UNIVERSITY FOR DEVELOPMENT STUDIES

SURVIVAL ANALYSIS OF MALE AND FEMALE HIV/AIDS PATIENTS IN NORTHERN REGION - A KAPLAN & MEIER APPROACH

BY

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Declaration

I hereby declare that this thesis with the exception of quotations and references contained in published works which have all been identified and acknowledged, is entirely my own original work, and it has not been submitted, either in part or whole for another degree elsewhere.

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Supervisor's Declaration

I hereby declare that the preparation and presentation of the thesis was supervised in accordance with the guidelines on supervision of thesis laid down by the University for Development Studies.

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ABSTRACT

Acquired Immune deficiency Syndrome (AIDS) is a disease caused by a virus known as Human Immunodeficiency virus (HIV). This virus attacks a person's immune system (white blood cells) and as such weakens the immune system and making the person vulnerable to opportunistic diseases e.g. tuberculosis, diarrhoea, to mention a few. HIV was first diagnosed more than twenty years ago and up to now there is no known cure for the disease. The rate at which HIV is spreading in sub-Sahara Africa is so high that the future generation is threatened with extinction. Thousands of people are dying daily of AIDS while tens of thousands are being infected. Different techniques have been used in campaign awareness programmes. These include; the media (Television, Radio, newspapers), books, schools, churches, etc. This project investigated the survival and hazards of both male and female HIV patients in the Northern Region. The main objective of the study was to compare the survival trends of both male and female HIV patients in the region who's $CD4^+$ T-cell count was below 350copies/µl as well as determine variables contributing to survival using Kaplan-Meier functions and the Cox regression. A retrospective study of the records of ninety HIV patients taken from the 2006 cohort group from seven HIV Sentinel Surveillance centres was conducted up to the end of2009. There were 36 males and 54 females representing 40% and 60% of the number of the number of patients enrolled in the study. At the end of the study period, 33 females and 25 males were censored representing 61.11% and 69.44% respectively with 32 deaths. In this cohort study, survival times varied by age and the HIV stage of infection, but not sex and the location of the patient. The mean survival times for male and female patients were 43.4 and 43.3 months respectively with standard errors of 1.3843 and 1.1888 (at a level significance of 0.05). The p-values of age and $CD4^+$ T-cell count of patients were found to be 0.0035 and 0.0025 respectively and thus contribute significantly to patient survival than sex and location since the hazard of old HIV/AIDS patients was significantly higher compared with younger patients. The potential working age group (25-49) years was found to be the most infected in the region.

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DEDICATION

This work is dedicated to my little boy, Michael N. Kambozieh and the entire Danzieh family for their contribution towards my education.

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GLOSSARY

AIDS: Acquired Immune deficiency Syndrome

ART: Anti-Retroviral Therapy

CDC: Centre for Disease Control (Atlanta, USA)

GDHS: Ghana Demographic Health Statistics

GHS: Ghana Health Service

GCS: Gay Compromise Syndrome

GRID: Gay Related Immune Deficiency

HAART: Highly Active Anti-Retroviral Therapy

HIV-RNA: Human Immune Virus-Ribonucleic Acid

HSS: HIV Sentinel Surveillance

KSOI: Kaposi Sarcoma Opportunistic Infection

MAC: Mycobacterium Avium Complex

MOH: Ministry of Health

MTCT: Mother to Child Transmission

NACP: National AIDS/STI Control Programme

NNRTI: Non-nucleoside Reverse Transcriptase Inhibitors

PCP: Pneumocystis Carinii Pneumonia

SIV: Simian Immunodeficiency Virus

SMM: Sooty Mangabey Monkey

VCT: Voluntary Counselling and Testing

WHO: World Health Organisation

CHAPTER ONE

INTRODUCTION

1.0 Background of the study

The Human Immune Virus/Acquired Immune deficiency Syndrome (HIV/AIDS) has had a devastating impact on mortality in Africa, which in 2006 experienced about 2.1 million of the 2.9 million deaths attributed to AIDS worldwide [UNAIDS, 2007]. HIV is currently estimated to account for between 35% and 75% of deaths of adults in the prime productive ages in sub-Saharan African populations [Lopman, *et al* 2006]. It is, however, not easy to obtain accurate information on HIV related mortality patterns in Africa, because most affected nations lack vital registration data that reliably inform the cause of death. HIV cohort studies thus have an important role to play in this respect, as their ability to measure HIV incidence and the survival of infected individuals allows analysts to make better use of the widely available data on national HIV prevalence trends.

The most informative comparative measures of HIV related mortality are based on life table estimates of survival after infection, obtained by follow-up of known sero-converters [Porter and Zaba, 2004]. Survival patterns after HIV infection before the introduction of antiretroviral therapy (ART) also form an important baseline for measuring the future success of treatment programmes. Previously published survival estimates in African populations suggested median times from infection to death ranging from 5 years for commercial sex workers in Nairobi [Anzala, *et al,* 1995] to 9.8 years; community study in Masaka district, Uganda [Morgan, *et al,* 2002]. This is lower than the average of 10.5 years observed in studies of infected individuals in high income countries such as Britain and the United States of America, to mention a few.

Estimates of survival of patients after the infection of the Human Immune Virus (HIV) are essential for understanding the trends of HIV infection and for planning healthcare resources for those infected. Understanding the natural history of HIV is essential for patient management and counselling, and enables an assessment of the impact of interventions to care for and treat people with HIV, including the provision of Anti-retroviral therapy (ART).

Most of the data on survival and progression to AIDS in low and middle income countries have come from cohorts of prevalent HIV infection or from cohorts of specific groups, taken from HIV Sentinel Surveillance centres and through voluntary counselling and testing centres [Crampin, *et al*, 2002].

1.1 HIV/AIDS in Ghana

The first HIV/AIDS case in Ghana was reported in 1986 and by the end of 2003 about 350,000 people were known to be living with the disease with an estimated 30,000 people already dead. The HIV/AIDS prevalence in the 15 to 49 year old age group rose from 2.7% in 1994 to 3.1% in 2004 and to 2.9% by the end of 2009 compared to 7.5% in sub- Saharan Africa and 1.1 % globally [MOH/NACP Sentinel Surveillance Report, 2009].

The Ghana Epidemiological Fact Sheet on HIV/AIDS and Sexually Transmitted infections (2008) indicates that HIV is primarily spread through heterosexual means accounting for about 80% of the cases, 15% for Mother to Child Transmission (MTCT) and 5% for others such as blood transfusion and intravenous drug usage. It also shows that women account for about 58% of adults estimated to be living with HIV/AIDS in Ghana and referred to the 5 to 14 year old age group as the "Window of Hope".

There is significant variation in HIV prevalence across the entire country with the highest in Eastern Region (4.2%), Greater Accra (3.2%), Brong Ahafo (2.9%), Central Region (3.0%), Volta Region (2.7%), Western Regions (3.1%), Ashanti Region (3.9%), Upper West Region 3.1%, Northern Region 2.0% and 2.2% for Upper East Region. This indicates a rise in the HIV prevalence rate in each region as contained in the reports of the GHS/NACP/HSS [2007, 2008, and 2009].

It is estimated that about 33.4 million people are living with HIV worldwide, 22.4 million of this lives in sub-Saharan Africa and about 273,000 people in Ghana [WHO Global Health Fact, 2009].

1.2 Ghana's Programmatic Response to HIV/AIDS

HIV/ AIDS has social, economic and development effects, and unless curtailed, could have a devastating effect on the overall wellbeing of the people of Ghana. The growing number of HIV/ AIDS cases can overwhelm the health care system, overburden the social system, hinder educational development, and inhibit agricultural production. For instance, the Joint United Nations Programme on HIV/AIDS (UNAIDS) has estimated that in Ghana the number of children under age 17 who have lost their mother or father or both parents to AIDS at the end of2003 was between 120,000 and 250,000 (UNAIDS, 2004). In some high prevalence areas, the social fabric (social support system) is no longer able to cope with the large number of orphans (USAID/Ghana, 2003; UNAIDS et al., 2004).

According to Akwara et al (2005), Ghana's response to the HIV/AIDS epidemic was initially characterized by a medical approach, whereby the disease was managed as an individual health issue. As the epidemic spread, a public health approach was taken. The first response was the formation of a technical committee in 1985 to advise the government. Working with the Ministry of Health and consultants from the World Health Organization (WHO), the committee was charged with the task to develop a short-term plan for HIV prevention and control. A medium-term plan was developed with the WHO's Global Program on AIDS in 1998.

In 1987, the National AIDS/STI Control Program (NACP) was established within the Disease Control Unit (DCU) of the Ministry of Health for the prevention, management, and control of HIV in the country. The functions of NACP include the organization of educational campaigns through mass media, workshops, video shows, and other channels to inform the public on how to reduce HIV-related risky behaviours, particularly through the use of condoms. Condom promotion was given considerable attention in Ghana by the joint effort of the Ghana Ministry of Health, Ghana Social Marketing Foundation, and other private and non-governmental organizations, For example, the Ministry of Health in Accra, in collaboration with Family Health International, embarked on an AIDS prevention program with condom promotion among commercial sex workers as its major goal. This program was initiated barely a year after the first AIDS case was reported in Ghana and continued through the early nineties.

HIV antibody testing and blood screening facilities were introduced in 1987.

In 1990, NACP established the national HSS system (described above). At the beginning of 2000, government and non-government partners launched a major HIV/AIDS awareness campaign for adolescents.

In the 21st century, the government of Ghana adopted a multi-sectoral approach to HIV/AIDS programming, and in September 2000, the Ghana AIDS/STI Commission (GAC) was established as a supra-ministerial and multi-sectoral body under the leadership of the President to direct and coordinate all HIV/AIDS-related activities in the country. GAC was given the mandate to formulate national policies and strategies; to provide high-level advocacy for HIV/AIDS prevention and control; to provide effective leadership in the national planning of programs; to expand and coordinate the national response; to mobilize, manage, and monitor resource allocation and utilization; and to foster linkages and networks among stakeholders.

In 2001, GAC published the Ghana HIV/AIDS Strategic Framework: 2001-2005 to guide the national response. Four key intervention areas were identified;

- Prevention of new transmission
- Care and support for people living with HIV/AIDS (PLWHA)
- Creation of an enabling environment for national response
- Decentralised implementation and institutional arrangements and research, monitoring, and evaluation (GAC, 2001a).

The National Monitoring and Evaluation Plan for HIV/AIDS in Ghana 2001-2005 was developed in 2001(GAC, 2001b).

In 2002, NACP published Guidelines for Management of Sexually Transmitted Diseases to improve the quality of STI management in health facilities in both the public and private sectors and to contribute to the reduction of transmission of STI's including HIV. Also in 2002, prevention of mother-to-child transmission (MTCT) of HIV interventions were introduced on a pilot basis and 2003 saw the beginning of national expansion. A comprehensive National HIV/AIDS and STI's Policy, approved by the cabinet was published in August 2004. The policy is intended to create a favourable environment for all aspects of HIV/AIDS and STI's prevention, care, and support. This is to address the complex range of policy issues such as the situation of orphans, AIDS education in the schools, human rights, treatment and care, research

ethics and as well as ensuring that all stakeholders would work toward a common goal to achieve the objectives of reducing the effects of HIV/AIDS on the individual, family, and the community at large (GAC, 2004).

1.3 Clinical Diagnosis and Recommended Treatment

Usually, HIV infection includes a long period (approximately 10 years) of clinical latency, between the time of primary infection or sere-conversion and the development of symptoms indicative of immunodeficiency. In the acute and early stages of the disease, there are some "flu-like" and "mononucleosis-like" illnesses such as fever, rash, pharyngitis, nausea, diarrhoea, and weight loss often referred to as opportunistic infections etc [Xingjian, 2007]. The clinical biomarkers used in predicting the HIV status of an individual among others include:

- The depletion of the $CD4^+$ T-cell lymphocytes and
- The plasma HIV-RNA viral load

When the CD4+ T-cell count falls below 500copies per micro litre *(*500/**µl***)*, the individual is said to be a carrier of HN. However, when the $CD4^+$ T-cell count falls below 200copies/µl, cellular immune responses are tremendously suppressed and thus, the individual is said to have developed AIDS (Ibid)

The RNA-plasma viral load measures the amount of human immunodeficiency virus in the blood. An initial measurement of the RNA-plasma viral load of a patient is used as a baseline for subsequent measurements. If the viral load shows a steady increase over several measurements, it gives an indication that the infection is getting worse and vice versa [Masur, et *al*, 1989].

Highly active anti-retroviral therapy (HAART) is a single or combination of several drugs. It has received much international publicity in suppressing or inhibiting the replication of HIV-RNA at different stages of the HIV life-cycle. HAART involves taking three or more drugs that fight HIV at the same time. HAART can strengthen the immune system and reduce the amount of HIV in the blood. Many medicines are available, and no one combination is best for everyone. Not everyone with HIV needs

HAART. Usually, it is started only when signs of immune system damage or symptoms of HIV appear.

Drugs that fight HIV are divided into several classes or types. The different classes of drugs are used in combination to strengthen the immune system and reduce the amount of HIV in the blood of a patient. Each class of drugs affects HIV in a different way:

- **NRTIs** (nucleoside and nucleotide reverse transcriptase inhibitors) interrupt the first step that HIV takes to "copy" itself inside a cell.
- **NNRTIs** (non-nucleoside reverse transcriptase inhibitors) also interrupt the first step that HIV takes to "copy" itself, but in a different way than NRTIs.
- **Protease inhibitors** interrupt the last step that HIV takes to copy itself and thus prevents it from multiplying.
- **Entry inhibitors** (including **fusion inhibitors)** stop HIV from entering a healthy cell.

New medicines in each of these drug classes are being developed. New drug classes, which attack HIV in new ways, are also being researched. HIV medicines can be hard to take and often have side effects, some of which are serious and even life threatening. Missing or delaying just a few doses of medicine can lead to the person developing "resistance" to the drugs, which means that the drug will stop working (Ibid).

Opportunistic illnesses such as PCP *(Pneumocystis carinii pneumonia)* and MAC *(Mycobacterium avium complex)* affect people whose immune systems are severely weakened by HIV. However, many of these illnesses can be prevented by taking certain medicines as soon as the immune system becomes weak. Since the immune system can be severely weakened before symptoms appear, it is important for people with HIV to see their doctors so that they can begin preventive treatment as soon as it is needed. A HAART regimen is the most effective way to strengthen the immune system [Fellay, *et al*, 2002].

1.4 Statement of the problem

The current HIV/AIDS status of Ghana stands at an estimated value of 273,000 people with a prevalence rate of 2.9%. This indicates a steady decline since the first incidence of the disease in 1986 [GNA, 2009; NACP/HSS Report, 2009].

The Ghana Demographic Health Statistics (2008) indicates that, HIV/AIDS is prevalent in urban areas, border towns, mining areas and communities where much education about the disease has not reached. It thus indicated a significant regional difference in people living with the disease.

What is explicit in most health records is the estimated number of people living with the disease, the trends of prevalence of the disease, the number of patients under anti-retroviral therapy, age distribution of patients, annual new infections, the ratio of males and females living with HIV/AIDS as well as government's policy direction in combating the spread of the disease. Much however, is not known about the hazard and survival trends of people living with HIV/AIDS under the auspices of these health centres as well as the factors/variables that contribute to these trends.

The inadequacy in HIV/AIDS data presentation, forecasting and knowledge of hazard and survival trends of patients enrolled in our health centres has thus necessitated this research.

1.5 Motivation and Purpose of the study

Since the discovery of the existence of HIV in Ghana in 1986, many interventions were made by the government of Ghana, Non-governmental Organisations and other concern institutions. These interventions were geared towards minimising the spread of the disease. Some of the interventions include:

- creating the awareness of the spread of the disease through education
- prevention of mother to child transmission of the disease
- promotion of voluntary counselling and testing centres
- provision of Anti-retroviral drugs for person's living with HIV/AIDS
- elimination of the public perception about HIV patients (stigmatisation)

The GHS/HSS report (2007, 2008, and 2009) indicates that, there is a marked gender difference in the number of people living with HIV/AIDS with about 58% of the number being female.

Despite the numerous interventions, reports on gender disparity and data on HIV /AIDS in the country, much effort has not been made in determining the gender survival trends of PLWHA. This has thus motivated the researcher to embark on this project. It is therefore hoped that the findings of this project will go a long way to creating the awareness of the trends of gender survival of PLWHA as well as pave the way for appropriate interventions

1.6 Research Questions

The following questions are to serve as benchmarks in formulating research objectives as well as serve as a baseline for analysing and interpreting the data gathered;

- Are there any gender differences in the survival of HIV/AIDS patients in northern region?
- Does the age of a patient during sero-conversion determine significantly the survival of the patient?
- Is sex a prognostic factor in determining the survival trends of HIV/AIDS patients in northern region?
- To what extent does the location (Urban or Rural) of a patient contribute significantly to a patient's survival?

1. 7 Objectives of the study

The typical goal in survival analysis is to characterize the distribution of the survival time for a given population, to compare the survival distributions among different groups, or to study the relationship between the survival time and some concomitant variables. With available data collected from the various HIV sentinel surveillance sites, the research is aimed at;

- Describing the survival and hazard trends of males and females living with HIV/AIDS in Northern Region.
- Determine the relationship of a patient's age to survival time.

- Determine the hazard rates in the stages of infection
- Determine the mean and variance of survival time of patients

1.8 Rationale of the study

It is hoped that this research will go a long way to enrich the knowledge about the trends and status of people living with HIV/AIDS in Northern Region as well as predict future trends of the virus that will go a long way in directing policy decisions in the region and the country as a whole.

1.9 Delimitation

The research is unable to capture all patients in the region that has the virus. This is because the data available captures only those who reported to hospitals, clinics, voluntary counselling and testing (VCT), and sentinel surveillance centres.

Time of origin has always been a hindrance to many health researchers. It describes the various points of entry of subjects into a study. Many are thus of the view that a patient's infection time is the first case of the diagnosis of the presence of the infection [Allison, 2008]. This will thus not affect the research since it is a retrospective study.

It is also worthy to mention, however, that the results of this research may be hindered in the absence of appropriate data and data collection methods.

1.10.1 HIV/AIDS

According to the Centre for Disease Control and Prevention (2000), a person is said to have the Human Immune Virus (HIV) if the person's $CD4^+$ T-cell count is less than 500copies/µl. People with HIV infection thus has AIDS when the person's $CD4^+$ T-cell count falls below 200copies/µl and in addition, develop any of the specific AIDS defining conditions such as loss of weight, skin infection and any opportunistic disease such as Tuberculosis, Syphilis etc.

1.10.2 Survivor Function S (t):

Let T to be a random variable describing an individual survival time and let to be any specific value of interest of the variable T. The cumulative distribution function

(c.m.f), F (t) of variable T is defined as the probability that the random variable T be less than or equal to a given value t. That is,

F (t) =P, (T≤ t) ..... Equation 1

In survival analysis, we are interested in two functions defined as survivor function S (t) and hazard function h (t). The survivor function **S (t) =P_r {T >t}**

= 1- F (t) ..... Equation 2

Survivor function, S (t) indicates the probability that an individual survives longer than some specified time t, as t ranges from 0 to 1. The survivor function has the following properties;

- It is non-increasing
- At time t = 0, S (t) = 1. In other words, the probability of surviving past time 0 is 1.
- At time t = 1, S (t) = S (l) = 0. As time goes to infinity, the survival curve goes to 0.

1.10.3 Hazard Function h (t):

The probability that an individual will die at a certain time t, conditioned on his/her survival up to the specified time

$$h(t) = \lim_{\delta t \to 0} \frac{\Pr(t \le T < t+\delta t / T \ge t)}{\delta t} \quad \text{.....Equation 3}$$

The cumulative hazard describes the accumulated risk up to time t, and is given as

$$H(t) = \int_0^t h(u)\delta u \quad \text{.....Equation 4}$$

$$\text{If } f(t) = \lim_{\delta t \to 0} \frac{\Pr(t \le T < t+\delta t)}{\delta t} \quad \text{.....Equation 5}$$

is a probability distribution function (p.d.f), the hazard and survivor functions can simply be expressed as

$$h(t) = \frac{f(t)}{S(t)} = -\left[\frac{d}{dt} \log S(t)\right] \quad \text{.....} \quad \text{Equation 6}$$

Integrating both sides of equation 6 gives an expression for the survivor function in terms of the hazard function

$$S(t) = \exp[-H(t)]$$

$$= \exp\left[-\int_0^t h(u)\delta u\right] \quad \text{.....} \quad \text{Equation 7}$$

1.10.4 Time of Origin:

In clinical research, it is referred to as the time of first diagnosis of an infection. Hence, the time of origin adopted for this research is the first time a patient is sero-converted

1.10.5 Censoring:

The occurrence of an event during observation of a sample of interest, before or after a specified time period. There are generally three reasons why censoring might occur:

- A subject does not experience the event before the study ends
- A person is lost to follow-up during the study period
- A person withdraws from the study.

The censoring type considered in this research is right censoring. Here, the period of observation expires, or an individual is removed from the study, before the event occurs. For example, some individuals may still be alive at the end of a clinical trial, or may drop out of the study for various reasons other than death prior to its termination (Allison, P. 2008)

CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

Acquired Immunodeficiency Syndrome (AIDS) and the Human Immune Virus (HIV) has puzzled many scientists ever since the illness first came to light in the early 1980's. For over twenty years, it has been the subject of fierce debate and the cause of countless arguments, with everything from a chimpanzee and a hunter, a promiscuous flight attendant to a suspect vaccine [Cohen, 2000]

Much was not known of this disease in the 1970's until the early part of 1980. Mann (1989) maintains that, the dominant features of this first period of the disease were silent and transmission was not accompanied by signs or symptoms. While rare sporadic case reports of AIDS and sero-archaeological studies documented human infections with the disease prior to 1970. He adds that, the pandemic started in the mid to late 1970s and by 1980, the disease had spread to at least America, Europe and Africa.

In the early part of 1981, a rare form of a relatively benign cancer known as *Kaposi Sarcoma* (KS) tended to occur in older people and by March, 1981 at least eight cases of a more aggressive form of KS had occurred amongst young gay men in New York.

About the same time, a number of cases of a rare lung infection known as *Pneumocystis Carinii Pneumonia* (PCP) had occurred in California and Los Angeles. This prompted the Centre for Disease Control (CDC) to publish a report about the occurrence, without identifiable causes of PCP and other rare life threatening opportunistic infections. This, however, marks the beginning of the awareness of HIV/AIDS in the United States of America [Dubois, *et al*, 1987]. Because there was little knowledge about the transmission of what seem to be a new disease, there was much concern about contagion and whether the disease could be passed on by people who had no apparent signs or symptoms. Knowledge about the disease was changing so quickly that certain assumptions made at this time were shown to be unfounded. For

example, in July 1981, Dr. Curran of the CDC was reported to have said, “There is no apparent danger to non-homosexuals from contagion, since no case has been reported outside the homosexual community or in women.” However, in December, 1981 it was clear that the disease affected other population groups [Moore, 1999].

By the first quarter of 1982, the disease still did not have a name, with different groups referring to it in different ways. The CDC generally referred to it by reference to the diseases that were occurring. For example, *Lymphadenopathy* (swollen glands), *Kaposi Sarcoma Opportunistic Infection* (KSOI). In contrast, some linked the disease to its initial occurrence in gay men. For example, Gay Compromise Syndrome (GCS), Gay related immune deficiency (GRID), gay cancer or community acquired immune dysfunction and many more [Henrad, 1995].

In June 1982, the CDC reported that the disease was occurring in non--homosexual Haitians and Haemophiliacs. This thus led to the speculation that the disease might have its origin in Haiti. Thus, the occurrence of the disease in non-homosexuals meant that, names such as GRID and GCS were redundant. The name Acquired Immune Deficiency Syndrome (AIDS) was thus suggested at a meeting in Washington DC in September, 1982. Many medical practitioners thought AIDS was an appropriate name because; it is acquired than inherited, resulted in a deficiency within the immune system, and a syndrome with a number of manifestations rather than a single disease [Henrad, 1995].

HIV/AIDS was first noticed in Africa in the early part of 1983 when a number of previously healthy African patients who were hospitalised in Belgium with opportunistic infections such as PCP and KS. These African patients had immune deficiency similar to the patients in America even though they had no previous history of blood transfusion, homosexuality or intravenous drug abuse. At this same time, a group of scientists working in parts of Zambia, Tanzania, Cameroun and the Democratic Republic of Congo, had noticed the emergence of a very aggressive form of KS coupled with opportunistic infections similar to that found in the United States of America and Belgium. This was described as *"slim"* disease in Congo, Uganda and Tanzania, *"esophageal candidiasis"* in Rwanda.

By the end of 1986, eighty five countries had reported AIDS cases to the World Health Organisation (WHO): Africa 2323, the Americas 31741, Asia 84, Europe 3858 and Oceania 3959 [WHO report, 2000].

2.1 Theories on the origin of HIV

The discovery of the origin of HIV was made soon after the discovery of the existence of AIDS. Many scientists were initially resistant to acknowledge that HIV causes AIDS. According to Grmek (1990), the how, when and where HIV first began to cause the disease in humans is bedeviled with many theories.

According to Henrad (1995), HIV is a Lentivirus (slow virus) and thus takes a long time to produce any adverse effects in the body (Lentiviruses forms a larger group of viruses called Retroviruses). They are found in a number of different animals including Cats, Sheep, Horses, and Monkeys etc. However, the investigation into the origin of HIV indicates that HIV is a descendant of a Simian Immunodeficiency Virus (SIV) found in the Sooty Mangabey Monkey (SMM) and the African chimpanzee (chimps). SIV is then believed to have crossed over to human as HIV through viral transfer (mutation).

2.1.1 The Hunter Theory

Simian Immunodeficiency Virus (SIVcpz) was transferred to humans as a result of chimps being killed and eaten or their blood getting into wounds on the hunter. It is believed that the hunter's body would have fought off the SIV, but on a few occasions, it adapted itself within its new human host as HIV (Science, 2003)

The Lancet journal (July, 2004) maintains that retroviral transfer from primates to human beings is still occurring even today. It stated that, of a sample of 1099 individuals taken in Cameroun, it was observed that about 10% were infected with Simian Foamy Virus (SFV); an ailment with similar characteristics to SIV cpz which was previously thought by scientists to infect only primates.

2.1.2 The Oral Polio Vaccine Theory (OPV)

This theory contends that polio vaccines played a role in the transfer of HIV. Blancou *et al* [Science, 2002] are of the opinion that the origin of HIV can be traced to the testing of a polio vaccine *Chat* given to people in Congo (DR), Rwanda and Burundi in the early 1950's. They emphasised that, to reproduce, live polio vaccine needs to be cultivated in a living tissue and so *Chat* was grown in the kidney cells taken from local chimps infected with SIV. It is thus clear that this theory takes its basis from the hunter theory.

2.1.3 The Contaminated Needle Theory

This theory suggests that health professionals working on inoculation and other medical programmes in Africa in the early 1950's used unsterilized syringes due to cost and the huge quantities of syringes needed for the inoculation. It is therefore likely that a single syringe would have been used to inject multiple patients without any sterilisation in between. This would rapidly have transferred any viral particles from one person to another, creating a huge potential for the virus to mutate and replicate in each new individual it entered, even if the SIV within the original person infected had not yet converted to HIV [Chitnis, *et al,* 2000].

2.1.4 The Conspiracy Theory

William Cooper (1991), a high ranking naval officer of the United States of America (USA), beliefs that HIV is man-made. He holds that the virus was spread deliberately or inadvertently. The theory is of the opinion that HIV was manufactured as part of a biological warfare programme, designed to wipe out large numbers of blacks and homosexuals in America, Africa and Asia through the small pox inoculation under the auspices of the United States Federal special cancer virus programme [Klonoff and Landrine, 1999].

2.1.5 The Colonialism Theory

This theory proposed by Moore (2000), an American specialist in primate behaviour is also known as *"Heart of Darkness"* theory. Its arguments are based on the Hunter and Contaminated Needle theories. He holds that, in the late 19th century, much of Africa was ruled by colonial forces. Colonial rule in French Equatorial Africa and

Belgian Congo (DR) was particularly harsh. Many Africans were forced into labour camps where sanitation was poor, food and physical demands extreme. With these poor health factors, SIV could easily have infiltrated the labour camps and taken advantage of their weakened immune systems to become HIV. He emphasized that a stray and perhaps sick chimpanzee with SIV would have made a welcome meal for the workers. He believes that many of the labourers would have been inoculated with unsterilized needles against diseases such as small pox and the virus could be passed on to uninfected individuals.

Despite these and many other theories about the origin of HIV, it still remains uncertain who the first infected person is, his/her race and exact place of origin. However, much research has indicated that HIV came into existence due to the mutation of the Simian Immunodeficiency Virus (SIVcpz) from a chimpanzee believed to be from central Africa. With this assertion, the Hunter theory thus has more scientific basis than the rest of the theories [Connor and Kingman, 1988].

2.2 Statistical Techniques related to HIV/AIDS

Since the advent of HIV in the early 1980's, many attempts has been made in the study of the pandemic in an attempt to predict future trends of the disease and its related effects on the human kind. In this light, several techniques were implored by researchers in the process of data collection, presentation and analysis of the trends of the pandemic.

2.2.1 HIV incidence using cross-sectional surveys

Prevalence and incidence are two most important indicators of the state of an epidemic. According to Brookmeyer and Quinn (1995), the prevalence of a disease is the proportion of a population that has contracted an infection, while incidence is a measure of the risk of uninfected individuals contracting the disease. The incidence of a disease is usually expressed as a rate [i.e. the proportion of the at-risk (uninfected) population that become infected per unit time]. Prevalence on the other hand, measures only the proportion of infected individuals sampled directly in the population of interest.

2.2.2 Measuring the incidence of HIV in a cohort study

The most common way in which the incidence of the disease is measured is by follow-up of an initially uninfected cohort. Over the duration of surveillance, individuals in the cohort are regularly tested, and incidence is estimated as the number of new infection events observed divided by the number of person-years of observation. The incidence estimated in this way is effectively an average incidence over the duration of the survey.

Unfortunately, such longitudinal surveillance is expensive, logistically complex and prone to biases. These biases include the fact that certain individuals become unavailable for follow-up, which may be correlated with risky behaviour (Janssen et al 1998).

2.2.3 Measuring HIV incidence in a cross-sectional survey

This technique identifies the number of individuals infected with the disease. Incidence is then calculated by inverting the well-known epidemiological relationship that prevalence is equal to incidence multiplied by the duration of infection (Mc Walter *et al*, 2009). In their view, incidence can be calculated by dividing prevalence by the average duration of infection (given that an accurate estimate of the mean duration is available). The incidence of the disease measured in this manner is thus effectively an average of the incidence over a historical period with length approximately equal to the duration of the infection (McDougal et al, 2006).

2.2.4 Measuring HIV incidence using biomarkers - The Serologieal Test Algorithm for Recent HIV Sero-conversion (STARHS)

The Serological Testing Algorithm for Recent HIV Sero-conversion (STARHS) holds that, HIV has a long asymptomatic phase before the onset of immune failure and AIDS. This means that HIV infections last for many years and may not be diagnosed until long after the infection event (Brookmeyer and Quinn, 1995; Mc Walter and Welte, 2009).

In the mid 1990s, however, a novel way of using cross-sectional surveys to estimate HIV incidence was to observe a biological marker (also known as a biomarker) indicating an immune system response to early infection and classify individuals as

either recently infected or non-recently infected. An incidence estimate is computed in the same way as in section 2.2.2 with one slight difference; the prevalence of recently infected individuals must be determined in the sub-population of the cross-section that excludes those that are non-recently infected (Janssen et al, 1998).

Brookmeyer and Quinn, the proponents of the biomarker-based approach in HIV monitoring, used a large sample of a *p24* antigen (an antigen present in the HIV protein shell) in a blood sample prior to HIV antibody production using the immune system (sere-conversion) as an indication of recent infection.

Similarly, Janssen *et al* (1998) proposed a method based on the increase of a serological response (in particular, they used 'detuned' assays to detect recently infected individuals). Depending on how the assays are applied, the mean window period for this approach is longer (between 100 and 200 days), facilitating better precision in the incidence estimates. This approach later became known as the Serological Testing Algorithm for Recent HIV Sero-conversion (STARHS).

The use of detuned assays however, did not prove reliable due to the variability in immune response due to subtype diversity. In order to improve biomarker characteristics, a number of other assays that test for recent HIV infection have been developed, including the much used BED assay, which is a capture enzyme immunoassay (CEIA) based on protein sequences from the B, E and D HIV subtypes (Parekh *et al*, 2002).

2.3 Gender Differences in Perception of HIV Risk

Zoë, *et al* (2002) examines the gender differentials in perceptions of HIV risk in Ghana and Uganda. They identified factors associated with high or low risk of HIV infection by using logistic regression methodology. Demographic and Health Survey (DHS) data containing information on perception of risk and sexual behaviour of HIV risk were taken from both countries. In addition, this survey also collected information on knowledge and attitudes on perception of risk and sexual behaviour. Logistic regression was used to analyse the perception of risk of HIV infection. In this application, the high reported risk of HIV was modelled for Uganda and Ghana separately. Separate models were also estimated for women and men, and these models were compared to the one in which both sexes were combined in order to see if there

were significant gender differences in the odds ratios. Principal findings include strong gender differentials in perceptions of risk, especially in Uganda; women felt at greater risk of HIV infection than men. In addition, strong power relationships exist as women felt at risk of HIV infection because of their partner's sexual behaviour, whereas the men's risk perception was related to their own behaviour.

This illustrates the subordinate position of women within sexual relationships as well as the need to empower women to enable them to negotiate safe-sex strategies. Individual knowledge exposure and sexual exposure factors were highly associated with perception of risk in Uganda whereas individual background characteristics were more influential in Ghana. Perceptions should therefore be influenced not just by objective circumstances, but by media campaigns that provide information and, societal views, and norms that mediate their impact (Shrader and Frechette, 1990). Other studies argue that perception is socially constructed, in that, social experiences influence the way in which people perceive superficially identical risks (Cross, 1992).

2.4 Managing HIV Spread using Time Series Analysis

To manage the spread of HIV in Ghana, a number of control measures have been introduced to reduce the number of incidence cases. The impact of these control measures has been assessed through the number of cases reported, descriptive statistics and graphical presentations (NACP/GHS/MOH, 2008).

Aboagye-Sarfo, *et al* (2009) considers three major control measures to limit the number of HIV cases using intervention analysis introduced by Box and Tiao (1975). These interventions include: the introduction of the female condom, the establishment of Ghana AIDS Commission by law (Act 613) to provide management and leadership of the HIV/AIDS epidemic, and the introduction of Voluntary Counselling and Testing as well as Prevention of Mother-to-Child Transmission (VCT/PMTC). One hundred and forty-four (144) consecutive monthly observations of sero-positive HIV cases were taken from the National AIDS Control Program and Biostatics Department in the ten (10) regions from 1996 to 2007. They observed in their pre-intervention analysis that HIV cases follow an integrated auto regression moving average models, *ARIMA (5, 1, 1)* in the northern and southern sectors of the country and as well suggest that the introduction of VCT/PMTCT caused the cases of HIV infection in the northern sector to

significantly reduce by a factor of 2.3%. This means that people who tested negative took steps to protect themselves from being infected and those tested positive avoided infecting others. The introductions of the female condom and the legislation have no impact in the reduction of the epidemic in the sector. The effect of the interventions on the various age groups cases in the northern sector reveals no different pattern as the VCT/PMTCT is the only intervention to have significantly impacted on persons of 30-39 years with negligible effect on the 60± years. On the other hand, the introduction of the female condom and the legislation have impacted on the number of cases of HIV infection in the southern sector, causing it to reduce by factors of 0.86% and 0.88% respectively. The female condom was observed to have resulted in the significant reduction in the new cases of the epidemic of people aged 15-59 years in the southern sector whereas the legislation was found to have impacted on persons aged 20-59 years.

2.5 Some approaches to HIV /AIDS using Survival Analysis

It is estimated that survival following HIV infection in adults is around ten years in all countries, irrespective of income (Morgan, *et al* 2002). Todd, *et al* (2006) used a dataset from a population-based cohort in rural Uganda to estimate the median survival among adults following HIV sero-conversion and to assess several risk factors, KaplanMeier functions were used to estimate survival patterns, and Weibull distributions to compare survival estimates. In this cohort, survival times varied by age, but not sex. The median survival was 9.6 years (95% CI 8.2-10.2). For those infected between 15 and 24 years of age, median survival was over 13 years, while in those infected at 45 years or more, median survival was under 6 years. There were no significant differences in survival by sex, tribe, religion, marital status, or sexual behaviour. They concluded that, survival is largely independent of social and environmental factors and thus reinforces the importance of universal access to antiretroviral therapy in order to extend survival of infected individuals.

This research, however, did not take into consideration the various stages of infection of the disease in analysing the mean survival time for the various age groups.

In the words of Spiegel et al (1989), "lifestyles and social support are related to survival with other life-threatening conditions such as cancer, tuberculosis". With HIV, perceptions of social support and stressful life events have been related to disease

progression, particularly end-stage disease (Patterson, *et al.* 1996; Leserman, *et al*, 1997). As the proportion of women infected with HIV continues to grow, the impact of parents' lifestyle (substance use and sexual behaviour) and social networks (e.g., their families, including children and partners) must be examined. Mothers are much more likely than fathers to be infected through heterosexual transmission, (USAIDS, 2000) typically through partners who are injecting drug users. Fathers living with HIV were often infected through injection drug use or are bisexual. Substance use may influence the survival of parents with HIV in several ways: those who are using drugs may be less adherent to medical regimens and medications, leading to an early death, or they may overdose and die early. Substances may also directly influence physical health. Thus, substance use is expected to be associated with decreased survival among parents (Lightfoot, *et al*, 2000).

In many developing countries, despite that anti-retroviral drugs has been subsidised by the governments of these countries access to these drugs has been a problem to patients (UNAIDS/WHO, 2007) Duncan *et al* (2007) indicated that patients with low income levels were more likely to be lost-to-follow-up. In their research, a retrospective chart review was performed on a data obtained from a registry of ninety-three patients attending self-pay clinic at the All India Institute of Medical Sciences (AIIMS) in Delhi. Multivariate Cox proportional hazard and logistic regression models were implored to assess the relationship between lost-to-follow-up status of the patients and the variables; age, sex, income, baseline $CD4^+$ T-cell count, and the distance from the clinic. It was realised that lost-to-follow-up rates were very high; 68% (63/93) were lost-to-follow-up. In the two models, younger age, low baseline $CD4^+$ T-cell count, and low income levels were significantly associated with increased risk of lost-to-follow-up. Additionally, there was a significant interaction between income and $CD4^+$ T-cell counts. In conclusion, they emphasised that, the model of health care delivery undertaken at that time was least effective for the most sick and poor patients.

The research, however, did not indicate the number of patients that survived or dead after the given period of study. Similarly, the researchers did not indicate the gender differences in survival and hazard functions since there could be gender differences in age, $CD4^+$ T-cell count and more particular income levels.

It is worthy to mention that, since this research was conducted in India there are all possibilities that there could be a significant difference if it was conducted elsewhere.

2.5.1 Socio-demographic and Psychosocial factors in HIV survival

Lee and Rotheram (2001) examined the socio-demographic and psychosocial factors that predict survival among people living with HIV. Survival was monitored among the sample (307), (81% mothers; 45% Latino, 34% African American). Over a median period of 28 months (range= 0-53 months), 44% (n = 135) of the parents died. Having an AIDS diagnosis and being African American were associated with earlier death. Sex, age, and financial status were not related to survival. Parents who survived had initially higher levels of anxiety that decreased over time; in contrast, parents who died reported initially lower, but constant, levels of anxiety over time. After HIV diagnostic status was controlled for, it was found that parents who reported having more children, using a coping style of seeking social support, and being sexually active at baseline survived longer.

These counter-intuitive findings raise hypotheses regarding the role of change and responsibilities in the survival of parents with HIV. The research, however, did not make any gender survival comparison of patients. It also did not consider variables such *as* the age of the patient during sero-conversion, the various stages of the HIV infection.

According to Mocroft *et al* (1996) factors found to predict survival in men also predict survival in women; for example, physical health status predicts survival in both men and women. In particular, a high $CD4^+$ T-cell count appears to be the best correlate of increased survival, and older age at diagnosis is linked to an earlier death.

Survival after diagnosis of acquired immunodeficiency syndrome (AIDS) have reported variation in temporal trends in association with age, gender, race, mode of transmission, lymphadenopathy, antiretroviral therapy, and presence of specific opportunistic infections at diagnosis (Hanson, *et al* 1993). A retrospective study carried out by Iatrakis et al (1994) analysed the survival of women diagnosed with AIDS from the beginning of 1990 until the end of 1992 in three major referral centres in London. The data were compared with a matched control group of male patients. Forty one

women were diagnosed with AIDS in three units; Jefferies wing, St Stephens Clinic and Charing Cross Hospital, London during the study period. Information regarding age at AIDS diagnosis, mode of transmission, ethnic origin, $CD4^+$ T-cell lymphocyte count at AIDS diagnosis, the AIDS defining diagnosis and the use of antiretroviral therapy and *Pneumocystis carinii pneumonia* (PCP) prophylaxis were recorded on a standardised information collection sheet .. The control group of men was matched for year of AIDS diagnosis, age and $CD4^+$ T-cell lymphocyte cell count. The data collected were analysed using Kaplan-Meier curves and the log-rank test. The mean age of the women and men was 33.4 yearrs and 35.6 years respectively. Thirteen women and seven men (not taking into account the patients with PCP at initial diagnosis) had PCP prophylaxis and 27 women and 22 men had AZT at some stage after AIDS diagnosis. There was no difference in survival between the two groups (Log-rank test: $x^2 = 0.15$, $p = 0.6949$).

2.5.2 Gender survival of HIV patients and the introduction of ART

In an earlier research conducted in the United States of America on *Survival for women and men with AIDS,* Lemp *et al* (1992) attributed a difference in survival between these two groups to factors such as age, initial diagnosis, antiretroviral therapy, $CD4^+$ T-cell lymphocyte count at initial diagnosis, and the use of health care resources.

Opportunistic infections (OIs) are common causes of death in HIV-infected patients in most developing countries (Holmes, *et al* 2003). The introduction of antiretroviral therapy (ART) has proven to reduce the incidence of opportunistic infections for patients with access to care. However, opportunistic infections still continue to cause substantial morbidity and mortality in patients with HIV infection in many third world countries (Mirza *et al,* 2003). Suthat *et al* (2007) conducted a retrospective cohort study into the survival time and risk factors of mortality among HIV-infected patients who had *cryptococcal meningitis* between January 2002 and December 2004 by reviewing five hundred and forty nine patients' medical records of those who had HIV-infection with newly diagnosed *cryptoccocal meningitis* in Bamrasnaradura Infectious Thailand. Each patient was classified into two groups during the follow-up period: received antiretroviral therapy (ART group) and did not receive antiretroviral therapy (ART group). A patient who was eligible to ART group defined as a patient who received antiretroviral therapy for at least two visits. The primary

outcome of interest was duration of time from diagnosed *cryptoccocal meningitis* to death. Patients were censored at the date of last visit if they were lost to follow-up or censored at the date of referral. The last event responsible for the patients' death was defined as the cause of death. Patients' baseline characteristics were described by descriptive statistics. Continuous variables were described by mean ± SD (standard deviation). Categorical variables were described by proportion and percentage. Survival time after *cryptococcal meningitis* was treated as a continuous variable. Due to distribution free survival time with unknown baseline hazard ratio, the Kaplan-Meier method for survival analysis was used. For variables that had more than one group, Log rank test was used for comparison.The research indicated that, the possibility of survival time after being diagnosed with *cryptococcal meningitis* estimated by the Kaplan-Meier survival analysis shows that patients who did not receive ART had higher chance to die of *cryptococcal meningitis* compared to patients who received ART.

It is evident, here that, the researchers did not make any gender comparison of the survival trends of the patients infected with the opportunistic disease (*cryptococcal meningitis).* In addition, the research did not state the HIV status of the patients under as well as the ages of the patients.

Isingo *et al* (2007) holds that survival patterns after HIV infection in African populations in the era before antiretroviral therapy (ART) form an important baseline for measuring future successes of treatment programmes. Few studies have followed sero-converters for ten or more years to describe such patterns.

In a related study in Kisesa, Tanzania, four rounds of village-based HIV testing and twenty rounds of household-based demographic surveillance on three hundred and sixty-nine HIV patients were conducted between 1994 and 2006. Approximate infection dates were established for individual sero-converters by allocating a date between the last negative and first positive test. Person-years lived post-infection were computed, allowing for left truncation and right censoring, and Kaplan-Meier survival functions were constructed, truncating the analysis at the start of 2005 when ART first became available in the community. Weibull models were fitted to estimate median survival time, and parametric regression methods were used to investigate the influence of sex and age at infection. The Kaplan-Meier function showed 67% surviving 9 years post-

infection, and the overall predicted median survival was 11.5 years. Survival was strongly related to age at infection (hazard ratio 1.06 for each additional year of age, and weakly to sex. A strong effect of age was evident even after allowing for mortality from non-HIV-related causes using cause deletion methods to estimate net mortality.

The researchers are therefore of the view that, the survival of HIV-infected individuals was comparable to that reported in developed country studies before the introduction of HAART and that Survival patterns in Kisesa are marginally more favourable than those reported in cohort studies in Uganda. They however, did not indicate the factors that might contributed to these favourable trends.

Considering the strengths and weaknesses of the various methodologies, statistics implored, and statistical tools implored in the various research works, it provides a benchmark for a careful selection of appropriate methodology and a good statistical tool for the analysis.

CHAPTER THREE

METHODOLOGY

3.0 Introduction

This chapter discusses the research methodology used in carrying out this project. It provides a brief description of the research area. The chapter provides a framework that informs the sources from which data was collected. It discusses the population, sample and sampling procedure, data management, data analysis and the Cox proportional hazard model that is implored by the SAS PHREG procedure to determine the maximum likelihood estimates of the explanatory variables.

The PHREG procedure, often referred to as Cox regression is a semi-parametric procedure that enables the estimation of the coefficients of the explanatory variables (8) of the proportional hazards model without having to specify a distribution or the baseline hazard function λo (t)

3.1 Brief Profile of the study area

This research work was conducted in the Northern Region of Ghana, which represents one of the ten administrative regions of the country (Figure 1). The region is made up of 20 administrative districts comprising; 1 Metropolis, 1 Municipality and 18 districts. Tamale, the capital of the region, is the country's fourth largest city as well as the largest amongst the three northern regions and as such serves as the nerve centre for all commercial activities in the whole of the three northern regions.

Tamale, the capital town of northern region is an incredible juxta-position of the ancient and modem; the traditional architecture of round huts with conical thatched roofs, smock as traditional attire accompanying a rich traditional festival (Damba) coupled with its slave routes and markets serves as a tourist destination.

3.1.1 Landmass and Boarders of northern region

The region covers about a third of the total land mass of Ghana (70,390km). It lies within the Guinea Savannah Agro-Ecological Zone and forms part of the Volta Basin, and lies between latitudes 8^0 30’ N and longitude 2^0 30’W and 0^0 00’W. The region is bounded on the north by the Upper East and Upper West regions,

on the west by Cote D'Ivoire and on the east by Togo. The regions on the south are the Brong Ahafo and Volta regions.

Its geographical features are mostly low lying, except in the north eastern comer with the Gambaga escarpment and the Black Volta along the western corridor. The land is drained by the tributaries of the Volta Lake: Rivers Nasia, Daka, Oti, the Black and White Volta.

3.1.2 Population and Major Ethnic Groups

The population of the study area is about 1.7 million and represents 9.6 % of the entire population of Ghana (Ghana Statistical Service, 2002). The main ethnic groups are Dagomba, Nanumba, Mamprusi, Gonja and Konkomba. Other smaller groups include Chekosis, Bimobas, Basaares and the Vagla.

3.1.3 Prevalence of HIV in Northern Region

The region has seven HSS centres (Adibo, Bole, Tamale, Yendi, Damongo, Nalerigu and Salaga) recording a total of 564 people living with HIV/AIDS with a prevalent rate of 2.0% (2009) an increase of 0.9% over the previous year (GHS/HSS, 2009). These centres are cited in the major health centres in the region and accessible to the districts closer to them. This is to insure that the region keeps track of the HIV cases as well as implement and monitor the health policies of the country.

Figure 1: Map of Northern Region showing the twenty districts

Curled from; *http://www.ghanaexpeditions.com/regions/region_detail.asp*

3.2 Data source

Data for the research was taken from all the new seven HIV sentinel surveillance (HSS) centres in the region. These centres include: Adibo, Bole, Damongo, Nalerigu, Salaga, Tamale and Yendi as shown in figure 1. For easy handling of the data collected, these sentinel surveillance centres are categorized into urban and rural zones. This categorization is based on the HIV sentinel surveillance format for collecting data (GHS/NACP/HSS, 2006-2009). The northern regional office of the national aids commission (NAC) was consulted to ascertain the government's policy direction in combating HIV/AIDS and sexually transmitted diseases and to ascertain the extent to which these policies were implemented. Notable among other policies include:

- Increased acess to anti-retroviral drugs
- Prevention of mother to child transmission (MTCT)
- Creating awareness of the disease through education

- Elimination of the stigma and promoting the rights and freedom of persons living with the disease
- Promoting the use of the condom.

3.3 Target Population

According to Amedahe (2002), Population is the entire aggregation of cases that meet a designated set of criteria. The target population therefore is the aggregate of cases about which a researcher would make generalisations.

It is common knowledge that a good number of people living with HIV/AIDS has not availed themselves to the appropriate medical centres for treatment probably due to lack of knowledge that these health centres could help them coup with the virus and counselling services to assist them from infecting others, stigmatisation (the fear of losing one's job or friends and relatives), and their inability to cater for medical bills, just to mention a few.

The target population thus considered for the research consist of all people living with HIV (PLWHA) that has reported to the hospitals, clinics, Voluntary Counselling and Testing centres (VCT), and the HIV Sentinel Surveillance (HSS) centres in the region from January 2006 to December 2009. This will make up a total study period of forty eight months (four years). By the World Health Organisation (Dec, 2004) definition of the status of an Individual living with HIV/ AIDS, the target population include all patients at stages II, III and IV that are undergoing anti-retroviral therapy (ART). Stages II, III and IV covers patients whose $CD4^{+}$T-cell count are below 300copies/µl, 200copies/µl and l00cpoies/µl respectively.

3.4 Sample and Sampling Procedure

In research, it is laborious studying the entire population. This thus calls for a scientific selection of a subset of the entire aggregates of a population that is representative (Yin, 1993).

There are currently five hundred and sixty four (564) HIV patients (148 males and 416 females) enrolled in the various sentinel surveillance centres, clinics, hospitals in northern region (NACP/HSS Report, 2009). The sample for this research is taken

from the 2006 cohort group who are in stages II, III and IV of the infection. Considering that about 50% of the cohort has these attributes at a 95% confidence level working with a 5% error of precision., and assuming that the population standard deviation is unknown, the resulting sample size of 90 is calculated using Cochran's formular: $\boldsymbol{n = (Z^2 pq)/ d^2}$. Where *n* is the sample size, *Z* the critical value of the normal distribution curve at 95% confidence level, *d* the margin of error (error of precision), *p* is the probability that patients in the cohort group are at stages II, III and IV of the infection and $\boldsymbol{q = 1-p}$.

The justification of this sample size and cohort group is based on the following reasons;

- This cohort group is chosen based on the fact that proper data keeping of HIV/AIDS cases in the region took effect from November 2005. This is to allow a reasonable time period for the study.
- A good percentage of the patients from each of the seven HSS centres are captured

Patients below ten (10) years are not captured in the study due the fact that they may be infected by their mothers during pregnancy, birth, or breastfeeding and thus have a short survival time. The inclusion of this age group will have an effect on the results of the research (WHO - Priority Interventions, April 2009; Besigin, T. et al, 2007). The table below illustrates the distribution of patients according to the HSS centres.

Table 1: Distribution of patients according to HSS centres

Centre	No. Of Patients	Sample		Total	Percentage of Centre
		Male	Female		
Tamale	73	23	28	51	69.86
Adibo	15	5	9	14	93.33
Salaga	9	3	5	8	88.89
Bole	12	4	7	11	91.67
Nalerigu	4	1	3	4	100.00
Damongo	3	-	2	2	66,67
TOTAL	116	36	54	90	

A retrospective study of the medical files of the ninety patients was conducted with effect from their first sero-conversion status from January 2006 up to December 2009 taking into consideration the different periods of entry into the study. This will enable the researcher obtain the number of patients at risk in each group, the number of patients dead, and the number of patients censored on or before time period t = 48 months.

3.5 Data Collection, Processing and Management

The retrospective data extracted from the medical records of the ninety HIV/AIDS patients is illustrated using tables or charts for the purpose of data analysis. Variables of interest extracted from the medical records of patients who form the sample include; patient's age, sex, CD4+ T-cell (stage), location (zone), number of people at risk at each age level.

Table 1 of the appendices illustrates the data obtained from the regional collation (Tamale Teaching Hospital) and Table 2 of the appendices shows a summary of the observations conducted for the forty eight months. It shows clearly the age groups, gender, status, stage, and the HSS zone classification (location). The age groupings considered include: 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, and 60+ with intervals of 4 years. This short age interval is to ensure that the patient's sero-conversion stages are immediately recognised and placed appropriately. The seven sentinel centres were classified into rural or urban for easy interpretation. These include: Rural (Adibo, Salaga, Yendi Nalerigu Damongo and Bole) and Urban (teaching, central and west hospitals-Tamale).

3.6 Data Analysis

Data analysis involves the ordering and summary of data using statistical tools and techniques into a more comprehensive form for easy interpretation or inference. It consists of the various statistical estimations of the population parameters. The data collected from the medical records of the ninety patients from the various HIV Sentinel Surveillance centres was analysed using SAS Version 9.1 (Cary Institute Inc. North Carolina, USA).

The LIFETEST procedure .was used to compute nonparametric estimates of the survivor functions by the Kaplan-Meier method. This procedure computes nonparametric tests to compare the survival curves of two or more groups. The procedure also computes rank tests of association of the survival time variable with other concomitant (prognostic) variables

Descriptive statistics were implored to determine the number and percentage of patients censored or dead, the distribution of the HIV stages according to sex and age group as well as the number and percentage of patients living in urban or rural areas.

The log-rank and Wilcoxon tests were implored to compare the survival times between the groups as well as check their significance. The p-values of these tests were used to test whether there is any significant gender difference between the survival times of the patients. The mean and standard errors of survival times were determined for both male and female patients. Any significant difference between the two means indicates that one group of patients has a longer survival time than the other.

The Cox's partial likelihood (a semi-parametric survival procedure) test was implored to estimate the coefficients of the parameters and the null hypothesis test (/J=O) used to test the statistical significance of the maximum likelihood estimates. All statistical tests were conducted at a level of significance of 0.05 (95% Confidence interval).

3. 7 The Cox's Proportional Hazard Model

The Cox Proportional Hazard (assuming hazard is constant for all patients) model is a semi parametric model in which the hazard function of the survival time is given by

$$\lambda_i (t, x) = \lambda_0(t)\, e^{\beta_i x_i(t)} \quad \text{..... Equation 4}$$

where $i = 1, 2, \ldots, n$.

Taking the natural logarithm (logs) of both sides of equation 4, we can rewrite the model as

$$log\,\lambda(t) = log\,\lambda_0(t) + \beta_1 x_{i1} + \beta_2 x_{i2} + \ldots + \beta_k x_{ik} \quad \text{..... Equation 5}$$

where $\lambda_0(t)$ is an unspecified baseline hazard function, *x(t)* is a vector of time-dependent covariate values, $\boldsymbol{\beta}$ is a $\boldsymbol{k \; x \; 1}$ vector of unknown regression parameters, and *n* is the number of variables considered in the study. It describes the relationship between the distribution of the survival time and the prognostic factors. The model is referred to as a semi parametric model since part of the model involves the unspecified baseline function over time (which is infinitely dimensional) and the other part involves a finite number of regression parameters. It is robust, easy to incorporate time-dependent covariates, and readily accommodate both discrete and continuous measurements of event times (Collett, 1994; Allison, 2008).

Taking survival time as the dependent variable and age, sex, $CD4^+$ T-cell count (HIV stage), and sentinel zone (location) as independent prognostic factors, and based on the fact that the ratio of the hazards for any two individuals *i* and *j* is constant over time the expected model will assume the form:

$$h(t, x) = e^{(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4)}, \quad \text{..... Equation 7}$$

where the β_i's are estimated coefficients of the regression model such that,

$\beta_0 = \log \lambda_0 (t)$, is the baseline constant for the regression model

x_1 =Age of the patients during first sero-conversion

x_2 = CD4+ T-cell count (WHO defined status since sero-conversion)

x_3 = sex of patient, and

x_4= location of patients (Urban or Rural based on the GHS/HSS classification). These variables in the SAS environment are represented by using dummy variables (1 or 0) except the age of the patients and survival time. The required model for the research is however, dependent on the significance of each of these factors at a level of significance of 0.05.

CHAPTER FOUR

DATA ANALYSIS

4.0 Introduction

This chapter presents vividly the data collected, the analysis of the data and the interpretation or inference of the results by using tables and charts. It consists of a preliminary presentation and analysis of data and a further analysis. The preliminary analysis presents information using descriptive statistics whilst the further analysis presents the maximum likelihood composite estimates of both sexes based on the significance of the global null hypothesis that, all the estimates of the parameters of the model are zero ($\boldsymbol{\beta}=0$)

4.1 Preliminary Analysis

This section analyses data using descriptive statistics. Data is presented using tables and charts. The tables indicates the frequency (counts) of observations as well as percentage occurrence of variables of interest (Age group, status, stage, sex, location, and survival time).

4.1.1 Analysis of Age and Sex distribution

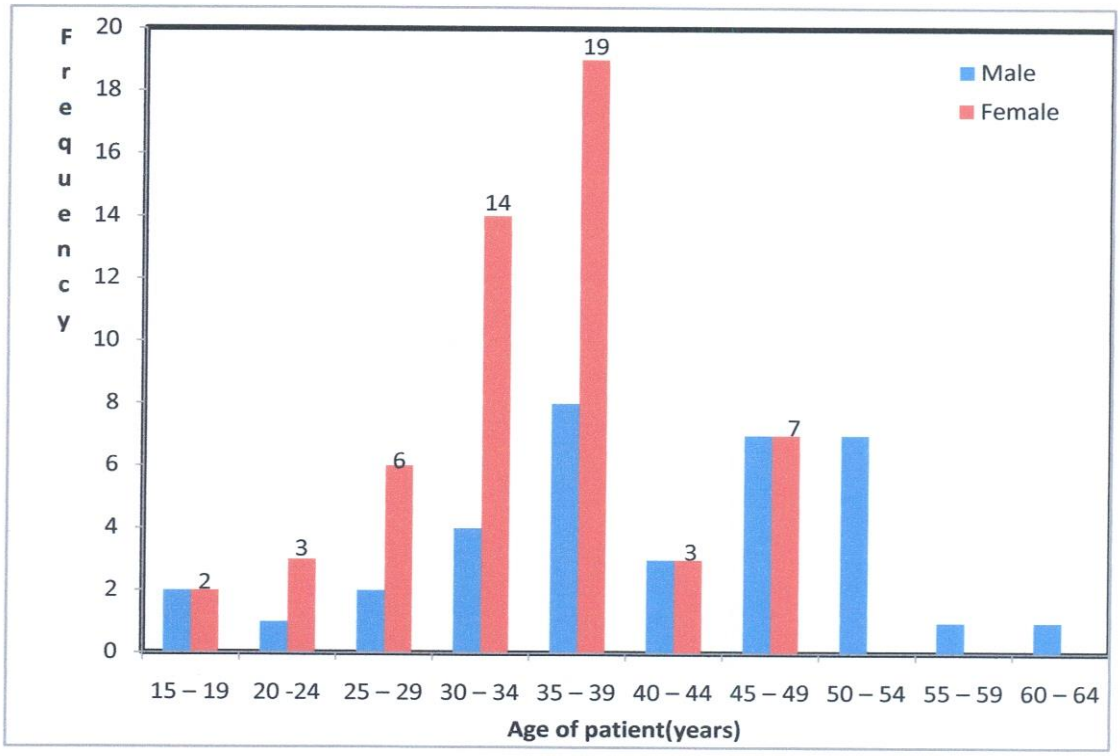
From the sample of ninety HIV patients taken from the 2006 cohort group representing all the seven HIV Sentinel Surveillance centres. Of this, 36 are males and 54 are females representing 40% and 60% respectively. The minimum age recorded is fifteen years and the maximum age is sixty three (63) years. From table 1 below, the age groups between 25 and 49 years has a higher percentage of the HIV infection in the region. This consists of 66.67% and 90.74% of the male and female populations respectively. The age group 30-39 years has the highest concentration of HIV infection for both sexes (12 males and 33 females). This accounts for about 50.0% of the total number of patients enrolled into the study. The table also illustrates that no female between the age group of 50-64 years is infected indicating that 10.0% (9 males) of the study group belongs to that age group. It is thus worthy to note that, the potential working population in the region is the most affected. This could thus have an adverse effect on the human resource of the economy in the medium and long term if frantic

efforts or measures are not taken to curb the trend. This is illustrated clearly by the bar chart in figure 1 below

Table 2: age and sex distribution of patients

Age group	Male	Female	No. Of patients	Percentage
15 – 19	2	2	4	4.44
20 -24	1	3	4	4.44
25 – 29	2	6	8	8.88
30 – 34	4	14	18	20.0
35 – 39	8	19	27	30.0
40 – 44	3	3	6	6.67
45 – 49	7	7	14	15.56
50 – 54	7	0	7	7.78
55 – 59	1	0	1	1.11
60 – 64	1	0	1	1.11
TOTAL	**36**	**54**	**90**	**100**

Figure 2: A Bar Chart showing Patient's Age Distribution



4.1.2 Analysis according to HIV Status and Stages of infection

Table 2 below shows the distribution of the ninety patients according to age group, WHO defined stages of infection (II, III, and IV), and status (censored or uncensored).

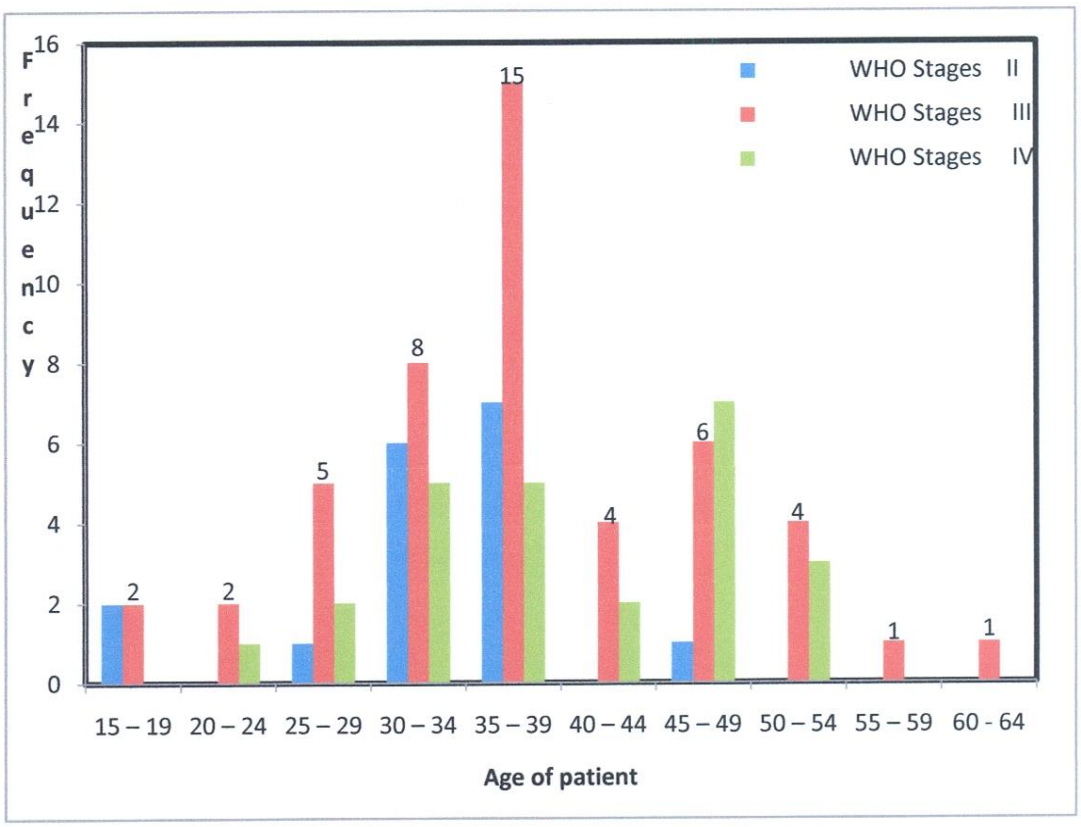
Table 3: Distribution of patients according to Stage and Status

Age group	WHO Stages			Status	
	II	III	IV	Censored	Uncensored
15 – 19	2	2	0	3	1
20 – 24	0	2	1	1	2
25 – 29	1	5	2	3	5
30 – 34	6	8	5	16	3
35 – 39	7	15	5	20	7
40 – 44	0	4	2	6	0
45 – 49	1	6	7	6	8
50 – 54	0	4	3	2	5
55 – 59	0	1	0	1	0
60 - 64	0	1	0	0	1
TOTAL	**17**	**48**	**25**	**58**	**32**

Table 3 above illustrates that, 18.89%, 53.33%, and 27.78% of the patients are in the stages II, III, and IV respectively of the HIV infection as defined by the World Health Organisation (WHO, 2004). This consists of seven males and ten females in stage II, nineteen males and twenty nine females in stage Ill, and ten males and fifteen females in stage IV. This is a clear indication that most of the HIV patients in the region are in stage III of the HIV infection.

Within the forty eight months of observation, 64.44% (58 patients) of the patients were censored and 35.56% (32 patients) deaths. This consists of 61.11% of the female and 69.44% of the male populations. From the bar chart below, it can be seen that most of the patients are classified into stage III of the HIV infection and belonging to the age group between 25 and 49 years as discussed earlier. The survival trends of patients according to their CD4+ T-cell count (stages) is illustrated in figure 4 of the further analysis.

Figure 3: A Bar chart showing the distribution of stages of HIV infection



4.1.3 Analysis of patients according to location (Urban or Rural)

A look at the demographic distribution of patients into either Urban or Rural based on the GHS/HSS report (2007, 2008, and 2009), it is observed that fifty three patients reside in urban areas (Tamale and her suburbs) and thirty seven patients reside in the rural areas (the other six HSS centres). This represents 58.89% and 41.11% of the patients classified as Urban and Rural dwellers respectively.

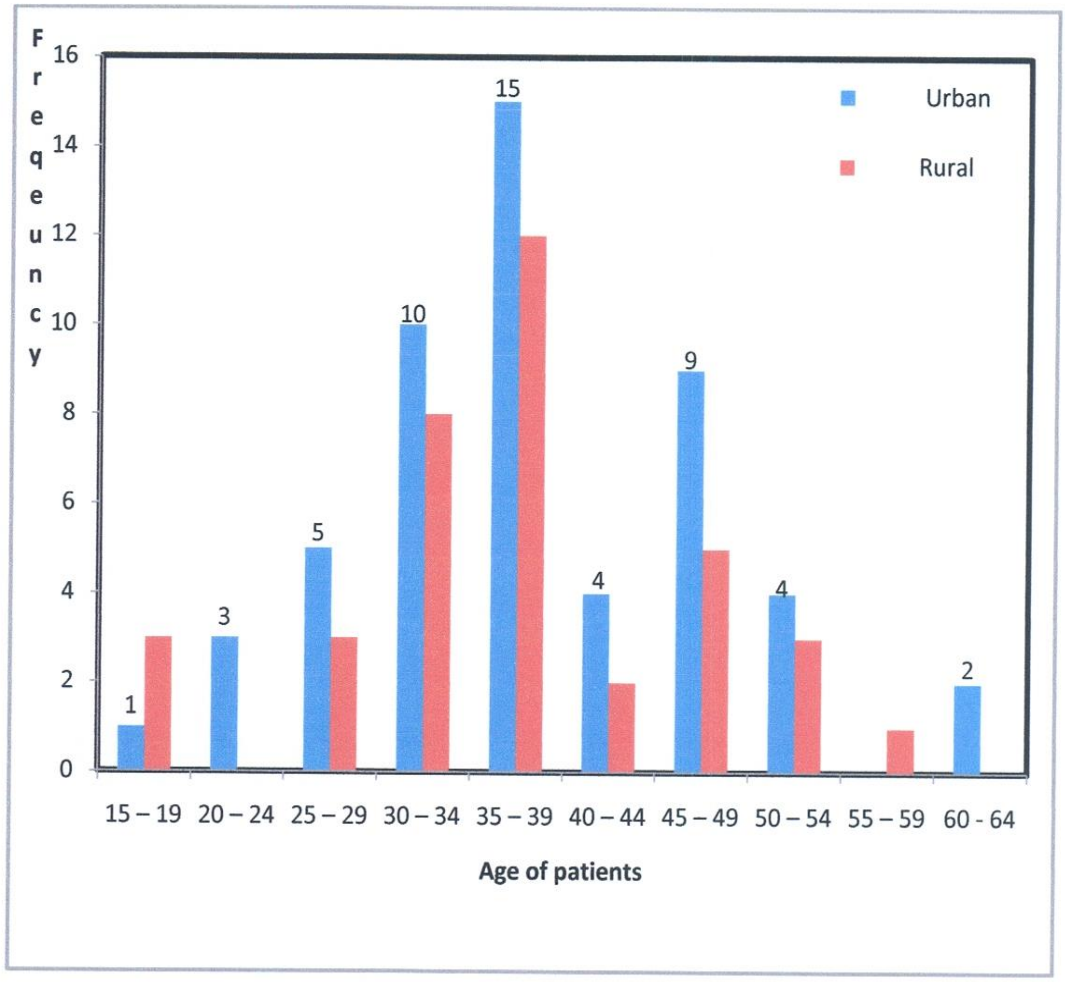
In the potential work group between 25 and 49 years, 41 and 30 patients were identified as urban and rural dwellers respectively. This represents 45.56% and 33.33% of the total number of patients enrolled into the study.

Table 4: Distribution of HIV patients according to location

	Location		
Age group	**Urban**	**Rural**	**Percentage**
15-19	1	3	4.44
20-24	3	0	3.33
25-29	5	3	8.89
30-34	10	8	20.00
35-39	15	12	30.00
40-44	4	2	6.67
45-49	9	5	15.56
50-54	4	3	7.78
55-59	0	1	1.11
60-64	2	0	2.22
TOTAL	53	37	**100%**

The bar chart below (Figure 3) illustrates the distribution of patients according to place of location. It points out facts as stated by the GHS/HSS Report (2007, 2008, and 2009) that, most infected cases are reported in the urban areas.

Figure 4: A bar chart showing the distribution of HIV patients according to location



4.2 Further Analysis

This section of the chapter presents the analysis obtained from the SAS 9.1 procedures (PROC LIFETEST and PROC PHREG).

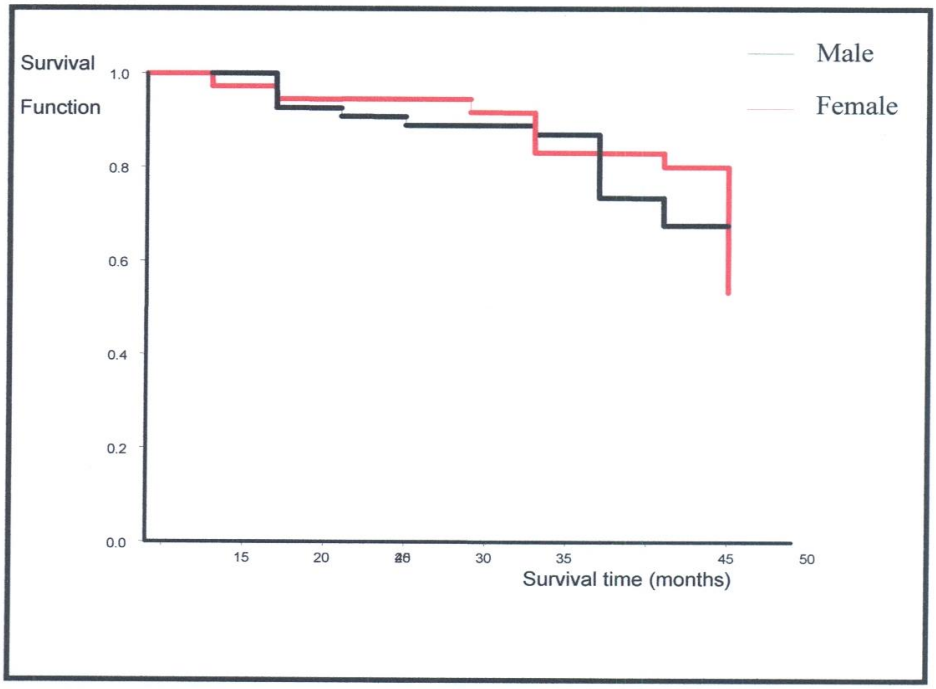
The LIFETEST procedure computes nonparametric estimates of the survivor functions by the Kaplan and Meier method (KM). The procedure computes nonparametric tests which are used to compare the survival curves of two or more groups. The procedure also computes the rank tests of association of the survival time variable with other prognostic or concomitant variables. Thus in line with this research, the life test procedure provides the survivor curves of both male and female patients superimposed on the same axes. It shows the log-rank and Wald's statistics that is used in determining

whether there exist any statistical significant differences in gender survivor time of the patient. The PHREG procedure, often referred to as Cox regression is a semi-parametric procedure that enables the estimation of the beta (8) coefficients of the proportional hazards model without having to specify the baseline hazard function lo(t).

4.2.1 Comparing Gender Survivor Curves

The PROC LIFETEST was implored to show the gender survival trends of the ninety patients. The results indicate mean survival times of 43.4 and 43.3 months (approximately 3.5years) for both male and female patients respectively with standard errors of 1.3843 and 1.1888 respectively. Figure 5 below shows the survivor curves of the ninety HIV patients superimposed on the same axes. Between time t=0 and t=l 3 months, the two survival curves are virtually indistinguishable. The curves, however, experience little overlaps after time t= 13 months suggesting a little longer survival time for the male cohort than female group. This is indicated by the little difference between their mean survival times. However, this difference as observed on the diagram is statistically insignificant as illustrated by the log-rank and Wald's test statistics.

Figure 5: Gender Survivor Curves

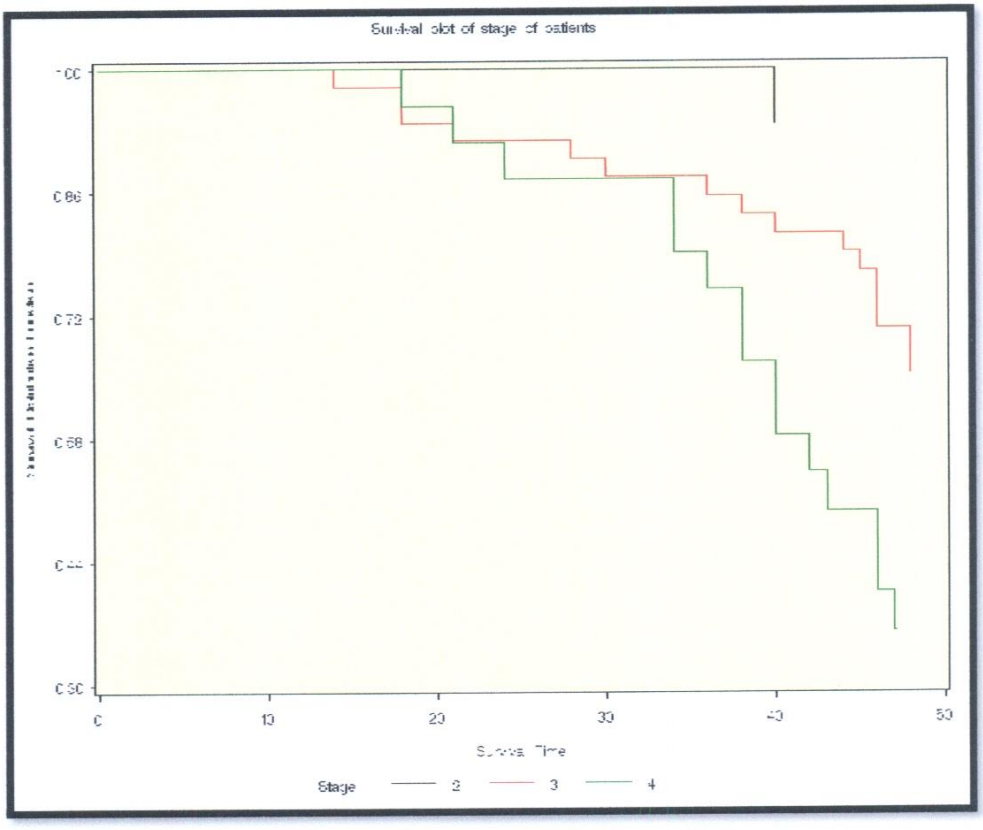


In general, despite the little differences in mean survival time of the male cohort over that of the female cohort, the p-values of the Log-rank (p>0.4603) and Wilcoxon (p>0.4608) test statistics indicates that, the difference between the two survival curves is statistically insignificant. This therefore implies that, there is no significant gender survival difference in HIV patients in the region. Tablet of the Appendices shows the data set collected from the regional HIV collation centre. Table 2 shows a summary of the data set. Other preceding tables shows the statistics of the number of patients censored and uncensored, a homogeneity test of gender survival curves for the period of study, and a test of equality over the strata obtained from the PROC LIFETEST.

4.2.2 Comparing trends of survival of patients in stages II, III, and IV

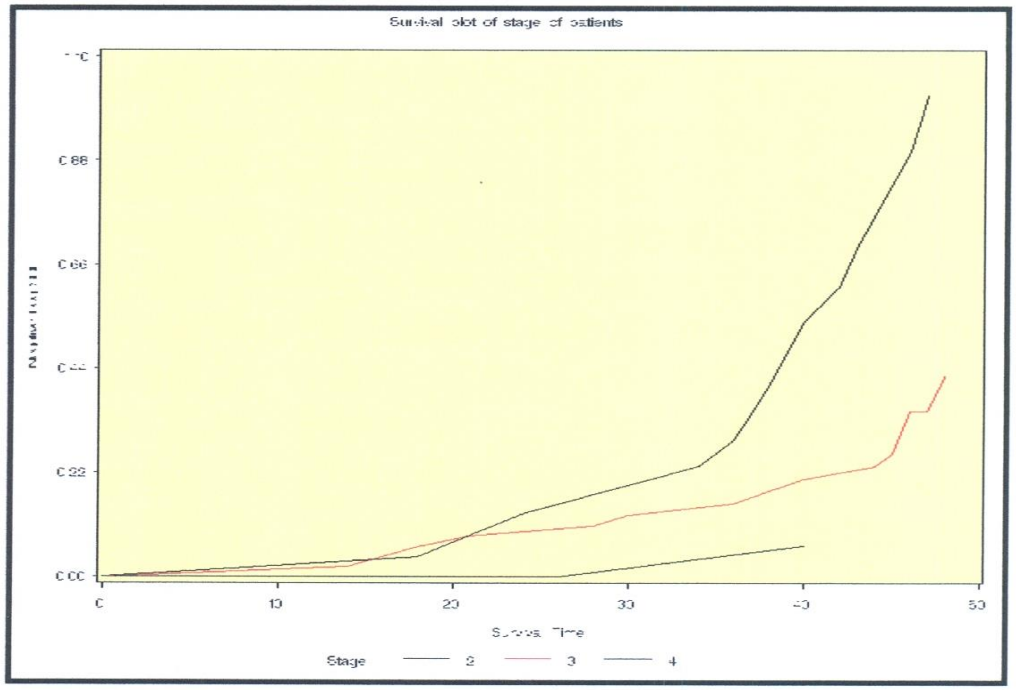
With reference to table 3 of section 4.1.2, indicating the number of patients in each stage of the HIV infection, figure 6 illustrates the survival trend of each stage of the infection as time increase (t☐0).

Figure 6: Survival curves of stages of HIV infection



The three curves are superimposed on the same axes. Between time t = 0 and t =13 months, the three survival curves are observed to be virtually indistinguishable. This implies that no death occurred during this period of the study. As time increase (t □ 0), patients in stage two (II) continue to record no death until after 42 months of the study period. Patients in stage three (III), however, experience their first death after the fourteenth month into the study and continue to experience more deaths until the end of the study period of forty eight months. However, patients in stage four (IV) experience their first death on the eighteenth month of the study and continue to experience more deaths than patients in stages II and III. The implication of this is that, for a unit increase in time, patients in stage four (IV) of the HIV infection has a higher risk of surviving than patients in stages two (II) and three (III). This stresses the point that age after sero-conversion is an attribute (concomitant factor) to patient survival. In other words, the age of an HIV patient at sero-conversion is a significant factor that accounts for his/her survival as illustrated by Todd et al (2006). This hazard differences in the various stages of the virus infection is adequately demonstrated by the negative log survival distribution in figure 7 below.

Figure 7:.Negative log survival distribution functions of stages of HIV infection



The curve representing stage two (II) of the HIV infection, as shown above, rises gently after a considerable period of no death. Stage three (III) has a marginal rise experiencing hazard risks earlier than stage two (II). Stage four experiences a sharp increase as compared to stages II and III. This indicates that, patients in stage *N* of the HIV infection are more vulnerable and thus have a high survival risk than patients in stages II and III In the words of Morgan et al (2002), patients are most vulnerable to death as they move from one stage of the infection to another.

4.2.3 Testing Global Null Hypothesis

Based on the fact that there is no statistically significant difference in gender survival trend, a composite Null Global Hypothesis Test (NGHT) and Maximum Likelihood Estimates (MLE) for both sexes is used to represent the Cox regression model taken into consideration the assumptions stated in section 4.3.

Testing the global null hypothesis that all the coefficients are zero (8=0) for the Cox regression model, three alternative chi-square statistics are given: a likelihood-ratio test, a score test, and a Wald test. Table *5* shows the Likelihood ratio, Score, and Wald test chi-square values to test the null hypothesis that all the parameter estimates of the Cox regression model are zero.

Table 5: Testing Global Null Hypothesis (8=0)

Test	Chi-Square	DF	Pr>Chi-Square
Likelihood Ratio	18.5623	4	0.0010
Score	18.5174	4	0.0010
Wald	17.9287	4	0.0013

All the three statistics, Likelihood ratio, Score, and Waid with 4 degrees of freedom has very small p-values (0.0010, 0.0010, and 0.0013 respectively) less than the given level of significance of 0.05. All the three statistics are thus significant indicating that, at least, one of the coefficients of the model is not zero and can thus be used to explain the model.

4.2.4 Analysis of Maximum Likelihood Estimates

In the PHREG procedure, the analysis of the maximum likelihood estimates of the variables forming the model (age, sex, stage, and location) for the associated statistics, there is no intercept (a characteristic feature of partial likelihood estimation). The intercept is part of l~t) = a(t) [the baseline hazard], the arbitrary function of time, which cancels out of the estimating equations after finding the hazard ratio of the ***ith*** and **jth** patients (Allison, 2008).

Table 6 below shows the maximum likelihood estimates of the coefficients of the model. The Age of a patient and his/her WHO (2004) HIV defined status are highly significant measures of survival since their p-values, 0.0035 and 0.0025 respectively, are extremely less than the level of significance (a=0.05)

The effect of sex is however more marginal with a p-value of 0.1610 whilst the demographic zone (location) of a patient as defined by the Ghana Health Service (OHS) and the HIV Sentinel Survey (GHS/HSS, 2007, 2008, and 2009) is apparently unrelated to the survival time of the patients (p=0.5753).Their p-values therefore indicates that they cannot be used to explain the model.

Table 6: Maximum Likelihood Estimates

		Parameter	Standard			Hazard	
Variable	**DF**	**Estimate**	**Error**	**Chi-Sq**	**Pr>Chi-Sq**	**Ratio**	**95% Hazard C I**
Age of patient	**1**	0.04280	0.02360	3.2880	0.0035	1.044	0.997 - 0.999
Sex	**1**	-0.55791	0.39798	1.9652	0.1610	0.572	0.262 - 0.265
Stage	**1**	0.93238	0.30842	9.1389	0.0025	0.541	0. 788 - 0. 792
Location	**1**	-0.20684	0.36922	0.3138	0.5753	0.813	0.394 - 0.398

The signs of the coefficients of the parameter estimates, indicates the direction of relationship of the variables and the survival time. The positive coefficient for Age indicates that patients below the mean survival time have longer survival time than patients whose age is above the mean survival time. This is illustrated more clearly

using the hazard ratio. For a unit change in age the risk of patient survival increases by 4.4% (95% Hazard Confidence Interval of 0.997 - 0.999). This further demonstrates the fact that, older patients have a higher risk of dying as compare with younger ones. Specifically, each additional year at the time of sero-conversion is associated with a 4.4% increase in the hazard of death.

A patient's status as he/she moves from one HIV stage of infection to another, experience about 45.90/o (95% Hazard Confidence Interval of 0.788-0.792) decrease in his/her chances of survival (controlling for covariates such as income levels and nutritional pattern of patients). Intimately, at sero-conversion, a patient's chance of survival is hindered as his/her $CD4^+$ T-cell count begins to reduce from 500copies/µl.

In summary, since sex and the demographic zone (location) of patients are not significant measures or determinants of the survival of patients, they do not form part or help to explain the Cox Regression model (partial regression). Hence, the Cox regression model for the ninety HIV patients (assuming proportional hazard for each prognostic variable) is thus illustrated as:

$$\mathbf{h(t, x)} = e^{(0.04280x_1 + 0.93238x_2)} \quad \text{..... Equation 8}$$

The above equation represents a composite model for both sexes, where, x_1 represents the age of the patient at sero-conversion, and x2 represents the amount of $CD4^+$ T- cells per micro litre.

The survival function S(t), is thus given as:

$$\mathbf{S(t)} = \exp\left[-\int_0^t \boldsymbol{h(t)}\right] \quad \text{..... Equation 9}$$

$$= \exp\left(-\int_0^t e^{(0.04280x_1 + 0.93238x_2)}\right) \quad \text{..... Equation 10}$$

Equations (8) and (10) above illustrate the composite hazard and survival functions of the patients enrolled into the study.

The survival function thus indicates that; the probability that age contributes to a patient's survival is about 0.043 and that a probability of about 0.93 of a patient's $CD4^+$ T- cells per micro litre accounts for a patients survival .Both functions indicate that age

at sero-conversion and the stage of HlV infection of a patient are attributes of a patient's survival.

4.3 Assumptions

The main interest of the study has been to compare gender survival times of patients and also to detect possible predictive variables of the survival time of the ninety HIV infection of a patients of the 2006 cohort in northern region.

The survival time has been measured (in months) from the day of first sero-conversion until the date of the patient's death or when lost-to-follow up (right censoring). Considering the demographic information recorded for the patients, the following assumptions are made;

- All the patients enrolled into the study are on the HAART regimen
- The income levels of patients believed to have much influence on the nutritional patterns of patients (UNAIDS report, 2004, 2006) is ignored since this was not captured in the various sentinel centres where data set was collected.
- Patients entered the study at different times and may have been infected before their first sero-conversion.

CHAPTER FIVE

SUMMARY OF FINDINGS, CONCLUSION AND RECOMMENDATION

5.0 Introduction

This final chapter summarizes the findings of the research work. It presents the limitations, suggestions and recommendations for further research to be carried out base on some of the short comings that this research has identified.

5.1 Discussion

A total of 116 people were recorded to have sero-converted to HIV positive in the 2006 cohort group in the seven HIV Sentinel Surveillance (HSS) centres in the region (each entering at different times) Some recorded demographic characteristics of the sero-converters were observed over a period of forty eight months. From the sample of ninety patients, 36 were male and 54 female. 17, 48 and 25 patients were in the World Health Organisation (WHO) defined stages II, III, and IV with $CD4^+$ T-cell count below 300 copies/µl, 200copies/µl, and 100copies/µl respectively. 58.890/o and 41.11% of the patients were classified as living in Urban or Rural areas respectively.

After the study period of forty eight months, thirty two deaths were recorded (21 females and 11males) representing 35.56% of the total number of patients enrolled into the study. The mean survival times for the 2006 cohort group are 43.4 and 43.3 months for both male and female patients respectively with the minimum death time occurring after fourteen months of first sero-conversion.

There is no indication of gender difference in survival. Patients in the age group 25-49 years have higher percentages of HIV infection. This consists of 55.56% and 90.74% of the male and female populations respectively with 78.7% and 85.2% belonging to stages III and IV of the HIV infection. A test of homogeneity of the survival curves indicates no survival difference between male and female patients for the given period of the study, since none of the test statistics was found to be significant.

The age of a patient during his/her first sero-conversion as well as the patient's $CD4^+$ T-cell count as he/she moves from one stage of HIV infection to another, are determinants of the survival trends of patients. That is, older patients have a higher risk of dying. Specifically, each additional year at the time of sero conversion is associated with a 4.4% increase in the hazard of death. A patient, whose age is more than the mean survival time bas a higher risk of survival than a patient below the mean survival time.

There exist significant differences in hazard among the patients in the various stages of the HIV infection. A patient's status as he/she moves from one HIV stage of infection to another experience about 45.9% decrease in his/her chances of survival At sero-conversion, a patient's chance of survival is hindered as his/her $CD4^+$ T-cell count reduces from 500 copies/µl A patient's sex and place of location does not help in explaining the survival trend of the patient

5.2 Summary of Findings

- There is no significant difference in gender survival time of HIV patients in northern region.
- The potential working age group (25-49 years) has the highest HIV infection in the region.
- The age and CD4+ T-cell count of a patient during his/her first sero-conversion are determinants of the survival trends of patients
- Each additional year at the time of sero-conversion is associated with a 4.4% increase in the risk of death of the patient
- A patient's status as he/she moves from one HIV stage of infection to another experience about 45.9% decrease in his/her chances of survival. This value increases with increasing time

• The sex of a patient and his or her location are not determinants of survival

5.3 Conclusion

Acquired Immune deficiency Syndrome (AIDS) is a disease that is caused by a virus known as Human Immunodeficiency virus (HIV). This virus attacks a person's immune system (white blood cells). This weakens the immune system and makes the person vulnerable to opportunistic diseases e.g. tuberculosis etc.

HIV was first diagnosed more than twenty years ago and up to now there is no known cure for the disease. The rate at which HIV is spreading in sub-Sahara Africa is so high that the future generation is threatened with extinction. Thousands of people are dying daily of AIDS while tens of thousands are being infected.

Different techniques have been used in campaign awareness programmes. These include; the media (Television, Radio, newspapers), books, schools, churches, the administration, parents/relatives, workshops etc.

The most common mode of transmission of HIV is through sexual relations. Other modes of transmission include transfusion of infected blood to a healthy person. HIV can also be transmitted from an infected mother to child during birth when the necessary precautions are not taken. The epidemic primarily affects the young, working age, sexually active adults- people between the ages of 15 and 50. Both women and men become infected in similar numbers, but women tend to become infected at a younger age than men, reflecting the biological and social vulnerability of teenage women.

The basic preventive methods that have been stressed upon in fighting AIDS include; abstinence, being in a monogamous relationship, being faithful to one's partner and the use of condoms. However due to cultural, social, economic, political and other secondary influences, these campaign programs have not been effective up to the desired level. There is therefore a need to explore other strategies that can be incorporated alongside the laid down strategies or any other strategy so that the effectiveness of these methods can be evaluated before implementation.

It is known that, due to the uniqueness of the backgrounds of people, different campaign methods and techniques have had different effects in different regions.

In Ghana, some of the challenging and unexplored issues in the study and management of HIV and its related cases are; the ability to determine spread patterns, predict future spread patterns, determine gender survival patterns as well as evaluate the

effectiveness of the methods that are used in curbing future spread patterns of the disease.

This project thus uses survival analysis to compare the gender survival trends of HIV patients, the risk of survival of the patients in the various stages of the infection in northern region. It is thus not a panacea to finding and solving the problems encountered in the fight against the epidemic, but throws more light in the gender survival trends of patients as well as eliciting the risk (hazards) of survival according to age distribution

5.4 Recommendation

The importance of age in determining survival following HIV sero conversion must be used in educational messages to all age groups in the region and the country at large. This will serve as a benchmark for measuring the prevalence and incidence of the disease.

The consequences of HIV infection is drastically reduced with the introduction of the Anti-retroviral therapy (ART). However, access to these drugs has generally, been a challenge in most developing countries and Sub-Saharan Africa in particular. All efforts should made by the governments of these countries to make the therapy (ART) accessible to patients. This will provide accurate benchmarks to gauging the effect of ART on the various stages of the HIV infection.

Consequently, considering the short comings of this research, the researcher therefore wishes to recommend that further research be conducted on the gender survival of HIV patients on the same Highly Active Anti-Retroviral Therapy (HAART) combination, taking into consideration some socio demographic and environmental factors such as income levels, religion, marital status, sexual behaviour, the HIV sub-type, and mode of transmission.

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APPENDICES

Appendix 1. Data set from. the regional HIV collation centre-Tamale Teaching Hospital

First sero-conversion	Age of patient	Sex	Stage	Status	Location	Duration (months)
09/06/2006	35	F	2	1	R	48
2010712006	31	F	3	0	R	21
06/1012006	35	F	4	0	R	18
01/0912006	38	M	2	1	R	45
01/0912006	30	F	2	1	R	48
01/09/2006	48	F	4	0	R	21
01/0912006	63	M	3	0	u	14
01/12/2006	30	F	2	1	u	47
01/1212006	16	M	2	1	R	42
03/03/2006	38	M	3	1	R	48
04/0512006	46	F	4	0	u	38
04/08/2006	53	M	4	0	u	43
04/08/2006	20	F	3	0	u	48
04/08/2006	34	M	3	1	u	47
04/08/2006	59	M	3	1	R	30
04/08/2006	32	F	4	1	u	48
06/10/2006	45	F	3	0	R	28
06/10/2006	50	M	3	0	u	18
06/1012006	36	F	2	1	u	48
06/10/2006	29	F	4	0	u	24
07/0712006	26	F	4	0	u	42
07/07/2006	33	F	3	1	u	48
0710712006	33	F	4	0	u	38
08/0912006	34	F	2	1	R	48
08/09/2006	35	F	3	0	u	46
08/09/2006	53	M	3	0	R	46
08/1212006	45	M	4	0	R	36
08/12/2006	26	F	3	1	R	48
08/1212006	18	M	3	0	R	36
09/06/2006	25	F	3	0	R	40
10/1112006	48	F	4	0	u	46
10/11/2006	36	M	3	1	u	48
11/08/2006	35	F	2	0	R	40
11/08/2006	49	F	2	1	u	48
11/08/2006	35	F	4	0	u	40
13/10/2006	40	F	3	1	R	48

13/10/2006	45	M	3	1	u	48
14/07/2006	46	M	3	0	R	30
14/07/2006	33	M	3	1	R	48
14/07/2006	39	F	3	1	u	48
14/07/2006	32	F	3	1	R	48
14/0712006	36	F	3	0	u	45
15/09/2006	24	M	4	0	u	47
15/09/2006	39	F	3	0	u	38
15/09/2006	36	F	2	1	u	44
15/09/2006	70	F	3	0	u	18
15/09/2006	33	F	2	1	u	48
16/06/2006	40	M	3	1	u	48
16/06/2006	35	M	3	1	u	48
16/06/2006	50	M	4	0	R	46
17/11/2006	48	M	4	1	u	48
17/11/2006	42	F	4	1	u	48
17/11/2006	35	F	4	1	u	48
17/11/2006	28	F	3	0	u	44
17/11/2006	32	F	2	1	R	48
17/11/2006	54	M	4	0	u	34
18/01/2006	47	M	3	1	u	48
19/05/2006	35	F	3	1	R	48
19/0512006	18	F	3	1	R	30
19/05fl006	30	F	3	1	R	48
21/07/2006	50	M	3	1	R	48
22/02/2006	35	F	3	1	u	48
22/05/2006	49	F	4	0	u	34
22/09/2006	37	M	3	1	u	48
22/09/2006	49	F	4	1	R	48
22/09/2006	38	M	3	1	R	47
22/0912006	35	F	2	1	u	48
22/1212006	36	F	2	1	u	48
2211212006	30	M	4	1	u	48
25/08/2006	37	M	4	1	R	42
25/08/2006	51	M	3	1	u	48
25/08/2006	15	F	2	1	u	26
25/08/2006	23	F	3	1	u	46
25/08/2006	35	F	3	1	R	48
27/10/2006	45	M	3	1	u	48
27/10/2006	32	M	2	1	u	48
28/0712006	42	F	3	1	R	45
28/07/2006	38	F	3	1	R	48
28/07/2006	30	F	3	1	u	48

28/07/2006	33	F	4	1	U	48
29/09/2006	49	M	3	0	U	46
29/09/2006	27	M	2	1	U	48
29/09/2006	32	F	3	1	R	48
29/09/2006	42	M	4	1	U	48
29/09/2006	35	F	3	1	U	48
29/12/2006	40	M	3	1	U	47
30/06/2006	29	M	3	1	U	48
/06/2006	38	F	3	1	R	48

Appendix 2: Summary of Data

Age	SEX		WHO			STATUS		LOCATION	
	ma	female	II	III	IV	Cens	Uncens	Urban	Rural
15–19	2	2	2	2	0	3	1	1	3
20-24	1	3	0	2	1	1	2	3	0
25–29	2	6	1	5	2	3	5	5	3
30–34	4	14	6	8	5	16	3	10	8
35–39	8	19	7	15	5	20	7	15	12
40–44	3	3	0	4	2	6	0	4	2
45–49	7	7	1	6	7	6	8	9	5
50–54	7	0	0	4	3	2	5	4	3
55–59	1	0	0	1	0	1	0	0	1
60–64	1	0	0	1	0	0	1	2	0
TOTAL	**36**	**54**	**17**	**48**	**25**	**58**	**32**	**53**	**37**

Appendix 3: Survivor Functions of Male and Female HIV patients (SAS output)

The LIFETEST Procedure

Stratum 1: sex = female

Product-Limit Survival Estimates

Duration months)	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.0000	1.0000	0	0	0	54
18.0000	.	.	.	1	53
18.0000	0.9630	0.0370	0.0257	2	52
21.0000	.	.	.	3	51
21.0000	0.9259	0.0741	0.0356	4	50
24.0000	0.9074	0.0926	0.0394	5	49
26.0000*	.	.	.	5	48
28.0000	0.8885	0.1115	0.0429	6	47
30.0000*	.	.	.	6	46
34.0000	0.8692	0.1308	0.0461	7	45
38.0000	.	.	.	8	44
38.0000	.	.	.	9	43
38.0000	0.8112	0.1888	0.0538	10	42
40.0000	.	.	.	11	41
40.0000	.	.	.	12	40
40.0000	.	.	.	13	39
40.0000	0.7340	0.2660	0.0610	14	38
42.0000	0.7147	0.2853	0.0624	15	37
44.0000	0.6954	0.3046	0.0636	16	36
45.0000	0.6760	0.3240	0.0647	17	35
45.0000*	.	.	.	17	34
46.0000	.	.	.	18	33
46.0000	0.6363	0.3637	0.0667	19	32
46.0000*	.	.	.	19	31
47.0000*	.	.	.	19	30
48.0000	.	.	.	20	29
48.0000	0.5939	0.4061	0.0687	21	28
48.0000*	.	.	.	21	27
48.0000*	.	.	.	21	26
48.0000*	.	.	.	21	25
48.0000*	.	.	.	21	24

48.0000*	.	.	.	21	23
48.0000*	.	.	.	21	22
48.0000*	.	.	.	21	21
48.0000*	.	.	.	21	20

The LIFETEST Procedure

Stratum 1: sex = female (continued)

Product-Limit Survival Estimates

uration onths)	Survival	Failure	Survival Standard Error	Number Failed	Number Left
8.0000*	.	.	.	21	19
8.0000*	.	.	.	21	18
8.0000*	.	.	.	21	17
8.0000*	.	.	.	21	16
8.0000*	.	.	.	21	15
8.0000*	.	.	.	21	14
8.0000*	.	.	.	21	7
8.0000*	.	.	.	21	6
8.0000*	.	.	.	21	5
8.0000*	.	.	.	21	4
8.0000*	.	.	.	21	3
8.0000*	.	.	.	21	2
8.0000*	.	.	.	21	1
8.0000*	.	.	.	21	0

Mean	Standard Error
43.3	1.1888

The LIFETEST Procedure

Stratum 2: sex = male

Product-Limit Survival Estimates

Duration months)	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.0000	1.0000	0	0	0	
.0000	0.9722	0.0278	0.0274	1	35
.0000	0.9444	0.0556	0.0382	2	34
.0000	0.9167	0.0833	0.0461	3	33
.0000*	.	.	.	3	32
.0000	0.8880	0.1120	0.0528	4	31
.0000	.	.	.	5	30
.0000	0.8307	0.1693	0.0630	6	29
.0000*	.	.	.	6	28
.0000*	.	.	.	6	27
.0000	0.8000	0.2000	0.0678	7	26
.0000*	.	.	.	7	25
.0000	.	.	.	8	24
.0000	.	.	.	9	23
.0000	0.7040	0.2960	0.0791	10	22
.0000	0.6720	0.3280	0.0818	11	21
.0000*	.	.	.	11	20
.0000*	.	.	.	11	19
.0000*	.	.	.	11	18
.0000*	.	.	.	11	17
.0000*	.	.	.	11	16
.0000*	.	.	.	11	15
.0000*	.	.	.	11	14
.0000*	.	.	.	11	13
.0000*	.	.	.	11	12
48.0000*	.	.	.	11	11
48.0000*	.	.	.	11	10
48.0000*	.	.	.	11	9
48.0000*	.	.	.	11	8
48.0000*	.	.	.	11	7
48.0000*	.	.	.	11	6
48.0000*	.	.	.	11	5

The LIFETEST Procedure

Stratum 2: sex = male (continued)

Product-Limit Survival Estimates

Duration (months)	Survival	Failure	Survival Standard Error	Number Failed	Number of Left
3.0000*	.	.	.	11	4
3.0000*	.	.	.	11	3
3.0000*	.	.	.	11	2
3.0000*	.	.	.	11	1
3.0000*	.	.	.	11	0

Mean	Standard Error
43.4	1.3843

ppendix 4: Summary of the Number of Censored and Uncensored Values

ercent tratum	sex	Total	Failed	Censored	Percent Censored
	female	54	21	33	61.11
	male	36	11	25	69.44
otal		90	32	58	64

Appendix 5: Testing Homogeneity of Survival Curves for Duration over Strata

Rank Statistics

Sex	Log-Rank	Wilcoxon
Female	2.0259	147.00
Male	-2.0259	-147.00

Appendix 6: Test of Equality over Strata

Test	Chi-Square	DF	Pr>Chi-Square
Log-Rank	0.5452	1	0.4603
Wilcoxon	0.5438	1	0.4608
-2Log (LR)	0.5024	1	0.4784

Appendix 7: Model Information

ata Set	HIV/AIDS	
ependent Variable	Duration months	Duration (months)
ensoring Variable	Status	Status
ensoring Value(s)	1	
ies Handling	BRESLOW	

Number of Observations Read	90
Number of Observations Used	90

Appendix 8: Testing Global Null Hypothesis: BETA=0

st	Chi-Square	DF	Pr > Chi-Square
kelihood Ratio	18.5623	4	0.0010
ore	18.5174	4	0.0010
ld	17.9287	4	0.0013

Appendix 9: Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr>Chi-Sq	Hazard Ratio
Age	1	0.04280	0.02360	3.2880	0.0035	1.044
Sex	1	-0.55791	0.39798	1.9652	0.1610	0.572
Stage	1	0.93238	0.30842	9.1389	0.0025	0.541
Location	1	-0.20684	0.36922	0.3138	0.5753	0.813