UNIVERSITY FOR DEVELOPMENT STUDIES

DETERMINANTS OF CD4 COUNT CHANGE IN PERSONS **ON ANTIRETROVIRAL THERAPY FOR HIV/AIDS IN THE KASSENA-NANKANA EAST DISTRICT OF UPPER EAST REGION OF** GHANA

BAWA **SIMON SUBINLEEB**

Thesis submitted to the Department of Statistics, **Faculty of Mathematical Sciences, University for Development Studies in Partial Fulfillment of the Requirements for the Award of Master of Science Degree in Biometry**

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B Y

BAWA SIMON SUBINLEEB (BSc. STATISTICS)

(UDS/MBM/0006/10)

Thesis submitted to the Department of Statistics, Faculty of Mathematical Sciences, University for Development Studies in Partial Fulfillment of the Requirements for the Award of Master of Science Degree in Biometry

October, 2012

DECLARATION

Student

I hereby declare that this thesis is the result of my own original work and that no part of it has been presented for another degree in this university or elsewhere except the references to other researchers or writers which have been duly acknowledged.

Candidate's Signature:..... Date: 18/10/12

Name: Bawa Simon Subinleeb

Supervisor

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

Supervisor's Signature:..... Date: 18/10/2012

Name: Bishop Dr. Albert Luguterah

ABSTRACT

HIV/AIDS was first recognized in the early 1980's and since then has affected humankind in different ways across all the continents. It has been a wake-up call to scientists, health experts, NGOs, individuals, and other stakeholders to handle such a menace since the virus depletes the CD4 T-lymphocytes which is a major cell of maintaining the body immune system against various infectious diseases. A secondary data of 142 persons living with HIV/AIDS on antiretroviral therapy was obtained from War Memorial Hospital of Navrongo in the Kassena-Nankana East District of Upper East Region of Ghana. The data excludes those who did not have their CD4 count taken at least once after treatment initiation. A generalized linear model (PROC GENMOD) was used in analyzing the data with SAS and SPSS software. The mean change in CD4 count of the 142 persons on treatment was 244.1 cells per micro litre with an average time of 13.6 months with females having the highest mean change in CD4 count of 259.8 cells per micro litre. The minimum and maximum CD4 count of change was 8 and 651 cells per micro litre within the time interval of 4 to 49 months. Poisson distribution was chosen since it best fitted the data among other distributions to model person's change in CD4 count on treatment. Number of months on treatment, weight, height, etc, were found to significantly determine the amount of change in CD4 count (P-values <0.05).

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DEDICATION

This work is dedicated to my late father, Nyam Bawa and the entire family.

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ACRONYMS

HIV — Human Immunodeficiency Virus

AIDS — Acquired Immunodeficiency Syndrome

MSM — Men having Sex with Men

IDUs — Injecting Drug Users

CSWs — Commercial Sex Workers

NACP — National AIDS/STI Control Program

PMTCT — Prevention of Mother-to-Child Transmission of HIV

ANC —Antenatal Care

ART — Antiretroviral Therapy

HSS — HIV Sentinel Survey

WHO — World Health Organization

UNAIDS — Joint United Nations Programme on AIDS

HAART — Highly Active Antiretroviral Treatment

GSS — Ghana Statistical Service

PLWHA — People Living with HIV/AIDs

NGOs — Non-Governmental Organizations

CHAPTER ONE

INTRODUCTION

1.1 Background

Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) is one of the devastating disease humankind has ever faced. HIV is the virus that causes AIDS. It destroys certain blood cells that are crucial to the normal function of the immune system, which defends the body against illness whereas AIDS occurs when the immune system is weakened by HIV to the point where a person develops any number of diseases or cancers.

In 1989, the medical historian Mirko Grmek asked the question, in a pioneering work, whether AIDS, whose clinical symptoms had been described eight years earlier, was a new disease. Yes, he answered, for it was the first time in history that a disease without specific symptoms and with no trace of organic lesions, certainly at first sight, had made its appearance. The speed with which it spread was also without precedent. On the other hand, he added that AIDS was not new for it had been present even if people were not aware of the fact, in humankind for several generations.

According to UNAIDS 2004, globally 37.8 million estimated people were living with **HIV/AIDS with 2.9 million people dead. 25 million people were estimated to be coming from Sub-Saharan Africa with 2.2 million dead. In Ghana 350, 000** people were estimated to be living with the disease with 30,000 dead.

HIV infections and AIDS deaths are unevenly distributed geographically and the nature of the epidemics vary by region. Epidemics are abating in some countries and burgeoning in others. More than 90 percent of people with HIV are living in the developing world (UNICEF, 2007).

There is growing recognition that the virus does not discriminate by age, race, gender, ethnicity, sexual orientation, or socioeconomic status — everyone is susceptible. However, certain groups are at particular risk of HIV, including men who have sex with men (MSM), injecting drug users (IDUs), and Commercial Sex Workers (CSWs). The impact of HIV/AIDS on women and girls has been particularly devastating. Women and girls now comprise 50 percent of those aged 15 and older living with HIV (UNAIDS and WHO, 2009).

The impact of HIV/AIDS on children and young people is a severe and growing problem. In 2008 for instance, 430,000 children under age 15 were infected with HIV and 280,000 died of AIDS. In addition, about 15 million children have lost one or both parents due to the disease (UNAIDS 2008a).

There are effective prevention and treatment interventions, as well as research efforts to develop new approaches, medications and vaccines. The sixth Millennium Development Goal (MDG) focuses on stopping and reversing the spread of HIV/AIDS by 2015 (UNAIDS 2008b). Global funding is increasing, but global need of treatment is growing even faster and widening the funding gap. Services and funding are disproportionately available in developed countries (NACP, 2001).

The HIV/AIDS epidemic has become a serious health and development problem in many countries around the world. The Joint United Nations Programme on AIDS (UNAIDS) estimates the number of HIV infections worldwide at about 36.1 million by the end of 2000, of which 25.3 million were found in sub-Saharan Africa. Another 21.8 million persons have already died from the disease since the beginning of the epidemic, mostly in Africa. And about 600,000 infants now become infected each year, about 90 percent of whom are African children.

The virus that causes AIDS has already infected and is infecting many Ghanaians. About three percent of the entire adult population of the country is HIV infected (NACP, 2001). Most of these people do not even know they carry the virus. In 2000, about 330,000 adults and 20,000 children were already infected. Between the beginning of the epidemic in the mid-1980s and the end of 2000, more than 185,000 persons may have already developed AIDS, although not all of these have been officially recorded. No cure is available for AIDS, and the disease is becoming one of the most serious development issues in the country and beyond (NACP, 2001).

Despite this situation, much can be done to alter the course of the HIV/AIDS epidemic in Ghana. HIV is not spread by casual contact or by mosquitoes or in the air or water. HIV is spread by certain types of human behaviour; therefore, it can be controlled and even be prevented by changes in those behaviours. What is needed is continued involvement from all sectors of Ghanaian society to promote interventions to reduce high-risk sexual behaviours, treat and control other

sexually transmitted diseases, maintain a safe blood supply, ensure safe use of needles, and mitigate the problems of those already infected with HIV or otherwise affected by the epidemic. More than 95 percent of the adult population aged 15 to 49 remains free of the infection and all of these people have the opportunity to protect themselves from the disease (NACP, 2001).

In 1995, the WHO estimated that twenty-four million adults had been infected since the beginning of the epidemic, of which sixteen million were in Africa. At least five million had died. From then on, AIDS has been the major cause of death amongst adults in cities in the USA, Europe and Africa.

In the middle of the 1990s, Uganda was the only African country to demonstrate that it is possible to stem the epidemic. At first noticed among young people in an urban environment, the rate of decline of HIV became general. From 30% amongst adults in Kampala in 1992-93, it progressively declined to level off at less than 6% in 2004.

It required that AIDS be seen as an obstacle to development and as a social and economic handicap and not only an illness. The creation of a global fund to fight against malaria, tuberculoses and AIDS was a response to these demands. In 2004 a battle which had been going on for three years about the price of antiretroviral and the conditions for fixing the prices resulted in a theoretic possibility of countries acquiring tri-therapy at a price of US$150-200 per person per annum compared to the $1200 in 1998. Access to medications became possible in-the South. The WHO began a "three by five" initiative so that three million AIDS sufferers could benefit from ART by the end of 2005 (World Bank, 2004).

1.2 Problem Statement

HIV causes immunodeficiency by infection, lyses and depletion of CD4 T-lymphocytes (Nwokedi et al, 2007). The CD4 T-lymphocytes occupy the central position in regulating immune functions' and are the primary targets of HIV. The relentless destruction of CD4 T- lymphocytes by HIV, either directly or indirectly, results in the loss of HIV-specific immune response; hence CD4 count has become a valuable indicator of immune function in the management of HIV infection (WHO, 2007) to boost or restore the CD4 count of those infected with the virus.

The HIV/AIDS pandemic has been characterized as the greatest natural challenge ever to confront humanity and one of the great moral causes of our time. The pandemic is on a rapid global march and is now impacting some of the world's most populous countries where forty million people worldwide are currently living with the disease and another 45 million may become infected by 2010. The disease is having a particularly devastating impact on Sub-Saharan Africa, where 2.3 million people died of HIV/AIDS in 2003; an estimated 26.6 million people are HIV positive with more than eleven million AIDS orphans. Also an estimated five to six million individuals in developing countries are in need of antiretroviral therapy (ART) today (World Bank, 2004).

In Sub-Saharan Africa alone, an estimated 450,000 children died from AIDS in 2004. Furthermore, an estimated 560,000 children were newly infected, and an estimated 1.9 million children are believed to be living with HIV/AIDS as of end of 2004 (UNAIDS, 2004). A UNAIDS report reveals that in the Sub-Saharan

African region, the estimated prevalence and death rates among children are drastically higher than anywhere else in the world.

The HIV/AIDS epidemic is a very serious problem in Ghana. Already in 2000, about 350,000 Ghanaians were infected with HIV. This includes 330,000 adults and 20,000 children and more than 150,000 Ghanaians have died from AIDS since the beginning of the epidemic in the early 1980s and it is also estimated that by 2014, AIDS will be responsible for 28 percent of deaths and no other single cause will come close to being responsible for so much mortality among Ghanaians (NACP, 2001).

The national prevalence rate of Ghana for 2008 and 2009 was 2.2% and 1.9% respectively. The Upper East Region recorded 2.0% and 2.2%. Within the region; Bawku recorded 1.4% and 2.4%, Bolgatanga, 2.0% and 2.6%, Navrongo maintained a constant prevalence of 2.8% for 2008 and 2009 which is extremely higher than both the national and the regional prevalence rate (HSS, 2009). Between 2007 and 2011, about 485 adults and 27 children infected with HIV were enrolled. Out of these people enrolled, 317 adults and 11 children were put on ART in the District (Navrongo Hospital, ART Clinic, 2011).

Though HIV/AIDS has gained several researches over the years both nationally and internationally in managing the affected, more people including both adults and children still suffer new infections and need to be put on treatment either sooner or later to avert the continuing depletion of their CD4 T-lymphocytes cells at a thresh hold of < 350 cells per micro litre since at this thresh hold the victims

suffers a number of opportunistic infections which intend has a serious economic, social, and psychological impact on the individual, the household, the family, and the nation at large.

The worry about HIV/AIDS is low life expectancy and the socio-economic impact. The increase in deaths has been among adults aged between 20 and 49 years. This group now accounts for 60% of all deaths in sub-Saharan Africa, compared to 20% between 1985 and 1990, when the epidemic was in its early stages and thus hitting adults in their most economically productive years and removing the very people who could be responding to the crisis (UNAIDS 2006). Through its impacts on the labour force, households and enterprises, AIDS has played a significant role in the reversal of human development in Africa (UNDP, 2005).

AIDS affects the economy by reducing the labour supply through increased mortality and illness. Amongst those who are able to work, productivity is likely to decline as a result of HIV-related illness. Government income also declineS, as tax revenues fall and governments are pressured to increase their spending to deal with the expanding HIV epidemic.

The abilities of African countries to diversify their industrial base, expand exports and attract foreign investment are integral to economic progress in the region. By making labour more expensive and reducing profits, AIDS limits the ability of African countries to attract industries that depend on low-cost labour and makes investments in African businesses less desirable (Rosen, 2004).

Also the impact that AIDS has had on the economies of African countries is difficult to measure. The economies of the worst affected countries were already struggling with development challenges, debt and declining trade before the epidemic started to affect the continent. AIDS has combined with these factors to further aggravate the situation. It is thought that the impact of AIDS on the gross domestic product (GDP) of the worst affected countries is a loss of around 1.5% per year; this means that after 25 years the economy would be 31% smaller than it would otherwise have been (Greener, 2004).

In Ghana, one of the major criteria for monitoring the victims response to immunity is the CD4 T-lymphocytes; hence the need to identify certain factors that might contribute in determining change in CD4 count and a model to predict ones expected change in CD4 count when initiated on treatment for better management of the victims response to immunity since an improved immune functioning means the risks of morbidity and mortality will be reduced.

1.3 Research Questions

For the achievement of the study objectives, the following questions are used as a guide:

i. What are the factors that influence change in CD4 count of PLWHA on ART?

ii. To what extent do these factors influence change in CD4 count of PLWHA on ART?

iii. **What distribution best describes a change in CD4 count of PLWHA on ART?**

iv. **Which model best** describes changes in CD4 count for PLWHA on ART?

1.4 Objectives of the Study

1.4.1 General Objective

To find out **how persons living with HIV/AIDS initiated on ART respond to** change in CD4 count in the Kassena-Nankana East District of the upper east region of Ghana.

1.4.2 Specific Objectives

i. **To determine the factors associated with, and their extent of influence on,** a change **in CD4 count of PLWHA on ART**

ii. To **determine the probability distribution of a change in** CD4 count of **PLWHA on** ART

iii. **To model the change in CD4 count of PLWHA on ART**

1.5 Significance of the Study

One of the life threaten and cause of mortality is HIV/AIDS hanging around the neck of global communities and a respecter **of no** category of mankind causing the **depletion of the CD4 T-lymphocytes. It poses a lot of challenges to the economic growth, education, and** social life since the virus weakens and destroys **certain vital cells (CD4 T-lymphocytes) in human body.**

In order to curb this situation or bring it to its minimal level, we need to identify some factors that could be used to monitor and predict the change in CD4 count

of infected clients once initiated on ART in Kassena-Nankana East district and the nation at large.

This research is therefore expected at the end of the day to uncover the best model in determining a change in CD4 count of PLWHA on ART for the health bodies and scientists, individuals, NGOs, and all stakeholders globally which hopefully will show guide intervention and hence reverse its consequences.

1.6 Limitation of the Study

This research as in any other researches is being time constraint and financially incapacitated in terms of scope and coverage. Thus, the inability of the researcher to have considered more than one district and other aspect of relevant areas that will seek to address issues that are pertinent to HIV/AIDS epidemic to all stakeholders globally.

It is therefore hoped that other researchers will after the findings of this study build on it in future.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

HIV/AIDS is perceived to be the most dreadful disease to mankind nationally and globally. To some people it is considered as a death sentence. Its mode of infection comes in several forms and is manifested in human with certain signs and symptoms that aids clinicians to diagnose and follow-up with clinical care and its associated management. A person once diagnosed to be positive might go through several consequences as an individual, the family, the nation, and the world at large. Below is some review of literature on HIV/AIDS menace.

2.2 Brief History of HIV/AIDS

In 1981, a new syndrome, the acquired immune deficiency syndrome (AIDS), was first recognized among homosexual men in the United States. By 1983, the etiological agent, the human immunodeficiency virus (HIV), had been identified. By the mid-1980's, it became clear that the virus had spread, largely unnoticed, throughout most of the world.

The HIV/AIDS pandemic consists of many separate epidemics. Each epidemic has its own distinct origin, in terms of geography and specific populations affected, and involve different types and frequencies of risk behaviours and practices, for example, unprotected sex with multiple partners or sharing drug injection equipment.

According to UNAIDS and WHO (2003), countries can be divided into three states: low, concentrated and generalized;

Low

Principle: Although HIV infection may have existed for many years, it has never spread to significant levels in any sub-population. Recorded infection is largely confined to individuals with higher risk behaviour: e.g. sex workers, drug injectors, men having sex with other men. This epidemic state suggests that networks of risk are rather diffuse (with low levels of partner exchange or sharing of drug injecting equipment), or that the virus has been introduced only very recently.

Numerical proxy: HIV prevalence has. not consistently exceeded 5% in any defined subpopulation.

Concentrated

Principle: HIV has spread rapidly in a defined sub-population, but is not well-established in the general population. This epidemic state suggests active networks of risk within the subpopulation.

The future course of the epidemic is determined by the frequency and nature of links between highly infected sub-populations and the general population.

Numeric proxy: HIV prevalence consistently over 5% in at least one sub-population at highest risk, and prevalence below 1% in the general adult population (age 15-49 years) in urban areas.

Generalized

Principle: In generalized epidemics, HIV is firmly established in the general population. Although sub-populations at high risk may continue to contribute disproportionately to the spread of HIV, sexual networking in the general population is sufficient to sustain an epidemic independent of sub-populations at higher risk of infection.

Numeric proxy: HIV prevalence consistently over 1% in pregnant women.

Industrialized Western Countries

HIV infections began to spread extensively shortly before or after 1980. Through the 1980s, the population "groups" affected predominantly were men who had,sex with other men and injecting drug users (IDU). In 1985, the majority (63 percent) of European adult AIDS cases were attributed to transmission among homo/bisexual men. In contrast, by 1992, only 42 percent of the reported adult AIDS cases were due to transmission among homo/bisexual men. The proportion of European AIDS case infected through IDU increased from 5 percent in 1985 to 36 percent in the early 1990's. In Spain and Italy, the major form of HIV transmission has been IDU. In France, Germany and the United Kingdom, it is through men who have sex with men. By the early 1990's, the United States reported that among adults, 57 percent of AIDS cases were infected through male-to-male sex Data on newly diagnosed HIV infections are now being used to track the HIV epidemic in Europe and provide more relevant information on the current HIV situation since the widespread use of highly active antiretroviral treatment (HAART) in 1996. The number of AIDS cases diagnosed in 2001 was only one-

third of that in 1995. However, data for the first 6 months of 2002 suggest that AIDS incidence is now levelling off.

The rate of newly diagnosed HIV infections has increased by 14% between 1997 and 2001. By transmission group the number of new diagnoses decreased slowly among homo/bisexual men and IDU while it has increased steadily among heterosexual contact. However, analysis'of these increases indicates that they are mostly due to persons originating from a country with a generalized HIV epidemic (UNAIDS and WHO, 2003).

Eastern Europe and Central Asia

Until the mid-1990s, most of the countries of Eastern Europe appeared to have been spared the worst of the HIV epidemic. But between 1995 and 1998, the former socialist economies of Eastern Europe and Central Asia saw infections increase around six-fold. Most of these epidemics are driven by IDU. In Ukraine for example, the number of diagnosed HIV infections jumped from virtually zero before 1995 to around 20,000 a year from 1996 onwards, about 80% of them in IDUs.

HIV/AIDS is spreading rapidly through the countries of this region, which continues to experience the fastest-growing epidemic in the world. Following the rapid increased in Ukraine and Belarus in 1995, the epidemic then started to take off in other countries of the region.

Moldova in 1996 and the Russian Federation in 1998, followed by Latvia and then Kazakhstan.

Latin America and the Caribbean

Extensive spread of HIV probably began in the early 1980s, initially predominately among MSM and IDU residing in large cities. The spread of HIV/AIDS has been slower in Latin America and the Caribbean than in other developing regions of the world, but sentinel surveillance data are rare and information on HIV prevalence is difficult to find. What can be determined to date is that the HIV epidemic varies from country to country.

Many of the epidemics can be described as being in the low level and concentrated stage. In these countries, the HIV epidemics are found mostly among MSM and IDU. However, 12 countries in this region have an estimated HIV prevalence of 1% or more among pregnant women. In several of the countries forming the Caribbean Basin, adult HIV prevalence rates are surpassed only by the rates experienced in sub-Saharan Africa, making this the second most affected region in the world (UNAIDS and WHO, 2003).

South and South-East Asia

The HIV/AIDS epidemic arrived later in Asia, in the mid- to late-80s. In the early 1990's Thailand and India accounted for the majority of reported infections. In Bangkok, Thailand, HIV prevalence among IDU increased from less than 1% in late 1987 to about 50% in 1990. In India, high levels of HIV prevalence were found among sex workers tested in Mumbai. By 1992, a number of countries were facing increasing numbers of infections. There were generally concentrated in groups such as IDU and sex workers. By 1993, 10% to 30% of IDUs in Yunnan

Province, China was found to be infected with HIV.

Thailand, which has experienced what is probably the best-documented epidemic in the developing world, began showing evidence of a fall in new infections, especially among sex workers and their clients. But Thailand is still one of the only three countries, including Cambodia and Myanmar with HIV prevalence among 15-49 year olds over 1% (UNAIDS and WHO, 2003).

Sub-Saharan Africa

Most of the available epidemiological data indicate that the extensive spread of HIV started in sub-Saharan Africa in the late 1970s. By the early 1980s, HIV was found in a geographic band stretching from West Africa across to the Indian Ocean, the countries north of the Sahara and those in the southern cone of the continent remained apparently untouched. By 1987, the epidemic began gradually to move south. Some of the most explosive epidemics have been seen in Southern Africa. South Africa has the largest number of people living with HIV/AIDS in the world, 5 million. Botswana and Swaziland have the highest prevalence levels, 38% and 33% respectively. West Africa has been relatively less affected by HIV infection than other regions of sub-Saharan Africa (UNAIDS and WHO, 2003). Uganda and Senegal represent two success stories. Uganda has brought estimated prevalence rate down to 5% by the end of 2001 from an estimated peak of close to 14% in the early 1990s with strong prevention campaigns. HIV prevalence has stabilized in Senegal at a relatively low level. (UNAIDS and WHO, 2003).

2.3 **Signs and Symptoms**

The symptoms of HIV vary depending on the stage of infection. Though people living with HIV tend to be most infectious in the first few months, many are unaware of their status until later stages. The first few weeks after initial infection, individuals may experience no symptoms or a flu-like illness including fever, headache, rash or sore throat.

As the infection progressively weakens the person's immune system, the individual can develop other signs and symptoms such as swollen lymph nodes, weight loss, fever, diarrhoea and cough. Without treatment, they could also develop severe illnesses such as tuberculosis, cryptococcal meningitis, and cancers such as lymphomas and Kaposi's sarcoma, among others (Priscilla *et al, 2005).*

2.4 Transmission Mode

HIV does not survive well outside the body. Therefore, it cannot be transmitted through casual, everyday contact. Mosquitoes and other insects do not transmit HIV.

HIV can be spread by sexual contact with an infected person, by sharing needles and/or syringes and/or other injecting equipment or, less commonly (and now very rarely in countries where blood is screened for HIV antibodies), through transfusions of infected blood or blood clotting factors. Babies born to HIV-infected women may become infected before or during birth or through breastfeeding after birth (IAS, 2005).

2.5 Diagnosis

An HIV test reveals infection status by detecting the presence or absence of antibodies to HIV in the blood. Antibodies are produced by individuals' immune systems to fight off foreign pathogens. Most people have a "window period" of 3 to 12 weeks during which antibodies to HIV are still being produced and are not yet detectable. This early period of infection represents the time of greatest infectivity but transmission can occur during all stages of the infection. Retesting should be done after three months to confirm test results once sufficient time has passed for antibody production in infected individuals.

People must agree to be tested for HIV and appropriate counselling should be provided. HIV test results should be kept confidential, and everyone should receive post-test counselling and follow-up care, treatment and prevention measures as appropriate.

2.6 Treatment

HIV can be suppressed by combination Antiretroviral Therapy (ART) consisting of three or more antiretroviral (ARV) drugs. ART does not cure HIV infection but controls viral replication within a person's body and allows an individual's immune system to strengthen and regain the power to fight off infections. With ART, HIV-infected individuals can live healthy and productive lives. An estimated 6.6 million people living with HIV in low- and middle-income countries were receiving ART at the end of 2010. Of this, an estimated 420 000-460 000 were children. This is a 16-fold increase in the number of

people receiving ART in developing countries between 2003 and 2010 (Priscilla *et al*, 2005).

The four classes of ARV drugs currently available are:

- Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs), which bind to and disable Reverse Transcriptase (RT), a protein that is essential for the reproduction of HIV;
- Nucleoside Reverse Transcriptase Inhibitors (NRTIs), which are faulty versions of building blocks that HIV needs to reproduce itself. When HIV uses NRTIs instead of normal building blocks, reproduction is stalled;
- Protease Inhibitors (PIs), which block the function of a protein called protease, essential for HIV reproduction; and
- Fusion Inhibitors, which block HIV from entering target cells — since HIV needs to be inside cells to replicate, this prevents reproduction.

2.6.1 Combination Therapy

This is a course of antiretroviral treatment that involves two or more ARVs in combination.

2.6.2 **Highly Active Antiretroviral Therapy**

Highly Active Antiretroviral Treatment (HAART) is a modality of antiretroviral treatment that involves the use of three or more ARVs. HAART strengthens the immune system and thus helps prevent opportunistic infections.

2.7 Role of CD4 T- lymphocytes in Disease Progression

The CD4 T-lymphocytes; a subpopulation of the lymphocytes also known as T helper cells, are coordinators of the body's immune response, e.g., providing help to B cells in the production of antibody, as well as in augmenting cellular immune response to antigens.

The "CD" or cluster of differentiation is a protein expressed on the surface of the cells of the hematopoetic system. The expression of these proteins is used in lymphocyte nomenclature.

These proteins are often associated with the specific function of the cells. Cells with different functions express different CD molecules (for example: CD3+ cells are total T-lymphocytes, CD4+ cells are T helper cells, CD8+ cells are cytotoxic T-lymphocytes and CD19+ are B lymphocytes).

CD4 T-lymphocytes occupy the central position in regulating immune functions. CD4 T-lymphocytes are the primary targets of HIV. The relentless destruction of CD4 T-lymphocytes by HIV, either directly or indirectly, results in the loss of HIV-specific immune response (WHO, 2007).

2.7.1 CD4 T-Iymphocytes and HIV

Within hours of exposure to HIV, CD4 T-lymphocytes are found to be infected showing active viral replication. The infected CD4 cells release virions by budding through the cell membrane or by lysis of the infected cells. The released virus particles then infect uninfected CD4 T-lymphocytes. CD4 T lymphocytes

also serve as important reservoirs of I-IIV: a small proportion of these cells carry HIV provirus integrated in the host DNA without active virus multiplication.

During the primary HIV infection, the number of CD4 T-lymphocytes in the bloodstream decreases by 20% to 40%. HIV brings about the lysis of HIV infected cells as well as bystander uninfected cells using various mechanisms such as lysis of the cells infected with HIV. Billions of CD4 T-lymphocytes may be destroyed every day, eventually overwhelming the immune system's regenerative capacity. In acute HIV-1 infection, in addition to the decline in CD4 T-lymphocytes counts, qualitative impairments of CD4 T-lymphocytes function are detected. The impairment of HIV-1-specific CD4 T-lymphocytes function occurs very early in acute infection. Following acute primary HIV infection, one may remain free of HIV-related illnesses, often for years, despite ongoing replication of HIV in the lymphoid organs and relentless destruction of the immune system. However, during the period, the immune system remains sufficiently competent to provide immune surveillance and to prevent most infections. Although the decrease in the total number of T-lymphocytes marks the decrease in immune competence, sometimes the quantitative loss of CD4 T-lymphocytes may not be matched by the qualitative functions. A number of assays such as cytokine induction, antigen induced proliferation, measurement of activation markers etc can assess the functions of lymphocytes. However, the total CD4 T-lymphocytes number still remains the most robust marker of immune competence (WHO, 2007).

The progressive loss of CD4 T-lymphocytes eventually results in the loss of an ability to mount desirable immune response to any pathogen and vulnerability to opportunistic pathogens characteristic of AIDS. The estimation of peripheral CD4 T-lymphocytes counts is relied upon for taking a decision on initiation of ART. The estimation of peripheral CD4 T-lymphocytes counts has also been used as a tool for monitoring disease progression and the effectiveness of antiretroviral treatment (ART). The changes in the CD4 T lymphocytes counts are important indicators of the response to ART. HIV plasma virus load is a sensitive indicator of the progression of HIV disease. However, due to the relatively high cost of virus load estimation, the CD4 T-lymphocytes count remains the most important key indicator for initiation and monitoring of ART and a measure of the effectiveness of the treatment in clinical trial evaluations (WHO, 2007).

2.7.2 CD4 T-lymphocyte Counts and Antiretroviral Therapy

2.7.2.1 CD4 Count not Available

In the absence of facilities for CD4 T-lymphocytes count, all patients with WHO stages 3 and 4 disease should start ART. Those with WHO stages 1 and 2 disease should be monitored carefully, with a minimum of three-monthly clinical reviews and at any time if new symptoms develop (WHO, 2007).

2.7.2.2 CD4 Count Available

The optimum time to commence ART is prior to patients becoming unwell or presenting with their first CH. Disease progression is greater in patients who commence ART with a CD4 T-lymphocytes count <200 cells per micro litre

compared with those who start therapy at counts above this level. If facilities for CD4 T-lymphocytes count measurement are available, ART should be started before the CD4 count drops below 200 cells per micro litre. The optimum time to initiate ART in patients with a CD4 cell count of 200-350 cells per micro litre remains unknown, and patients with CD4 counts in this range require regular clinical and immunological evaluation. Initiation of ART is recommended for all patients with pulmonary TB or severe bacterial infections and CD4 counts <350 cells per micro litre. Initiation of ART is also recommended for all pregnant women with any stage 3 disease and a CD4 count <350 cells per micro litre. The decision to initiate ART in adults and adolescents is based on clinical and immunological assessment. In many resource-limited settings, clinical staging alone will be available to guide the decision of when to start ART. Measuring viral load (HIV RNA) is not recommended to guide decision on when to start ART. In the era of highly active anti-retroviral therapy, it has been possible to reverse the decline in CD4 T-lymphocytes numbers as a result of potent anti-HIV treatment and control of plasma viremia. As untreated HIV infection progresses, the CD4 T-lymphocytes count declines about 4% per year. In response to successful ART, the CD4 T-lymphocytes count typically increases by >50 cells per micro litre within weeks after viral suppression, and then increases 50-100 cells per micro litre per year thereafter until a threshold is reached. In some patients, CD4 T-lymphocytes counts may not increase as quickly or as steadily, even with durable viral load suppression (WHO, 2007).

2.7.2.3 Relevant of CD4 Count in Monitoring HIV Clients on ART

Since the introduction of HAART, much has been studied regarding which factors best predict a patient's success on HAART. Previously described predictors of treatment failure include poor adherence to medications, one or more missed visits in the previous year, prior virologic failure, a regimen consisting only of nucleosides, higher baseline viral loads and lower baseline CD4 cell counts, (Robbins *et a!,* 2007). Scoring systems have been designed and validated to assess the incidence of clinical disease progression among patients receiving HAART. In a model designed by the EuroSIDA study group, the most recent CD4 cell count, viral load and haemoglobin level were independently related to the risk of disease progression, as was a late presentation of persons with advanced disease, before the start of HAART (Lundgren *et al,* 2002).

Several cohort studies and clinical trials have shown that the CD4 count is the strongest predictor of subsequent disease progression and survival, (Egger *et al,* 2002). The use of the CD4 count as an independent and reliable marker for treatment outcome is attractive from various aspects. First, CD4 counts are already the most important factor in deciding whether to initiate antiretroviral therapy and opportunistic prophylaxis — all HIV-positive patients in high-income countries, and an increasing number of patients in low-income countries have a baseline CD4 count at entry into care. Second, the CD4 count is a relatively objective and simple marker to follow. Finally, the cost of CD4 counts has become more affordable, including developing countries (MacLennan *et al,* 2007). This article further evaluates the use of the CD4 count in assessing the

clinical status of HIV-infected individuals, in making informed decisions regarding the initiation of antiretroviral therapy and in monitoring the success of such therapy.

2.7.3 ART Adherence and CD4 Count

A decrease in viral load generally goes hand in hand with an increase in CD4 count. However, over the shorter term the impact of adherence on viral load is more apparent than a change in CD4 count, largely because of the time delay between the two responses (Gross *et a!*, 2001; Press *et al,* 2002). Falling CD4 counts are usually a result of virologic failure. This sequence of events was appreciated in recent research which suggested that pharmacy refill adherence can accurately predict patient's response to treatment (in particular virologic failure) and allow time for intervention, when compared to the use of CD4 counts which the WHO recommends in resource-limited settings to monitor treatment success (Bisson *et al,* 2008).

Only a few studies have chosen to evaluate immunologic outcomes of adherence specifically (Wood *et al,* 2004; Safren *et al,* 2005), probably because of the concerns highlighted above. However, there are many studies that have assessed both virologic and immunologic outcomes (Haubrich *et al,* 1999; Paterson *et al,* 2000; Gross *et al*, 2001; Mannheimer *et al,* 2002; Kitahata *et* al, 2004). Not surprisingly, these found adherence to be the most significant factor influencing the increase in CD4 count. The study by Wood et al (2004) in particular put an end to concerns that late initiation on ART (after CD4 count drops below 350 cells per micro litre) might cause irreparable damage to the immune system, so

precluding a CD4 response to ART. It found that substantial CD4 count gains are possible in patients with advanced stage infection, provided they are adherent to treatment.

Among those with a CD4 count of less than 50 cells per micro litre, absolute CD4 counts in adherent patients rose to 200 cells per micro litre during the fifth 15-week period of treatment, compared to 60 cells per micro litre in non-adherent patients. As with viral load, any adherence level less than 100% was associated with a less-than-optimal CD4 count response (Veenstra *et al,* 2009).

2.8 Opportunistic Infections

Opportunistic Infections (01s) are illntsses caused by organisms that do not usually cause disease in persons with normal immune systems. The most common °Is in people living with HIV/AIDS include:

- Candidiasis (Thrush), a fungal infection of the mouth, throat or vagina;
- Cytomegalovirus (CMV), a viral infection that causes eye disease that can lead to blindness;
- Herpes simplex viruses, which can cause oral or genital herpes. (These are common infections, but outbreaks for people living with HIV/AIDS can be more frequent and more severe.);
- Mycobacterium avium complex (MAC or MAI), a bacterial infection that can cause recurring fevers, problems with digestion and serious weight loss;
- Pneumocystis pneumonia (PCP), a fungal infection that can cause a fatal pneumonia;

- Toxoplasmosis (Toxo), a protozoal infection of the brain; and
- Tuberculosis (TB), a bacterial infection that attacks the lungs and can cause meningitis. TB is one of the leading causes of death for people living with HIV/AIDS.
- Malaria is common in the developing world. It is more common and severe in people with HIV infection.

2.9 HIV Prevention

2.9.1 Microbicides

These are substances that can substantially reduce transmission of one or more sexually transmitted diseases (STDs). They work by either destroying the microbes or preventing them from establishing an infection. An HIV microbicide would provide a user-controlled method of prevention. Scientists are currently exploring microbicide development as a potential HIV prevention method.

2.9.2 Condom

Condom use is one of the least expensive, most cost-effective methods for preventing HIV transmission. Consistent, correct condom use significantly reduces the risk of HIV and other STDs.

2.9.3 Vaccines

Vaccines to prevent HIV infection or improve the ability of the immune system to defend itself are being tested by researchers. Global investment in HIV vaccine research is estimated at US$650 million per year, but it is likely that a successful vaccine is still a number of years away (International AIDS Vaccine Initiative: http://www.iavi.org/viewpage.cfm?aid=13).

2.9.4 Mother-To-Child Transmission

The prevention of Mother-to-Child Transmission (PMTCT) of HIV can. be reduced significantly through the use of antiretroviral by HIV-positive women during pregnancy and delivery, and by their infants following birth. These regimens reduce the risk of MTCT by decreasing viral replication in the mother and through prophylaxis of the infant during and after exposure to the virus.

2.9.5 Post Exposure Prophylaxis

Post Exposure Prophylaxis (PEP) involves the short-term use of antiretroviral to prevent infection in people who have recently been exposed (such as health care workers through needles tick injuries or women who have been raped). PEP significantly reduces the risk of infection, but is not 100% effective.

2.9.6 Socio-Behavioural Interventions

These are educational programmes designed to encourage individuals to change their behaviour to reduce their exposure to HIV and risk for infection. Such efforts include encouraging proper and consistent condom use, the use of sterile syringes, a reduction in the number of sexual partners, abstinence and the delaying of sexual debut among youth (U.S. National Institutes of Health: http://aidsinfo.nih.gov/other/cbrochure/english/cbrochure_en.pdt).

2.10 The Impact of IIIV/AIDS **in Africa**

Two-thirds of all people infected with HIV live in sub-Saharan Africa, although this region contains little more than 10% of the world's population. AIDS has caused immense human suffering in the continent. The most obvious effect of this

crisis has been illness and death, but the impact of the epidemic has certainly not been confined to the health sector; households, schools, workplaces and economies have also been badly affected.

During 2009 alone, an estimated 1.3 million adults and children died as a result of AIDS in sub-Saharan Africa. Since the beginning of the epidemic more than 15 million Africans have died from AIDS.

Although access to antiretroviral treatment is starting to lessen the toll of AIDS, fewer than half of Africans who need treatment are receiving it. The impact of AIDS will remain severe for many years to come.

2.10.1 The Impact on the Health Sector

In all heavily affected countries the AIDS epidemic is adding additional pressure on the health sector. As the epidemic matures, the demand for care for those living with HIV rises, as does the toll of AIDS on health workers.

2.10.2 The Effect on Hospitals

As the HIV prevalence of a country rises, the strain placed on its hospitals is likely to increase. In sub-Saharan Africa, people with HIV-related diseases occupy more than half of all hospital beds. Government-funded research in South Africa has suggested that, on average, HIV-positive patients stay in hospital four times longer than other patients.

Hospitals are struggling to cope, especially in poorer African countries where there are often too few beds available. This shortage results in people being admitted only in the later stages of illness, reducing their chances of recovery.

2.10.3 Health Care Workers

While AIDS is causing an increased demand for health services, large numbers of healthcare professionals are being directly affected by the epidemic. Botswana, for example, lost 17% of its healthcare workforce due to AIDS between 1999 and 2005. A study in one region of Zambia found that 40% of midwives were HIV-positive. Healthcare workers are already scarce in most African countries. Excessive workloads, poor pay and migration to richer countries are among the factors contributing to this shortage.

Although the recent increase in the provision of antiretroviral drugs (which significantly delay the progression from HIV to AIDS) has brought hope to many in Africa, it has also put increased strain on healthcare workers. Providing antiretroviral treatment to everyone who needs it requires more time and training than is currently available in most countries.

2.10.4 The Impact on Households

The toll of HIV and AIDS on households can be very severe. Although no part of the population is unaffected by HIV, it is often the poorest sectors of society that are most vulnerable to the epidemic and for whom the consequences are most severe. In many cases, the presence of AIDS causes the household to dissolve, as parents die and children are sent to relatives for care and upbringing. A study in

rural South Africa suggested that households in which an adult had died from AIDS were four times more likely to dissolve than those in which no deaths had occurred. Much happens before this dissolution takes place: AIDS strips families of their assets and income earners, further impoverishing the poor.

2.10.5 Impact of the HIV Epidemic on TB

HIV infection also influences the incidence of other diseases due to its suppression of the body's immune response. There is abundant evidence that PLHIV are vulnerable to a variety of renal and rheumatological autoimmune diseases, while some cancers, such as Kaposi sarcoma, are almost exclusively linked to HIV. And there are of course a multitude of other infections that are usually suppressed by an intact immune system.

2.10.6 Household Income

In Botswana it is estimated that, on average, every income earner is likely to acquire one additional dependent over the next ten years due to the AIDS epidemic. A dramatic increase in destitute households — those with no income earners — is also expected.

Other countries in the region are experiencing the same problem, as individuals who would otherwise provide a household with income are prevented from working — either because they are ill with AIDS themselves or because they are caring for another sick family member.

Such a situation is likely to have repercussions for every member of the family. Children may be forced to abandon their education and in some cases women may be forced to turn to sex work ('prostitution'). This can lead to a higher risk of **HIV** transmission, which further exacerbates the situation.

2.10.7 **Food Production**

The AIDS epidemic adds to food insecurity in many areas, as agricultural work is neglected or abandoned due to household illness. In Malawi, where food shortages have had a devastating effect, it has been recognised that HIV and AIDS have diminished the country's agricultural output. It was calculated in 2006 that by 2020, Malawi's agricultural workforce will be 14% smaller than it would have been without HIV and AIDS. In other countries, such as Mozambique, Botswana, Namibia and Zimbabwe, the reduction is likely to be over 20%.

A study in Kenya demonstrated that food production in households in which the head of the family died of AIDS were affected in different ways depending on the sex of the deceased. As in other sub-Saharan African countries, it was generally found that the death of a male reduced the production of 'cash crops' (such as coffee, tea and sugar), while the death of a female reduced the production of grain and other crops necessary for household survival.

2.10.8 Healthcare Expenses and Funeral Costs

Taking care of a person sick with **AIDS is not only an emotional strain for household members, but also a major strain on household** resources. Loss of income, additional care-related expenses, the reduced ability of caregivers to

work, and mounting medical fees push affected households deeper into poverty. It is estimated that, on average, HIV-related care can absorb one-third of a household's monthly income.

The financial burden of death can also be considerable, with some families in South Africa easily spending seven times their total household monthly income on a funeral. Furthermore, although many South Africans contribute to some sort of funeral insurance plan, many of these are inadequately funded, and it is arguable that such financial arrangements detract from other savings plans or health insurance.

Aside from the financial burden, providing home based care can impose demands on the physical, mental and general health of carers — usually family and friends of the sick person. Such risks are amplified if carers are untrained or unsupported by a home-based care organisation.

2.10.9 The Impact on Children

It is hard to overemphasise the trauma and hardship that children affected by HIV and AIDS are forced to bear. The epidemic not only causes children to lose their parents or guardians, but sometimes their childhood as well.

As parents and family members become ill, children take on more responsibility to earn an income, produce food, and care for family members. It is harder for these children to access adequate nutrition, basic health care, housing and clothing.

Because AIDS claims the lives of people at an age when most already have young children, more children have been orphaned by AIDS in Africa than anywhere else. Many children are now raised by their extended families and some are even left on their own in child-headed households.

As projections of the number of AIDS orphans rise, some have called for an increase in institutional care for children. However this solution is not only expensive but also detrimental to the children. Institutionalisation stores up problems for society, which is ill equipped to cope with an influx of young adults who have not been socialised in the community in which they have to live. There are other alternatives available. One example is the approach developed by church groups in Zimbabwe, in which community members are recruited to visit orphans in their homes, where they live either with foster parents, grandparents or other relatives, or in child-headed households.

The way forward is prevention. Firstly, it is crucial to prevent children from becoming infected with HIV at birth as well as later in life. Secondly, if efforts are made to prevent adults becoming infected with HIV, and to care for those already infected, then fewer children will be orphaned by AIDS in the future.

2.10.10 The Impact on the Education Sector

The relationship between AIDS and the education sector is circular — a s the epidemic worsens, the education sector is damaged, which in turn is likely to increase the incidence of HIV transmission. There are numerous ways in which AIDS can affect education, but equally there are many ways in which education

can help the fight against AIDS. The extent to which schools and other education institutions are able to continue functioning will influence how well societies eventually recover from the epidemic.

"Without education, AIDS will continue its rampant spread. With AIDS out of control, education will be out of reach." *Peter Piot, Director of UNAIDS*

A decline in school enrolment is one of the most visible effects of the epidemic. This in itself will have an effect on HIV prevention, as a good, basic education ranks among the most effective and cost-effective means of preventing HIV.

There are numerous barriers to school attendance in Africa. Children may be removed from school to care for parents or family members, or they may themselves be living with HIV. Many are unable to afford school fees and other such expenses — this is particularly a problem among children who have lost their parents to AIDS, who often struggle to generate income.

Studies have suggested that young people with little or no education may be around twice as likely to contract HIV as those who have completed primary education. In this context, the devastating effect that AIDS is having on school enrolment is a big concern. In Swaziland and the Central African Republic, it was reported that school enrolment fell by 25-30% due to AIDS at the beginning of the millennium.

2.10.11 The Impact on Teachers

HIV and AIDS are having a devastating effect on the already inadequate supply of teachers in African countries; for example, a study in South Africa found that 21% of teachers aged 25-34 were living with HIV.

Teachers who are affected by HIV and AIDS are likely to take periods of time off work. Those with sick families may also take time off to attend funerals or to care for sick or dying relatives, and further absenteeism may result from the psychological effects of the epidemic.

When a teacher falls ill, the class may be taken on by another teacher, may be combined with another class, or may be left untaught. Even when there is a sufficient supply of teachers to replace losses, there can be a significant impact on the students. This is particularly concerning given the important role that teachers can play in the fight against AIDS.

The illness or death of teachers is especially devastating in rural areas where schools depend heavily on one or two teachers. Moreover, skilled teachers are not easily replaced. The impact of AIDS in Tanzania for example means that in 2006 it was estimated that around 45,000 additional teachers were needed to make up for those who had died or left work because of HIV and AIDS. The greatest proportion of staff that have been lost, according to the Tanzania Teacher's Union, were experienced staff between the ages of 41 and 50.

2.10.12 The **Impact** on **Enterprises and Workplaces**

HIV and AIDS dramatically affect labour, setting back economic and social progress. The vast majority of people living with HIV in Africa are between the ages of 15 and 49 - in the prime of their working lives.

AIDS damages businesses by squeezing productivity, adding costs, diverting productive resources, and depleting skills. Company costs for health-care, funeral benefits and pension fund commitments are likely to rise as the number of people taking early retirement or dying increases. Also, as the impact of the epidemic on households grows more severe, market demand for products and services can fall. The epidemic hits productivity through increased absenteeism. Comparative studies of East African businesses have shown that absenteeism can account for as much as 25-54% of company costs.

A study in several Southern African countries has estimated that the combined impact of AIDS-related absenteeism, productivity declines, health-care expenditures, and recruitment and training expenses could cut profits by at least 6-8%. Another study of a thousand companies in Southern Africa found that 9% had suffered a significant negative impact due to AIDS. In areas that have been hit hardest by the epidemic, it found that up to 40% of companies reported that HIV and AIDS were having a negative effect on profits.

Some companies, though, have implemented successful programmes to deal with the epidemic. An example is the gold-mining industry in South Africa. The gold mines attract thousands of workers, often from poor and remote regions. Most live

in hostels, separated from their families. As a result a thriving sex industry operates around many mines and HIV is common. In recent years, mining companies have been working with a number of organizations to implement prevention programmes for the miners. These have included mass distribution of condoms, medical care and treatment for sexually transmitted diseases, and awareness campaigns. SOme mining companies have started to replace all-male hostels with accommodation for families, in order to reduce the transmission of HIV and other sexually transmitted diseases.

In Swaziland, an employers' anti-AIDS coalition has been set up to promote voluntary counselling and testing. The coalition not only includes larger companies but also small and medium sized enterprises. In Botswana, the Debswana diamond company offers all employees HIV testing, and provides antiretroviral drugs to HIV positive workers and their spouses. This policy was introduced in 1999 when the company found that many of their workforce were HIV positive. With a skilled workforce, it is financially worth their while to protect the health and therefore the productivity of their workers. Nevertheless, workplace programmes for HIV treatment and prevention remain scarce in Africa.

2.10.13 The Impact on Life Expectancy

In many countries of sub-Saharan Africa, AIDS is erasing decades of progress in extending life expectancy. In the worst affected countries, average life expectancy has fallen by twenty years because of the epidemic. Life expectancy at birth in Swaziland is just 31 years - less than half of what it would be without AIDS.

The impact that AIDS has had on average life expectancy is partly attributed to child mortality, as increasing numbers of babies are born with HIV infections acquired from their mothers. The biggest increase in deaths, however, has been among adults aged between 20 and 49 years. This group now accounts for 60% of all deaths in sub-Saharan Africa, compared to 20% between 1985 and 1990, when the epidemic was in its early stages. By affecting this age group so heavily, AIDS is hitting adults in their most economically productive years and removing the very people who could be responding to the crisis.

2.10.14 The Economic Impact

Through its impacts on the labour force, households and enterprises, AIDS has played a significant role in the reversal of human development in Africa. One aspect of this development reversal has been the damage that the epidemic has done to the economy, which, in turn, has made it more difficult for countries to respond to the crisis.

One way in which AIDS affects the economy is by reducing the labour supply through increased mortality and illness. Amongst those who are able to work, productivity is likely to decline as a result of HIV-related illness. Government income also declines, as tax revenues fall and governments are pressured to increase their spending to deal with the expanding HIV epidemic.

The abilities of African countries to diversify their industrial base, expand exports and attract foreign investment are integral to economic progress in the region. By making labour more expensive and reducing profits, AIDS limits the ability of

African countries to attract industries that depend on low-cost labour and makes investments in African businesses less desirable.

The impact that AIDS has had on the economies of African countries is difficult to measure. The economies of the worst affected countries were already struggling with development challenges, debt and declining trade before the epidemic started to affect the continent. AIDS has combined with these factors to further aggravate the situation. It is thought that the impact of AIDS on the gross domestic product (GDP) of the worst affected countries is a loss of around 1.5% per year; this means that after 25 years the economy would be 31% smaller than it would otherwise have been.

2.10.15 The Future Impact of HIV/AIDS

This page has outlined just some of the ways in which the AIDS epidemic has had a significant impact on countries in sub-Saharan Africa. Although both international and domestic efforts to overcome the crisis have been strengthened in recent years, the people of sub-Saharan Africa will continue to feel the effects of HIV and AIDS for many years to come. It is clear that as much as possible needs to be done to minimize this impact.

As access to treatment is slowly expanded throughout the continent, millions of lives are being extended 'and hope is being given to people who previously had none. Unfortunately though, the majority of people in need of treatment are still not receiving it, and campaigns to prevent new infections (which must remain the central focus of the fight against AIDS) are lacking in many areas.

2.11 HIV/AIDS Situation in Ghana

The first case of HIV/AIDS was reported in Ghana in 1986 and it is spread primarily through heterosexual sex in Ghana (USAID, 2003) The HIV/AIDS prevalence rate (the percent of people living with the disease) in Ghana is still relatively low compared to the sub-Saharan African region overall, and appears to be fairly stable, but there are an increasing number of people living with HIV/AIDS in this low-income country, posing challenges to both prevention and treatment efforts (UNAIDS, 2004). The Government of Ghana created a National Advisory Commission on AIDS (NACA) in 1985 and established NACP in 1987. The GAC was inaugurated in 2000, followed by the implementation of the country's National Strategic Framework (NSF) on HIV/AIDS for 2001-2005 (GAC, 2004.)

There is significant variation in HIV prevalence rates across the country with the highest rates found in the Eastern Region and the lowest in the Upper West and Northern Regions. HIV prevalence rates are also higher in border regions, in mining areas and along major transportation routes (GOG and MOH, *2004*). The national prevalence rate as at 2009 was 1.9% (2005-2009, HSS Reports).

CHAPTER THREE

METHODOLOGY

3.1 Background of the Study Area

This research is comprise of all HIV/AIDS clients receiving clinical care and only those initiated on treatment as at 2007 to 2011 of Kassena-Nankana East District in the Upper East Region of Ghana. Clients who did not have their CD4 count repeated were excluded in the study.

The district has a population of 109,944 people (53,676 males and 56,268 females) as against the regional population of 1,046,545 people of which 506,405 are males and 540,140 females (GSS, May 2012). The district is 11km away to Ghana - Burkina Faso border with only one ART clinic providing services to PLWHA in the district with 14 PMTCT sites purposely for PMTCT services as at November, 2011 (DHMT, Navrongo, 2011). HIV prevalence rate in the district is 2.8 per cent higher than that of the regional, 2.2 per cent (HSS, 2009).

3.2 Source of Data and Data Collection

The data for this research was mainly secondary data from War Memorial Hospital ART clinic under the National AIDS/STI Control Programme in Kassena-Nankana East District of the Upper East Region of Ghana covering a period of five (5) years from 2007 to 2011. The variables or factors studied includes: initial CD4 count, next CD4 count after treatment initiation, age, gender, education, marital status, alcohol consumption, smoking, height, weight, religion,

and number of months in between initial and next CD4 count taken. Statistical packages used for the analysis include SAS and SPSS.

3.3 Generalized Linear Model

Generalized linear model (GLM) is a flexible generalization of ordinary linear regression that allows for response variables that have other than a normal distribution. The GLM generalizes linear regression by allowing the linear model to be related to the response variable via a link function and by allowing the magnitude of the variance of each measurement to be a function of its predicted value.

Generalized linear models were formulated by John Nelder and Robert Wedderburn as a way of unifying various other statistical models, including linear regression, logistic regression and Poisson regression.

In a generalized linear model (GLM), each outcome of the dependent variables, Y, is assumed to be generated from a particular distribution in the exponential family, a large range of probability distributions that includes the normal, binomial and Poisson distributions, among others. The mean, *p,* of the distribution depends on the independent variables, X, through:

$$E(Y) = ,u = g^{-t}(\mathrm{X},\mathrm{o}) \qquad (3.1)$$

where E(Y) is the expected value o f Y; Xfi is the *linear predictor,* a linear combination of unknown parameters, ,8; *g* is the link function.

In this framework, the variance is typically a function, V, of the mean:

$$\text{Var}(Y) = V(p) = V(g^{1}\ (NO \qquad (3.2)$$

It is convenient if V follows from the exponential family distribution, but it may simply be that the variance is a function of the predicted value.

The unknown parameters, /3, are typically estimated with maximum likelihood, maximum quasi-likelihood, or Bayesian techniques.

3.3.1 Model Components

The GLM consists of three elements:

i. A probability distribution from the exponential family

ii. A linear predictor / = Xfi

iii. A link function g such that E(Y) = μ =

3.3.2 **Probability Distribution**

The over dispersed exponential family of distributions is a generalization of the exponential family and exponential dispersion model of distributions and includes those probability distributions, parameterized by 0 and T , whose density functions f (or probability mass function, for the case of a discrete distribution) can be expressed in the form

$$iy(Y10,T)=h(y,r)exp\left(\frac{b(0)T\ T(y)-\ A(0)}{d(r)} \right| \qquad (3.3)$$

T, called the *dispersion parameter*, typically is known and is usually related to the variance of the distribution. The functions $h(y, z^{-})$, $b(6)$, $T(y)$, $A(9)$, and $d(r)$ are known. Many, although not all, common distributions are in this family.

For scalar Y and 9, this reduces to

$$fy(y\ I\ 0,r) = h(y, r)\ \exp\frac{b(0)\ T(y) - A(0)}{d(r)} \qquad (3.4)$$

9 is related to the mean of the distribution. If $b(0)$ is the identity function, then the distribution is said to be in canonical form (or *natural form)*. It should be noted that any distribution can be converted to canonical form by rewriting 0 as $0'$ and then applying the transformation $0 = b(0^{1})$. It is always possible to convert $A(0)$ in terms of the new parameterization, even if $b(0')$ is not a one-to-one function. If, in addition, $T(y)$ is the identity and r is known, then 0 is called the *canonical parameter* (or *natural parameter)* and is related to the mean through

$$= E(Y) = VA(9) \qquad (3.5)$$

For scalar Y and 0 , this reduces to

$$p = E(Y) = \qquad (0) \qquad (3.6)$$

Under this scenario, the variance of the distribution can be shown to be

$$Var(Y) = \text{VV}\ A(0)\ d(r) \qquad (3.7)$$

For scalar Y and 9, this reduces to

$$Var(Y) = A''(0)d(r) \qquad (3.8)$$

3.3.3 Linear Predictor

The linear predictor is the quantity which incorporates the information about the independent variables into the model. The symbol (Greek "eta") is typically used to denote a linear predictor. It is related to the expected value of the data (thus, "predictor") through the link function.

ri is expressed as linear combinations (thus, "linear") of unknown parameters fl. The coefficients of the linear combination are represented as the matrix of independent variables X. can thus be expressed as

$$= \quad (3.9)$$

The elements of **X** are either measured by the experimenters or stipulated by them in the modelling design process.

3.3.4 Link Function

The link function provides the relationship between the linear predictor and the mean of the distribution function. There are many commonly used link functions, and their choice can be somewhat arbitrary. It can be convenient to match the domain of the link function to the range of the distribution function's mean.

When using a distribution function with a canonical parameter *0,* the *canonical link* function is the function that expresses *0* in terms of p , i.e. $0 = b(p)$. For the most common distributions, the mean p is one of the parameters in the standard form of the distribution's density function, and then $b(p)$ is the function as defined above that maps the density function into its canonical form. When using

the canonical link function, $b(p) = B = X/3$, which allows X' Yto be a sufficient statistic for P.

3.4 Negative Binomial Distribution

In probability theory and statistics, the negative binomial distribution is a discrete probability distribution of the number of successes in a sequence of Bernoulli trials before a specified (non-random) number of failures (denoted *r)* occur. "For example, if one throws a die repeatedly until the third time **"1"** appears, then the probability distribution of the number of non-"1"s that had appeared will be negative binomial.

3.4.1 Definition of Negative Binomial Distribution

Suppose there is a sequence of independent Bernoulli trials, each trial having two potential outcomes called "success" and "failure". In each trial the probability of success is p and of failure is $(1 — p)$. We are observing this sequence until a predefined number r of failures has occurred. Then the random number of successes we have seen, X, will have the negative binomial (or Pascal) distribution:

$$X \quad NB(r, , p) \tag{3.10}$$

When applied to real-world problems, outcomes of *success* and *failure* may or may not be outcomes we ordinarily view as good and bad, respectively. Suppose we used the negative binomial distribution to model the number of days a certain machine works before it breaks down. In this case "success" would be the result

on a day when the machine worked properly, whereas a breakdown would be a "failure". If we used the negative binomial distribution to model the number of goal attempts a sportsman makes before scoring a goal, though, then each unsuccessful attempt would be a "success", and scoring a goal would be "failure". If we are tossing a coin, then the negative binomial distribution can give the number of heads ("success") we are likely to encounter before we encounter a certain number of tails ("failure").

The probability mass function of the negative binomial distribution

$$\text{is } f(k) = \Pr(X = k) = \binom{k + r - 1}{k} p^k \text{ for } k = 0,1,2,... \qquad (3.11)$$

Here the quantity in parentheses is the binomial coefficient, and is equal to

$$\frac{(k + r - 1)}{k!\,(r-1)!} = \frac{(k + r - 1)(k + r - 2)\cdots(r)}{k!} \qquad (3.12)$$

This quantity can alternatively be written in the following manner, explaining the name "negative binomial":

$$\frac{(k + r - 1)}{k!} = \frac{(-1)^k (-r)(-r-1)\cdots(-r-k+1)}{k!} = (-1)^k \binom{-r}{k} \qquad (3.13)$$

3.4.2 Mean, Variance, and MGF of Negative Binomial Distribution

If the random variable X has a negative binomial distribution with parameters r and p, then the

i. Mean;

$$E(X) = \frac{pr}{q} \tag{3.14}$$

ii. Variance;

$$Var(X) = \frac{pr}{q^2} \tag{3.15}$$

iii. Moment Generating Function;

$$M_X(t) = \left(\frac{pe^t}{1-qe^t}\right)^k \tag{3.16}$$

where $q = 1 - p$

Negative binomial regression handles dispersion (i.e. zero – inflated or over dispersed) issues by modelling the dispersion parameter of the response variable in place of Poisson and its model expression can be written as

$$\log \mu_i = \beta_0 + \beta_i Z_i \tag{3.17}$$

3.5 Poisson Distribution

The Poisson distribution is named after the French mathematician Simeon Denis Poisson (1781-1840) who developed the distribution. The first application of this distribution was by the Polish economist Ladislaus von Bortkiewics (1868-1931), who studied the probability of deaths from the kick of a horse in a Prussian army and the number of deaths by suicide of women and children. It is used to model the number of occurrences of events of a specified type in a period of time

of length *t*, when events of this type are occurring randomly at a mean rate 2 per unit time.

The Poisson distribution is given by the formula

$$f(x) \qquad \frac{A^x e^{-2}}{x!} \qquad ; \; x = 0\,1\,2 \,,\bullet\bullet\bullet \tag{3.18}$$

where

X = the number of times a particular event occurs in cases where non-occurrences cannot be enumerated

> 0 is the average number of occurrences per unit of time or space e =

the mathematical constant that is the base of natural logarithms

The Poisson distribution is a discrete and it is defined for all non-negative integers indicated by the dots trailing after the values of x in equation 3.1. It is applied to problems in order to find the probability of the number of occurrences, x, of a particular event when non-occurrences have no meaning or cannot be enumerated. It is sometimes said that the Poisson applies to isolated events in a continuum or to rare events.

3.5.1 The Cumulative Distribution Function of Poisson Random Variable The cumulative distribution function of a Poisson random variable X with a parameter 2, , denoted by *P(r;2)* is obtained by adding the successive Poisson probabilities for all values less than or equal to *r*. It is mathematically expressed as

$$P(r;2) = P(X < r) \qquad \underset{x\,=\,o}{} \qquad p(x;2) \tag{3.20}$$

3.5.2 Characteristics of Poisson Distribution

A Poisson distribution is a single parameter distribution, A and is both the mean and the variance. Hence, both the location and spread of the Poisson distribution will change as *A,* changes. For small values of*t,* the distribution is skewed to the right and as 2 is increased, the Poisson distribution tends to be symmetric.

The mathematical expression of the mean and variance are

1. $At = E(X) = A,$ (3.21)
2. $a2 \; E(x\,2) \; [E(x)]2$ ___ (3.22)

3.5.3 Moment Generating Function for Poisson Distribution

If *X* is a random variable having Poisson distribution then the moment generating function of *X* is

$$M\,x\,(t) = e^{\,1(e' -1)} \quad (3.23)$$

There are two assumptions underlying the Poisson distribution:

i. Occurrences must be independent, and

ii. The average number of occurrences must be constant. For instance, consider HIV/AIDS clients arrivals at a clinic for initiation of ART. In order for the Poisson to apply, the arrival of a client must not change the arrival pattern of other clients, and the average rate at which clients arrive must be the same for each time period.

3.5.4 Model Expression of Poisson Distribution

For a specified distribution of Poisson with a link function of log, the Poisson mean parameter, A. is related to the linear predictor by

log (2)= X,/3

The model of a Poisson regression therefore expresses the log outcome rate as a linear function of a set of predictors. i.e.

$$\log_e (0 = A + Ax, + Ax_2 + ... + fi_k x_k \quad (3.24)$$

and so

$$Y = \exp(flo + /^3, X_1 + ,2X2 + ... + flkXk) \quad (3.25)$$

CHAPTER FOUR

RESULTS

4.1 Descriptive Statistics

Table 4.1: Descriptive Statistics of CD4 **Count of Clients on Treatment**

Variable	Min	Max	Mean	Std. Deviation
ICD4 Count Before ART	4	350	158.9	101.5
Next CD4 Count After Start of ART	58	927	403.0	186.4
Change in CD4 Count	8	651	244.1	152.3

The table above (Table 4.1) shows the distribution of three of the variables measured for the 142 persons on ART. The minimum and maximum CD4 count before starting ART was 4 and 350 cells per micro litre with mean CD4 count of 158.9. The next CD4 count, which represents the CD4 count after a person has been on treatment for some time, had a minimum value of 58, and a maximum of 927 cells per micro litre respectively, with mean count of 403. Thus these individuals, after being on treatment for varying periods, experienced changes in CD4 count that ranged from 8 to 651 cells per micro litre.

Table 4.2: Descriptive Breakdown of CD4 Count by Gender

Descriptive Statistics	CD4/Gender					
	ICD4		NCD4		CCD4	
	Male	Female	Male	Female	Male	Female
Mean	160	158.6	352.2	418.4	192.2	259.8
Std dev	95.8	103.6	189.9	183.4	129.4	155.7
Min	11	4	88	58	8	10
Max	343	350	884	927	573	651

Table 4.2 shows the distribution of these three variables by gender. The average initial CD4 count for Males and Females are approximately the same (males= 160, Females=158.6) while after varying periods of treatment, females had a higher CD4 count than males (Females=418.4, Males=352.2). Individually, females experienced a greater change in CD4 count (259.8) on average, than males (192.2).

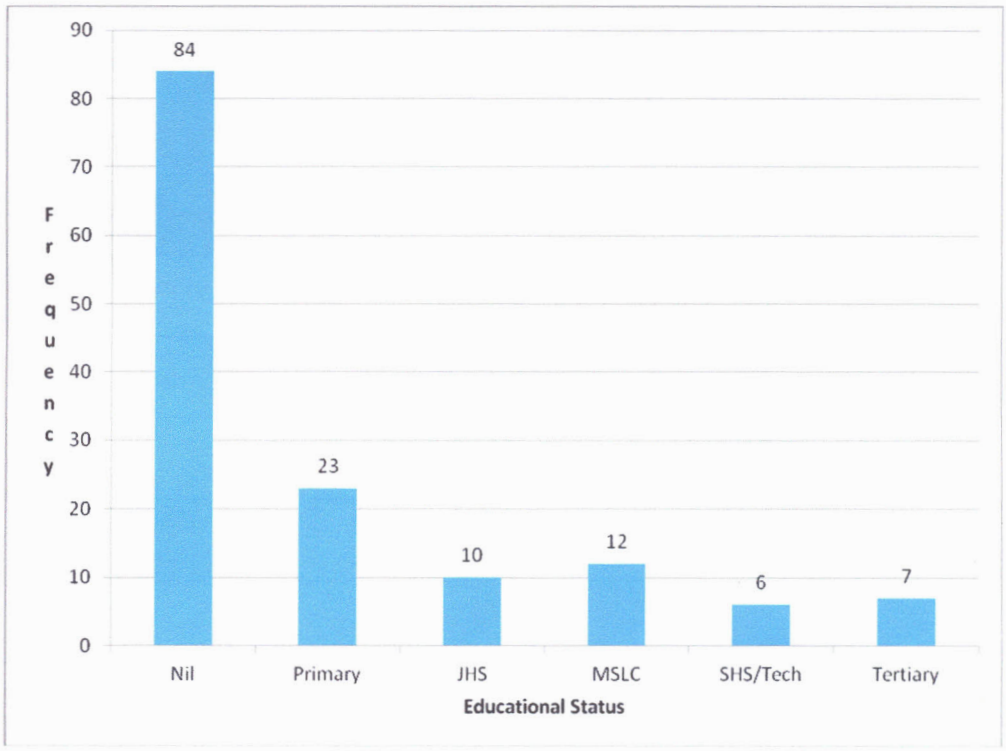

Figure 4.1: Educational Status

Figure 4.1 shows that the educational distribution of the respondents is skewed towards higher education. More than half (84 out of 142) of the persons on ART never had education. The rest of the 58 who have had education, many (23 out of 58) had primary educational attainment. However, clients with a JHS level education, had the best change (295.4) in CD4 count followed by the Primary level clients (260.1), while clients with a MSLC level of education had the worse change (202.6) followed by clients with a Tertiary level education (213.3) as shown in Table A1 in Appendix A.

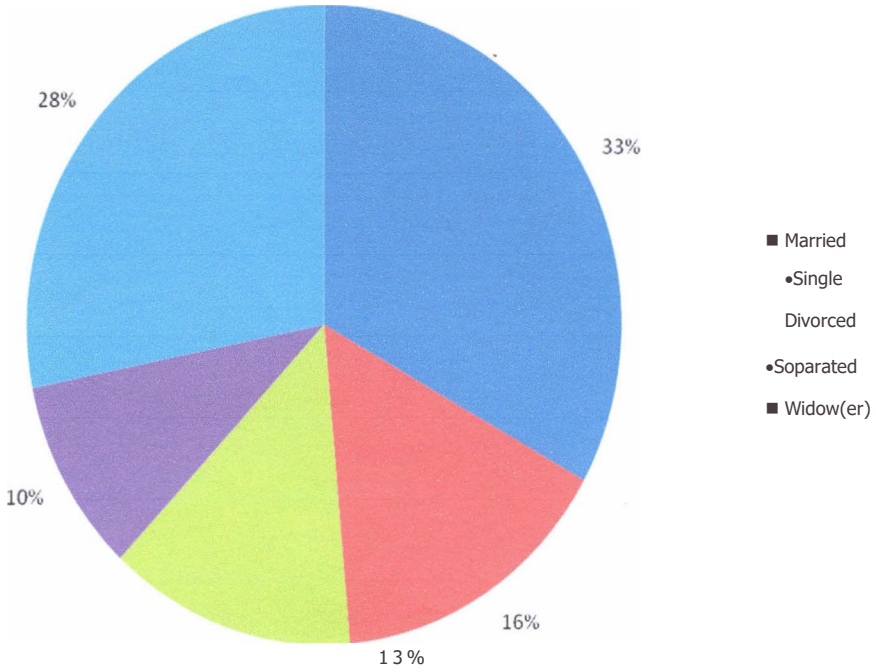

Figure 4.2: Marital Status

The greatest proportion of the persons on ART (33%) in the district as married followed by widow(er) with 28% and the least was those who have separated (representing 10%).

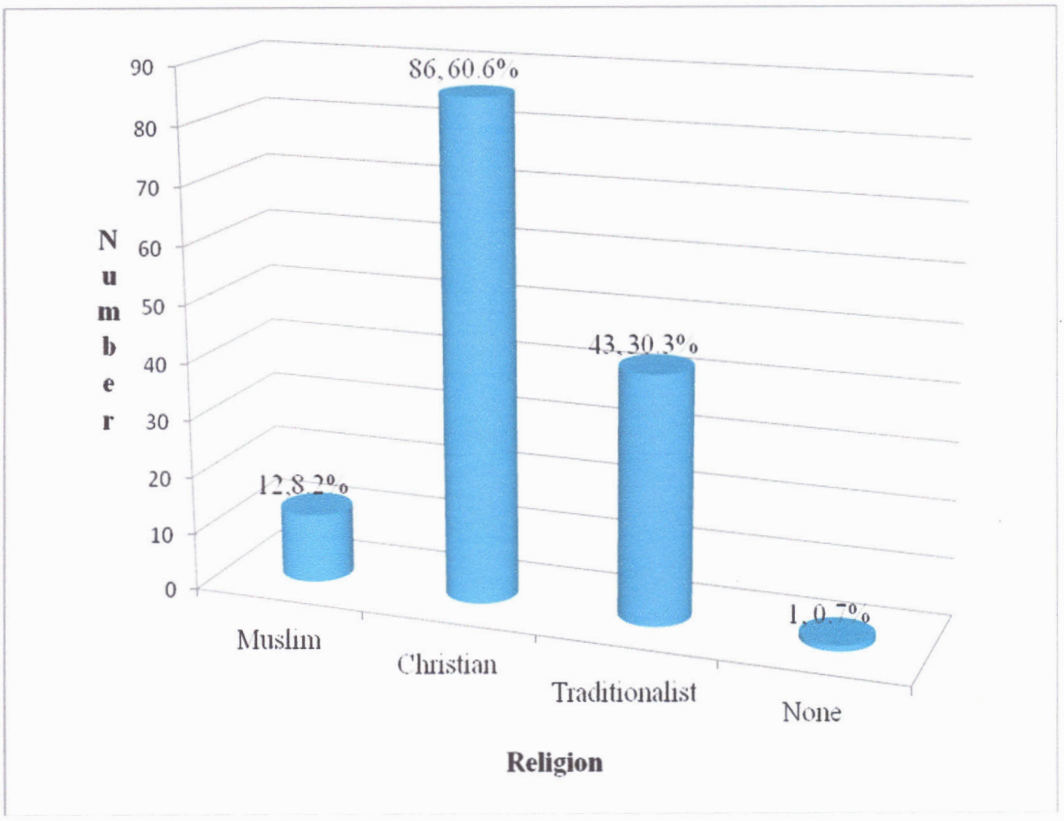

Figure 4.3: Religious Affiliation

The distribution of respondents by religion is shown in Figure 4.3 above. Most clients are Christians (60.6%) followed by Traditionalist (30.3%) and Muslims (8.2%), with only one person who does not belong to any religion.

Table 4.3: Smoking Habit of Clients on ART

Smoking	Frequency	Percent	Mean	Std dev	Min	Max
Yes	3	2.1	160.0	143.3	31	317
No	129	90.8	251.3	152.2	8	651
Stopped	10	7	173.8	129.1	19	435
Total	142	100				

Most (90.8 %) of the HIV/AIDS clients on ART have never been smokers: These clients experienced the highest change in CD4 count on average (251.3 cells per

micro litre). Clients who still smoke (2.1%), experienced on average, the worse change in CD4 count (160 cells per micro litre) as shown in Table 4.3.

Table 4.4: Drinking Habit of Clients on ART

Alcohol intake	Frequency	Percent	Mean	**Std** dev	Min	Max
Yes	31	21.8	213.5	140.6	10	494
No	86	60.6	274.4	158.3	8	651
Stopped	25	17.6	177.8	117.0	42	435
Total	142	100				

Table 4.4, also shows that clients who have stopped the habit of drinking (17.6%) on average experienced the worse change in CD4 count (177.8 cells per micro litre) while those who never developed the habit of drinking, have the best change (274.4 cells per micro litre).

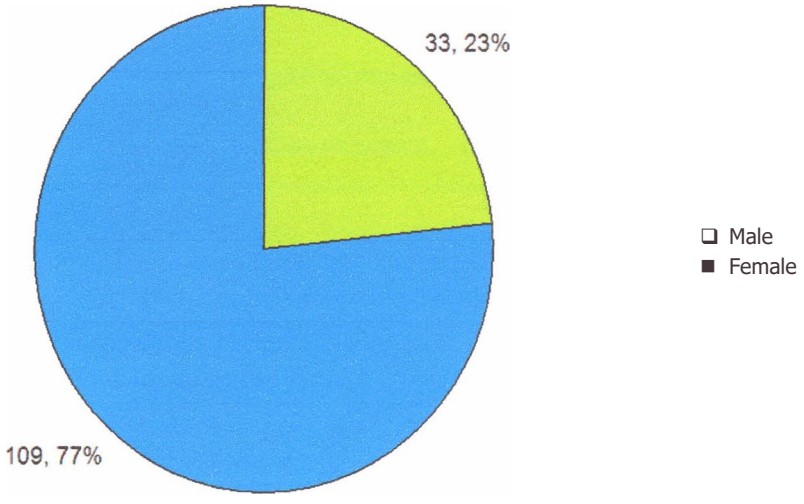

Figure 4.4: Gender Distribution of Clients on ART

Most clients are females (77%) as shown in figure 4.4. This is probably because females are screened during pregnancy and their HIV status is therefore more likely to be known, and therefore captured as clients, as compared to men.

4.2 Analysis of Parameters

The results of the Generalised linear models, depicting the parameter estimates and their significance or otherwise to the model, are shown in Table 4.5 below. The table shows that the period of treatment (months), as well as the weight and height of the client are significant determinants of change in CD4 counts. The Initial CD4 count is not significant.

Table 4.5: Statistical Output for Poisson Distribution

Parameter	DF	Estimate	Standard error	Wald 95% confidence Limits		Chi-square	Chisq p-value
Intercept	1	6.0039	0.1076	5.7929	6.2149	3110.87	<0.0001
Months	1	0.0166	0.0007	0.0152	0.0179	564.12	<0.0001
Age	1	-0.0013	0.0007	-0.0027	0	3.58	0.0585
Gender							
Male	1	-0.287	0.0179	-0.322	0.2519	257.17	<0.0001
Female	0	0	0	0	0	.	.
Education							
Nil	1	0.0802	0.0295	0.0223	0.138	7.38	0.0066
Primary	1	0.1882	0.0316	0.1264	0.2501	35.56	<0.0001
JHS	1	0.3766	0.0342	0.3095	0.4437	120.93	<0.0001
MSLC	1	0.147	0.0372	0.0742	0.2199	15.65	<0.0001
SHS/Tech	1	0.0204	0.0397	-0.0575	0.0982	0.26	0.6079
Tertiary	0	0	0	0	0	.	.

*5% Significance level chosen.

Table 4.5: Statistical Output for Poisson Distribution Continuous

Parameter	DF	Estimate	Standard error	Wald 95% confidence Limits		Chi-square	Chisq p-value
Weight	1	0.0065	0.0006	0.0052	0.0078	100.61	<0.0001
Height	1	-0.0021	0.0007	-0.0034	-0.0007	9.38	0.0022
ICD4	1	0	0.0001	-0.0001	0.0001	0.06	0.8137
Marital Status							
Married	1	0.0061	0.0168	-0.0269	0.0391	0.13	0.7165
Single	1	0.119	0.0207	0.0785	0.1596	33.09	<0.0001
Divorced	1	0.0464	0.0199	0.0073	0.0855	5.42	0.02
Separated	1	0.0172	0.0232	-0.0284	0.0627	0.55	0.4602
Widow(er)	0	0	0	0	0	.	.
Religion							
Muslim	1	-1.1874	0.0488	-1.283	-1.0918	592.71	<0.0001
Christian	1	-1.0142	0.0453	-1.1029	-0.9255	502.12	<0.0001
Traditionalist	1	-0.9262	0.0444	-1.0132	-0.8391	434.96	<0.0001
None	0	0	0	0	0	.	.
Smoking							
Yes	1	-0.2132	0.0549	-0.3208	-0.1055	15.06	<0.0001
No	1	0.0647	0.0295	0.0069	0.1224	4.82	0.0281
Stoped	0	0	0	0	0	.	.
Alcohol intake							
Yes	1	0.0896	0.0221	0.0463	0.1329	16.47	<0.0001
No	1	0.2292	0.0198	0.1903	0.2681	133.4	<0.0001
Stopped	0	0	0	0	0	.	.

*5% Significance level chosen.

For the categorical variables, males differed significantly from females in the change in CD4 counts, while only SHS/Tech level clients did not differ from Tertiary level students in change in CD4 counts. Also, only Single and Divorced clients differed significantly from widow(er) while clients who were religious (Christian, Muslim and Traditional) differed from those with no religious

persuasion. Clients who developed, or did not develop drinking or smoking habits, significantly differed from clients who stopped drinking or smoking.

4.3 General Model Expression for Prediction

$Log_e(Y) = 6.004 - 0.287X, + 0.080X_2 + 0.188X_3 + 0.377X_4 + 0.147X_5 + 0.020X_6 + 0.006X_7 + 0.119X_8 + 0.046X_9 + 0.017X_{10} - 1.187X_1, -1.014X_{12} - 0.926X_{13} + 0.017X_{14} - 0.001X_{15} + 0.007X_{16} - 0.002X_{17} - 0.213X_{18} + 0.065X_{,9} + 0.090X_{20} + 0.229X_{21}$

Implies

$$Y = \exp(6.004 - 0.287 + 0.080X_2 + 0.188X_3 + 0.377X_4 + 0.147X_5 + 0.020X_6 + 0.006X_7 + 0.119X_8 + 0.046X_9 + 0.017X_{10} - 1.187X_1, -1.014X_{12} - 0.926X_{13} + 0.017X_{14} - 0.001X_{15} + 0.007X_{16} - 0.002X_{17} - 0.213X_{18} + 0.065X_{19} + 0.090X_{20} + 0.229X_{21})$$

where

X_1= Male X_2 = No education X_3 = Primary X_4 = JHS X_5 = MSCL X_6 = SHS/Tech X_7 = Married X_8 = Single X_9 = Divorced X_{10} = Separated X_{11}= Muslim X_{12} = Christian X_{13} = Traditionalist X_{14} = Month X_{15} = Age X_{16}= Weight X_{17}= Height X_{18} = Smoke X_{19}= Not Smoking X_{20} = Alcohol X_{21}= No Alcohol

4.4 Reduced Model for Prediction

$Log_e(Y) = 6.004 — 0.287X_1 + 0.080X_2 + 0.188X_3 + 0.377X_4 + 0.147X_5 + 0.119X_6 + 0.017X_7 — 1.187X_8 — 1.014X_9 — 0.926X_{10} + 0.017X_{11} + 0.007X_{17} - 0.002X_3 - 0.213X_{14} + 0.065X_{15} + 0.090X_{16}, + 0.229X_{17}$

Implies

$Y = \exp(6.004 — 0.287X_1 + 0.080X_2 + 0.188X_3 + 0.377X_4 0.147X_5 + 0.119X_6 + 0.017X_7 — 1.187X_8 — 1.014X_9 — 0.926X_{10} + 0.017X_{11} + 0.007X_{12} - 0.002X_{13} - 0.213X_{14} + 0.065X_{15} + 0.090X_{16} + 0.229X_{17})$

where

$X,$ = Male X_2 = **No education** X_3 = Primary X_4 = **JHS** X_5 **= MSCL** X_6 = Single

X., = Divorced

X_8= Muslim X_9= **Christian** X_{10} **= Traditionalist** $X_{,,}$ **= Month** X_{12}= **Weight**

X_{13} = Height X_{14} = Smoke X_{15} = Not Smoking X_{16} = Alcohol X_{17} = No Alcohol

4.5 Model Evaluation

The evaluation of our model is shown in the residual plots of Figure 4.5 and Table 4.6 of the Deviance for two of the distributions tested. Table 4.6 shows that the Poisson distribution is the better model of these two, while the residual plots show that the assumptions of Normality, constant variance and random distribution for the transformed Poisson distribution are not violated.

Table 4.6: Deviance Output for Choice of Best Distribution

Distribution	DF	Value	Deviance Ratio (Value/DF)
Poisson	119	67.8	0.6
Negative Binomial	119	152.7	1.3

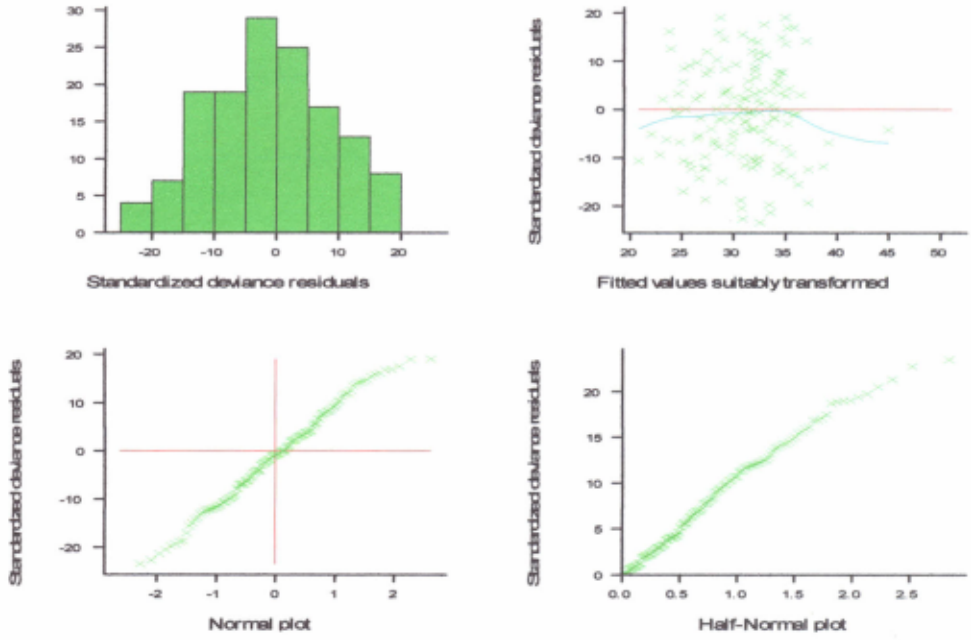

Figure 4.5 Residual Plot of Poisson Distribution

4.6 Example for Model Application

Consider a Male client with ICD4 count of 100 with no education, smokes, takes alcohol, Single, Weight = 49.4, Height = 159.6, and a traditionalist. What is the expected time, t of months is he to take to improve his CD4 count to normal state (Minimum of 500 count per micro litre) if he follows the prescription faithfully?

Solution:

Y = 500-100 = 400

$$400 = \exp(6.004 - 0.287 + 0.080 + 0.119 - 0.926 + 0.007(49.4) - 0.002(159.6) - 0.213 + 0.090 + 0.017t)$$

$$= e^{4.8936 + 0.017t}$$

$$= e^{4.8936} \times e^{0.017t} = 133.4331\, e^{0.017t}$$

$$\Rightarrow \ln(e^{0.017t}) = \ln\left(\frac{400}{133.4331}\right)$$

$$t = \frac{1.0979}{0.017} = 64.6 months$$

Hence it will take him 64.6 months to get the minimum normal CD4 count of 500 cells per micro litre.

CHAPTER FIVE

DISCUSSIONS, CONCLUSION AND RECOMMENDATIONS

5.1 Discussions

The majority (77%) of the clients put on treatment between 2007 and 2011 were females as compared to their males' counterparts of 23% in figure 4.4. In terms of CD4 count performance, females had a mean change of 259.8 cells per micro litre with an average time of 13.03 months whilst the males had 192.2 cells per micro litre with 15.45 time average in months. The higher number of females and mean change in CD4 count as against their males' counterparts could be attributed to the routine PMTCT protocol screening through ANC and adherence to ART.

16.9 per cent of the total clients had their CD4 count less than 100 cells per micro litre which is a bit lower than 19.4 per cent of a similar study in Kano of northern Nigeria.

In table 4.2, the minimum ICD4 count for males was 11 cells per micro litre which is greater than that of females' minimum ICD4 count of 4 cells per micro litre. The corresponding males and females minimum NCD4 counts were 88 and 58 cells per micro litre. On the other hand, the maximum ICD4 count for females was 350 cells per micro litre greater than that of males' maximum ICD4 count of 343ce11s per micro litre and their corresponding maximum NCD4 counts were 927 and 884 for females and males respectively. This means that clients can be expected to have their CD4 count improved faster if they start ART at a relatively higher CD4 count.

The overall mean change in CD4 count for the 142 persons on ART was 244.1 cells per micro litre lesser than 302, and 270 cells per micro litre compared to a similar study in London, UK and Kano, Nigeria. This mean change in CD4 count is also less than half the minimum normal CD4 count of 500 cells per micro litre. On educational status, the 142 people who are on ART, 84 of them representing 59.2% had no education followed by 23 (16.2%) of them attaining primary education. Those who attained SHS/Tech and Tertiary were the least with 6 and 7 representing 4.2 and 4.9% respectively. When the clients educational status were tested statistically, all (no education, primary, JHS, MSLC) except SHS/Technical education contributes significantly (P-values < 0.05) in determining change in CD4 count of persons on ART.

It was also realized that clients who do not smoke and are on treatment perform well with a mean change in CD4 count of 251.3 cells per micro litre with a minimum and maximum CD4 count of 8 and 651 as compare to a mean CD4 count of 169 cells per micro litre of those who smoke. Those who quitted smoking had a mean CD4 count of 173.8 cells per micro litre with a minimum and maximum CD4 count of 19 and 435 cells per micro litre respectively as can be seen in table 4.3.

Similarly to the smoking habit of clients, it can be seen in table 4.4 that 86 of the clients representing 60.6% of those who do not drink had a better CD4 count change, 274.4 cells per micro litre (mean value) as compare to those who take alcohol, 213.5 cells per micro litre (mean value). Interestingly, those who rather

stopped drinking were worst of in response to change in CD4 count with mean and standard deviation of 177.8 and 117..0 respectively in table 4.4.

From table 4.5, the duration in months contribute significantly (P-value = 0.0001) in determining of change in CD4 count of clients initiated on ART with an estimated Poisson regression coefficient of 0.0166 implying that if a client were to increase his/her number of months on ART by one point, the difference in the logs of expected counts would be expected to increase by 0.0166 unit, while holding the other variables in the model constant (CI: 0.0152±0.0179). In the same table, the difference in the logs of expected counts is expected to be 0.2870 unit lesser for males compared to females, whiles holding the other variables constant in the model for a change in CD4 count within the confidence interval of -0.3220±-0.2519 for a Poisson regression. However age is not necessary in the determination of clients change in CD4 count (P-value =0.0585). 59.2% representing 84 (P-value=0.0066) of the clients with no education had a mean change in CD4 count of 242.5 cells per micro litre. Those who attained primary education, 23(16.2%) with p-value <0.0001 had mean change in CD4 count of 260.1 cells per micro litre and that of those who attained tertiary education had the least mean (213.3 cells per micro litre) change in CD4 count within 5 to 26 months. The other educational attainment had estimated coefficients greater than zero compared to tertiary education set at zero (see table 4.5). Both weight and height of clients are significant (P-values; < 0.0001 and 0.0022) in prediction of change in CD4 count of clients after initiation of ART. For a unit increase in weight of a client, the difference in the logs of expected CD4 count would be

expected to increase by 0.0065 unit, while holding the other variables in the model constant and that of height is expected to decrease by 0.0008 unit, holding the other variables constant. Also the starting or initial CD4 count (ICD4) of clients put on ART does not contribute (P-value = 0.8137) in predicting change in CD4 count of the clients.

Similarly on marital status, those who are either married or separated do not (P-values; 0.7165 and 0.4602) influence the prediction of change in CD4 count of clients. However, those who are single or divorced contributes to the prediction of change in CD4 count with P-values of <0.0001 and 0.0200, with an estimated Poisson regression coefficients of 0.1190 and 0.0464 respectively in table 4.5.

The three common religions, Muslim, Christianity, and Traditionalist also contributes significantly (P-values all <0.0001) for prediction of change in CD4 count with an estimated Poisson regression coefficients of -1.2627, -1.0026, and -0.9891 respectively and thus implies that for one point change in those religious affiliations, the difference in the logs of expected counts would be expected to decrease by -1.2627, -1.0026, and -0.9891, holding other variables constant respectively.

5.2 Conclusion

The determinants of change in CD4 are Gender, Educational status, Marital Status, Religion, Months, Weight, Height, Smoking and Drinking Habit. The overall mean change in CD4 count was 244.1cells per micro litre.

The distribution that was used to model the data for predicting an individual change in CD4 count once the factors are known was Poisson.

Generally all the clients considered in the study between 2007 and 2011 had their CD4 count appreciated at a varying margin after been put on treatment at a certain initial CD4 count though very few of them attained the normal CD4 count of > 500 cells per micro litre.

The model for predicting the change in CD4 count of a particular client on treatment is

$$Log_e(Y) = 6.004 - 0.287X_1 + 0.080X_2 + 0.188X_3 + 0.377X_4 + 0.147X_5$$
$$+0.119X_6 + 0.017X_7 - 1.187X_8 - 1.014X_9 - 0.926X_{10} + 0.017X_{11}$$
$$+ 0.007X_{12} - 0.002X_{13} - 0.213X_{14} + 0.065X_{15} + 0.090X_{16} + 0.229X_{17}$$

5.3 Recommendations

Based on the findings of the work, the following recommendations are given; Clinicians and health care givers as well as other stakeholders should monitor the life habit or style, such as drinking and smoking habits, of persons living with **HIV/AIDS** on ART since this will help clients improve their CD4 counts better. Also, Educational Status, Marital Status, and Weight should inform Clinicians to better advice and monitor clients for a better response and restoration of CD4 count to curb the breakdown of their immunity system against common opportunistic infections.

Investigations into the reasons why females respond better to treatments than males, is recommended. This will help clinicians provide better care for their male clients. Further research should also consider different treatment combinations to determine which category or regimen gives a better CD4 count improvement.

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APPENDICES

Appendix A

Table A1: Descriptive Statistics on Educational Level with Change in CD4 Count of Clients

Education	Mean	Standard deviation	Minimum	Maximum
Nil	243.5	141.7	8	651
Primary	260.1	146.5	31	638
JHS	295.4	201.7	30	596
MSLC	202.6	163.5	19	623
SHS/Tech	239.2	146.7	77	494
Tertiary	213.3	224.9	10	523

Source: Data from ART Clinic, Navrongo Hospital

Table A2: Descriptive Statistics on Marital Status with Change in CD4 Count of Clients

Marital Status	Mean	Standard deviation	Minimum	Maximum
Married	228.4	149.9	11	596
Single	283.5	182.0	8	638
Divorced	240.7	150.7	22	623
Separated	236.2	110.7	109	433
Widow(er)	245.2	153.9	30	651

Source: Data from ART Clinic, Navrongo Hospital

Table A3: An Output of Parameter Estimates for Negative Binomial Distribution

Parameter	DF	Estimate	Standart error	Wald 95% confidence Limits		Chi-square	Chisq p-value
Intercep	1	5.3832	1.2075	3.0165	7.7498	19.87	<0.0001
Months	1	0.0215	0.0083	0.0052	0.0378	6.69	0.0097
Male	1	-0.3223	0.182	-0.6791	0.0344	3.14	0.0766
Female	0	0.0000	0.0000	0.0000	0.0000	0.00	0.0000
Age	1	-0.0017	0.0072	-0.0159	0.0125	0.05	0.8146
Weight	1	0.0065	0.0068	-0.0053	0.0215	1.41	0.2344
Height	1	-0.0008	0.0068	-0.0140	0.0125	0.01	0.9114
ICD4	1	0.0001	0.0007	-0.0012	0.0014	0.01	0.9028
Education							
Nil	1	0.3123	0.2961	-0.2682	0.8927	1.11	0.2917
Primary	1	0.3332	0.3114	-0.2771	0.9435	1.15	0.2846
JHS	1	0.5651	0.3528	-0.1264	1.2566	2.57	0.1092
MSLC	1	0.3638	0.3841	-0.3890	1.1167	0.90	0.3435
SHS/Tech	1	0.2297	0.4045	-0.5631	1.0224	0.32	0.5701
Tertiary	0	0.0000	0.0000	0.0000	0.0000	0.00	0.0000
Marital Status							
Married	1	0.0141	0.1756	-0.3301	0.3583	0.01	0.9361
Single	1	0.1848	0.2256	-0.2573	0.6270	0.67	0.4126
Divorced	1	0.0336	0.2105	-0.3791	0.4462	0.03	0.8733
Separated	1	0.1087	0.2429	-0.3674	0.5848	0.20	0.6545
Widow(er)	0	0.0000	0.0000	0.0000	0.0000	0.00	0.0000
Religion							
Muslim	1	-1.2627	0.7201	-2.6740	0.1487	3.07	0.0795
Christian	1	-1.0026	0.7005	-2.3755	0.3703	2.05	0.1523
Traditionalist	1	-0.9891	0.6946	-2.3505	0.3723	2.03	0.1545
None	0	0.0000	0.0000	0.0000	0.0000	0.00	0.0000

Table A3 Continuous

Smoking							
Yes	1	-0.1108	0.4891	-1.0694	0.8479	0.05	0.8208
No	1	0.1258	0.2814	-0.4258	0.6774	0.20	0.6549
Stoped	0	0.0000	0.0000	0.0000	0.0000	0.00	0.0000
Alcohol intake							
Yes	1	0.0914	0.2250	-0.3497	0.5325	0.17	0.6846
No	1	0.2371	0.1975	-0.1499	0.6240	1.44	0.2299
Stoped	0	0.0000	0.0000	0.0000	0.0000	0.00	0.0000
Dispersion	1	0.4339	0.0493	0.3373	0.5305		

Source: SAS GENMOD output (Data from ART Clinic, Navrongo Hospital)

APPENDIX B

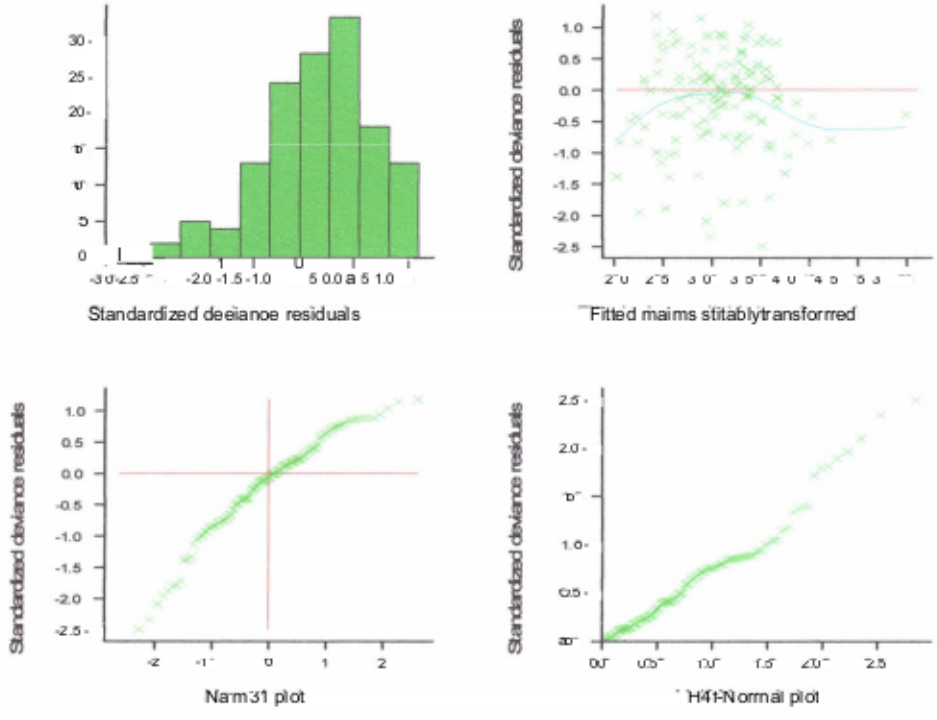

Figure BI: Residual Plots of Negative Binomial Distribution

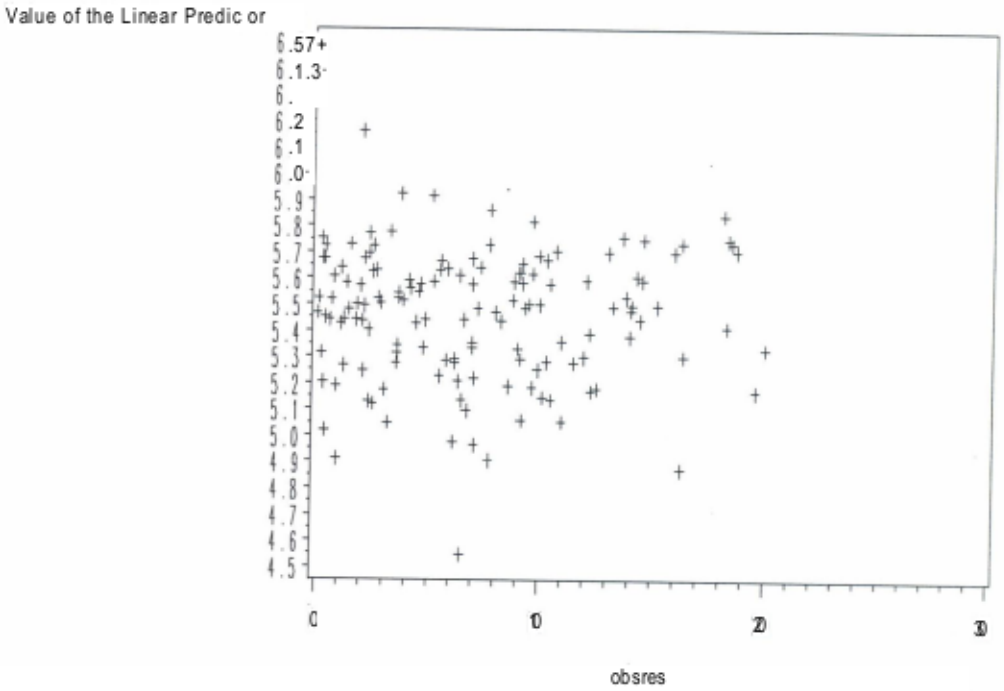

Figure B2: Plot of Linear Predictor Against Absolute. Residuals of Poisson Distribution

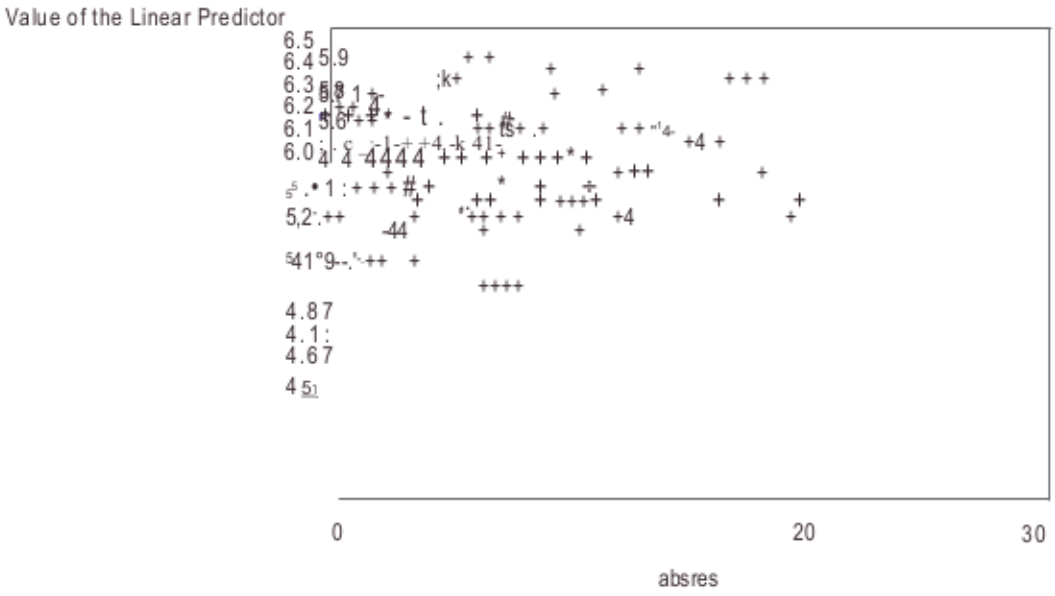

Figure B3: Plot of Linear Predictor Against Absolute Residuals of Negative Binomial Distribution

Figure B4: Map of Study Area

Source: http://www.kassenanankana.ghanadi strict s.gov.gh/