\right)\right]\right)\right\}\right) \tag{3.19}$$

This is derived by differentiating (3.18) with respect to β component and equating it to zero.

3.5.5 Accelerated Failure Time Model (AFT)

AFT models follow a known distribution. They are comprised of the Exponential model, Weibull, Lognormal, Log-logistics and Gamma model. The underlying assumption for this model is that the effect of the covariate is multiplicative with respect to the survival time. The AFT model is the natural logarithm of the survival time (*logt*). It is expressed as a linear function of the covariates.

$$\log t=\beta X_j+z_j \tag{3.20}$$

Where, X_j is the vector of covariates, β is the vector of regression coefficient, z_j is the error term.

3.5.5.1 Exponential Distribution

This distribution is described as one parameter model because the hazard is constant over time. The risk of an event happening is flat over time. The hazard function is given as; $h(t) = \lambda$, with the cumulative hazard given as:

$$H(t) = \lambda t \tag{3.21}$$

For survival function we know that, $H(t) = -\ln[S(t)]$.

$$S(t) = e^{-H(t)} = e^{-\lambda t} \tag{3.22}$$

For density function we multiply the hazard function by the survival function

$$f(t) = h(t)S(t) = \lambda e^{-\lambda t} \tag{3.23}$$

3.5.5.2 Weibull Distribution

This model is flexible as compared to the exponential model because its hazard rates are not constant. It is a two-parameter model i.e. λ and p where, λ is the location parameter, p is the shape parameter. Thus, it informs whether the hazard is increasing, decreasing, or constant over time.

The hazard for the Weibull model is represented as;

$$h(t, X) = \lambda p(\lambda t)^{p-1} \tag{3.24}$$

$$\lambda_i = e^{X_i \beta} \tag{3.25}$$

The shape parameter can be interpreted as:

If $p < 1$, then the hazard is monotonically decreasing with time.

If $p > 1$, then the hazard is monotonically increasing with time.

If $p = 1$, then the hazard is flat and we have the exponential model.

The survivor function is given as;

$$S(t) = e^{(-\lambda t)p} \tag{3.26}$$

The density function represented as;

$$f(t) = \lambda p(\lambda t)^{p-1} e^{(-\lambda t)p} \tag{3.27}$$

3.5.5.3 Log-Logistic Model

The hazard function for Log-Logistic is defined as;

$$h(t, X) = \frac{\frac{\lambda t}{\gamma}\left[\frac{1}{\gamma} - 1\right]}{\gamma\left(1 + (\lambda t)^{1/\gamma}\right)} \tag{3.28}$$

$$\lambda_i = e^{-(X_i \beta)} \tag{3.29}$$

The log-logistic model have two parameters as the Weibull model, -λ been the location parameter and γ as the shape parameter. The hazard for Log-logistic is not monotonic. The shape parameter is defined as:

If $\hat{\gamma} < 1$then the conditional hazard first rises, then falls.

If $\hat{\gamma} \geq 1$ then the hazard is declining

The survivor function for the log-logistic is

$$S(t) = \frac{1}{1 + (\lambda t)^{1/\gamma}} \tag{3.30}$$

The density function defined as;

$$f(t) = \frac{\frac{\lambda t}{\gamma}\left(\frac{1}{\gamma} - 1\right)}{\left\{\gamma\left(1 + (\lambda t)^{1/\gamma}\right)\right\}^2} \tag{3.31}$$

3.5.5.4 Log-Normal Model

The survivor function for log-normal model is:

$$S(t)=1-\Phi\left\{\frac{\ln(t)-\mu}{\sigma}\right\} \tag{3.32}$$

Where Φ is the standard Normal Cumulative distribution function and $\sigma = \beta X$.

The density function denoted as:

$$f(t)=\frac{1}{\sigma t\sqrt{2\pi}}\exp\left\{-\frac{1}{2\sigma^2}(\ln(t)-u)^2\right\} \tag{3.33}$$

The hazard function for the Log-normal is given as:

$$h(t)=\frac{\frac{1}{\sigma t\sqrt{2\pi}}\exp\left\{-\frac{1}{2\sigma^2}(\ln(t)-u)^2\right\}}{1-\Phi\left\{\frac{\ln(t)-\mu}{\sigma}\right\}} \tag{3.34}$$

The hazard rate for this model is similar to the log-logistic that is, where $\hat{\gamma}<1$ the hazard first rises and then falls.

3.5.5.5 The Gamma Model

The gamma distribution is a two parameter model with λ and k. The density function for the model is defined as:

$$f(t)=\frac{\lambda(\lambda t)^{k-1}e^{-\lambda t}}{\Gamma(k)} \tag{3.35}$$

Survival function denoted as;

$$S(t)=1-I_k(\lambda t) \tag{3.36}$$

Where $I_k(x)$is the incomplete gamma function, and is represented as;

$$I_k(x) = \int_0^x \frac{\lambda^{k-1} e^{-x}}{\Gamma(k)} dx \qquad (3.37)$$

k is the shape parameter and $1/\lambda$ the scale parameter.

The hazard function is obtained by taking the ratio of the density and the survivor function. i.e. $\lambda(t) = \frac{f(t)}{S(t)}$ .The hazard for Gamma increases monotonically if, $k > 1$ from a value of 0 at the origin to a maximum of λ, is constant if $k = 1$ decreases monotonically if, $k < 1$, from 1 at the origin to an asymptotic value of λ.

3.6 Model Selection Criteria

Akaike information criterion (AIC) and Bayesian information criterion (BIC) is used to compare the goodness-of-fit between the Cox model and the AFT model. These models are based on the log-likelihood $l(b)$, the number of parameters in the distribution, p, and the total number of observations, n. Where $\hat{b}$ denotes the MLE of all the parameters in the distribution. Models with smaller AIC or BIC values show a better fit. However, the BIC is preferred if the distribution have a sufficiently large sample size because it penalises models more severely than the AIC does.

$$BIC = l(\hat{b}) - \frac{p}{2} \log n \qquad (3.38)$$

$$AIC = l(\hat{b}) - 2p \qquad (3.39)$$

3.7 Model Development

Since it is likely that the available covariates to be included in the model based on the clinical importance and statistical significance can be more than

expected. It is necessary we decide on a reasonable method to select our covariates (Hosmer and Lemeshow, 1999). In this study, covariates that were insignificant were removed one at a time through the backward elimination system. The stepwise selection criterion was also used to select the covariates for the AFT model.

3.7.1 The Likelihood Ratio Test (LR)

The likelihood ratio (LR) is statistic used to test the significance of the interaction terms. This test statistic is computed by taking the difference between the log likelihood statistic of the reduced model which does not contain the interaction term and the log likelihood statistic of the full model containing the interaction. The decision rule to reject the null hypothesis is that: H_0: there is no interaction. Thus, if: $LR = (2LL_R - (-2LL_F)) > \chi^2_{1,0.10} = 2.71$. This test statistic approximates a chi-square distribution (Kleinbaum and Klein, 2005).

3.8 Assessing the Adequacy of the Models

Statistical inferences that lead to the identification of important risk or prognostic factors depend largely on the adequacy of the model selected. It is therefore very imperative to diagnose the Cox model to see whether it satisfies the proportionality assumption. Also, the AFT model is checked to ensure that it is well fitted. Thus, we employed the Cox-Snell residual, the martingale residual, Deviance residual and Schoenfeld residual.

3.8.1. Cox-Snell Residual

This is instituted to estimate the overall fitness of the model. For the i^{th} patient the Cox-Snell residual is given as;

$$rz_i = \exp\left(\hat{\beta}x_i\right)\hat{H}_0(t_i) \tag{3.40}$$

$\hat{H}_0(t_i)$, is plot of the estimate of the baseline cumulative hazard function at time t_i, the observed survival time for each patient. If the fitted model is correct, the value rz_i will have a unit exponential distribution (Collet, 2003).

3.8.2 Martingale Residual

The martingale residuals have a mean of zero when the observations are uncensored. It takes values between -∞ and 1. The residuals sum to zero. In large samples the martingale residuals are uncorrelated and the expected values are zero. The properties of martingale residual are similar to the linear regression.

$$r_{Mi} = \varphi_i - rz_i \tag{3.41}$$

The quantity r_{Mi} is the difference between the observed numbers of deaths for the i^{th} patient in the interval (0, t). The interval (0, t) is the expected number of deaths.

r_{Mi} is an estimate of $H_i(t_i)$ the cumulative hazard or the cumulative probability of death for the i^{th} patient (Collet, 2003).

3.8.3 Deviance Residual

The martingale residuals are not symmetrically distributed about zero, even when the fitted model is correct making the result difficult to interpret. As a result the Therneau *et al.*, (1990) introduced the deviance residual which is more symmetrically distributed about the zero.

$$r_{Di} = sign(r_{Di})\{-2[r_{Di} + \varphi_i \log(\varphi_i - \varphi\, r_{Mi})]\}^{1/2} \qquad (3.42)$$

Where; $sign(r_{Di})$ is a function that take values of +1 if the argument is positive and -1 if otherwise. This ensures that the variance residual have the same sign as the martingale residual. The original motivation for these residuals is that they are components of the deviance. The deviance is a statistic used to summarize the extent to which the fit of the model of current interest deviates from that of a model which is a perfect fit to the data. The statistic is given by;

$$D = -2\left(\log \hat{L}_c - \log \hat{L}_f\right) \qquad (3.43)$$

Where, $\hat{L}_c$ is the maximized partial likelihood under the current model and $\hat{L}_f$ is the maximized partial likelihood of the full model. The model with a smaller deviance value is considered the best (Collet, 2003).

3.8.4 Schoenfeld Residual

This method was proposed by Schoenfeld (1982) which differ from the previously mentioned. It is computed for the covariate of each patient. It is based on the first derivative of the log-likelihood function. Asymptotically, the Schoenfeld residuals have a mean of zero. These residuals will not be correlated with the covariates if the model is well fitted. A Schoenfeld residual

for the j^{th} covariate of the i^{th} patient with the observed survival time t_i is deduced as;

$$R_{ji} = \varphi_i \left\{ X_{ji} - \frac{\sum_{l \in R(t_i)} X_{jl} \exp\left(\hat{\beta} x_l\right)}{\sum_{l \in R(t_i)} \exp\left(\hat{\beta} x_l\right)} \right\} \qquad (3.44)$$

Where, $\hat{\beta}$ is the maximum partial likelihood estimator of the Schoenfeld residuals are defined only at uncensored survival times, for censored observations they are set as missing. The sum of the Schoenfeld residuals for a covariate is zero.

3.9 Conclusion

The chapter dealt with the statistical techniques employed in this study. It presented the techniques in a clear, detailed and concise manner.

CHAPTER FOUR

DATA ANALYSIS AND DISCUSSION OF RESULTS

4.0 Introduction

This chapter analyses, interprets and discusses the results from the study. The chapter is grouped into Descriptive analyses, further analysis and discussion of results.

4.1 Descriptive Analyses

This segment explains the descriptive statistics of the data on the survival of HIV/AIDS, TB and the HIV/TB co-infected patients on treatment.

Table 4.1 revealed that a total of 590 patients at St. Mathias Hospital were on treatment. The patients were grouped into three, the HIV/AIDS, TB and HIV/TB co-infection. Of the 295 HIV/AIDS patients, 58 (19.7%) died; 219 were TB patients, 23 (10.5%) died and 76 were HIV/TB co-infection, 25 (32.9%) died during the period 2008 to 2013. It was also revealed that the co-infected patients experienced the worse survival followed by the HIV/AIDS patients. The TB patients were shown to have the best survival among all the three categories.

Table 4.1: Descriptive statistics for the three categories

Category	Total	Death	Censored	Percent Death
HIV/AIDS	295	58	237	19.7%
TB	219	23	196	10.5%
CO-INFECTED	76	25	51	32.9%
GRAND TOTAL	**590**	**106**	**484**	**18.0%**

Table 4.2 shows the summary statistics for continuous covariates of the patients. The maximum age of the HIV/AIDS patient was 75 years. The mean age of HIV/AIDS patient was 35 years. The median weight of the HIV/AIDS patients was 50 kg. The minimum and maximum weights were 8 kg and 90 kg respectively. The minimum survival time for HIV/AIDS patients was 1 month. The median and maximum survival times were 8 and 69 months respectively. The HIV/TB co-infected patients had a mean age of 37 years and a maximum age of 70 years. The minimum weight of the patients was 9 kg. The maximum weight was 93 kg. The mean and maximum survival time was 11 and 68 months respectively. Also, the minimum age of the TB patients was seven (7) years and the maximum age recorded was 102 years. The minimum weight of the TB patients was 15 kg which is little above the weight of HIV/AIDS and the co-infected patients. The maximum weight was 76 kg quite lower than the HIV/AIDS and the co-infection. The mean survival time was approximately five months. The maximum survival time for TB patients was 14 months.

Table 4.2: Descriptive statistics for continuous covariates for the patients

	Mean	Median	Std. Dev.	Min.	Max.
HIV/AIDS					
AGE	35.47	34.00	11.51	6.00	75.00
WEIGHT	50.98	50.00	11.22	8.00	90.00
TIME	17.07	8.00	19.30	1.00	69.00
CO-INFECTION					
AGE	37.09	35.500	14.96	6.00	70. 00
WEIGHT	42.96	43.00	13.77	9.00	93.00
TIME	11.24	6.00	15.50	1.00	68.00
TB					
AGE	45.031	42.00	20.04	7.00	102.00
WEIGHT	45.12	45.00	11.14	15.00	76.00
TIME	4.92	5.00	2.36	1.00	14.00

Table 4.3 Hazard, density and survival estimates of HIV/AIDS patients on treatment

Mid-point	Hazard	SE	Density	SE	Upper limit	Survival	SE
1	0.0249	0.0069	0.0243	0.0066	2	1.0000	0.0000
3	0.0098	0.0049	0.0092	0.0046	4	0.9514	0.0131
5	0.0117	0.0058	0.0107	0.0053	6	0.9329	0.0158
7	0.0096	0.0055	0.0086	0.0049	8	0.9114	0.0187
9	0.0104	0.0060	0.0092	0.0053	10	0.8942	0.0209
11	0.0074	0.0052	0.0064	0.0045	12	0.8757	0.0230
13	0.0000	0.0000	0.0000	0.0000	14	0.8629	0.0244
15	0.0000	00000	0.0000	0.0000	16	0.8629	0.0244
17	0.0046	0.0046	0.0039	0.0039	18	0.8629	0.0244
19	0.0000	0.0000	0.0000	0.0000	20	0.8550	0.0254
21	0.0000	0.0000	0.0000	0.0000	22	0.8550	0.0254
23	0.0055	0.0055	0.0047	0.0047	24	0.8550	0.0254
25	0.0181	0.0104	0.0150	0.0085	26	0.8456	0.0268
27	0.0065	0.0065	0.0053	0.0052	28	0.8156	0.0310
29	0.0000	0.0000	0.0000	0.0000	30	0.8051	0.0323
31	0.0216	0.0125	0.0170	0.0096	32	0.8051	0.0323
33	0.0157	0.0111	0.0120	0.0083	34	0.7710	0.0364
35	0.0168	0.0118	0.0123	0.0086	36	0.7471	0.0390
37	0.0275	0.0159	0.0194	0.0109	38	0.7224	0.0415
39	0.0204	0.0144	0.0137	0.0095	40	0.6837	0.0448
41	0.0110	0.0110	0.0071	0.0070	42	0.6564	0.0470
43	0.0240	0.0168	0.0149	0.0104	44	0.6421	0.0481
45	0.0132	0.0132	0.0080	0.0079	46	0.6122	0.0503
47	0.0147	0.0147	0.0086	0.0086	48	0.5963	0.0515
49	0.0000	0.0000	0.0000	0.0000	50	0.5791	0.0528
51	0.0164	0.0164	0.0093	0.0092	52	0.5791	0.0528
53	0.0179	0.0179	0.0098	0.0097	54	0.5604	0.0543
55	0.0204	0.0204	0.0108	0.0107	56	0.5407	0.0558
57	0.0000	0.0000	0.0000	0.0000	58	0.5191	0.0576
59	0.0690	0.049	0.0335	0.0224	60	0.5191	0.0576
61	0.0476	0.0476	0.0206	0.0198	62	0.4521	0.0669
63	0.0000	0.0000	0.0000	0.0000	64	0.4110	0.0723
65	0.0000	0.0000	0.0000	0.0000	66	0.4110	0.0723
67	0.0000	0.0000	0.0000	0.0000	68	0.4110	0.0723
69	0.0000	0.0000	0.0000	0.0000	70	0.4110	0.0723

Table 4.3 shows the hazard, density and survival estimates of HIV/AIDS patients. The life table estimates indicate that the 59th month after the patient was diagnosed of HIV/AIDS is the riskiest month as approximately 7% of the patients failed [$\widehat{HR} = 0.068966$]. This is followed by the 61st month where approximately 5% failed. This is represented graphically in Figure 4.1.

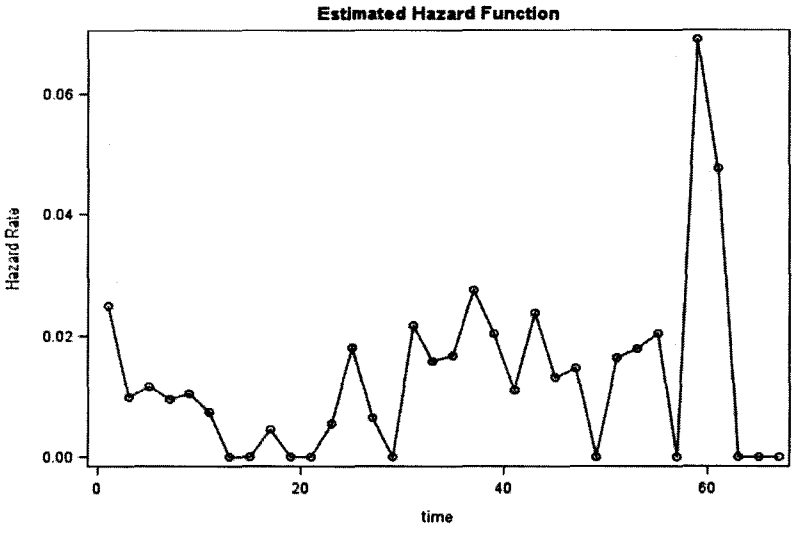

Figure 4.1: Hazard curve for HIV/AIDS

Table 4.4 shows the hazard, density and the survival estimates of the TB patients. The life table estimates revealed that about 3% of the risk occurred in the 1st month [$\widehat{HR} = 0.029557$]. The 13th month was the riskiest month, as approximately half of the TB patients experienced the event [$\widehat{HR} = 0.50000$], this is graphically represented in Figure 4.2.

Table 4.4: Hazard, density and survival estimates of TB patients on treatment

Mid-point	Hazard	SE	Density	SE	Upper limit	Survival	SE
1	0.0296	0.0085	0.0287	0.0081	2	1.0000	0.0000
3	0.0143	0.0064	0.0133	0.0059	4	0.9426	0.0161
5	0.0038	0.0038	0.00344	0.0034	6	0.9160	0.0196
7	0.0165	0.0117	0.0148	0.0103	8	0.9091	0.0206
9	0.0000	0.0000	0.0000	0.0000	10	0.8795	0.0286
11	0.1429	0.1414	0.1099	0.0953	12	0.8795	0.0286
13	0.5000	0.3062	0.2199	0.1102	14	0.6596	0.1916

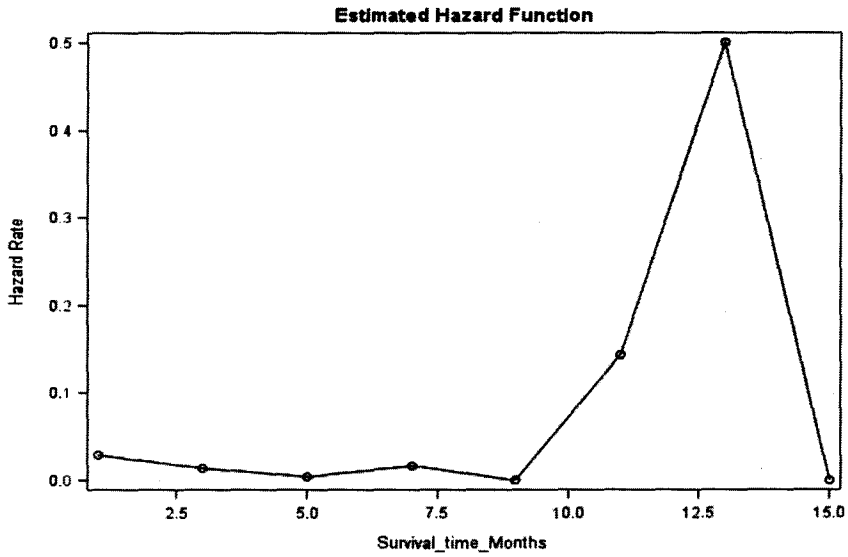

Figure 4.2 Hazard curve for TB Patients

About 7% of the co-infected patients $[\widehat{HR} = 0.066667]$ failed in the first month of the treatment as shown in the Table 4.5 and Figure 4.3. The 63^{rd} month was the riskiest month for the patients$[\widehat{HR} = 0.333333]$. Thus, approximately 33% of the patients failed.

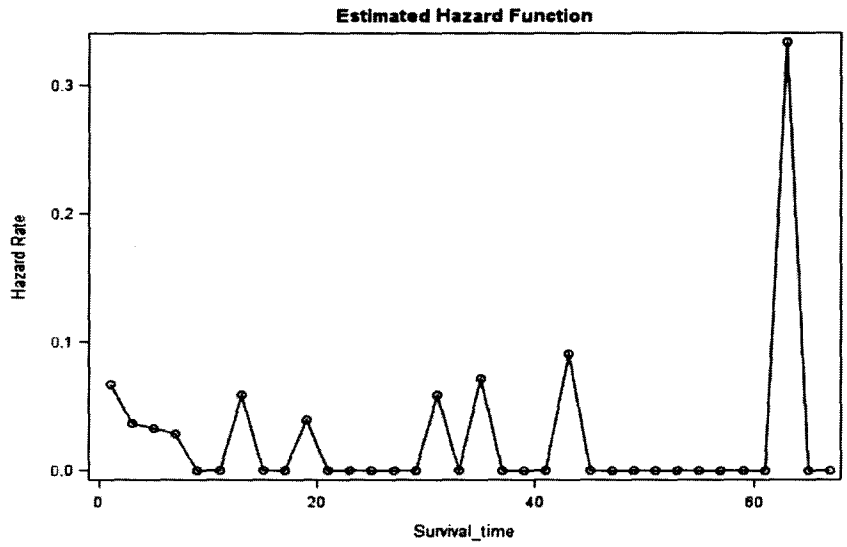

Figure 4.3: Hazard Curve for co-infection

Table 4.5: Hazard, density and survival estimates for co-infected patients on treatment

Mid-point	Hazard	SE	Density	SE	Upper-limit	Survival	SE
1	0.0667	0.0222	0.0625	0.0195	2	1.0000	0.0000
3	0.0367	0.0183	0.0310	0.0150	4	0.8750	0.0390
5	0.0333	0.0192	0.0262	0.0147	6	0.8131	0.0469
7	0.0286	0.0201	0.0211	0.0146	8	0.7606	0.0528
9	0.0000	0.0000	0.0000	0.0000	10	0.7183	0.0577
11	0.0000	0.0000	0.0000	0.0000	12	0.7183	0.0577
13	0.0588	0.0415	0.0399	0.0268	14	0.7183	0.0577
15	0.0000	0.0000	0.0000	0.0000	16	0.6385	0.0739
17	0.0000	0.0000	0.0000	0.0000	18	0.6385	0.0739
19	0.0400	0.0399	0.0246	0.0238	20	0.6385	0.0739
21	0.0000	0.0000	0.0000	0.0000	22	0.5894	0.0829
23	0.0000	0.0000	0.0000	0.0000	24	0.5894	0.0829
25	0.0000	0.0000	0.0000	0.0000	26	0.5894	0.0829
27	0.0000	0.0000	0.0000	0.0000	28	0.5894	0.0829
29	0.0000	0.0000	0.0000	0.0000	30	0.5894	0.0829
31	0.0588	0.0587	0.0327	0.0312	32	0.5894	0.0829
33	0.0000	0.0000	0.0000	0.0000	34	0.5239	0.0962
35	0.0714	0.0712	0.0349	0.0331	36	0.5239	0.0962
37	0.0000	0.0000	0.0000	0.0000	38	0.4541	0.1057
39	0.0000	0.0000	0.0000	0.0000	40	0.4541	0.1057
41	0.0000	0.0000	0.0000	0.0000	42	0.4541	0.1057
43	0.0909	0.0905	0.0378	0.0356	44	0.4541	0.1057
45	0.0000	0.0000	0.0000	0.0000	46	0.3784	0.1120
47	0.0000	0.0000	0.0000	0.0000	48	0.3784	0.1120
49	0.0000	0.0000	0.0000	0.0000	50	0.3784	0.1120
51	0.0000	0.0000	0.0000	0.0000	52	0.3784	0.1120
53	0.0000	0.0000	0.0000	0.0000	54	0.3784	0.1120
55	0.0000	0.0000	0.0000	0.0000	56	0.3784	0.1120
57	0.0000	0.0000	0.0000	0.0000	58	0.3784	0.1120
59	0.0000	0.0000	0.0000	0.0000	60	0.3784	0.1120
61	0.0000	0.0000	0.0000	0.0000	62	0.3784	0.1120
63	0.3333	0.3143	0.0946	0.0725	64	0.3784	0.1120
65	0.0000	0.0000	0.0000	0.0000	66	0.1892	0.1450
67	0.0000	0.0000	0.0000	0.0000	68	0.1892	0.1450
69	0.0000	0.0000	0.0000	0.0000	70	0.1892	0.1450

In determining whether there is significant difference among different groups of the covariates, the log rank test of equality was employed as shown in Table 4.6. With the null hypothesis that: there is no significant difference between the survival curves of the patients.

Table 4.6: Test of equality using the log rank

Variable	df	χ^2			*p*-value		
		HIV	TB	Co-infected	HIV	TB	Co-infected
Gender	1	0.50	0.29	0.71	0.4811	0.5899	0.3991
Mstatus	3	1.92	0.93	4.36	0.5890	0.8185	0.2254
Religion	2	2.09	0.28	6.37	0.3520	0.6887	0.0414
WHO	3	39.17	*	1.62	0.0000	*	0.6555
Disclosure	1	0.66	*	0.39	0.8819	*	0.5313
Regimen	2	7.43	*	0.31	0.1901	*	0.8559
		*	1.06	*	*	0.0040	*
TB Type	1	*	0.05	0.57	*	0.8287	0.4508

df: degrees of freedom
*: Means empty cell

The log-rank test of equality shows a significant difference of survival among the groups; WHO Clinical Stage of HIV/AIDS patients, the Drug regimen of TB patients and Religion of the co-infected patients. However, covariates including Sex, Marital status, Religion of HIV and TB patients, Disclosure to sexual partner, Drug regimen of HIV/AIDS patients and TB type were not significantly different.

4.2 Further Analysis

4.2.1 The Cox Proportional Hazard Model for HIV/AIDS Patients

The proportional hazard model for HIV/AIDS patients in Table 4.7 showed that, the predictor variables Gender, WHO clinical stage and Weight are statistically significant at 10% significance level. The hazard estimate for Gender is given as [$\widehat{HR}$=0.4800, *p*-value =0.0370]. Thus, the result indicates that the rate of dying among female patients is approximately 50% lower than the male patients holding the other predictors constant. WHO clinical stages I, II and III of the patients showed an estimated hazard ratio and *p*-value as [$\widehat{HR}$ =0.1640, *p*-value =0.0008], [$\widehat{HR}$ =0.3080, *p*-value =0.0751] and [$\widehat{HR}$=0.3670, *p*-value =0.0179] respectively. This means that, the risk of death

for patients at WHO clinical stages I, II and III is about 16%, 30% and 36% respectively lower than the patients at WHO clinical stage IV assuming that all other predictors are constant. The estimated hazard ratio and p-value of weight is $[\widehat{HR} = 0.9420,\ p < 0.0016]$ denoting that a unit change in the weight will reduce the risk of the patient by 0.9420 holding all other explanatory variables constant.

Table 4.7: The Cox proportional hazard regression model for HIV/AIDS patients

Variables	Level	df	β	SE	χ^2	p-value	Exp(β)
Gender	Female	1	-0.7349	0.3524	4.3492	0.0370	0.4800
Age		1	0.0066	0.0188	0.1238	0.7250	1.0070
		Religion compared with Traditionalists					
Religion	Christian	1	-0.1587	0.6612	0.0576	0.8104	0.8530
	Islam	1	-0.0387	0.7116	0.0030	0.9566	0.9620
		Marital status compared with Divorced					
Mstatus	Divorced	1	-0.6248	0.8084	0.5974	0.4396	0.5350
	Married	1	-0.3471	0.5455	0.4049	0.5246	0.7070
	Single	1	-0.0251	0.7373	0.0012	0.9728	0.9750
Weight		1	-0.0602	0.0191	9.9625	0.0016	0.9420
		Regimen compared with CBV/NVP					
AZT/3TC/EFV		1	0.3207	0.4621	0.4818	0.4876	1.3780
		1	0.5308	0.4451	1.4224	0.2330	1.7000
AZT/3TC/NVP							
		WHO clinical stage compared with IV					
WHO	I	1	-1.8051	0.5359	11.3462	0.0008	0.1640
	II	1	-1.1780	0.6619	3.1674	0.0751	0.3080
	III	1	-1.0018	0.4233	5.6018	0.0179	0.3670
Disclosure	No	1	-0.0750	0.5023	0.0223	0.8813	0.9280

df: degrees of freedom

In fitting the reduced model, the covariate that were insignificant at 10% significance level were removed one at a time from the model assessing at each stage the AIC values. Covariates including Disclosure, Regimen, Marital status and Religion were dropped from the full model with only Sex, Weight and WHO clinical stage retained as the only significant covariates as shown in appendix Table A1.

We assessed the importance of the insignificant covariates in the reduced Cox model for the HIV/AIDS patients to ensure that the spurious relationships are avoided. Thus, these covariates are added one at a time to the three significant covariates in the reduced model. The study revealed that none of those covariates were significant and therefore cannot be retained in the model. This implies that, the insignificant covariates are not as a result of confounding elements in the model as shown in appendix Table A2-A6.

Table 4.8: Reduced model for HIV/AIDS

Effects	Model	AIC
0	Sex weight WHO Disclosure Regimen MSTATUS Religion AGE	347.611
1	Sex Weight WHO Disclosure Regimen Mstatus Religion	343.739
2	Sex Weight WHO Disclosure Regimen Mstatus	338.900
3	Sex Weight WHO Disclosure Regimen	336.902
4	Sex Weight WHO Disclosure	335.076
5	Sex Weight WHO	332.965

In determining the interaction effects of the model, the possible interactions of the covariates were formed to see if their effects can increase or decrease the hazard rate of the patients. The study revealed that none of the covariates significantly interact at 10% significance level as shown in appendix Table A18. Therefore, the final model will be the model involving Sex, weight and WHO clinical stage.

For the model to be adequate for statistical inferences it is necessary to cross check the model with it assumptions. If the assumptions are duly met then the model is good enough for statistical predictions.

Table 4.9: Test of proportional hazard assumption

Time	rho	χ^2	df	*p*-value
Gender	0.0971	0.34	1	0.5619
Age	-0.0061	0.00	1	0.9663
Religion	-0.0071	0.00	1	0.9667
Mstatus	0.0069	0.00	1	0.9607
Weight	-0.0944	0.24	1	0.6210
Regimen	-0.0870	0.24	1	0.6208
Who	0.1629	1.61	1	0.2039
Disclosure	-0.0918	0.31	1	0.5787
Global test		**5.90**	**8**	**0.7502**

df: degrees of freedom

In supporting the fact that the proportionality assumption was not violated, the Schoenfeld residual was performed as shown in Table 4.9. The correlation between the Schoenfeld residual for each of the covariate and the rank of the survival time was determined. The *p*-value and the global test were greater than the 5% significance level. Hence, we cannot reject the model that the proportionality assumption is violated. Thus, the Cox proportional hazard model is appropriate since all the covariates satisfied the proportionality assumption.

To validate this, we employed the graphical residuals to test if the assumption is duly met. The Scaled Schoenfeld residual in Figure 4.4 was used. This further suggests that there was no enough evidence that the Scaled Schoenfeld residual graphically violates the proportionality assumption. Undoubtedly, the plots support the proportionality assumption since the residuals are random and LOESS curves are smooth and horizontal with zero gradients.

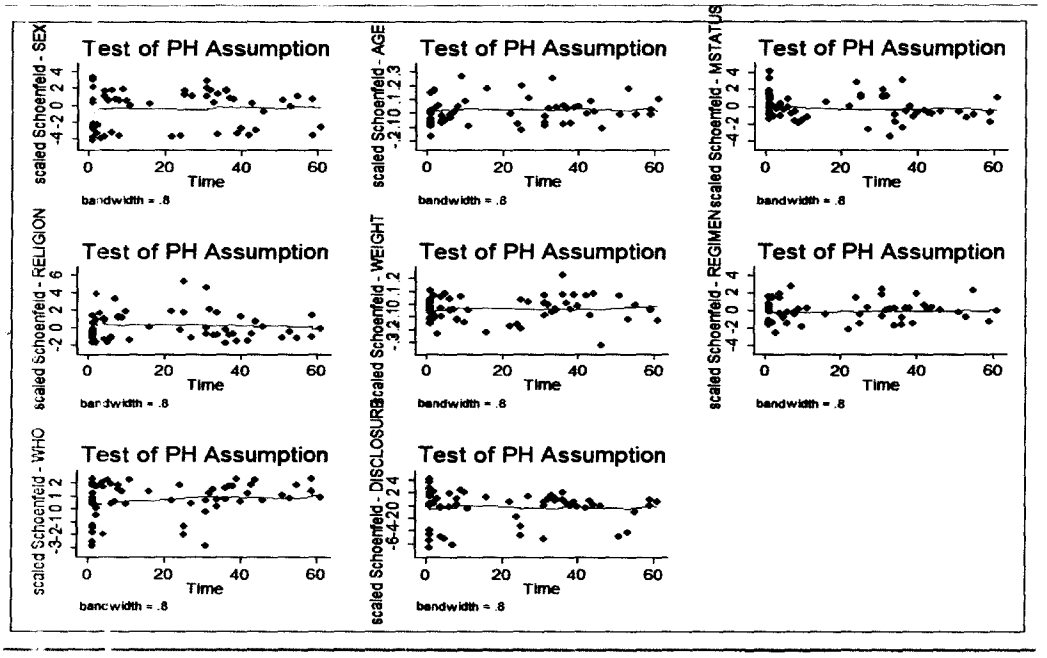

Figure 4.4 Scaled schoenfeld residual for HIV/AIDS covariates

The martingale residual plot is conducted to determine whether the assumption of the correct functional form of the model is satisfied and to establish whether the data support the hypothesis that the effect of the covariate is linear in the residual plot.

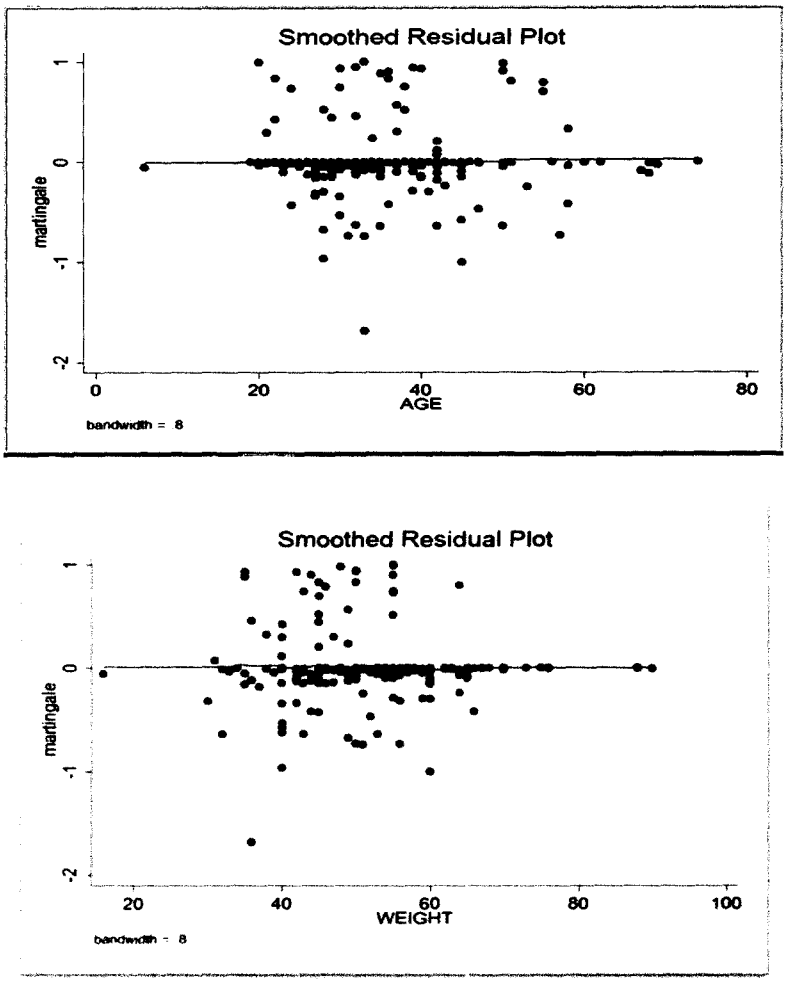

Figure 4.5: Martingale residual plot for continuous covariates of HIV/AIDS patients.

Figure 4.5 shows the plot of martingale residuals against the two continuous predictor variables Age and Weight. For each of the predictors the plot does not show trend and the resulting smoothed plots (LOESS) are approximately horizontal straight lines. Consequently, the martingale residual plot confirms that Age and Weight of the patients have a linear relationship with the survival time.

4.2.2 The Cox Proportional Hazard Model for Co-infection Patients

The proportional hazard model for the co-infected patients confirmed that the weight and Gender are significant as shown in Table 4.10. The estimated

hazard ratios are $[\widehat{HR} = 0.9150,\ p-\text{value} = 0.0052]$ and $[\widehat{HR} = 0.2980,\ p-\text{value} = 0.0415]$ respectively. This implies that an increase in the Weight of a patient will decrease the estimated hazard by 0.9150 assuming that all covariates are constant.

Table 4.10: Cox proportional hazard regression model for co-infection patients

Variables	Level	df	β	SE	χ^2	*p*-value	Exp(β)
Gender	Female	1	-1.20975	0.59342	4.1559	0.0415	0.2980
Age		1	-0.0220	0.02166	0.0000	0.9872	1.0000
		Religion compared with Traditionalists					
Religion	Christian	1	-0.0861	0.69072	0.0155	0.9008	0.9170
	Islam	1	0.7263	0.70620	1.0577	0.3037	2.0670
		Marital status compared with widowed					
Mstatus	Divorced	1	0.5313	0.86656	0.3759	0.5398	1.7010
	Married	1	-0.7354	0.66948	1.2067	0.2720	0.4790
	Single	1	-4.3838	1.99875	4.8103	0.0283	0.0120
Weight		1	-0.0886	0.03169	7.8204	0.0052	0.9150
		Regimen type compared with CBV/NVP					
AZT/3TC/EFV		1	-0.3794	0.69116	0.3013	0.5831	0.6840
AZT/3TC/NVP		1	-0.1414	0.57940	0.0596	0.8072	0.8680
		WHO clinical stage compared with IV					
WHO	I	1	-0.5896	0.61837	0.9092	0.3403	0.5550
	II	1	0.3599	0.78890	0.2082	0.6482	1.4330
	III	1	0.0369	0.67695	0.0030	0.9566	1.0380
Disclosure	No	1	-0.0109	0.58111	0.0004	0.9850	0.9890

df: degrees of freedom

Also, a female patient will have a decreased hazard of 0.2980 compared to the male patients assuming that all other covariates are constant. The Single patient is also significant $[\widehat{HR} = 0.0120, p-\text{value} = 0.0283]$. This implies that a Single patient have his/her estimated hazard decreased by approximately 98% compared to the widowed patient holding other factors constant.

The reduced model for the co-infection data was reached when the covariate that were insignificant at 10% significance level were removed one at a time from the model assessing at each stage the AIC values. Covariates including Disclosure, WHO clinical stage, Regimen, and Religion were dropped from

the full model with only Sex, Weight and Marital status maintained as the only significant covariates as shown in appendix Table A7.

Table 4.11: Reduced model for co-infection patients

Effects	Model	AIC
0	Sex Weight Mstatus Religion WHO Regimen Disclosure Age	181.710
1	Sex Weight Mstatus Religion WHO Regimen Disclosure	179.710
2	Sex Weight Mstatus Religion WHO Regimen	177.710
3	Sex Weight Mstatus Religion WHO	174.024
4	Sex Weight Mstatus Religion	169.654
5	Sex Weight Mstatus	169.323

The importance of the insignificant covariates in the reduced model for the co-infected patients was assessed to ensure that they do not confound the analysis. These insignificant covariates are added one at a time to the covariates in the reduced model. It is observed that none of those covariates were significant and therefore cannot be retained in the model. This implies that, the insignificant covariates are not as a result of confounding elements in the model as shown in appendix Tables A8-A12.

In assessing the interaction effects of the model, possible interactions of the covariates were formed to see if their effects can increase or decrease the hazard rate of the patients. The LR test was used to compare the log likelihood statistics for the interaction model and the no-interaction model. It is observed that none of the covariates significantly interact at 10% significance level to be included in the model as shown in appendix Table A19.

Table 4.12 shows the proportionality assumption for the co-infection. This provides enough evidence that the proportionality assumption is not violated

since the *p*-values are statistically insignificant. Hence, the Cox proportional hazard model is appropriate since all the covariates satisfied the proportionality assumption. This implies that the covariate does not correlate with the survival time.

Table 4.12: Test of proportional hazard assumption

Time	rho	χ^2	df	*p*-value
Gender	0.1320	0.67	1	0.4141
Age	-0.0324	0.02	1	0.8901
Religion	0.1693	0.45	1	0.5037
Mstatus	0.1032	0.29	1	0.5884
Weight	0.2295	1.43	1	0.2316
Regimen	0.1009	0.34	1	0.5592
WHO	0.2242	1.18	1	0.2783
Disclosure	-0.1400	1.02	1	0.3128
Global test		**12.00**	**8**	**0.2130**

df: degrees of freedom

Figure 4.6 of the scaled Schoenfeld residual demonstrates that the proportionality assumption is duly satisfied. That is, since the residual plots are random and LOESS curves are smooth and horizontal with their slope being zero.

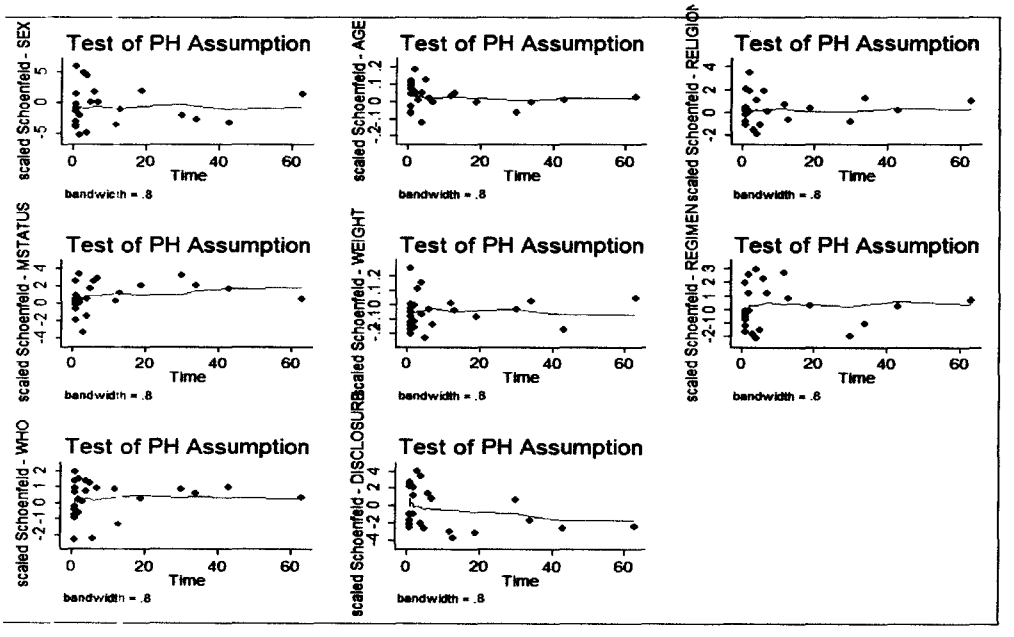

Figure 4.6 Scaled Schoenfeld residual for co-infected covariates

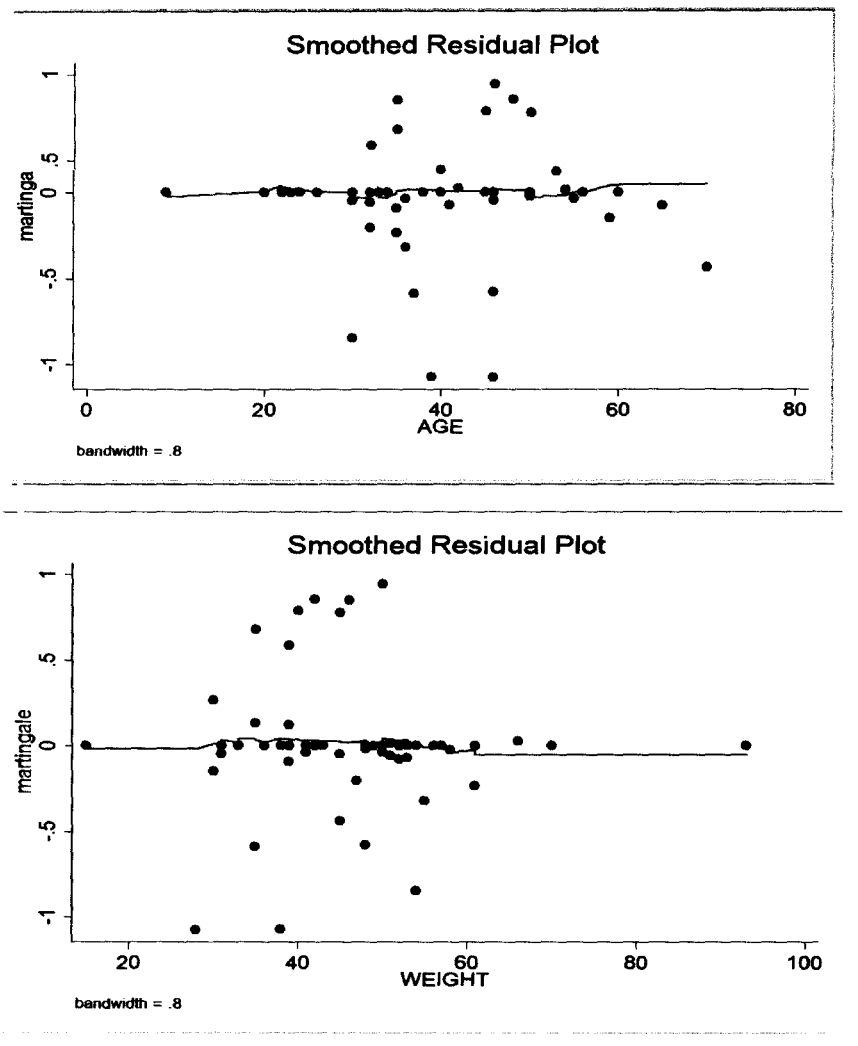

Figure 4.7: Martingale residual plot for continuous covariates for HIV/TB co-infection

We plotted the martingale residuals against two continuous predictor variables in the co-infection model: Age and Weight as shown in Figure 4.7. For each of the predictor variables, the plots showed a correct functional form. The result does not show any trend and the smoothed plots (LOESS) can be described as horizontal straight lines. The martingale residual plot confirms the model as having a linear relationship with the survival time. As such the model is appropriate.

4.2.3 The Cox Proportional Hazard Model for TB patients

Table 4.13 shows the fitted Cox proportional hazard model for TB patients. The weight and combine drug regimen shows a significant influence on the survival of the patients at 10% significant level. The estimated hazard ratio and p-value of the weight of patients is $[\widehat{HR} = 0.9600,\ p - \text{value} = 0.0892]$. This implies that a unit increase in the weight of a patient will eventually lower the risk of the patients by 0.9600 holding all other predictor variables constant. The estimated hazard ratios for drug regimen administered are $[\widehat{HR} = 0.024,\ p - \text{value} = 0.0590]$ and $[\widehat{HR} = 0.3320,\ p - \text{value} = 0.0773]$ for patients on the Drug regimens (HRZ) and (HRZE) respectively. This implies that as a patient uses this Drug regimen, the hazard of death decreases by 92% and 66% respectively compared to patients who are on (HRZES) drug regimen.

Table 4.13: Cox proportional hazard model for TB patients

Variables	Level	df	β	SE	χ^2	p-value	Exp(β)
Gender	Female	1	0.30481	0.50217	0.3684	0.5439	1.3560
Age		1	0.01345	0.01557	0.7463	0.3876	1.0140
		Religion compared with Traditionalists					
Religion	Christian	1	-0.53001	0.64541	0.6744	0.4115	0.5890
	Islam	1	-0.46550	0.70062	0.4414	0.5064	0.6280
		Marital status compared with Widowed					
Mstatus	Divorced	1	-0.59622	1.1912	0.256	0.6167	0.5510
	Married	1	-0.20446	0.7282	0.0788	0.7789	0.8150
	Single	1	0.02914	1.1233	0.0007	0.9793	1.0300
Weight		1	-0.04110	0.02418	2.8885	0.0892	0.9600
TB type	Extra Pul	1	-0.36376	0.82393	0.1949	0.6589	0.6950
		Regimen type compared with HRZES					
Regimen	HRZ	1	-2.83010	0.93189	9.2230	0.0024	0.0590
	HRZE	1	-1.10377	0.62486	3.1203	0.0773	0.3320

df: degrees of freedom

The reduced model for the TB data was reached when the covariate that were insignificant at 10% significance level were removed one at a time from the cox model assessing at each stage the AIC value. Among the covariates

removed included: Age, Sex, Religion, TB type and Marital status with only weight and Regimen retained as the only significant variables as shown in appendix Table A13.

Table 4.14: Reduced model for TB patients

Effects	Model	AIC
0	Weight Regimen Age Sex Religion TB type Mstatus	215.910
1	Weight Regimen Age Sex Religion TB type	210.345
2	Weight Regimen Age Sex Religion	208.538
3	Weight Regimen Age Sex	205.408
4	Weight Regimen Age	203.822
5	Weight Regimen	203.067

The insignificant covariates were assessed to ensure that the variables that will make the model bias are avoided in the TB data. Thus, these covariates were added one at a time to the reduced model. It is observed that, none of those covariates were significant and therefore cannot be retained in the model. This implies that, the insignificant covariates are not as a result of confounding elements in the model as shown in appendix Tables A14-A18.

In assessing the interaction effects of the model, possible interactions of the covariates were formed to see if their effects can increase or decrease the hazard rate of the patients. The LR compares the log likelihood statistics for the interaction model and the no-interaction model. The study revealed that none of the covariates significantly interact at 10% significant level as shown in Appendix A19. Therefore, interaction of the covariates will not be included in the model.

This shows that the proportionality assumption of the Cox PH model for TB patients is satisfied as shown in Table 4.15. The *p*-value is not significant at 5% significance level confirming that the proportionality assumption is satisfied

Table 4.15: Test of proportional hazard assumption

Time	rho	χ^2	df	*p*-value
Gender	0.0638	0.10	1	0.7548
Age	-0.2237	1.21	1	0.2710
Mstatus	0.1415	0.56	1	0.4555
Religion	0.0460	0.04	1	0.8342
Regimen	0.1223	0.47	1	0.4923
Weight	-0.0300	0.03	1	0.8734
TB type	-0.0267	0.01	1	0.9089
Global test		**2.36**	**7**	**0.9373**

df: degrees of freedom

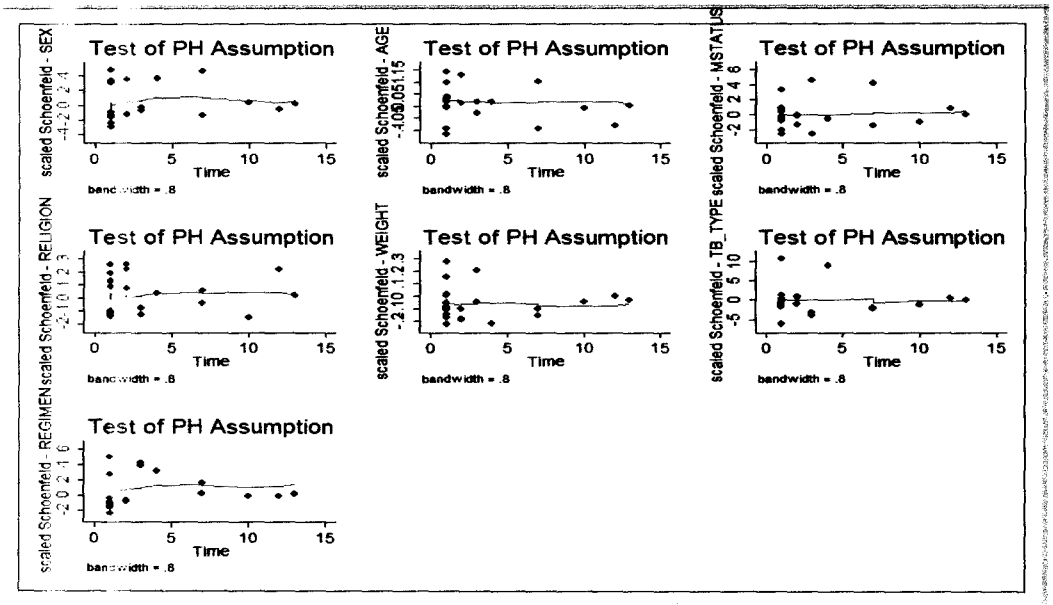

Figure 4.8 Scaled Schoenfeld residual for TB patients

Additionally, to affirm the adequacy of the proportionality assumption, the scaled Schoenfeld residual was duly examined in Figure 4.8. The residual plots are random and LOESS curves are smooth and horizontal with a slope zero. This suggests that the proportionality assumption is satisfied. Figure 4.9 is the plot of martingale residuals against the two continuous predictor variables age and weight in the TB Cox model. This is to aid us check for the linearity assumption. For each of the predictor variables age and weight, the plots display a correct functional form. It does not show trend and the resulting smoothed plots (LOESS) is described as horizontal straight lines. Thus, the

martingale residual plot confirms the model as having a linear relationship with the survival time. As such the model is adequate.

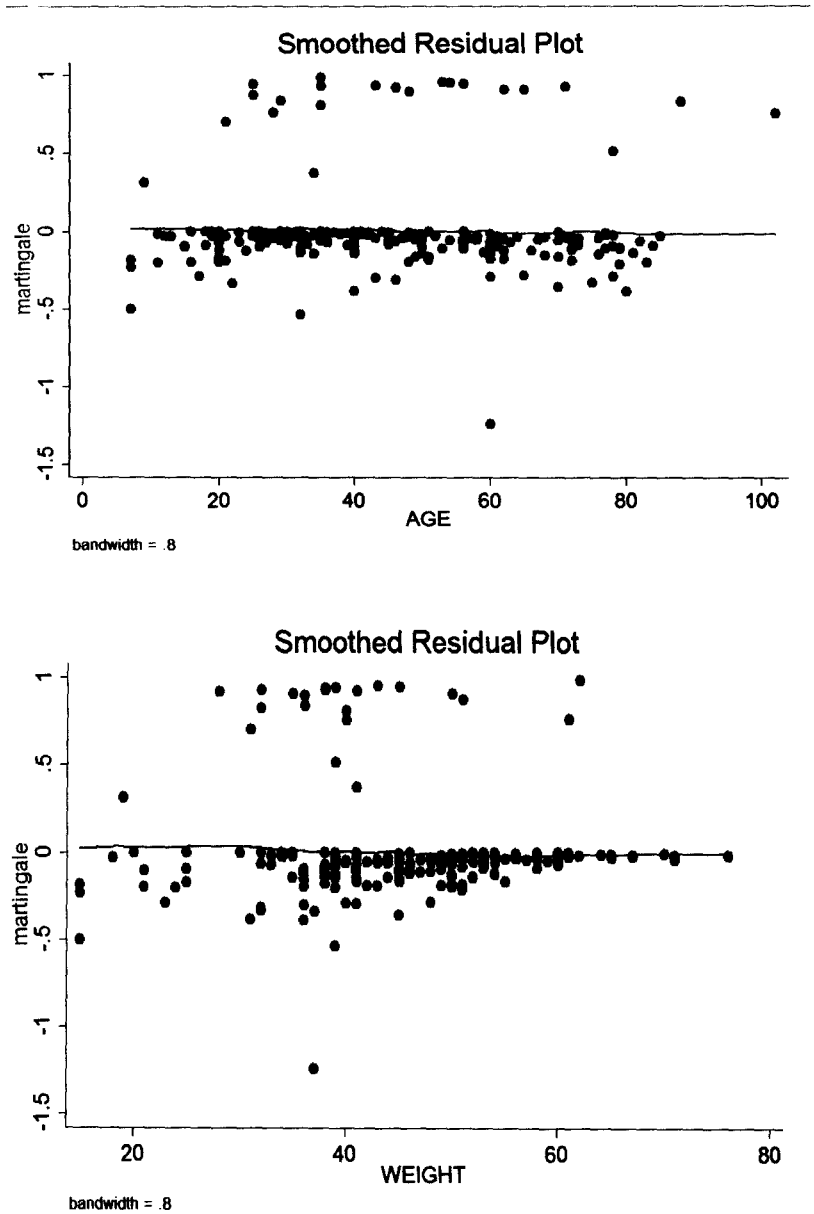

Figure 4.9: Martingale residual plot for continuous covariates of TB patients

4.3 Accelerated Failure Time Model (AFTM)

The HIV/AIDS and HIV/TB co-infection survival data shows that the AFT (Gamma) model is the best based on the AIC and BIC values. However, the TB data shows that the Cox model has the least BIC values as shown in Table 4.16.

Table 4.16: Model comparison

Criterion	Weibull	Exponent.	Gamma	Llogistic	Lnormal	Cox
HIV/AIDS						
AIC	273.362	274.138	246.477	278.993	280.761	347.611
BIC	328.510	325.839	305.072	334.141	335.908	370.901
Co-infection						
AIC	135.472	134.551	129.336	136.916	136.007	181.710
BIC	172.764	169.512	168.958	174.207	173.299	198.774
TB						
AIC	198.394	196.750	200.839	197.777	195.669	215.970
BIC	242.451	237.419	248.286	241.829	239.727	228.461

The Gamma model shown in Table 4.17 revealed that Gender, Weight and WHO Clinical Stage are significant at 10% significance level. However, age, religion, regimen, marital status and disclosure of status to partner are insignificant.

The estimated survival time of a female patient will increase since the time ratio is greater than one $[TR = e^{0.9427} = 2.57]$. Moreover, a unit increase in the weight of a patient will eventually increase the estimated survival time$[TR = e^{0.0658} = 1.09]$. In other words, the survival time is 1.09 times longer for a unit increase in weight of a patient. Again, patients at WHO Clinical Stage I, II and III will have their predicted survival time accelerated by $[TR = e^{2.3345} = 10.32]$, $[TR = e^{1.7459} = 5.73]$ and $[TR = e^{1.6392} = 5.15]$ respectively.

Table 4.17: Gamma model for HIV/AIDS patients

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	0.7449	2.8028	-4.7484	6.2382	0.07	0.7904
Gender	Female	1	0.9427	0.4874	-0.0125	1.8979	3.74	0.0531
Age		1	-0.0089	0.0327	-0.0730	0.0552	0.37	0.7851
		Religion compared with Traditionalist						
Religion		1	0.0319	0.8424	-1.6192	1.6829	1.34	0.2469
Christian								
	Islam	1	-0.1733	0.9317	-1.9993	1.6528	0.66	0.4166
		Marital status compared with Widowed						
Mstatus	Divorced	1	0.5889	1.2211	-1.8044	2.9822	0.23	0.6296
	Married	1	-0.2117	0.8744	-1.9255	1.5021	0.06	0.8087
	Single	1	-0.5911	1.0712	-2.6906	1.5084	0.30	0.5811
Weight		1	0.0658	0.0349	-0.0027	0.1343	3.55	0.0597
		Regimen compared with (CBV/NVP)						
AZT/3TC/EFV		1	0.1568	0.5683	-1.2706	0.9570	0.08	0.7826
AZT/3TC/NVP		1	0.7137	0.6589	-2.0050	0.5777	1.17	0.2787
		WHO Clinical Stage compared with IV						
WHO	I	1	2.3345	0.8933	0.5836	4.0853	6.83	0.0090
	II	1	1.7459	0.9872	-0.1889	3.6807	3.13	0.0770
	III	1	1.6392	0.6535	0.3584	2.9200	6.29	0.0121
Disclosure	No	1	0.3030	0.6692	-1.0087	1.6147	0.21	0.6507
Scale		1	0.2209	0.0573	0.1328	0.3673		
Shape		1	7.2105	1.8461	3.5923	10.8288		

df: degrees of freedom

In fitting a reduced model for prediction, stepwise model selection was employed, with AIC criterion. The variables; Age, Regimen, Disclosure, Religion and Marital status were dropped with only Sex, Weight and WHO clinical stage as the significant covariates as shown in Table 4.18. Estimates of the reduced model are shown in Table 4.19.

Table 4.18 Stepwise model selection

Effects	Model	AIC
0	Sex Weight WHO Age Regimen Disclosure Mstatus Religion	215.910
1	Sex Weight WHO Age Regimen Disclosure Mstatus	210.345
2	Sex Weight WHO Age Regimen Disclosure	208.538
3	Sex Weight WHO Age Regimen	205.408
4	Sex Weight WHO Age	203.822
5	Sex Weight WHO	203.067

Table 4.19 Estimate of reduced model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	1.6664	1.2859	-0.8540	4.1868	1.68	0.1950
Gender	Female	1	0.3565	0.2966	-0.2247	0.9378	1.45	0.0393
Weight		1	0.0493	0.0297	-0.0089	0.1075	2.76	0.0967
		WHO Clinical Stage compared with IV						
WHO	I	1	1.4427	0.6951	0.0803	2.8050	4.31	0.0379
	II	1	1.0510	1.8068	-2.4902	4.5923	0.34	0.5608
	III	1	0.9583	0.4620	0.0528	1.8639	4.30	0.0381
Scale		1	0.1881	0.0441	0.1188	0.2977		
Shape		1	9.4916	2.1905	5.1982	13.7849		

df: degrees of freedom

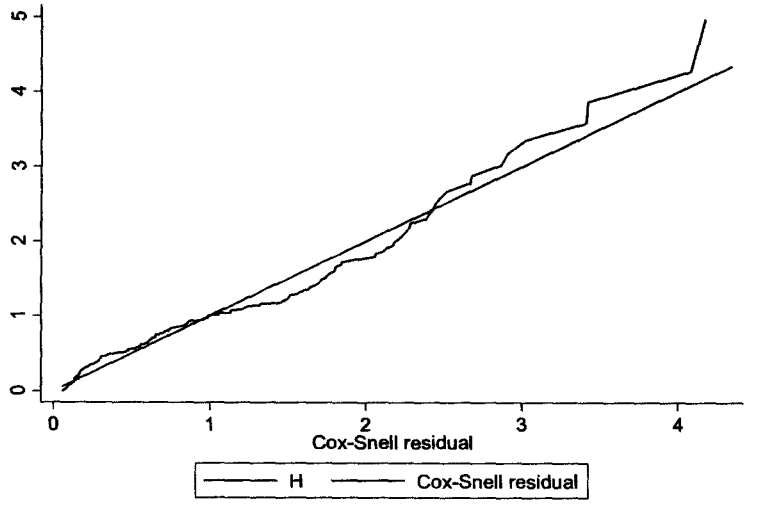

Figure 4.10 Gamma Cox-Snell residual for HIV/AIDS

The Cox-Snell residual graph as shown in Figure 4.10 compared to the rest of the AFT model in the appendix implies that the gamma graph is closer to the bisector than the rest of the models; as a result, the gamma model best fit the HIV/AIDS data in this study.

Table 4.20: Gamma model for co-infection patients

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	-2.7195	1.5647	-5.7862	0.3472	3.02	0.0822
Gender	Female	1	0.7499	0.4391	-0.1108	1.6106	2.92	0.0877
Age		1	0.0049	0.0012	0.0026	0.0072	17.56	<.0001
			Religion compared with Traditionalist					
	Christian	1	0.2927	0.5665	-0.8176	1.4031	0.27	0.6054
	Islam	1	0.2875	0.6466	-0.9798	1.5547	0.20	0.6566
			Marital status compared with Widowed					
Mstatus		1	-0.2219	0.7405	-1.6734	1.2295	0.09	0.7644
Divorced								
	Married	1	0.1907	0.5508	-0.8888	1.2703	0.12	0.7291
	Single	1	2.7347	1.3184	0.1506	5.3188	4.30	0.0381
Weight		1	0.0882	0.0240	0.0410	0.1353	13.44	0.0002
			Regimen compared with (CBV/NVP)					
AZT/3TC/EFV		1	0.2338	0.6450	-1.0304	1.4980	0.13	0.7170
AZT/3TC/NVP		1	0.1261	0.5497	-0.9514	1.2035	0.05	0.8186
			WHO Clinical Stage compared with IV					
WHO	I	1	-0.4564	0.5366	-1.5081	0.5954	0.72	0.3951
	II	1	-0.7908	0.6457	-2.0564	0.4749	1.50	0.2207
	III	1	-0.3266	0.6711	-1.6420	0.9888	0.24	0.6265
Disclosure	No	1	-0.3633	0.5162	-1.3749	0.6484	0.50	0.4815
Scale		1	0.6634	0.1070	0.4836	0.9100		
Shape		1	0.8089	0.1083	0.6222	1.0516		

df: degrees of freedom

The Gamma model shown in Table 4.20 indicated that Gender, Age and Weight were significant. However, Religion, Marital status, Drug regimen, WHO Clinical Stage and Disclosure were statistically insignificant.

The study reveals that female patients will survive longer with an estimated time ratio of; $[TR = e^{0.7499} = 2.1167]$. A unit increase in the age of a patient will accelerate his/her predicted survival time by $[TR = e^{0.0049} = 1.0049]$. Also, a unit increase in the weight of TB patient corresponds to an increase in the survival time by $[TR = e^{0.0882} = 1.0922]$.

In fitting a reduced model for prediction, stepwise model selection was employed, with AIC criterion. The variables; Age, Regimen, Disclosure,

Religion and Marital status were dropped with only Sex, Weight and WHO clinical stage retained as the significant covariates as shown in Table 4.21.

Table 4.21: Stepwise model selection

Effects	Model	AIC
0	Mstatus Weight Age Sex WHO Religion Disclosure Regimen	129.336
1	Mstatus Weight Age Sex WHO Religion Disclosure	125.589
2	Mstatus Weight Age Sex WHO Religion	123.661
3	Mstatus Weight Age Sex WHO	119.922
4	Mstatus Weight Age Sex	117.874
5	Mstatus Weight Age	113.687

Table 4.22: Estimates of reduced model

Variables	df	β	SE	95% C.I		χ^2	*p*-value
Intercept	1	-0.3323	1.1709	-2.6273	1.9627	0.08	0.7766
Age	1	0.0033	0.0023	-0.0012	0.0078	2.08	0.0488
		Marital status compared with Widowed					
Divorced	1	-0.9679	0.5165	-1.9802	0.0444	3.51	0.0609
Married	1	-0.0226	0.2773	-0.5662	0.5209	0.01	0.9349
Single	1	2.8596	0.7462	1.3971	4.3221	14.69	0.0001
Weight	1	0.0763	0.0283	0.0209	0.1317	7.29	0.0069
Scale	1	0.1401	0.0494	0.0702	0.2796		
Shape	1	10.6269	3.6709	3.4320	17.8218		

df: degrees of freedom

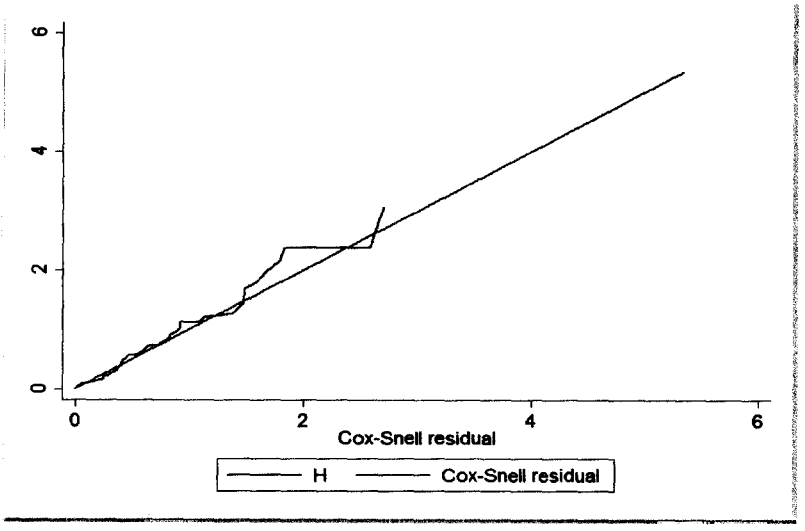

Figure 4.11 Cox-Snell residual plot for co-infection

The Cox-Snell residual graph as shown in Figure 4.11 implies that the Gamma model is the best fit for the co-infection data. This is because the model is closer to bisector than the rest of the models in the appendix.

4.3 Discussion of Results

There were 590 patients on treatment from 2008 to 2013, of which two hundred and ninety-five (295) patients were diagnosed of HIV/AIDS; two hundred and nineteen (219) were TB patients and seventy-six (76) were HIV/TB co-infected. The study discovered that the percentage of death among the co-infected patients (32.9%) was higher than the deaths recorded from both HIV/AIDS and TB patients (30.2%). The survival estimates at the end of 70th month for HIV/AIDS and the co-infection was [$\hat{S}_{(HIV/AIDS)} = 0.4110$, $\hat{S}_{(Co-infection)} = 0.1892$] respectively. This suggests that the co-infected patients experienced the worse survival rate compared to the HIV/AIDS, evident in Table 4.2. This agrees with the Interagency Coalition on AIDS and Development in 2010 report, that 33% of all AIDS deaths worldwide can be attributed to TB. This could also be as a result of the difficulty in diagnosing the HIV patients of TB since HIV patients were more susceptible to contracting extra-pulmonary TB. It was also revealed that the youth are the most affected in HIV contraction with the average age of 35 years. The mean age of a TB patient was 45 years.

The hazard plot (Figure 4.1) for HIV/AIDS showed the 59th month of treatment as the riskiest month. About 50% of the risk of TB patients occurred in the 13th month [$\widehat{HR} = 0.5000$]. This could be attributed to the Drug resistance strain resulting in hazard increase after the minimum recovery period of six month. The 63rd month of HIV/TB co-infection was the risky

month ($\widehat{HR} = 0.3333$). This could be that the co-infected patients were not diagnosed of TB at the earlier state resulting in the higher risk at the later state of treatment.

In addition, the log rank test revealed that the WHO Clinical Stage is statistically significant for the HIV/AIDS patients. The Drug regimen for TB patients is also significant. There is a statistically significant difference among the religious denominations of HIV/TB co-infected patients. However, covariates including Gender, Marital status, Religion of both HIV and TB patients, Disclosure to sexual partner, Drug regimen for HIV/AIDS patients and TB type were statistically insignificant.

Further, Weight, Gender and WHO Clinical Stage of HIV/AIDS patients are clinically and statistically significant for the patient's survival in the Cox model. This suggests that, patients with higher Weight will have lower hazard hence an improvement in their survival rate. The result of the Gender showed female patients of recording a lower mortality rate than male. The patients at WHO clinical stage I, II and III have a better survival than the patient at stage IV. This could be as a result of the opportunistic infections such as the extra-pulmonary TB and radiological bacterial pneumonia that the patients at WHO Clinical Stage IV usually surfer from.

The Weight, Gender and Marital status was also significant among the co-infected patients. The weight and the Drug regimen used were significant for the survival of the TB patients in the Cox model. Patients that used the combined drug regimen (HRZ) and (HRZE) have a better survival rate than the patients that used the drug regimen (HRZES). Thus, the patients on the (HRZ) and (HRZE) drug regimens are children and new cases of TB reported

respectively. Whereas, the patients on (HRZES) drug regimen are on re-treatment due to relapse or the drug resistant strain hence the higher risk of survival.

The possible interactions of the covariates that were formed to see if their effects can increase or decrease the hazard rate of the patients revealed that none of the covariates significantly interact at 10% significant level.

Furthermore, comparing the Cox model with the Accelerated Failure Time model (AFT) showed that the AFT (Gamma) model was the best in the HIV/AIDS and HIV/TB co-infection survival data. However, the Cox model was adjudged the best model among the TB category based on the BIC values. In determining the prognostic effects among the HIV/AIDS patients using the Gamma model we observed that Gender, Weight and WHO Clinical Stage are statistically significant. The model deduced that the female patients had a better and longer predicted survival time. This is consistent with Owiti, (2013) where she argued that men naturally seek healthcare late and find it difficult to visit hospital regularly resulting in higher mortality rate among male. This suggests that a unit change in the Weight of patient will increase the predicted survival time. Rafera, (2012) asserts that the rate of dying among patients with higher weight in Ethiopia is proportionally lower compared to patients with lower Weight. Similarly, patients at WHO Clinical Stage I, II and III experienced an improved survival time. This could be as a result of the opportunistic infections at stage IV. The Gamma model for the co-infected patients showed that Gender, Age and Weight is statistically significant. Thus, an increase in the age of a patient will increase their predicted survival time.

The diagnostic evaluation of the Cox proportional hazard model proves that the proportionality assumption was satisfied. The global test revealed that there was no significant difference in the survival of the patients. Therefore, the proportionality assumption is satisfied. The scaled Schoenfeld residual plot was also performed to further justify the proportionality assumption. The test was adequate since the residual plots were random and LOESS curves smooth and horizontal with zero gradients. The martingale residual plot was also undertaken among the continuous covariates to check the correct functional form of the model. For each of the covariates, the plots do not show trend and the resulting smoothed plots (LOESS) were approximately horizontal straight lines. This confirms that the martingale residual plots have a linear relationship with the survival time. The Cox-Snell residual plot shows that the gamma model's graph is closer to the bisector than the rest of the models; as a result, the gamma model best fit the HIV/AIDS and HIV/TB co-infection survival data in the study.

4.4 Conclusion

This chapter dealt with the analysis and discussion of results. It presented the major findings of the study in a clear, detailed, precise and concise manner.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.0 Introduction

This chapter covers the conclusion of the findings and some recommendations based on the study.

5.1 Conclusion

In this study, the survival and the prognostic factors that affect HIV/AIDS, TB and HIV/TB co-infection between 2008 and 2013 were studied. The summary statistics and the survival estimate based on the life table showed that the HIV/TB co-infected patients experienced the worse survival rate.

Factors such as Weight, Gender and WHO clinical stage significantly determine the survival of the HIV/AIDS patients. We also observed that Gender, Age and Weight significantly determine the survival of the co-infected patients. While the Weight and the Drug regimen influenced the survival of the TB patients. Of the three categories the study deduced that Weight significantly determines the patient's survival.

The study showed the Cox proportional hazard model to be adequate for the TB survival data. However, the accelerated failure time model indicates that the Gamma model is well fitted for the HIV/AIDS and co-infection.

5.2 Recommendations

Following the outcome of this study, the following recommendations were made;

i. Government and stakeholders should support health institutions and physicians to initiate routine tests on opportunistic infections for HIV/AIDS patients to avoid deterioration in the health of the patients before the tests are conducted.

ii. Health authorities and workers should be very cautious and pay much attention to patients who weighed lesser than the minimum weights of 8, 9 and 15 kilograms of HIV/AIDS, co-infection and TB respectively because it is observed in the study that this factor significantly affects the survival of the patients.

iii. Researchers and authors who study in HIV/AIDS and TB co-infection should consider AFT (Gamma) model even if the proportionality assumption of the Cox model is satisfied.

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APPENDIX I PUBLICATION

Nawumbeni, N. D., Luguterah, A., Adampah, T. (2014): Performance of Cox Proportional Hazard and Accelerated Failure Time Models in the Analysis of HIV/TB Co-infection Survival Data. *International Institute for Science Technology and Education,* **21**: 2224-5766.

APPENDIX II

TABLES AND FIGURES FOR COX MODEL FOR HIV/AIDS PATIENTS

Figure A1: Survival curve for HIV/AIDS patients

Table A1: Reduced model

Variable		df	β	SE	χ^2	*p*-value	Exp(β)
Gender	Female	1	-0.63551	0.32537	3.8150	0.0508	0.530
Weight		1	-0.05591	0.01813	9.5124	0.0020	0.946
		WHO clinical stage compared IV					
I		1	-1.69419	0.49097	11.9073	0.0006	0.184
II		1	-1.04785	0.64047	2.6767	0.1018	0.351
III		1	-0.84955	0.37430	5.1516	0.0232	0.428

The insignificant covariates added one at a time to the reduced model.

Table A2: Age added

Testing Global Null Hypothesis: BETA=0			
Test	χ^2	df	*p*-value
Likelihood Ratio	33.2814	6	<.0001
Score	36.0206	6	<.0001
Wald	30.6384	6	<.0001

Type III analysis of effects			
Effect	**df**	χ^2	**p-value**
Age	**1**	**0.2689**	**0.6040**
Sex	1	3.6204	0.0571
Weight	1	9.7245	0.0018
WHO	3	12.6745	0.0054

Table A3: Religion added

Testing Global Null Hypothesis: BETA=0			
Test	χ^2	**df**	***p*-value**
Likelihood Ratio	33.3633	7	<.0001
Score	36.7277	7	<.0001
Wald	30.8192	7	<.0001

Type III analysis of effects			
Effect	df	χ^2	*p*-value
Religion	**2**	**0.3514**	**0.8389**
Sex	1	3.6583	0.0558
Weight	1	9.2738	0.0023
WHO	3	12.9346	0.0048

Table A4: Marital status added

Testing Global Null Hypothesis: BETA=0			
Effect	χ^2	**df**	***p*-value**
Likelihood Ratio	33.0693	6	<.0001
Score	35.9773	6	<.0001
Wald	30.5789	6	<.0001

Type III analysis of effects			
Effect	**df**	χ^2	***p*-value**
Mstatus	**3**	**1.4485**	**0.6942**
Sex	1	4.8066	0.0284
Weight	1	9.2872	0.0023
WHO	3	14.3856	0.0024

Table A5: Regimen added

Testing Global Null Hypothesis: BETA=0			
Test	**χ^2**	**df**	***p*-value**
Likelihood Ratio	34.4491	8	<.0001
Score	36.2176	8	<.0001
Wald	30.0188	8	0.0002

Type III analysis of effects			
Effect	**df**	**χ^2**	***p*-value**
Regimen	**2**	**1.2463**	**0.5362**
Sex	1	2.7820	0.0953
Weight	1	6.0695	0.0138
WHO	3	8.3091	0.0400

Table A6: Disclosure added

Testing Global Null Hypothesis: BETA=0			
Test	**χ^2**	**df**	***p*-value**
Likelihood Ratio	33.0693	6	<.0001
Score	35.9773	6	<.0001
Wald	30.5789	6	<.0001

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
Disclosure	**1**	**0.0515**	**0.8205**
Sex	1	3.8542	0.0496
Weight	1	9.5380	0.0020
WHO	3	13.4087	0.0038

APPENDIX III

TABLES AND FIGURES FOR COX MODEL FOR HIV/TB CO-INFECTION PATIENTS

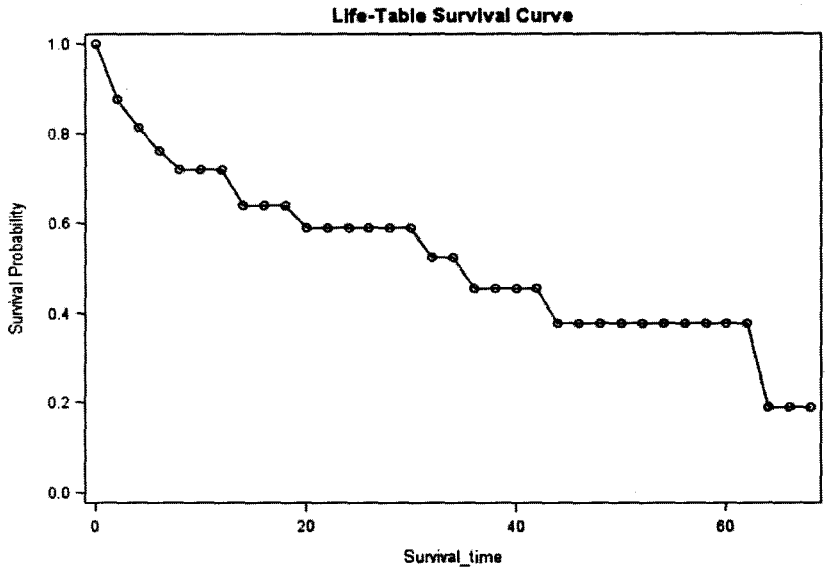

Figure A2: Survival curve for Co-infection

Table A7: Reduced model co-infection

Variables		df	β	SE	χ^2	*p*-value	Exp(β)
Gender	Female	1	-0.97975	0.46433	4.4522	0.0349	0.375
Marital status compared with widowed							
Divorced		1	0.44978	0.68316	0.4335	0.5103	1.568
Married		1	-0.54453	0.53716	1.0276	0.3107	0.580
Single		1	-4.01271	1.27652	9.8814	0.0017	0.018
Weight		1	-0.07735	0.02588	8.9330	0.0028	0.926

The insignificant covariates added one at a time to the reduced model

Table A8: Age added

Testing Global Null Hypothesis: BETA=0			
Test	χ^2	**df**	***p*-value**
Likelihood Ratio	17.6452	6	0.0072
Score	12.8043	6	0.0463
Wald	12.5717	6	0.0504

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
Age	**1**	**0.0956**	**0.7571**
Sex	1	4.4589	0.0347
Mstatus	3	8.8360	0.0316
Weight	1	8.9743	0.0027

Table A9: Disclosure added

Testing Global Null Hypothesis: BETA=0			
Test	**χ^2**	**df**	***p*-value**
Likelihood Ratio	17.5662	6	0.0001
Score	12.8713	6	0.0001
Wald	12.5245	6	0.0012

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
Disclosure	**1**	**0.0151**	**0.9021**
Sex	1	4.4314	0.0353
Mstatus	3	11.0102	0.0117
Weight	1	8.2187	0.0041

Table A10: Religion added

Testing Global Null Hypothesis: BETA=0			
Test	**χ^2**	**df**	***p*-value**
Likelihood Ratio	21.2193	7	0.0035
Score	17.1290	7	0.0166
Wald	14.3141	7	0.0459

Type III analysis test			
Effect	df	χ^2	*p*-value
Religion	**2**	**4.0960**	**0.1290**
Sex	1	4.2498	0.0393
Mstatus	3	10.2395	0.0166
Weight	1	8.2340	0.0041

Table A11: WHO added

Testing Global Null Hypothesis: BETA=0			
Test	**χ^2**	**df**	***p*-value**
Likelihood Ratio	20.4200	8	0.0089
Score	13.8725	8	0.0851
Wald	12.7230	8	0.1217

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
WHO	**3**	**2.5724**	**0.4623**
Sex	1	5.9679	0.0146
Mstatus	3	10.6039	0.0141
Weight	1	9.5509	0.0020

Table A12: Regimen added

Testing Global Null Hypothesis: BETA=0			
Likelihood Ratio	18.1331	7	0.0114
Score	12.6946	7	0.0799
Wald	12.6400	7	0.0814

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
Regimen	**2**	**0.5936**	**0.7432**
Sex	1	4.5735	0.0325
Mstatus	3	11.3586	0.0099
Weight	1	8.9828	0.0027

APPENDIX IV TABLES AND FIGURES FOR COX MODEL FOR TB PATIENTS

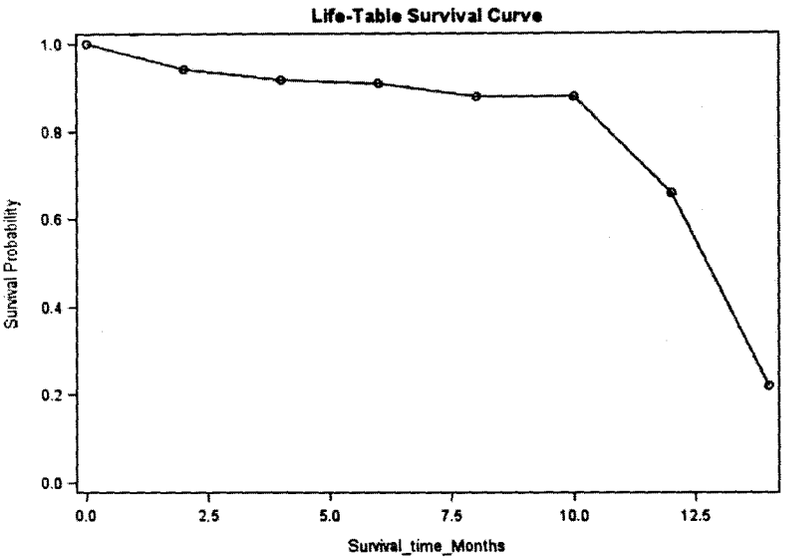

Figure A3: Survival curve for TB patients

Table A13: Reduced model for TB

Variable		df	β	SE	χ^2	*p*-value	Exp(β)
Weight		1	-0.03462	0.01864	3.4493	0.0633	0.966
Regimen type compared with HRZES							
Regimen	HRZ	1	-2.54039	0.89020	8.1437	0.0043	0.079
Regimen	HRZE	1	-0.69685	0.52833	1.7397	0.1872	0.498

The insignificant covariates added one at a time to the reduced model

Table A14: Marital status added

Testing Global Null Hypothesis: BETA=0			
Test	χ^2	**df**	***p*-value**
Likelihood Ratio	15.8786	6	0.0144
Score	15.1595	6	0.0191
Wald	12.8979	6	0.0447

Type III analysis test			
Effect	df	χ^2	*p*-value
Mstatus	**3**	**1.2528**	**0.7404**
Weight	1	2.9185	0.0876
Regimen	2	8.3768	0.0152

Table A15: TB type added

Testing Global Null Hypothesis: BETA=0			
Test	**χ^2**	**df**	***p*-value**
Likelihood Ratio	14.8956	4	0.0049
Score	14.6059	4	0.0056
Wald	12.5293	4	0.0138

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
TB type	**1**	**0.1398**	**0.7085**
Weight	1	3.5616	0.0591
REGIMEN	2	8.3916	0.0151

Table A16: Religion added

Testing Global Null Hypothesis: BETA=0			
Test	χ^2	df	*p-value*
Likelihood Ratio	16.1692	5	0.0064
Score	15.7532	5	0.0076
Wald	13.4479	5	0.0195

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
Religion	**2**	**1.6126**	**0.4465**
Weight	1	3.4747	0.0623
Regimen	2	8.6743	0.0131

Table A17: Gender added

Testing Global Null Hypothesis: BETA=0			
Test	**χ^2**	**df**	***p-value***
Likelihood Ratio	14.9824	4	0.0047
Score	14.6292	4	0.0055
Wald	12.4685	4	0.0142

Type III analysis test			
Effect	**df**	**χ^2**	***p*-value**
Gender	**1**	**0.2408**	**0.6236**
Weight	1	3.1944	0.0739
Regimen	2	8.1994	0.0166

Table A18: Age added

Testing Global Null Hypothesis: BETA=0			
Test	χ^2	**df**	***p-value***
Likelihood Ratio	15.9917	4	0.0030
Score	15.0804	4	0.0045
Wald	12.8190	4	0.0122

Type III analysis test			
Effect	**df**	χ^2	***p*-value**
Age	**1**	**1.2746**	**0.2589**
Weight	1	4.1040	0.0428
Regimen	2	8.4816	0.0144

Table A19: Interaction effects

Interaction	$-2LL_R$	$-2LL_F$	$-2LL_R-(-2LL_F)$	**DECISION**
HIV/AIDS				
Sex*Weight	525.149	524.990	0.159	Fail to reject
Sex*WHO	500.145	497.600	2.545	Fail to reject
Weight*WHO	495.987	493.747	2.240	Fail to reject
CO-INFECTION				
Sex*Mstatus	170.252	167.603	2.649	Fail to reject
Sex*WEIGHT	175.572	173.318	2.254	Fail to reject
Weight*Mstatus	163.922	161.448	2.474	Fail to reject
TB				
Weight*Regimen	197.067	195.871	1.196	Fail to reject

APPENDIX V TABLES AND FIGURES FOR AFT MODEL FOR HIV/AIDS PATIENTS

Table A20: Weibull model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	-1.5506	2.5841	-6.6155	3.5142	0.36	0.5485
Gender	Female	1	0.8039	0.4767	-0.1305	1.7383	2.84	0.0918
Age		1	-0.0024	0.0287	-0.0585	0.0538	0.01	0.9337
		Religion compared with Traditionalist						
Christian		1	2.0442	0.9364	0.2089	3.8795	4.77	0.0290
Islam		1	1.7962	1.0033	-0.1703	3.7626	3.20	0.0734
		Marital status compared with Widowed						
Mstatus	Divorced	1	0.4206	1.0482	-1.6337	2.4750	0.16	0.6882
	Married	1	0.8233	0.7924	-0.7297	2.3764	1.08	0.2988
	Single	1	-0.3782	0.9909	-2.3203	1.5639	0.15	0.7027
Weight		1	0.0433	0.0272	-0.0100	0.0966	2.53	0.1115
		Regimen compared with (CBV/NVP)						
AZT/3TC/EFV		1	-0.5295	0.6592	-1.8215	0.7625	0.65	0.4218
AZT/3TC/NVP		1	-1.2319	0.6632	-2.5316	0.0679	3.45	0.0632
		WHO Clinical Stage compared with IV						
WHO	I	1	0.4217	0.7180	-0.9855	1.8290	0.35	0.5569
	II	1	0.5910	0.8599	-1.0943	2.2763	0.47	0.4919
	III	1	1.1856	0.5591	0.0897	2.2814	4.50	0.0340
Disclosure	No	1	0.1199	0.7150	-1.2815	1.5213	0.03	0.8668
Scale		1	1.2362	0.1655	0.9509	1.6072		
Shape		1	0.8089	0.1083	0.6222	1.0516		

Table A21: Exponential model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	-1.0675	2.1343	-5.2506	3.1157	0.25	0.6170
Gender	Female	1	0.7438	0.3887	-0.0181	1.5057	3.66	0.0557
Age		1	-0.0030	0.0238	-0.0496	0.0436	0.02	0.8988
		Religion compared with Traditionalist						
	Christian	1	1.8633	0.7646	0.3648	3.3619	5.94	0.0148
	Islam	1	1.5467	0.8107	-0.0423	3.1357	3.64	0.0564
		Marital status compared with Widowed						
	Divorced	1	0.4488	0.8613	-1.2393	2.1370	0.27	0.6023
	Married	1	0.8142	0.6499	-0.4597	2.0881	1.57	0.2103
	Single	1	-0.3383	0.8039	-1.9139	1.2374	0.18	0.6739
Weight		1	0.0361	0.0220	-0.0070	0.0792	2.70	0.1006
		Regimen compared with (CBV/NVP)						
AZT/3TC/EFV		1	-0.4863	0.5418	-1.5483	0.5756	0.81	0.3694
AZT/3TC/NVP		1	-1.0408	0.5339	-2.0873	0.0057	3.80	0.0513
		WHO Clinical Stage compared with IV						
WHO	I	1	0.4218	0.5989	-0.7520	1.5956	0.50	0.4813
	II	1	0.4747	0.6946	-0.8866	1.8360	0.47	0.4943
	III	1	1.0732	0.4577	0.1761	1.9703	5.50	0.0190
Disclosure	No	1	0.1772	0.5955	-0.9899	1.3443	0.09	0.7661
Scale		1	1.0000	0.0000	1.0000	1.0000		
Weibull scale		1	1.0000	0.0000	1.0000	1.0000		

Table A22: Log-normal model

Parameter Level		df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	-0.0623	2.7586	-5.4692	5.3445	0.00	0.9820
Gender	Female	1	0.8077	0.5670	-0.3035	1.9190	2.03	0.1543
Age		1	-0.0112	0.0302	-0.0704	0.0480	0.14	0.7110
		Religion compared with Traditionalist						
	Christian	1	1.5201	1.0090	-0.4575	3.4978	2.27	0.1319
	Islam	1	1.3939	1.0542	-0.6722	3.4601	1.75	0.1861
		Marital status compared with Widowed						
	Divorced	1	0.0269	1.1970	-2.3191	2.3730	0.00	0.9821
	Married	1	0.5114	0.8915	-1.2358	2.2586	0.33	0.5662
	Single	1	-0.6922	1.1622	-2.9701	1.5856	0.35	0.5514
Weight		1	0.0428	0.0322	-0.0204	0.1060	1.76	0.1844
		Regimen compared with (CBV/NVP)						
AZT/3TC/EFV		1	-0.8269	0.7625	-2.3214	0.6675	1.18	0.2781
AZT/3TC/NVP		1	-1.2465	0.7132	-2.6444	0.1513	3.05	0.0805
		WHO Clinical Stage compared with IV						
WHO	I	1	0.3636	0.7916	-1.1880	1.9152	0.21	0.6460
	II	1	0.6811	0.9231	-1.1281	2.4902	0.54	0.4606
	III	1	0.9965	0.6813	-0.3388	2.3319	2.14	0.1436
Disclosure	No	1	-0.2583	0.8097	-1.8453	1.3286	0.10	0.7497
Scale		1	2.1091	0.2563	1.6621	2.6764		

Table A23: Log-logistic model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	-0.8969	2.7604	-6.3073	4.5134	0.11	0.7452
Gender	Female	1	0.8628	0.5531	-0.2213	1.9469	2.43	0.1188
Age		1	-0.0125	0.0292	-0.0697	0.0447	0.18	0.6692
		Religion compared with Traditionalist						
	Christian	1	2.0011	0.9669	0.1061	3.8961	4.28	0.0385
	Islam	1	1.8129	1.0370	-0.2196	3.8455	3.06	0.0804
	Divorced	1	-0.0412	1.1606	-2.3160	2.2336	0.00	0.9717
	Married	1	0.5654	0.8589	-1.1180	2.2488	0.43	0.5103
	Single	1	-0.6831	1.1052	-2.8493	1.4830	0.38	0.5365
Weight		1	0.0433	0.0313	-0.0180	0.1045	1.91	0.1665
		Regimen compared with (CBV/NVP)						
AZT/3TC/EFV		1	-0.6806	0.7275	-2.1064	0.7451	0.88	0.3494
AZT/3TC/NVP		1	-1.2478	0.6997	-2.6192	0.1236	3.18	0.0745
		WHO Clinical Stage compared with IV						
WHO	I	1	-0.0190	0.8214	-1.6289	1.5910	0.00	0.9816
	II	1	0.3399	0.9144	-1.4523	2.1320	0.14	0.7101
	III	1	0.9787	0.6348	-0.2656	2.2229	2.38	0.1232
Disclosure	No	1	-0.0713	0.7649	-1.5704	1.4278	0.01	0.9257
Scale		1	1.0840	0.1441	0.8354	1.4065		

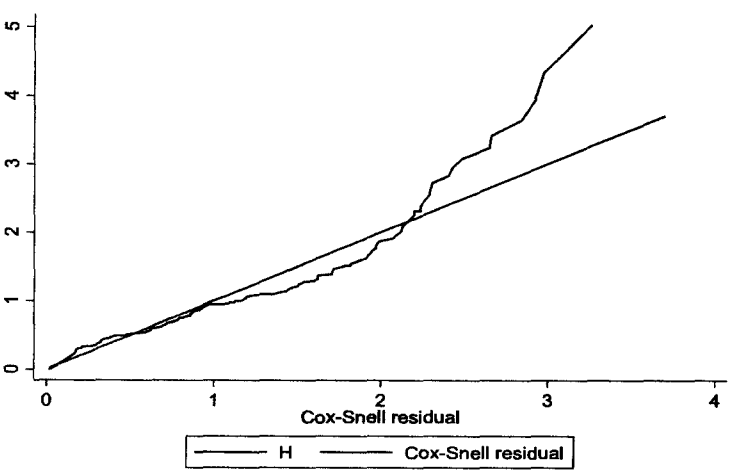

Figure A4: Cox-Snell residual plot for Weibull

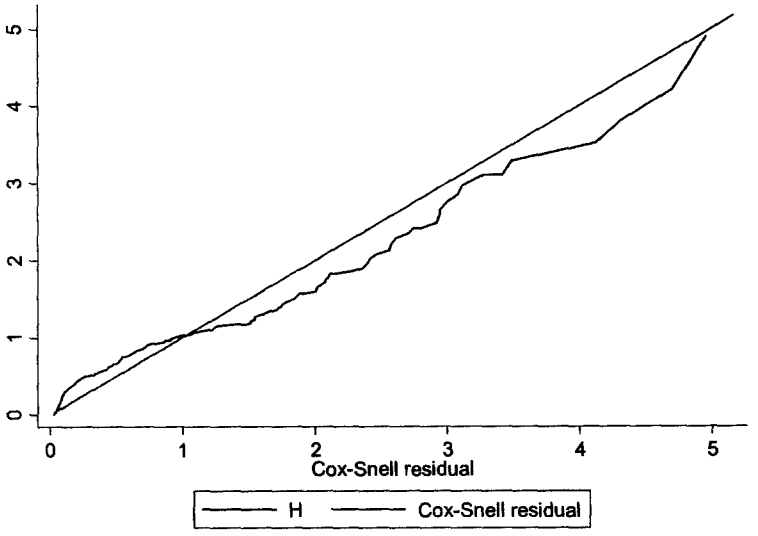

Figure A5: Cox-Snell residual plot for Exponential

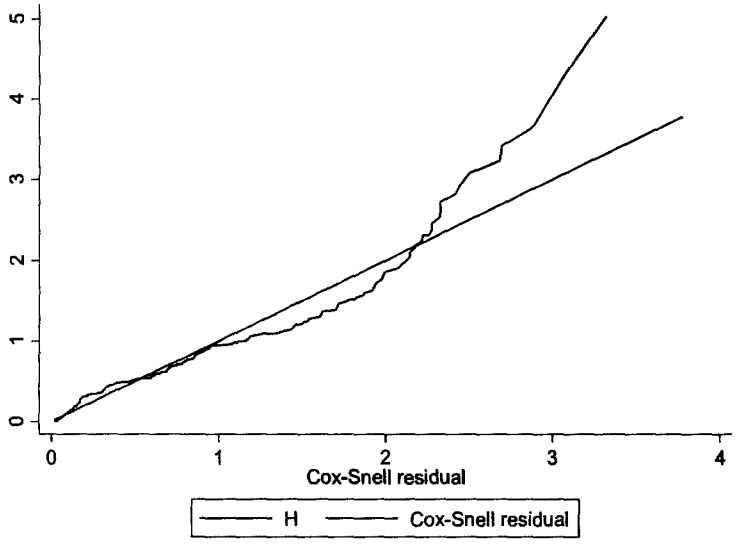

Figure A6: Cox-Snell residual plot for Log-normal

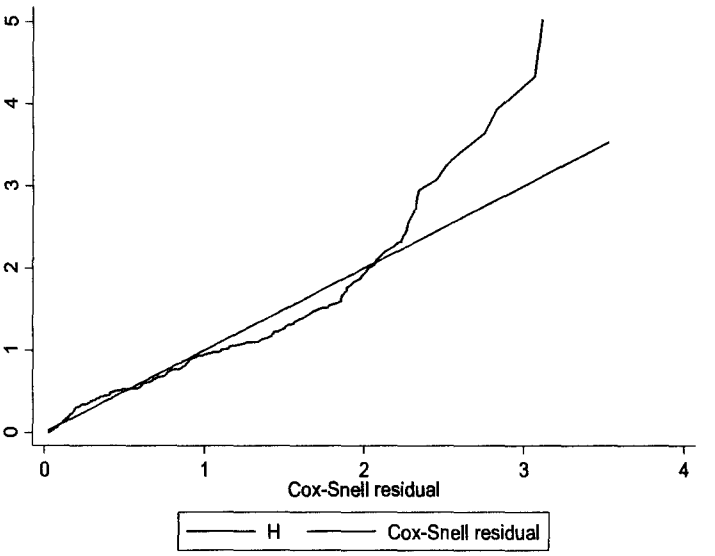

Figure A7: Cox-Snell residual plot for Log-logistic

APPENDIX VI

TABLES FOR AFT MODEL FOR TB PATIENTS

Table A24: Weibull model

Parameter	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	0.7280	1.4408	-2.0959	3.5518	0.26	0.6134
Gender	Female	1	-0.0965	0.4305	-0.9403	0.7472	0.05	0.8226
Age		1	-0.0135	0.0138	-0.0405	0.0135	0.96	0.3261
		Religion compared with Traditionalist						
	Christian	1	0.6344	0.5834	-0.5091	1.7778	1.18	0.2769
	Islam	1	0.2261	0.6166	-0.9824	1.4346	0.13	0.7139
		Marital status compared with Widowed						
	Divorced	1	0.5295	1.0564	-1.5411	2.6001	0.25	0.6162
	Married	1	-0.0040	0.6190	-1.2172	1.2093	0.00	0.9949
	Single	1	0.0197	0.9801	-1.9013	1.9408	0.00	0.9839
Weight		1	0.0437	0.0228	-0.0009	0.0883	3.68	0.0550
		Regimen compared with (HRZES)						
	HRZ	1	1.8359	0.6473	0.5671	3.1046	8.04	0.0046
	HRZE	1	1.1560	0.5876	0.0044	2.3076	3.87	0.0491
		TB type compared with Pulmonary						
TB type	Extra Pul	1	0.1470	0.7415	-1.3064	1.6004	0.04	0.8429
Scale		1	0.8895	0.1704	0.6110	1.2950		
Shape		1	1.1242	0.2154	0.7722	1.6365		

Table A25: Exponential model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	0.6132	1.6119	-2.5461	3.7725	0.14	0.7036
Gender	Female	1	-0.1063	0.4824	-1.0517	0.8391	0.05	0.8256
Age		1	-0.0150	0.0152	-0.0449	0.0148	0.97	0.3236
		Religion compared with Traditionalist						
	Christian	1	0.6972	0.6471	-0.5711	1.9655	1.16	0.2813
	Islam	1	0.2454	0.6942	-1.1152	1.6060	0.12	0.7237
		Marital status compared with Widowed						
	Divorced	1	0.5947	1.1825	-1.7229	2.9123	0.25	0.6150
	Married	1	-0.0051	0.6950	-1.3674	1.3572	0.00	0.9941
	Single	1	0.0330	1.0986	-2.1201	2.1861	0.00	0.9760
Weight		1	0.0500	0.0231	0.0047	0.0952	4.68	0.0305
		Regimen compared with (HRZES)						
	HRZ	1	1.9776	0.6825	0.6400	3.3152	8.40	0.0038
	HRZE	1	1.2731	0.6254	0.0474	2.4988	4.14	0.0418
		TB type compared with Pulmonary						
Extra Pul TB		1	0.2115	0.8239	-1.4033	1.8262	0.07	0.7974
Scale		1	1.0000	0.0000	1.0000	1.0000		
Weibull Shape		1	1.0000	0.0000	1.0000	1.0000		

Table A26: Log-normal model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	0.3663	1.6095	-2.7884	3.5209	0.05	0.8200
Gender	Female	1	-0.0147	0.4496	-0.8959	0.8665	0.00	0.9739
Age		1	-0.0108	0.0140	-0.0383	0.0166	0.60	0.4388
		Religion compared with Traditionalist						
	Christian	1	0.4843	0.6629	-0.8149	1.7835	0.53	0.4650
	Islam	1	0.0798	0.7076	-1.3070	1.4666	0.01	0.9102
		Marital status compared with Widowed						
	Divorced	1	0.7955	1.1376	-1.4341	3.0250	0.49	0.4844
	Married	1	0.0425	0.6561	-1.2435	1.3284	0.00	0.9484
	Single	1	0.1611	0.9407	-1.6827	2.0049	0.03	0.8640
Weight		1	0.0481	0.0219	0.0051	0.0910	4.80	0.0284
		Regimen compared with (HRZES)						
	HRZ	1	2.2859	0.7303	0.8545	3.7173	9.80	0.0017
	HRZE	1	1.1857	0.6499	-0.0880	2.4594	3.33	0.0681
		TB type compared with Pulmonary						
	Extra Pul	1	0.3900	0.8477	-1.2714	2.0515	0.21	0.6454
Scale		1	1.6695	0.2888	1.1894	2.3433		

Table A27: Log-logistic model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	0.2043	1.5697	-2.8724	3.2809	0.02	0.8965
Gender	Female	1	-0.0522	0.4407	-0.9160	0.8116	0.01	0.9057
Age		1	-0.0127	0.0137	-0.0395	0.0141	0.87	0.3516
		Religion compared with Traditionalist						
	Christian	1	0.6033	0.6043	-0.5811	1.7877	1.00	0.3181
	Islam	1	0.2169	0.6406	-1.0387	1.4725	0.11	0.7349
		Marital status compared with Widowed						
	Divorced	1	0.6362	1.0866	-1.4934	2.7658	0.34	0.5582
	Married	1	0.0354	0.6407	-1.2204	1.2911	0.00	0.9560
	Single	1	0.1056	0.9829	-1.8207	2.0320	0.01	0.9144
Weight		1	0.0471	0.0232	0.0017	0.0925	4.13	0.0420
		Regimen compared with (HRZES)						
	HRZ	1	2.0548	0.6891	0.7042	3.4054	8.89	0.0029
	HRZE	1	1.2502	0.6311	0.0132	2.4872	3.92	0.0476
		TB type compared with Pulmonary						
	Extra Pul	1	0.3411	0.8065	-1.2396	1.9218	0.18	0.6723
Scale		1	0.8433	0.1579	0.5843	1.2172		

Table A28: Gamma model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	1.0491	1.3192	-1.5364	3.6346	0.63	0.4264
Gender	Female	1	-0.1650	0.4197	-0.9877	0.6576	0.15	0.6942
Age		1	-0.0139	0.0139	-0.0412	0.0133	1.00	0.3164
		Religion compared with Traditionalist						
	Christian	1	0.6472	0.5577	-0.4460	1.7404	1.35	0.2459
	Islam	1	0.2164	0.5881	-0.9364	1.3691	0.14	0.7129
		Marital status compared with Widowed						

	Divorced	1	0.4205	1.0174	-1.5735	2.4145	0.17	0.6794
	Married	1	-0.0589	0.5850	-1.2054	1.0877	0.01	0.9199
	Single	1	-0.0733	0.9574	-1.9498	1.8031	0.01	0.9389
Weight		1	0.0404	0.0223	-0.0033	0.0841	3.28	0.0703
	Regimen compared with (HRZES)							
	HRZ	1	1.6114	0.6064	0.4228	2.8000	7.06	0.0079
	HRZE	1	1.0709	0.5478	-0.0028	2.1446	3.82	0.0506
	TB type compared with Pulmonary							
	Extra Pul	1	-0.0849	0.6783	-1.4143	1.2446	0.02	0.9004
	Scale	1	0.3699	0.0730	0.2513	0.5445		

APPENDIX VII

TABLES AND FIGURES FOR AFT MODEL FOR HIV/TB CO-INFECTION PATIENTS

Table A29: Weibull model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	-2.5546	1.7573	-5.9987	0.8896	2.11	0.1460
Gender	Female	1	1.0524	0.4613	0.1482	1.9566	5.20	0.0225
Age		1	-0.0125	0.0191	-0.0500	0.0250	0.43	0.5139
		Religion compared with Traditionalist						
	Christian	1	0.3891	0.5336	-0.6567	1.4349	0.53	0.4658
	Islam	1	0.3943	0.5918	-0.7657	1.5542	0.44	0.5053
		Marital status compared with Widowed						
	Divorced	1	-0.3430	0.6965	-1.7081	1.0222	0.24	0.6224
	Married	1	0.2911	0.5612	-0.8089	1.3911	0.27	0.6040
	Single	1	3.2286	1.5803	0.1314	6.3259	4.17	0.0410
Weight		1	0.0944	0.0250	0.0455	0.1434	14.31	0.0002
		Regimen compared with (CBV/NVP)						
AZT/3TC/EFV		1	0.0217	0.5850	-1.1249	1.1683	0.00	0.9704
AZT/3TC/NVP		1	0.3156	0.5140	-0.6918	1.3230	0.38	0.5392
		WHO Clinical Stage compared with IV						
	I	1	-0.3860	0.4859	-1.3383	0.5664	0.63	0.4270
	II	1	-0.9368	0.6349	-2.1811	0.3075	2.18	0.1401
	III	1	0.5779	0.6914	-0.7772	1.9330	0.70	0.4033
Disclosure	No	1	-0.5185	0.4684	-1.4365	0.3995	1.23	0.2683
Scale		1	0.8247	0.1354	0.5977	1.1378		
Shape		1	1.2126	0.1992	0.8789	1.6731		

Table A30: Exponential model

Variables Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept	1	-2.8773	2.0672	-6.9289	1.1744	1.94	0.1640
Gender Female	1	1.0791	0.5382	0.0242	2.1339	4.02	0.0450
Age	1	-0.0102	0.0222	-0.0536	0.0333	0.21	0.6467
Religion compared with Traditionalist							
Christian	1	0.4256	0.6310	-0.8111	1.6623	0.45	0.5000
Islam	1	0.3610	0.6939	-0.9991	1.7210	0.27	0.6029
Marital status compared with Widowed							
Divorced	1	-0.4007	0.8206	-2.0090	1.2077	0.24	0.6254
Married	1	0.3664	0.6564	-0.9201	1.6528	0.31	0.5767
Single	1	3.4057	1.8051	-0.1321	6.9435	3.56	0.0592
Weight	1	0.0983	0.0295	0.0406	0.1560	11.14	0.0008
Regimen compared with (CBV/NVP)							
AZT/3TC/EFV	1	0.0971	0.6832	-1.2419	1.4361	0.02	0.8870
AZT/3TC/NVP	1	0.3126	0.6030	-0.8692	1.4945	0.27	0.6041
WHO Clinical Stage compared with IV							
I	1	-0.3369	0.5866	-1.4867	0.8129	0.33	0.5658
II	1	-0.8940	0.7562	-2.3761	0.5881	1.40	0.2371
III	1	0.4929	0.7771	-1.0301	2.0159	0.40	0.5259
Disclosure No	1	-0.5211	0.5520	-1.6030	0.5608	0.89	0.3452
Scale	1	1.0000	0.0000	1.0000	1.0000		
Shape	1	1.0000	0.0000	1.0000	1.0000		

Table A31: Log-normal model

Variables Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept	1	-1.3353	1.5512	-4.3755	1.7049	0.74	0.3893
Gender Female	1	0.5629	0.3929	-0.2073	1.3330	2.05	0.1520
Age	1	-0.0146	0.0185	-0.0509	0.0216	0.63	0.4286
Religion compared with Traditionalist							
Christian	1	0.2226	0.5378	-0.8315	1.2767	0.17	0.6789
Islam	1	0.1725	0.5972	-0.9979	1.3430	0.08	0.7726
Marital status compared with Widowed							
Divorced	1	-0.2197	0.7502	-1.6901	1.2507	0.09	0.7696
Married	1	-0.0215	0.5747	-1.1479	1.1049	0.00	0.9701
Single	1	1.8603	1.1666	-0.4262	4.1467	2.54	0.1108
Weight	1	0.0786	0.0221	0.0353	0.1219	12.68	0.0004
Regimen compared with (CBV/NVP)							
AZT/3TC/EFV	1	0.1086	0.5697	-1.0080	1.2253	0.04	0.8488
AZT/3TC/NVP	1	0.0419	0.4864	-0.9114	0.9953	0.01	0.9313
WHO Clinical Stage compared with IV							
I	1	-0.4779	0.5224	-1.5019	0.5460	0.84	0.3603
II	1	-0.6304	0.6506	-1.9055	0.6447	0.94	0.3326
III	1	-0.1706	0.5826	-1.3124	0.9713	0.09	0.7697
Disclosure No	1	-0.2974	0.4479	-1.1752	0.5804	0.44	0.5066
Scale	1	1.1233	0.1652	0.8420	1.4985		

Table A32: Log-logistic model

Variables	Level	df	β	SE	95% C.I		χ^2	*p*-value
Intercept		1	-1.7967	1.9366	-5.5923	1.9989	0.86	0.3535
Gender	Female	1	0.7145	0.4277	-0.1238	1.5528	2.79	0.0948
Age		1	-0.0152	0.0209	-0.0561	0.0257	0.53	0.4670
		Religion compared with Traditionalist						
	Christian	1	0.2826	0.5473	-0.7901	1.3553	0.27	0.6056
	Islam	1	0.2154	0.6386	-1.0363	1.4672	0.11	0.7359
		Marital status compared with Widowed						
	Divorced	1	-0.2912	0.7119	-1.6866	1.1042	0.17	0.6825
	Married	1	0.0181	0.5908	-1.1399	1.1761	0.00	0.9755
	Single	1	2.0319	1.5282	-0.9633	5.0272	1.77	0.1837
Weight		1	0.0852	0.0233	0.0394	0.1309	13.33	0.0003
		Regimen compared with (CBV/NVP)						
AZT/3TC/EFV		1	0.2085	0.6279	-1.0222	1.4391	0.11	0.7399
AZT/3TC/NVP		1	0.0917	0.5392	-0.9651	1.1485	0.03	0.8650
		WHO Clinical Stage compared with IV						
	I	1	-0.4213	0.5192	-1.4390	0.5964	0.66	0.4171
	II	1	-0.7207	0.6408	-1.9767	0.5352	1.27	0.2607
	III	1	-0.2023	-1.5395	1.1350	0.09	0.77	0.6823
Disclosure	No	1	-0.3472	0.4975	-1.3223	0.6280	0.49	0.4853
Scale		1	0.6508	0.1061	0.4728	0.8958		

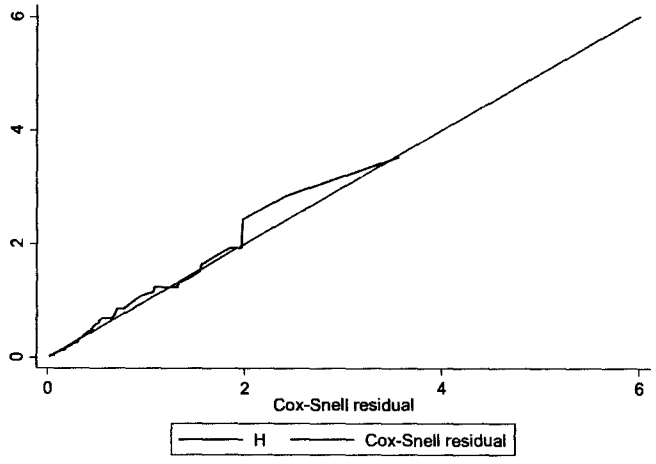

Figure A8: Cox-Snell residual plot for Weibull

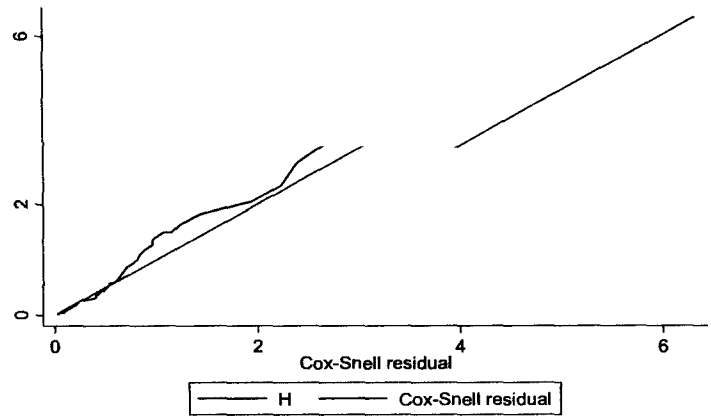

Figure A9: Cox-Snell residual plot for Exponential

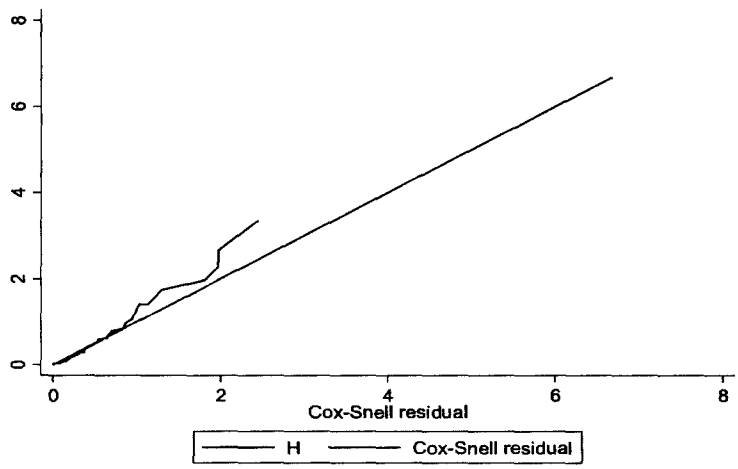

Figure A10: Cox-Snell residual plot for Log-normal

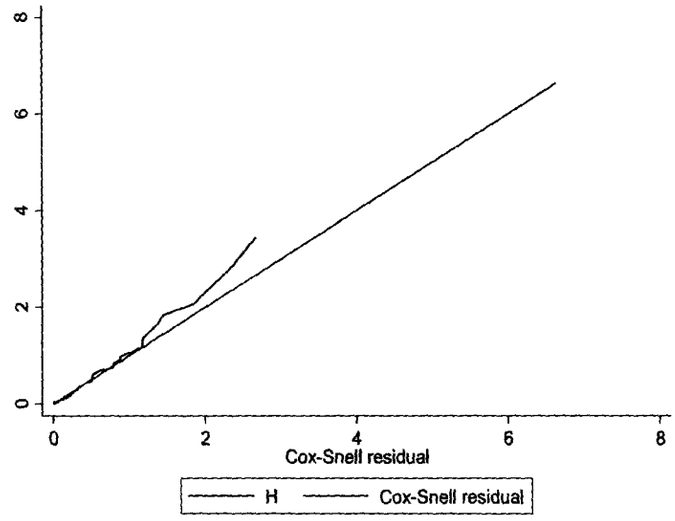

Figure A11: Cox-Snell residual plot for Log-logistic