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CHRONIC CONDITIONS AMONG HIV/AIDS INFECTED PATIENTS RECEIVING ANTIRETROVIRAL THERAPY AT THE PANTANG HOSPITAL

BY

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THIS DISSERTATION IS SUBMITTED TO THE SCHOOL OF PUBLIC HEALTH, THE UNIVERSITY OF GHANA, LEGON IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF MASTER OF PUBLIC *HEALTH (MPH) DEGREE*

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DECLARATION

I, **KOTEY, MARTHA,** declare that I am the author of this dissertation. I do declare that except for references of others' works, which I have duly cited, and that this dissertation, either in whole or in part, has not been presented elsewhere for another degree. This study results from my research work at the University of Ghana, School of Public Health, Legon, under the supervision of **Dr Bismark Sarfo**.

28/10/2020

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DEDICATION

This dissertation is dedicated to my late father, Mr Emmanuel Kotey, for his constant advice and correction, which have made me a better person. To my dearest mother, Mrs Monica Abeka-Asirifi Kotey, for her unending prayer and support. To my siblings (Samuel, Glory, Mary, and Ruth) for always being there for me and providing shoulders I could always lean on.

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ABSTRACT

Background

The number of persons living with HIV/AIDS (PLWHA) is increasing partly due to improved screening, earlier diagnosis, the use, acceptance, and greater accessibility to antiretroviral therapy (ART). The HIV disease, coupled with ART, results in chronic disease complications such as hypertension, cardiovascular disease, diabetes, and renal failure, among other diseases. Therefore, HIV patients must be assessed to identify other chronic diseases associated with HIV disease for effective management.

Objectives

The main objective of this study was to assess chronic conditions among HIV patients receiving ART at the Pantang hospital.

Method

The study adopted a retrospective study design. Two hundred and twenty-two (222) medical records of HIV patients receiving care at the Pantang Hospital were randomly sampled, extracted and entered in an Epi-Info designed template, and imported into STATA IC version 16 for analysis. The analysis was done using means, standard deviation, frequency, and percentages. The Kaplan Meier failure curve was used to determine the experience of at least one chronic condition during the first three years on Antiretroviral drugs (ARV). The simple cox proportional hazard model was used to assess the association between the study variables. All statistical significance was set at ≤ 0.05 at a 95% confidence interval.

Results

Out of two hundred and twenty-two (222) patients records reviewed, 53.6% developed chronic conditions during the first three years on antiretroviral medication. The mean age of participants was 39.01±9.64years. Females constituted 65.32% (n=145), majority were married (42.79%, n=95), employed (82.88%, n=184) and Christians (84.68, n=188). Age and drug combinations were associated with the experience of chronic conditions within the first three years on antiretroviral medication based on the simple cox-proportional hazard model at a $p<0.05$. Compared to patients below 30 years, those aged 40-49 (ARR: 2.17, 95% CI: 1.04-4.54) and those 50 and above (ARR: 3.34, 95% CI: 1.43-7.76) had an increased risk of experiencing chronic conditions. Again, the risk of developing chronic conditions was high among patients on TDF+3TC+EFV (ARR: 2.15, 95% CI: 1.16-3.98), TDF+3TC+NVP (ARR: 4.07, 95% CI: 1.64-10.08), AZT+3TC+EFV (ARR: 3.05, 95% CI: 1.37-6.80), and AZT+3TC+NVP (ARR: 2.12, 95% CI: 1.06-4.22).

Conclusion

The majority of patients developed at least one chronic condition while on antiretroviral drugs within the first three years. Since some drug combinations are associated with the experience of chronic conditions, patients' characteristics must be carefully considered before administering medications.

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AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
AZT	Zidovudine
BMI	*Body Mass Index*
cART	combined Antiretroviral Therapy
CDC	Centers for Disease Control and Prevention
CD4	*Cluster of Differentiation Four*
CVD	Cardiovascular Disease
CCR5	C-C chemokine receptor type 5
CXCR4	C-X-C chemokine receptor type 4
DDI	Didanosine
D4T	Stavudine
DM	Diabetes Mellitus
DNA	Deoxyribonucleic Acid
EFV	Efavirenz
HbA	Hemoglobin A
HBV	Hepatitis B Virus
HIV	*Human Immunodeficiency Virus*
LMICs	Low and Middle-Income Countries
MI	Myocardial Infarction
MLSC	*Middle School Leaving Certificate*
NACP	National AIDS Control Program
NCDs	Non-Communicable Diseases
NRTIs	Nucleoside/ Nucleotide reverse transcriptase inhibitors
NNRTIs	Non-nucleoside reverse transcriptase inhibitors
NVP	Nevirapine

OI	Opportunistic infection
PGL	Persistent Generalized Lymphadenopathy
PIs	Protease Inhibitors
PLWHA	Persons Living With HIV/AIDS
PPE	Pruiritic Papular Eruption
RNA	Ribonucleic Acid
RTI	Respiratory Tract Infection
SSA	Sub-Saharan Africa
TB	Tuberculosis
TDF	Tenofovir
WHO	World Health Organization
3TC	Lamivudine

CHAPTER ONE

1.0 INTRODUCTION

This chapter includes the study background, problem statement, justification, research questions, objectives, and the conceptual framework of this research work.

1.1 Background

The Joint United Nations Program on HIV and AIDS (UNAIDS) (2019) has estimated that about thirty-eight million people worldwide live with HIV/AIDS. Out of this number, Sub-Saharan Africa (SSA) remains the region that is poorly affected, and this keeps increasing. This may be due to an improvement in screening for the disease, early diagnosis, better methods of treating the infection, greater accessibility, as well as the increased acceptance of antiretroviral therapy (Esté & Cihlar, 2010; Jain et al., 2014; Kalra, Kalra, Agrawal, & Unnikrishnan, 2011; Mesquita et al., 2019; World Health Organisation (WHO), 2016; Yang, Beymer, & Suen, 2019). The HIV pandemic is continuously spreading, with a more significant disease burden in SSA, which is responsible for about 67% of all HIV/AIDS cases (Esté & Cihlar, 2010; Quinn, 2009). Globally, out of the 38 million children and adults that are affected, about 24.5 million patients have access to antiretroviral therapy (UNAIDS, 2019). The current treatments cannot cure the HIV infection; hence patients are bound to take the drugs for the rest of their lives as it helps suppress viral replication and minimize their effects (Esté & Cihlar, 2010). HIV infection as a chronic medical condition has become manageable since the discovery of active Antiretroviral Therapy (ART) (Feinstein et al., 2019; Mrus, Williams, Tsevat, Cohn, & Wu, 2005; Palella & Phair, 2012; Quinn, 2009). There has been a significant extension of the predicted lifespan (Jain et al., 2014; Mesquita

et al., 2019; Nsagha et al., 2015; Reynolds, 2011) and a positive impact on the survival of individuals with the HIV infection, as they now live longer but have to depend on the drugs for the rest of their lives (Yang et al., 2019). Since patients now live longer and have to rely on antiretroviral therapy (ART), the morbidity associated with ART has become a global concern, and this has exacerbated the emergence of non-communicable diseases (NCDs) and further increased the burden on developing countries (Art et al., 2019; Esté & Cihlar, 2010). Higher rates of NCDs among HIV/AIDS patients receiving ART have been demonstrated in developed countries and are linked to four different factors, including the virus (DiMauro, Tay, & Mancuso, 2004; Dinoso et al., 2009; Hunt, 2012; Jain et al., 2014), the ART medication (Deeks & Phillips, 2009; Jain et al., 2014; Reiss et al., 2010; Worm et al., 2010; Zuber et al., 2019), individual patient characteristics (Bisson et al., 2008; Goulet et al., 2019; Kirk & Goetz, 2009) and a combination of these factors (Jain et al., 2014).

Out of the total number of people living with HIV globally, about 32.1 million of them are adults (Nsagha et al., 2015; UNAIDS, 2019). The introduction and widespread use of antiretroviral therapy (ART) has led to HIV-infected individuals experiencing a dramatic decline in immunodeficiency-related events. This has increased life expectancy (Deeks, Lewin, & Havlir, 2014; Hyle et al., 2019). However, the ART medications have exposed PLWHA to the effects of ageing itself as they tend to have extended lives, as well as the influence of environmental risk factors known to act in the general population and contributing to the occurrence of obesity, diabetes mellitus, and cardiovascular diseases (Nsagha et al., 2015; World Health Organization, 2013). The number of patients accessing HIV treatment in Ghana has increased; over 120,000 are currently accessing ART (UNAIDS, 2019).

According to Kalra et al. (2011), as HIV treatment develops and access to therapy improves, the incidence of HIV-associated diabetes is bound to grow. The use of some antiretroviral drugs tends to increase the risk of cardiovascular diseases, thereby causing pro-atherogenic serum lipid elevations, induction of insulin resistance, and increases in visceral adiposity (subcutaneous fat loss) (Cunha, Ferreira, Stern, Spada, & Bydlowsk, 2015; Feinstein et al., 2019). Abacavir's use tends to increase myocardial infarction risk by reducing vascular reactivity and platelet activation increase (Fahme, Bloomfield, & Peck, 2018; Lin et al., 2018). Some traditional risk factors, such as advancing age, smoking, hyperlipidemia, and hypertension, continue to be significant predictors of cardiovascular disease (CVD) among HIV patients on ART (Palella & Phair, 2012). The use of specific ARVs can adversely impact CVD risk. Studies in some high-income countries have reported that ART increases the risk of diabetes and myocardial infarction (Lin et al., 2018; Samaras, 2009; Serrano-villar et al., 2016; Yoon, Gulick, Hoover, Vaamonde, & Glesby, 2004). The prevalence of diabetes mellitus and metabolic syndrome among HIV individuals on antiretroviral therapy has increased (Jantarapakde et al., 2014; Karamchand et al., 2016). Since a more significant proportion of HIV patients on ART live in sub-Saharan Africa, the ART associated metabolic complications and comorbidities will likely be very high in this region (Deeks et al., 2014; Feinstein et al., 2019).

1.2 Problem Statement

The National AIDS Control Program (NACP) reported that the prevalence of PLWHA in Ghana has decreased from about 3.60% in 2003 to about 1.69% in 2018 (Ghana AIDS

Commission, 2019). However, chronic conditions associated with the ARTs cannot be overlooked, which has raised public health concerns over the years.

Treatment of HIV/AIDS with ART leads to a reduction in viral replication, an increase in CD4+ cell counts, and decreased mortality and morbidity due to the disease. HIV patients are "destined" to live on ART for the rest of their lives. PLWHA on ART are faced with major complications, including cardiovascular diseases, renal disease, liver disease, bone disease, and some neurological complications (Deeks & Phillips, 2009).

Chronic conditions associated with HIV patients have been increasing since the advent of combination antiretroviral therapy (cART), including non-communicable diseases (NCDs) (Abebe et al., 2016; Hemkens & Bucher, 2014; Mesquita et al., 2019). Among NCDs, cardiovascular diseases such as heart diseases and hypertension pose a more significant threat. According to Nsagha et al. (2015), studies on cardiovascular diseases and their risk factors associated with PLWHA on ART have been highly reported in the developed world. However, data are scarce on this subject in Africa, even though it has a tremendous HIV/AIDS burden and increasing access to ART. There has been an increase in prevalence and incidence of chronic conditions, including insulin resistance and diabetes mellitus, together with other NCDs in the general population (Art et al., 2019). With the increasing cases of HIV related diseases and with greater access to antiretroviral medications among HIV/AIDS patients in Ghana, chronic conditions in these patients is expected to be high (Zicari et al., 2019)

There is an increase in the number of HIV patients receiving ART generally in the Accra metropolis. However, most people are unaware of some chronic conditions associated with these drugs. Therefore, there is a need to investigate the chronic conditions among HIV

patients and the factors responsible for their onset. Long-term exposure to antiretroviral drugs leads to increased metabolic dysfunction, lipodystrophy, and insulin resistance (Dube & Sattler, 2010; Langs-barlow, Renner, Katz, Northrup, & Paintsil, 2013), just to name a few. Also, drugs used to treat comorbidities associated with HIV/AIDS have a high tendency to increase the risk of developing complications. Some patients are non-adherent to the ART treatment hence further increasing their complications. From a cohort study in the Netherlands by Smit et al. in 2015, it was projected that by 2030, 28% of HIV-infected individuals would have more than three non-communicable diseases, and 54% will be on medications to treat these conditions.

This study aims to determine chronic disease conditions and their associated factors among HIV/AIDS patients receiving ART at Pantang ART clinic in the Greater Accra Region of Ghana.

1.3 Justification of the Study

This study is vital because HIV/AIDS remains a global public health issue as more people are being infected, resulting in an increased number of people accessing ART. Thus, without adequate knowledge of ART's chronic conditions, HIV/AIDS-related mortality is bound to increase.

There has been an increase in prevalence and incidence of chronic disease complications, including insulin resistance and diabetes mellitus, and other NCDs in the general population in sub-Saharan Africa, including Ghana. However, there is a paucity of data and limited studies on HIV and ART associated complications among HIV patients. This research aims

to determine the association between ART usage and the development of chronic disease complications with this background. The results should help provide context-specific findings and knowledge in the interactions between HIV medications and the disease. This will be relevant in HIV treatment policies and clinical guidelines.

1.4 Research questions

In considering the problem presented, this study is faced with the following questions:

1. What is the proportion of HIV patients receiving antiretroviral therapy at the Pantang hospital who developed chronic disease conditions?

2. What are the socio-demographic factors associated with experiencing chronic disease conditions in patients receiving antiretroviral therapy at the Pantang hospital?

3. Which line(s) of ART medication(s) is/are associated with developing chronic disease conditions in HIV patients receiving antiretroviral therapy at Pantang hospital?

1.5 Objectives

1.5.1 General *Objective*

To assess chronic disease conditions among HIV/AIDS-infected patients receiving antiretroviral therapy at Pantang hospital.

1.5.2 Specific Objectives

1. To determine the proportion of HIV patients receiving antiretroviral therapy at the Pantang hospital who developed chronic disease conditions.

2. To assess the socio-demographic factors associated with experiencing chronic disease conditions in HIV patients receiving antiretroviral therapy at Pantang hospital.

3. To determine the line(s) of ART medication associated with developing chronic disease conditions in HIV patients receiving antiretroviral therapy at Pantang hospital

1.6 Conceptual framework

This conceptual framework (*Figure 1*) explains the relationship between the various factors and the experience of chronic conditions among PLWHA.

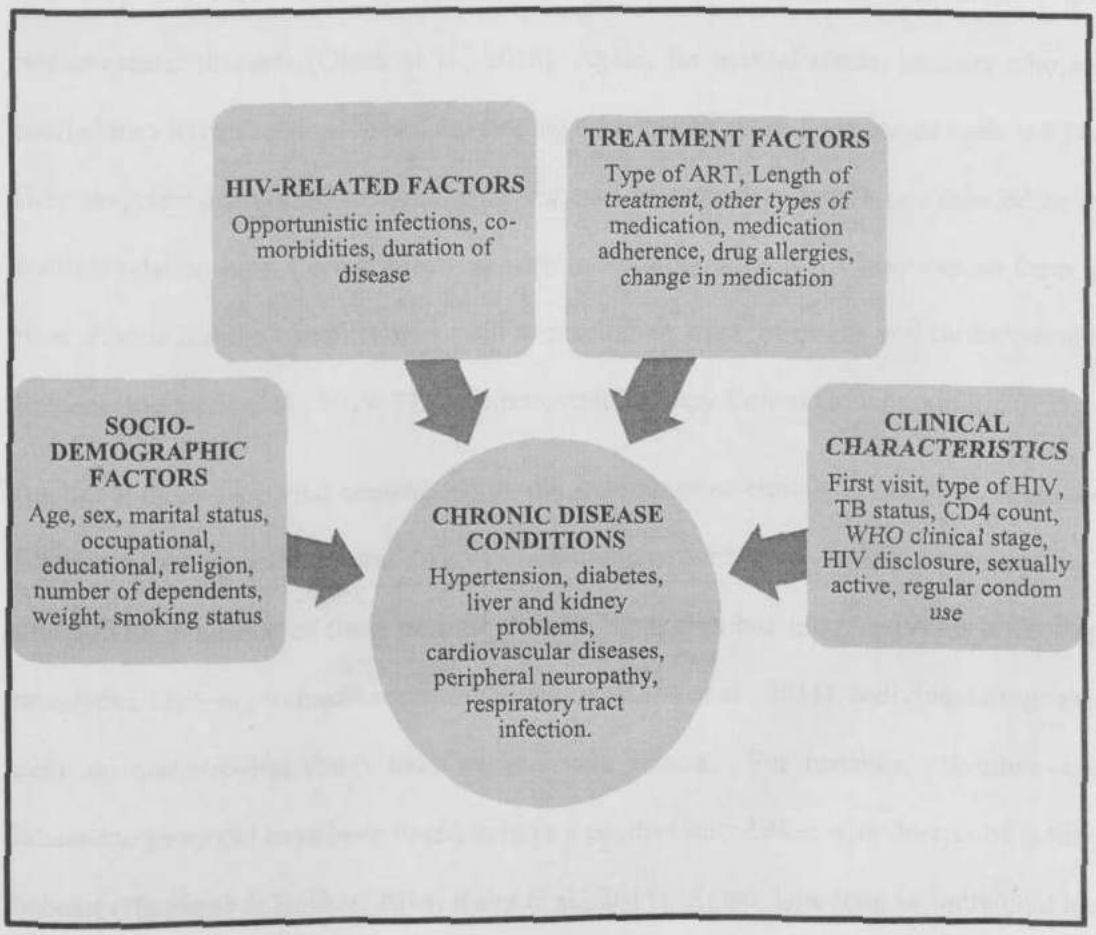

Figure 1: Conceptual Framework of the study showing factors associated with *experiencing chronic* disease conditions

1.6.1 Narrative of the conceptual framework

The conceptual framework shows an interplay of various factors associated with experiencing chronic disease conditions among HIV-infected patients. Based on the

epidemiology of HIV/AIDS-infected patients, PLWHA are at risk of developing chronic disease complications due to their socio-economic factors such as age, educational level of patients, marital status, and smoking status, among other factors. As PLWHA reach older age, they are faced with age-related health conditions such as hypertension and cardiovascular diseases (Olack et al., 2015). Again, for marital status, patients who are married may have a reduced risk of developing other health-related conditions such as STIs. They may remain faithful to a partner compared to patients who are not married or in multiple relationships. Certain lifestyles such as smoking in PLWHA may expose them to other chronic disease complications such as respiratory tract infections and cardiovascular diseases (Moorthie et al., 2019; The Antiretroviral Therapy Cohort Collaboration, 2013).

Treatment factors are vital contributors to the experience of chronic conditions. There are different types of antiretroviral (ARV) combinations, with each having its unique side effects. The incidence of these chronic disease conditions has increased with increasing cumulative exposure to medication combinations (Kalra et al., 2011). Individual drugs that make up antiretroviral drugs have various side effects. For instance, stavudine and didanosine treatment have been found to have a positive correlation with the risk of getting diabetes (Hemkens & Bucher, 2014; Kalra et al., 2011). Again, how long an individual has been on antiretroviral therapy can affect the onset of chronic conditions. Patients who have been on ARV for a more extended period have a higher probability of developing chronic disease conditions (Serrano-villar et al., 2016; Zicari et al., 2019). Also, patients who are adherent to ARV experience undetectable viral loads and an increase in CD4 cells, which aids in boosting the body's immune system, thus fighting other chronic conditions that may arise.

The clinical stage of an HIV-infected patient may trigger the onset of chronic conditions. HIV patients with either stage III or IV (a severe form of the infection) are more prone to co-or multi-morbidities compared with those with the mild form of the infection (stages I and II) (Rastogi et al., 2011). Patients whose CD4 counts are above 350 cells/mm^3 have a reduced risk of developing chronic conditions (Deeks & Phillips, 2009). CD4 lymphocyte cells are blood cells that fight any form of infection that enters the body. Thus, when a larger number of CD4 cells are lost (CD4 below 350), the body will be unable to fight infections, making the body prone to chronic conditions.

Opportunistic infections (OI) are frequent in HIV-infected patients. They occur because the CD4 count of the patient is low or when the viral load is high. When this happens, their immune system is unable to fight off infections. Some common opportunistic infections include candidiasis, cancer, tuberculosis, and recurrent pneumonia. These opportunistic infections serve as a gateway for the onset of other chronic disease conditions as they further weaken the immune system. Also, some of these OIs are risk factors for other chronic conditions; thus, their presence triggers these conditions.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 History of HIV/AIDS and ART

According to the World Health report (2003), AIDS was first discovered in 1981. It was identified when young adults (mostly men) who were previously healthy in the United States began to fall ill. They experienced opportunistic infections, and these same signs were described in Africa, Europe and the Caribbean. Since its discovery, the HIV disease has been a pandemic and is still one of the most massive pandemics today. This same virus causes AIDS. The human immunodeficiency virus is a member of a family of primate lentiviruses. "HIV, like other retroviruses, contains a viral capsid, which consists of the major capsid protein, the nucleo-capsid protein, the diploid single-stranded RNA genome, and the viral enzymes protease reverse transcriptase, and integrase" (Chen, 2019).

HIV is transmitted through the percutaneous membrane's exposure to infected blood, breast milk, and secretions from the genitalia. The efficient transmission of HIV varies based on the type of exposure. The transmission may occur via sexual contact, vertical transmission from mother to child, injection drug users sharing infected needles, and the transfusion of infected blood products. HIV cannot be transmitted through nonsexual casual contact (COPRESIDA, 2010; Kassaye & Levy, 2009). For transmission to occur, any fluid that contains the virus must successfully get into the bloodstream of an HIV-negative person through a mucous membrane (typically found in the rectum, vagina, tip of the penis, or mouth); open sores; or by direct injection (Centre for Disease Control (CDC), 2018; UNAIDS, 2000; Washington State Department of Health, 2014).

HIV is successfully transmitted when there is direct contact between an infectious viral particle and a susceptible host cell. The virus primarily targets CD4+ T-lymphocytes and binds with the CD4+ T-cell receptor and either the CCR5 or CXCR4 chemokine co-receptor (Février, Dorgham, & Rebollo, 2011; Taylor et al., 2016; Washington State Department of Health, 2014).

Ghana's progress report in 2018 indicated that about 334,713 persons were living with HIV, 29,514 (8.8%) of which were children, and 305,199 (91.2%) were adults. It was estimated that 34% of PLWHA were on ART, and about 66% had a suppressed viral load. People with HIV/AIDS on prescribed ARVs get to maintain an undetectable viral load and have little or no possibility of transmitting the virus to their HIV-negative partner via sex (Ghana AIDS Commission, 2019).

The introduction of ART has averted over 5.5 million deaths in low and middle-income countries (LMICs) from the peak in 1995 to 2019 (UNAIDS, 2019). About 2.5 million people globally were accessing antiretroviral therapy as of June 2019. Sub-Saharan Africa (SSA) accounted for most of those lives saved, constituting approximately 71% of all PLWHA (UNAIDS, 2019; Zicari et al., 2019). HIV has become a manageable chronic disease (Zicari et al., 2019).

There are six distinct classes of antiretroviral drugs that are currently used to treat HIV infection. These drugs act at different stages in the virus's replication cycle (Arts & Hazuda, 2012; Bisson et al., 2008; Desai, Iyer, & Dikshit, 2012; Hance & Clavel, 2004; National Centre for AIDS & STD Control (NCASC) 2009). They are given in combinations of three or more drugs, depending on the severity of the infection or the presence of opportunistic infections (OI). ARVs aim to suppress viral load, improve CD4 count, reduce opportunistic

infections, and generally lead to a reduction in mortality caused by HIV/AIDS (Jain et al., 2014; Kalra et al., 2011). One of ART's greatest successes is its tendency to convert HIV/AIDS from a previously deadly disease to a chronic one requiring long-term management (Palmisano & Vella, 2011; Vella, Schwartländer, Sow, Eholie, & Murphy, 2012).

The six classes of ARV drugs work such that each drug class attacks HIV differently. In general, drugs from either two or three classes are combined to ensure a much more powerful attack on the virus. Many PLWHA begin the treatment on two drugs from the nucleoside/nucleotide reverse transcriptase inhibitors class, combined with either an integrase inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a protease inhibitor – hence, the name 'triple therapy.' The classes of drugs are:

I. Nucleoside/ Nucleotide reverse transcriptase inhibitors (NRTIs): These drugs work by targeting the HIV protein activity, reverse transcriptase. This class of drugs is often referred to as the 'backbone of a first-line HIV treatment combination. It includes; emtricitabine, lamivudine, tenofovir (both disoproxil and alafenamide), abacavir, stavudine, zidovudine, didanosine, and zalcitabine.

II. Non-nucleoside reverse transcriptase inhibitors (NNRTIs): These drugs also target the reverse transcriptase differently from the NRTIs. NNRTIs directly bind to the reverse transcriptase enzyme and blocks its processes. They include efavirenz, nevirapine, rilpivirine, etravirine, delavirdine, and doravirine.

III. Protease inhibitors (PIs): PIs mainly block the activity of the protease enzyme. The virus uses the protease enzyme to break down large polyproteins into smaller pieces required for assembling new viral particles. However, in the presence of protease

inhibitors, the virus can still replicate, but the resulting virions are immature and unable to infect new cells. They include; atazanavir, darunavir, and lopinavir.

IV. Integrase inhibitors: These drugs target an HIV protein called integrase, essential for viral replication and prevent the virus from inserting itself into the human DNA. The integrase enzyme binds to host cell DNA, prepares an area on the viral DNA for integration, and then transfers this processed strand into the host cell's genome. They include bictegravir, dolutegravir, elvitegravir, and raltegravir.

V. Entry inhibitors: These drugs prevent the virus from entering human cells. There are two main types: CCR5 inhibitors and fusion inhibitors. The virus to enter a host cell binds to the CD4 receptor and a co-receptor (CCR5 or CXCR4). Once this happens, the virus's envelope fuses with the host's cell membrane and releases the viral components into the cell. The CCR5 inhibitors stop HIV from using the CCR5 co-receptor by binding to it and block viral entry. An example is maraviroc.

VI. Booster drugs: they help to 'boost' the effects of protease inhibitors. A small dose added to an antiretroviral cause the liver to break down the primary drug much slower. The drugs then get to stay in the body for much longer times, thereby making the drug effective. Ritonavir and cobicistat are examples of booster drugs.

2.2 Chronic Conditions and HIV patients

Chronic conditions in this context are unfavourable health conditions that arise due to the long-term use of ART among PLWHA. HIV infection generally weakens the immune system, leading to an increase in the risk of developing numerous conditions and certain cancers. As PLWHA are put on ART, it increases their life span. However, it exposes them

to a series of other health-related complications such as CVDs, non–AIDS-related cancers, bone diseases, cognitive disorders, diabetes, liver, lung, and renal disease (Deeks et al., 2014; Desai et al., 2012; Serrano-villar et al., 2016; Top Antivir Med, 2018). Obesity, high cholesterol, diabetes, lack of exercise, hypertension, smoking, older age, and family history are risk factors for cardiovascular disease (The Antiretroviral Therapy Cohort Collaboration, 2013).

Some researchers asserted that the proportion of HIV-infected persons with at least one non-communicable disease from among CVD and non-AIDS infections would increase from 29% to 84% (Art et al., 2019; Deeks et al., 2014; Quinn, 2009). Controlling HIV with ART comes at a cost as patients are faced with several adverse effects (Mrus et al., 2005).

2.2.1 Cardiovascular diseases and HIV patients

Cardiovascular disease (CVD) is referred to as any abnormal heart or blood vessels (Women Of Color, 2012). It is mainly characterized by a buildup of fat deposits inside the arteries and increased blood clot risk. The different CVDs include coronary heart diseases, aortic disorders, strokes, peripheral arterial disease, and transient ischemic attack (American Stroke Association, 2005). The main risk factors of CVDs are high blood pressure, smoking, high cholesterol, and obesity, etc. (American Stroke Association, 2005; Moorthie et al., 2019).

HIV infection involves every system in the human body. 'The cardiac involvement is due to the virus, opportunistic infections, protozoa, fungi, side effects of ARVs and also a combination of all or some of these factors' (Hemkens & Bucher, 2014; Jain et al., 2014). CVDs have been reported to contribute to about 20% of all deaths in PLWHA (Feinstein et al., 2017; So-Armah & Freiberg, 2019).

Go et al. (2014) reported that CVDs are the most common cause of mortality among adults in the United States. CVDs usually occur earlier and more commonly in HIV-infected subjects, who have an estimated 50% greater risk of developing myocardial infarction (MI) than uninfected subjects. Again, HIV-infected patients have an estimated 4.5-fold greater risk for sudden cardiac death. A review by Deeks et al. (2014) indicated approximately a 1.5 fold increased risk of developing a myocardial infarction (MI) among HIV-infected adults.

2.2.2 Respiratory Tract Infection and HIV-infected patients

HIV infection primarily targets the lungs. Respiratory infections are the most frequent health conditions most HIV-infected patients face (The Antiretroviral Therapy Cohort Collaboration, 2013). Non-AIDS diseases are the leading causes of mortality in HIV-infected patients, and respiratory tract infections constitute 3.1% of all lives lost (Hunt, 2012). According to Raj, Rijal, Palpasa, Gupta, & Shakya (2015) and Hunt (2012), HIV-infected patients typically develop pulmonary diseases and respiratory symptoms such as sputum production, chronic cough and dyspnea. These patients also tend to develop lower and upper respiratory tract infections.

In a cross-sectional study by Raj et al. (2015) to determine RTI among HIV positive individuals in Nepal, they reported that patients with a CD4 count lower than 200 cells/mm^3 developed RTI. Also, lower respiratory tract infections were found to be significantly higher in the HIV/AIDS population than in the general population (Lamas, Coelho, Grinsztejn, & Veloso, 2018). Hunt (2012) and Lamas et al. (2018) also reported that high CD4 count and decreased viral load were associated with a reduced risk of lower respiratory tract infections.

2.2.3 Peripheral neuropathy and HIV patients

Peripheral neuropathy is one of the most occurring health conditions in HIV type I patients (Wang et al., 2015). The symptoms include numbness, paresthesia, and burning pain. This disease typically affects the quality of life of PLWHA. Some common neuropathy PLWHA experience is distal symmetrical polyneuropathy, mono-neuropathy multiplex, autonomic neuropathy, and demyelinating polyneuropathy (Tagliati, Grinnell, Godbold, & Simpson, 1999; Wang et al., 2015).

About 30-67% of all PLWHA experience peripheral neuropathy (Tumusiime, Venter, Musenge, & Stewart, 2014; Widyadharma et al., 2019). Age and low haemoglobin levels are risk factors for peripheral neuropathy in HIV-infected individuals (Gunasekaran & Sivakumar, 2018; Widyadharma et al., 2019). Also, the female sex has been associated with ten times increased risk of developing peripheral neuropathy during the first year on ART than men (Widyadharma et al., 2019).

According to Gunasekaran & Sivakumar (2018), Tumusiime et al. (2014) and Luma et al. (2012), more than 35% of all PLWHA are bound to develop peripheral neuropathy in their lifetime. Reports by Gunasekaran & Sivakumar (2018) indicated that about 43.3% of HIV patients with clinical stages III and IV have an increased risk of developing peripheral neuropathy. However, low CD4 count and reduced viral load have no association with the experience of peripheral neuropathy.

2.2.4 *Hypertension* and HIV patients

Hypertension is one of the leading causes of mortality worldwide (Lloyd-sherlock, Beard, Minicuci, Ebrahim, & Chatterji, 2014). Initially seen as a problem only in high-income countries, hypertension is currently a global problem and increases CVD risk in low, middle-

and high-income countries. More than 85% of the deaths globally from CVD occur in low and middle-income countries (LMICs) (WHO, 2010). The prevalence of hypertension in African adults is almost the same as the prevalence in high-income countries, which poses a public health problem (Olack et al., 2015). The HIV infection keeps the immune system active at all times. This may cause inflammation and stiffen the blood vessels, and this may cause hypertension (Jericó et al., 2005). Amusa et al. (2016) reported that the prevalence of hypertension was 46% in HIV-infected patients.

2.2.5 Diabetes and HIV patients

Shaw, Sicree, & Zimmet (2010) reported that globally, the total number of diabetics is predicted to rise from 285 million in 2010 to 439 million in the next 20 years. Of all diabetes cases recorded, 80% of them live in low-income and developing countries (Baghaei, Marjani, Javanmard, Tabarsi, & Masjedi, 2013). In Ghana, over 500,000 cases of diabetes were reported in 2016 (Gatimu, Milimo, & Sebastian, 2016). Despite the increasing emergence of the diabetes epidemic in Africa (Whiting, Guariguata, Weil, & Shaw, 2011), only a few works have been done on the continent to establish a link between HIV and diabetes.

It has been reported that PLWHA have two times increased risk of developing diabetes mellitus compared to the general population (Sharma, Young, & Glesby, 2013). In a cohort study conducted by Moyo et al. (2014) on diabetes in HIV-infected adults, it was demonstrated that there was an increase in CD4 counts in patients with higher glycated HbA 1c levels. HIV patients who have diabetes tend to have a higher CD4 count. Other demographic characteristics, such as obesity, genetics, ethnicity, and physical inactivity, predisposes patients to diabetes. A study conducted in the USA indicated that among HIV

patients on ART, African-Americans and Hispanics were at an increased risk of developing diabetes as compared to non-Hispanic whites (Misra et al., 2013)

2.3 Antiretroviral therapy and chronic disease conditions

Cohorts of PLWHA on ART have a higher prevalence of hypertension, cancer, gout, and chronic HBV infection than the non-ART cohort (Art et al., 2019). Kalayjian et al. (2012) reported that the incidence of diabetes mellitus (DM) in an ART cohort over a period of ten years was significantly greater than those in the non-ART group. Before introducing ARV as a routine treatment for HIV/AIDS, the prevalence of diabetes was estimated to be 2.0-2.6% in patients who were not on treatment (Kalayjian et al., 2012; Krishnan et al., 2012), this has increased after the introduction of ARV (Misra et al., 2013).

Long-term exposure to ART is associated with an increased risk of DM among PLWHA (Art et al., 2019; Esté & Cihlar, 2010; Zicari et al., 2019). Several rapid-onset diabetes cases have been recorded following protease inhibitor initiation (De Wit et al., 2011). In a prospective study consisting of 11 cohorts from Europe, the USA, Argentina, and Australia, a significant relationship was established between diabetes and exposure to ART (De Wit et al., 2011; Lin et al., 2018). A study conducted in Gabon by Moyo et al. (2014) showed that patients comorbid for diabetes and HIV have a more excellent immune reconstitution with increased CD4 count after initiating ART. It is speculated that hyperglycemia in diabetic patients influences activities of humoral immunity (Moyo et al., 2014). Evidence suggests that PLWHA on ART have an increased risk of cardiomyopathy and coronary heart diseases

(Jain et al., 2014). ARTs tend to induce dyslipidemia, reduce insulin sensitivity and promote body fat redistribution hence increasing the risk of CVDs (Hemkens & Bucher, 2014).

Even though NRTIs are considered a cornerstone of ART regimens, they have been found to have the potential to expose its users to adverse side effects (White, 2001). ART tends to affect the mitochondria's function by inhibiting the replication of mitochondrial DNA (Cunha et al., 2015; Flint et al., 2009; Pacheco, Tuboi, Faulhaber, Harrison, & Schechter, 2008; White, 2001).

Amusa et al. (2016) reported that using ART was associated with a much higher prevalence of hypertension. Again, Fiseha, Belete, Dereje, & Dires (2019) also indicated that globally, about 35% of all HIV-infected adults on ART have hypertension compared to 30% of all HIV uninfected adults.

It is rather unfortunate to note that PLWHA on long-term ART, especially NRTIs, have a higher risk of developing peripheral neuropathy. In a study involving 1,116 patients by Moore et al. (2000) (as cited in White, 2001), the risk of developing peripheral neuropathy in patients treated with D4T and DDI was about four times greater than those given only DDI.

2.4 Socio-demographic factors that influence chronic conditions in HIV-infected patients

2.4.1 Age and chronic conditions in HIV-infected patients

Yang et al. (2019) report that in the US, about half of the PLWHA as of 2015 were 50 years and older, about 18% were 60-64 years, and 16% were 65 and older due to treatment with

ARV. Thus, they are faced with the problem of an ageing population among PLWHA. Consequently, chronic conditions associated with ageing, such as stroke, hypertension, and cardiovascular diseases, are bound to increase.

In a cross-sectional survey conducted in Nairobi, Kenya, by Olack et al. in 2015, it was established that the likelihood of hypertension increased with advancing age. It was observed that study participants over 55 years were five times more at risk of developing hypertension than participants aged 34–44 years.

Data obtained from research in the Netherlands also indicated that the rate of survival for HIV-infected individuals aged 50 years or older who were on treatment has increased steadily from 1996 to 1999 and again from 2006 to 2014 and is approaching that among uninfected individuals in the same age group (Smit et al., 2015). HIV patients are thus exposed to age-related conditions. Smith, Boer, Brul, Budovskaya, & Spek (2015), however, indicated that even when survival analysis is limited to only HIV-infected persons who did not have comorbidities before initiating antiretroviral therapy and who have maintained viral suppression throughout treatment, there remains a significant gap between the rates of survival of such persons and the general population.

Another study that was done in the Netherlands also stated that the proportion of PLWHA aged 50 years and above would increase from 28%, as of 2010, to about 73% in 2020 (Top Antivir Med., 2018; Smith, Boer, Brul, Budovskaya, & Spek, 2015). A study by Deeks & Phillips (2009) indicated that some comorbidities, such as cardiovascular disease, bone diseases, and diabetes, are usually associated with natural ageing and were increasingly dominant among PLWHA.

2.4.2 Sex of patient and chronic conditions in HIV-infected patients

The United Nations AIDS estimated in 2019 that about 1.7 million people became newly infected with HIV. More than 95% of these new infections are in low and middle-income countries. Out of the new infections each day, half are women, and 40% are young people (15-24 years old) (UNAIDS, 2019). Also, of the estimated 38 million adults living with HIV worldwide, nearly 18 million are women (Centre for Disease Control (CDC), 2018). Women are more prone to being infected as compared to men, as women and girls accounted for more than 48% of new HIV infections worldwide and 59% in SSA. More than 5,500 women aged 15-24 years every week become infected with HIV (UNAIDS, 2019). Globally, the proportion of women living with HIV/AIDS is steadily increasing. Mrus et al. (2005) asserted that the number of women infected has tripled over the years, from about 7% since the disease's discovery to 26%.

Research by Widyadharma et al. (2019) indicated that females are ten times more likely to develop a chronic condition while on ARV compared to men. A study by Karamchand et al. (2016) reported the opposite. They indicated that males on NNRTIs have an increased risk of developing diabetes compared to women. The sex of HIV patients on ARV may be associated with the risk of developing chronic conditions. However, the type of ARV used, among other factors, may contribute to the experience of several chronic disease conditions.

2.5 Treatment Factors that influence chronic conditions in HIV-infected patients

2.5.1 Type of ART use and chronic conditions in HIV-infected patients

The use of thymidine analogues (ART medications) exacerbates the risk of diabetes (Misra et al., 2013). Nucleoside analogues such as reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase (NNRTIs), the predominant ART medication used in Ghana and sub-Saharan Africa under the public health approach, have been positively associated with hyperglycemia, increased insulin resistance, hyperlipidemia, and lipodystrophy in patients (John, Nolan, & Mallal, 2001; Langs-barlow et al., 2013). The development of diabetes and insulin resistance has been attributed to hyperlipidemia and lipodystrophy (Dube & Sattler, 2010; John et al., 2001). The NRTIs antiretroviral drug class causes depletion in the amount and quality of mitochondrial DNA by inhibiting the mitochondrial DNA polymerase-γ. Aside NRTIs, some other ARV drug classes, such as protease inhibitors, also cause severe damage to the mitochondria. They do so by increasing oxidative stress and reducing mitochondrial function (Smith et al., 2015). Stavudine and zidovudine (NRTIs) were found to be associated with diabetes after adjusting for other risk factors for diabetes and lipids (De Wit et al., 2011; Kalra et al., 2011). Quite a number of antiretroviral drugs have been reported to cause diabetes, including NRTIs (stavudine and zidovudine) as well as PIs (indinavir and ritonavir) (De Wit et al., 2011; Hemkens & Bucher, 2014; Murata, Hruz, & Muecklesr, 2002).

Currently, the most preferred NNRTI for first-line ART in LMICs is efavirenz (EFV) because it is associated with a slight increase in blood glucose levels and cheaper than the other drugs (Erlandson et al., 2015; Lennox, Jeffery et al., 2018). However, efavirenz's use

exposes PLWHA to numerous health complications (Karamchand et al., 2016; Lennox, Jeffery et al., 2018).

2.5.2 Length of treatment and chronic conditions in HIV-infected patients

A range of diverse combinations of drugs is used in ART treatment, each having its peculiar side effects. These drugs are administered to reduce viral load and replication and boost immune function (Ford, Meintjes, & Vitoria, 2017). In a multivariate analysis conducted by Karamchand et al. in 2016, while adjusting for age, sex, BMI, baseline CD4 count, viral load, NRTI backbone, and exposure to other diabetogenic medicines, long term treatment with EFV rather than nevirapine (NVP) was associated with an increased risk of developing diabetes. Also, patients who were on long-term zidovudine (AZT) and stavudine (D4T) were identified to have an increased risk of the onset of diabetes (Araujo et al., 2014; Karamchand et al., 2016). It was also established that long-term use of EFV and D4T, and AZT increased the risk of incident diabetes (Araujo et al., 2014). The study concluded that it is prudent to prevent and detect diabetes in antiretroviral therapy programs. Also, ARVs that have a reduced risk of metabolic complications should be encouraged.

2.5.3 Medication adherence and chronic conditions in HIV-infected patients

According to WHO (2013), medication adherence is 'the degree to which an individual's behaviour corresponds with the agreed recommendations from a health care provider.' For PLWHA, medication adherence includes starting HIV treatment, attending all medical appointments, and taking HIV medicines each day and exactly as prescribed by the clinician. This is important to staying healthy. This suggests that adherence depends both on the patient as well as the health professional. Without proper adherence, there is a likelihood of treatment failure, leading to avoidable HIV-related morbidity and mortality; thus, adherence

is the most critical factor in ensuring the success of ART. Again, imperfect/non-adherence has the tendency to increase the risk of developing HIV resistant strains and transmitting the virus to others (Chaiyachati, Ogbuoji, & Price, 2014; Rodrigues da Silva reis, Guerra, & Lencastre, 2013). ART adherence is measured by some indicators, including patient self-reports, provider reports, pill count and pharmacy reports, electronic devices like medication Event Monitoring System, biochemical reports, and surrogate markers are also used (Chalker et al., 2009).

The World Health Organization has categorized adherence into subjective and objective measures, as Chalker et al. (2009) stated. In measuring adherence subjectively, self-report and provider assessment is used chiefly to determine the rate of adherence. However, this method will cause patients to report good adherence only about themselves, while the opposite is true. With the objective measures, there is actual evidence to determine the rate of adherence. Health providers usually lead the counting of pills, using electronic and biochemical monitoring. The objective measurement is assumed to be the best method as both patients and providers are involved; hence a higher adherence rate could be recorded (Baah-Danso, 2017).

According to Siedner (2016) and Deeks & Phillips (2009), patients who are non-adherent to ART have an increased risk of developing CVD complications and renal diseases. Again, the study reported that CVD events had a probability of occurring five times more than any other opportunistic infections among HIV-patients non-adherent to ART.

Patients adherent to ARV can maintain a suppressed viral load, thus, building up their immune system, which prevents the development of other opportunistic infections (Iacob,

Iacob, & Jugulete, 2017). Also, some patients may, however, become non-adherent to antiretroviral drugs due to drug toxicity.

2.6 Immune factors that influence chronic conditions in HIV-infected patients

2.6.1 Cluster of differentiation four (CD4) count and chronic conditions in HIV-infected patients

The CD4 T lymphocytes are a small population of the lymphocytes, also called T-helper cells. They coordinate the body's immune response by sending help to the B-lymphocytes during antibody production and increasing cellular immune response to antigens (World Health Organisation, 2007). The term CD4 count is a laboratory test used to measure CD4 T lymphocytes in blood samples. The CD is a protein that expresses itself on the surface of the hematopoietic system (Vogt & Schulte, 2010.). HIV primarily targets CD4 T lymphocytes, destroys them, and hence directly or indirectly leads to a loss of specific immune response, recall antibody response, and, eventually, non-specific immune response in the AIDS stage.

For PLWHA, the CD4 count is the strongest predictor of HIV progression and one of the most critical laboratory indicators of immune function and life expectancy (Ford et al., 2017) and death (Moorhouse, Conradie, & Venter, 2016). Again, to monitor the response to ART by a patient, the CD4 count is used.

When the virus attacks a susceptible host, there is a decline in CD4 T lymphocytes counts. As the CD4 T lymphocytes cells begin to decrease gradually (below 200 cells/mm^3), there is an ultimate loss of control over the immune activity of the human body, and various

opportunistic infections start appearing (Ford et al., 2017; Hanna, Vijayan, Karthigeyan, & Tripathi, 2017; Raji et al., 2019). A research conducted by (Deeks & Phillips, 2009) reported that patients with low CD4 count (below 350 cells/mm^3) tend to develop several non-AIDS complications. Again, low CD4 levels lead to an increased risk of developing cardiovascular disease, myocardial infarction and hypertension (Fahme et al., 2018; Feinstein et al., 2019).

2.6.2 *World Health Organization (WHO) stages and chronic conditions in HIV-infected patients*

Table 1 summarizes the WHO clinical stages of HIV and their related diseases in PLWHA.

Table 1: WHO clinical stages of HIV and their related disease in adults and adolescents aged 15 years or more (WHO, 2007)

Clinical stage I (Asymptomatic)
Asymptomatic
Persistent Generalized Lymphadenopathy (PGL)
Clinical stage II (Mild form of infection)
Unexplained moderate loss of weight (<10% of the measured weight of the body)
Recurrent respiratory tract infections (*sinusitis, tonsillitis, otitis media* and pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulcerations
Pruritic Papular Eruption
Seborrheic dermatitis
Fungal nail infections
Clinical stage III (Moderate form of the disease)
Unexplained severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhoea for longer than one month
Unexplained persistent fever (above 37.5 °C, intermittent or constant, for longer than one month)
Persistent oral candidiasis
Oral hairy leukoplakia (OHL)
Pulmonary TB
Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)

Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis Unexplained anaemia (<8 g/dl), neutropenia (<0.5 x 109/litre) or chronic thrombocytopenia (<50 X 109/litre3)
Clinical stage IV (Severe disease)
HIV wasting syndrome Pneumocystis *jiroveci* pneumonia (PCP) Recurrent severe bacterial pneumonia Chronic herpes simplex infection (orolabial, genital or anorectal, of more than one month's duration or visceral at any site) Oesophageal candidiasis (or candidiasis of the trachea, bronchi, or lungs) Extrapulmonary TB (EPTB) Kaposi sarcoma Cytomegalovirus (CMV) infection (retinitis or infection of other organs) Toxoplasmosis of the central nervous system (CNS) HIV encephalopathy Extrapulmonary cryptococcosis including meningitis Disseminated non-tuberculous mycobacterial infection Progressive multifocal leukoencephalopathy (PML) Penicilliosis Chronic cryptosporidiosis Chronic isosporiasis Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis) Recurrent septicemia (including due to non-typhoidal Salmonella) Lymphoma (cerebral or B-cell, non-Hodgkin) Invasive cervical carcinoma Atypical disseminated leishmaniasis Symptomatic HIV-associated nephropathy or HIV-associated Cardiomyopathy

2.6.3 Viral burden and chronic conditions in HIV-infected patients

The viral burden is a term that describes the amount of human immune virus in the blood of PLWHA. The higher the viral load in the blood, the faster the fall in CD4 cell count, and the greater the possibility of falling ill due to HIV. However, an undetectable viral load means a reduced risk of HIV being passed on to an HIV-negative person. The viral load test is defined as the number of copies of HIV RNA in a millilitre of blood (copies/ml) (Avert, 2017; Kalra et al., 2011). HIV viral load predicts how fast the disease will progress. Therefore, PLWHA must keep their viral load very low by adhering to ART to maintain a healthy immune system, thereby reducing the risk of developing HIV/AIDS-associated health complications and increasing life expectancy (Avert, 2017; Www.i-Base.info, 2020).

According to Serrano-Villar et al. (2016), a high viral burden increases the risk of experiencing a stroke. Again, cardiovascular diseases have been found to cause more deaths in HIV patients with high viral load.

CHAPTER THREE

3.0 METHODS

3.1 Study site

The Pantang Antiretroviral therapy (ART) Centre is located within the Pantang Hospital, situated in the Pantang sub-municipality within the La-Nkwantanang Madina Municipality of the Greater Accra Region of Ghana. Pantang sub-municipal occupies 68.1sq/km and is bounded by the Abokobi district, Adenta Municipal, Damfa sub-municipal, La-Nkwantanang Madina Municipal, and Accra Metropolis (Figure 2).

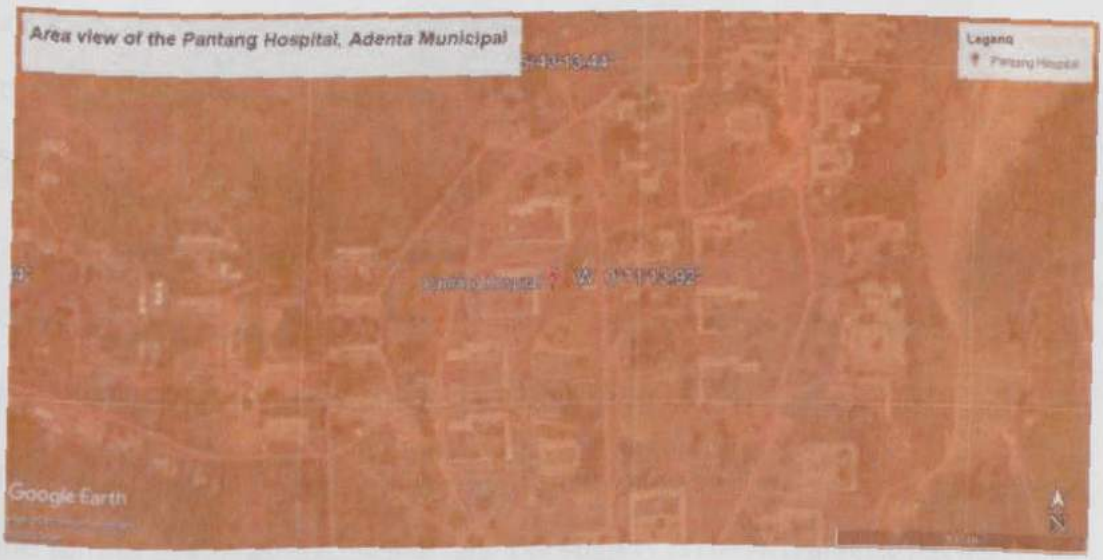

Figure 2: A location map of Pantang Hospital (source: Google Earth)

The projected sub-municipality population was 24,932, with an annual population growth rate of 4.2% (Ghana Statistical Service, 2014).

The sub-municipal has a total of four (4) health facilities. These facilities include a government hospital (Pantang hospital), one private hospital, one clinic, and one maternity home. There are, however, sixteen (16) outreach points for public health activities within the sub-municipality.

The Pantang Hospital, where the research was carried out, has two primary health departments: the general hospital and the specialized psychiatry care hospital. The ART centre is a part of the general hospital.

The ART centre started in 2006 as an HIV testing and counselling unit of the Pantang general Hospital. It referred suspected HIV positive clients to The Greater Accra Regional Hospital and Korle-Bu Teaching Hospital (the regional and tertiary hospitals in the Greater Accra Region of Ghana) for confirmatory test and further management.

In 2008, the unit was designated as an ART centre to begin offering complete ART services. Currently, the centre provides services that include HIV testing and counselling, provision of antiretroviral drugs (ARVs), prevention of mother-to-child transmission (PMTCT) services, and community health education on HIV/AIDS.

HIV patients receiving care at the centre attend to the same primary health care physician as other patients seeking general medical care. The Ministry of Health is piloting this integrated primary health and HIV care in Ghana to reduce the stigma associated with HIV treatment. Against this background, some patients from other centres seek transfer to Pantang ART centre; hence the centre is recording exponential growth in patients seeking HIV treatment and could serve as the clinic for many HIV/AIDS-related studies in the coming years.

3.2 Study population

The target population for this study was HIV/AIDS patients receiving ART treatment in the Greater Accra Region of Ghana, and the study population was those patients receiving their treatment at the antiretroviral clinic at Pantang Hospital in Accra. Presently, there are over 900 patients receiving ART services in the Hospital.

3.3 *Research Study design*

This research is a retrospective cohort study. Records of HIV patients receiving antiretroviral therapy at the Pantang hospital in the Greater Accra region were reviewed.

3.4 Description of study Variables

3.4.1 Dependent Variable

The dependent variable was chronic disease condition, defined as any chronic condition developed by a patient after testing positive for HIV and given ARVs. It includes hypertension, peripheral neuropathy, diabetes, liver and kidney problems, cardiovascular diseases, respiratory tract infection, and other defined chronic diseases. The dependent variable was considered a binary or dichotomous variable.

3.4.2 Independent Variables

Table 2 below shows the independent variables that were considered in this study.

Table 2: Independent variables considered in the study

INDEPENDENT VARIABLE	TYPE OF VARIABLE	LEVEL OF MEASUREMENTS	CATEGORIES
PATIENT'S SOCIO-DEMOGRAPHIC CHARACTERISTICS			
Sex	Categorical	Nominal	Female, Male
Age	Categorical/ continuous	Ordinal	<29, 30-39, 40-49,>49
Marital status	Categorical	Nominal	Never married, married, divorced/separated/widowed, cohabiting
Occupational status	Categorical	Nominal	Employed, not employed
Educational level	Categorical	Ordinal	None, Primary, JSS/MSLC, Secondary/technical/vocational, tertiary
Religion	Categorical	Nominal	Christian, Muslim, others
Number of dependents	Discrete	Count	None, one, two, >two
Weight in kg	Categorical/ continuous	Ordinal	<50, 50-70, >70
Smoking status	Categorical	Binary	Yes/No
CLINICAL CHARACTERISTICS			
First visit	Categorical	Nominal	HIV testing, in VCT site, transfer in
Type of HIV	Categorical	Ordinal	HIV I, HIV II, HIV I&II
TB status	Categorical	Nominal	Not screened, screened negative, screened positive
Drug allergies	Categorical	Binary	Yes/no
HIV disclosure	Categorical	Nominal	Disclosed, not disclosed
Sexually active	Categorical	Binary	Yes/no
Regular condom use	Categorical	Binary	Yes/no
WHO clinical stage	Categorical	Ordinal	Stage I, stage II, stage III, stage IV
Drug combination	Categorical	Nominal	Other combinations, TDF+3TC+EFV, NVP+3TC+D4T, TDF+3TC+NVP, AZT+3TC+EFV, AZT+3TC+NVP
Change in ART medication	Categorical	Binary	Yes/no
TREATMENT FACTORS			

Prescribed drug regime	Categorical	Ordinal	1st line 1st choice, 1st line 2nd choice, 2nd line 1st choice, 2nd line 2nd choice
Medication adherence	Categorical	Binary	Yes/no
HIV related factors			
Opportunistic infections	Categorical	Binary	Yes/No
Comorbidities	Categorical	Binary	Yes/No
Immune factors			
CD4 count	Categorical/ continuous	Ordinal	<350 counts, ≥350 counts
WHO clinical stage	Categorical	Ordinal	Stages I, II, III, IV

3.5 Sampling Method

3.5.1 Sample size calculation

A cohort study from Uganda estimated the prevalence of hypertension (a chronic condition) among HIV patients on ART to be 14.5% (Mayanja et al., 2017). This value was used as the expected prevalence of chronic conditions among patients on ART. Sample size calculation was done using Cochran's formula as presented below:

$$n^a = \frac{z_{\alpha/2}^2 * p * (1-p)}{e^2}$$

Where:

n^a *is the sample size estimate from the Cochran's sample size formula ,*

p *is the prevalence estimate of* 14.5

e *is the margin of error of* 0.05 *and*

$z_{\alpha/2}$ *is the standardized normal score at* 0.05 *alpha level which is* 1.96.

Hence:

$$n^a = \frac{1.96^2 * 0.145 * (1 - 0.145)}{0.05^2} = 190.5 \approx 191$$

Since the study used health facility records, most of the variables had missing observations; hence, a 20% upward adjustment was used to cater for missing data within patients records.

Considering an upward adjustment of 20%, an estimated final sample size of

$n \approx 1.20 * n^a = 1.20 * 191 \approx 229.2 \approx 230$ was used.

Hence a minimum sample size of 230 records was reviewed.

3.6 Sampling Technique.

The list of folder numbers of all HIV patients on ART was obtained from the ART clinic's records unit. A simple random sampling process using the "sample" command in STATA version 16 was used to select 230 folder numbers from the list randomly. Selected records that did not satisfy the inclusion and exclusion criteria were replaced using another simple random selection procedure, excluding the already chosen records. Selected folder numbers were reviewed and used for the analysis of this study.

3.7 Inclusion / Exclusion Criteria

3.7.1 Inclusion criteria

- Medical records of HIV positive patients who were 15 years and above and receiving ART treatment for at least three years at the Pantang ART clinic were reviewed.

- The medical records of selected participants were reviewed to ensure that they were negative for tuberculosis, serum hepatitis, and inflammatory conditions other than HIV before they started taking the ART medication.

3.7.2 *Exclusion criteria*

- HIV positive pregnant women and
- Patients diagnosed with diabetes, cardiovascular disease, kidney complications, and other chronic conditions before being diagnosed with HIV and given medication were excluded from the study.

3.8 *Missing values*

For each of the chronic conditions considered the outcome variable in the study, only patients with complete data on the condition were considered for analysis. No missing values were imputed for the data used in the study.

3.9 Medical record extraction

A secondary data source was used for the study. Information from the medical records of patients who visit the ART clinic of the Pantang Hospital was extracted. Relevant information, which included patients' socio-demographic data, and clinical characteristics were taken.

3.10 Data collection

The extraction of data related to this study was carried out by two trained research assistants and the Principal Investigator.

Reviewed records of patients were captured and entered in an Epi-Info designed template. The template had skipped patterns designed to aid in consistency checking and data validation. The collected data was exported as a comma-separated values (CSV) file, which was then imported into STATA IC version 16 for further data cleaning, coding, and analysis.

3.11 *Quality control*

This was ensured by putting the following measures in place: training of research assistants who helped to collect data to capture the objectives of the research; and also, research assistants were keenly supervised during data collection; data was entered twice each day and again checked for accuracy. Folders for which key data were missing were not included in the analysis.

3.12 Data analysis

STATA IC version 16 was used to analyse the data set. Socio-demographic characteristics, clinical characteristics, and symptoms screened before ARV administration were described using frequency and percentages. The mean and standard deviation were used to summarize continuous variables. The frequency and percentages of the various chronic disease conditions observed during the first three years on ARVs among patients whose records were reviewed in this study were also described using the bar chart.

The Kaplan Meier failure curve for experiencing at least one chronic condition was plotted to show the hazard curves' differences across selected baseline socio-demographic and clinical characteristics. The log-rank test was used to test the equality of hazard curves for some selected variables and shown on the graph.

The unadjusted or simple cox-proportional hazard model was employed to assess the risk of experiencing at least one chronic condition in the first three years on ARVs after adjusting for time to experience of the conditions. All variables from the unadjusted or simple cox-proportional hazard model that were significant were then modelled together to estimate the adjusted risk of experiencing at least one chronic condition in the first three years on ARVs. The unadjusted and adjusted cox-proportional hazard model was also used to assess the risk of experiencing some selected chronic disease complications in the first three years on ARVs among HIV positive patients.

Statistical significance for this study was considered at an alpha of 0.05. A 95% confidence interval was used for all risk ratios estimates.

3.13 Ethical Considerations.

This study's ethical clearance was obtained from the Ghana Health Service Ethics Review Committee (GHS-ERC 017/02/20) and the ART centre at Pantang Hospital granted permission. There were no medical or financial benefits to any participant in this study. However, the study would benefit the patients since the information collected would improve health intervention and promote health activities for HIV/AIDS patients visiting the ART clinic. It would also add up to the existing knowledge of ART medication use.

The confidentiality of the participants was not breached in this study. Trained research assistants assisted the principal investigator in extracting data from the record, after which only the principal investigator and supervisor had access to the collated data.

3.14 Risks

There were minimal risks associated with this study. Due to the COVID-19 pandemic, all research assistants and principal investigators were in full PPEs. Also, all COVID-19 protocols were duly observed.

3.15 Consent form

No consent was obtained directly from patients. However, permission was sought from the clinic to use the patient's data. Also, no contact of the study participant was taken. No follow-up on any patient was done; thus, there was no need to provide any form of supervisory contact information for redress purposes.

CHAPTER FOUR

4.0 RESULTS

From the sample size calculated, two hundred and thirty records were to be reviewed; however, two hundred and fifty-six records were reviewed. Out of this number, due to missing data, only two hundred and twenty-two records were analysed and used in the study.

4.1 Background/socio-demographic characteristics of study participants

Table 3 below shows the background characteristics of all 222 records reviewed for the study. The age range with the highest frequency was 40-49, with a percentage of 35.59. Individuals aged >49 were the least with a percentage of 14.41. Females (65.32%, n=145) were more than males (34.68%, n=77) in the study. Majority of participants were married (42.79%, n=95), employed (82.88%, n=184) and Christians (84.68%, n=188). The study's records showed that most respondents had their highest education level as JSS/MSLC (47.75%, n=106), and 92.79% (n=206) had never smoked. (Table 3)

Table 3: Background/socio-demographic characteristics of study participants

Variables	Frequency (n)	Percentage
Age (mean ± SD)	**39.01 ± 9.64**	
<29	35	15.77
30-39	76	34.23
40-49	79	35.59
>49	32	14.41
Sex		
Male	77	34.68
Female	145	65.32
Marital status		
Never married	59	26.58
Cohabiting	18	8.11
Married	95	42.79
Divorced/separated/widowed	50	22.52
Occupation		
Employed	184	82.88
Unemployed	38	17.12
Education		
None	34	15.32
Primary	28	12.61
JSS/MSLC	106	47.75
Secondary/technical/vocational	36	16.22
Tertiary	18	8.11
Religion		
Muslim	25	11.26
Christian	188	84.68
Others	9	4.05
Number of dependent children (Mean ± SD)	**(0.96 ± 1.17)**	
None	106	47.75
One	55	24.77
Two	34	15.32
>Two	27	12.16
Weight in kg (Mean ± SD)	**(58.23 ± 11.23)**	
<50	41	18.47
50-70	149	67.12
>70	23	10.36
Missing	9	4.05
Smoking status		
Never smoked	206	92.79
Ever smoked	16	7.21

JSS: Junior Secondary School. MSLC: Middle school leavers certificate

4.2 *Clinical characteristics of study participants*

Table 4 reports on the frequencies and percentages of clinical characteristics of study participants. Most of the patients got to know their HIV status by diagnostic HIV testing (84.68%, n=188), had HIV I (72.97%, n=162), had not screened for TB (88.29%, n=196), had no drug allergies (95.95%, n=213), had not disclosed their HIV status (56.76%, 126). Only 21.17% (n=47) patients had stage I HIV infection, with a majority (32.88%, n=73) of them with the severe form (stage IV) of the disease. The majority of patients also had a CD4 count below 350 (60.36%, 134). Most of the patients were on 1st line, 1st choice as a prescribed drug regime (64.41%, n=143) and given TDF+3TC+EFV as a prescribed drug combination (40.09%, n=89). The study established that only 52.70% (n=117) of the participants were adherent to their ARV medication during the first three years on ARVs, and 31.98% (n=71) had a change in ART medication within the first three years on ARV. (Table 4)

Table 4: Clinical characteristics of study participants

Variables	Frequency	Percentage
First visit		
HIV testing	188	84.68
In VCT site	24	10.81
Transfer in	10	4.50
Type of HIV		
HIV I	162	72.97
HIV I & II	7	3.15
Unknown	53	23.87
TB status		
Not screened	196	88.29
Screened negative	18	8.11
Screened positive	8	3.60
Drug allergies		
Yes	9	4.05
No	213	95.95
HIV disclosure		
Disclosed	96	43.24
Not disclosed	126	56.76
Sexually active		

Yes	101	45.50
No	117	52.70
Unknown	4	1.80
Regular condom use		
Yes	24	10.81
No	177	79.73
Unknown	21	9.46
WHO clinical stage		
Stage I	47	21.17
Stage II	29	13.06
Stage III	44	19.82
Stage IV	29	13.06
Unknown	73	32.88
CD4 below 350 (Mean ± SD)	(244.56 ± 197.61)	
Yes	134	60.36
No	42	18.92
Unknown	46	20.72
Prescribed drug regime		
1st line 1st choice	143	64.41
2nd line 2nd choice	79	35.59
Drug combinations		
Other combination	39	17.57
TDF+3TC+EFV	89	40.09
NVP+3TC+D4T	17	7.66
TDF+3TC+NVP	15	6.76
AZT+3TC+EFV	17	7.66
AZT+3TC+NVP	45	20.27
Adherence to ARV medication		
Non-adherent	105	47.30
Adherent	117	52.70
Change in ART medication		
Yes	71	31.98
No	151	68.02

VCT: Voluntary Counselling and Testing. TDF: Tenofovir. 3TC: Lamivudine. EFV: Efavirenz. NVP: Nevirapine. D4T: Stavudine. AZT: Zidovudine

4.3 *Conditions screened* before ARV administration

Regarding the conditions screened before ARV administration, figure 3 shows that the conditions with the highest percentages were severe weight loss (38.83%), fever (26.1%), chronic cough (24.8), chills (24.3%), and skin rash itching (24.3%). The conditions with the least percentages were STI (9.9%), body pains (9.5%), vomiting (9%), jaundice (1.4%), and other conditions (anaemia, herpes, dermatitis, among others) (8.1%). (Fig. 3)

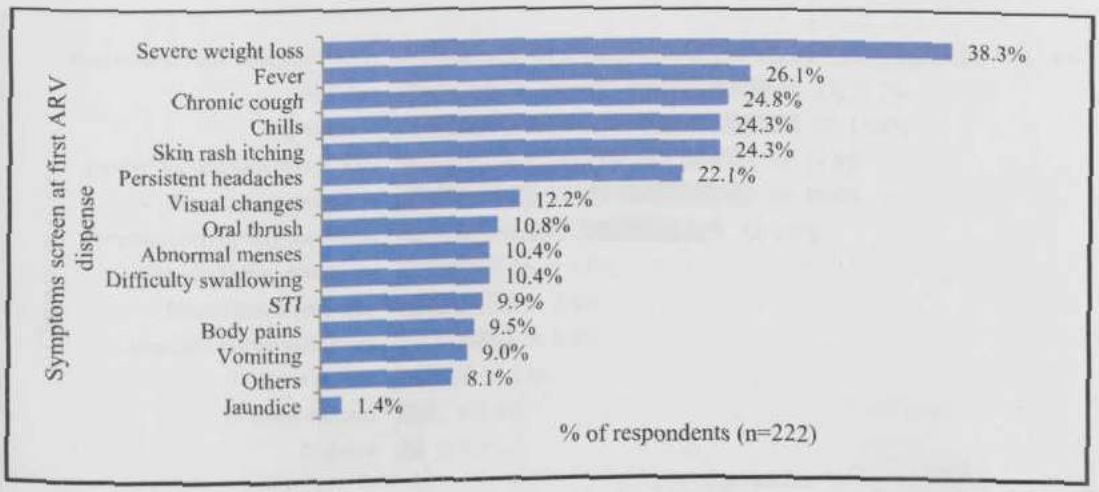

Figure 3: Conditions screened before ARV administration

4.4 Chronic conditions developed during the first three years on ARVs

Figure 4 shows that during the first three years on ARV, 39 (17.6%) patients developed RTIs, 27 (12.2%) had anaemia and hypertension, and 24 (10.8%) developed cardiovascular diseases and neurological conditions. Few respondents had mental health problems and lymphatic system conditions (8; 3.6%), bone disease (5; 2.3%), liver diseases (3; 1.4%), and diabetes (2; 0.9%). (Fig. 4).

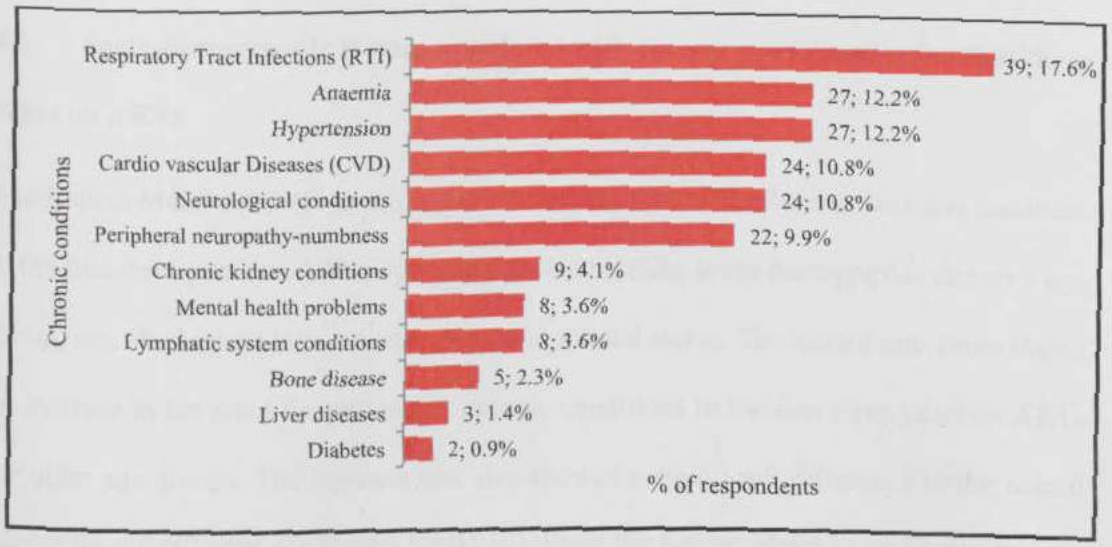

Figure 4: Chronic conditions developed during the first three years on ARVs

Overall, the prevalence of experiencing at least one of the mentioned chronic disease conditions in the first three years on ARV among HIV patients was 53.6%, with a 95% confidence interval estimate of 46.4% to 53.6% (Fig. 5).

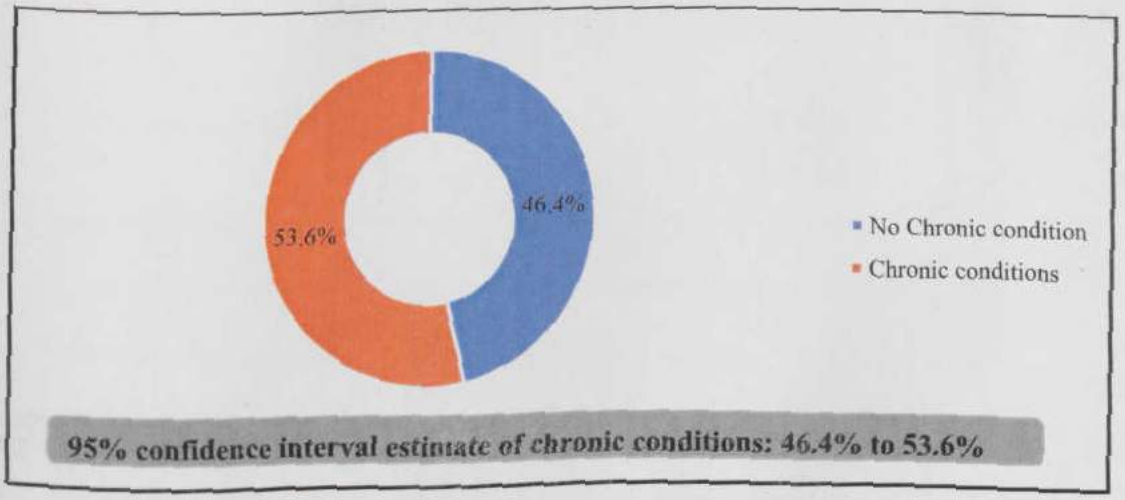

Figure 5: Prevalence of chronic conditions during the first three years on ARVs

4.5 Socio-demographic factors associated with chronic conditions in the first three years on ARVs

The Kaplan Meier curve (Figure 6) shows the hazard rate of developing a chronic condition in the first three years on ARVs by some selected baseline socio-demographic factors – age group, sex, the highest level of education, and marital status. The hazard rate curve shows an increase in the rate of experiencing chronic conditions in the first three years on ARTs for older age groups. The log-rank test also showed a significant difference in the hazard curves for the different age groups ($p=0.010$). From the Kaplan Meier hazard curve and the log-rank test of equality of hazard curves, the hazard curves were not significantly different across the sex, highest level of education, and patients' marital status ($p>0.05$).

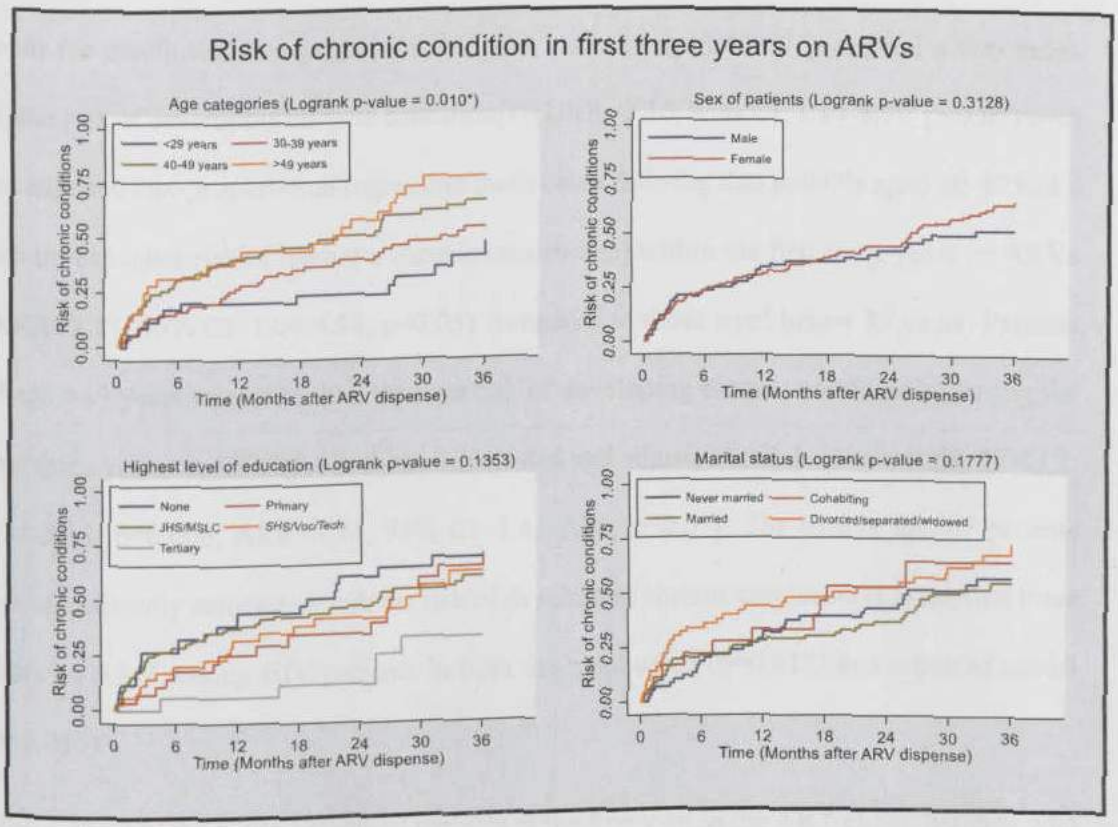

Figure 6: Kaplan Meier curve of the risk of developing chronic condition(s) in the first three years on ARTs among HIV patients for selected socio-demographic factors

4.6 Socio-demographic factors associated with chronic condition(s) in the first three years on ARVs

The frequency and percentage distribution of socio-demographic factors and their association with the experience of chronic condition(s) during the first three years on ARVs are shown in Table 5. The cox-proportional hazard model was used to estimate both the crude (unadjusted) and adjusted odds of chronic condition(s) experience among patients visiting the ART clinic within the first three years on ARVs.

The experience of chronic condition(s) within the first three years on ARV was 71.9% (n=23/32) among patients >49 years, 58.2% (n=46/79) among patients aged 40-49, 48.7% (n=37/76) among patients aged 30-39, and 37.1% (n=13/35) among patients <30 years.

From the unadjusted cox-proportional model, patients aged 40-49 years had a two times higher risk of developing chronic condition(s) (URR=2.10, 95% CI: 1.14-3.90, p<0.05) with the adjusted cox-proportional regression model also showing that patients aged 40-49 had a two times higher risk of having a chronic condition(s) within the first three years on ARVs (ARR=2.17, 95% CI: 1.04-4.54, p<0.05) compared to those aged below 30 years. Patients of age >49 years were over two times at risk of developing chronic condition(s) during the first three years on ARVs for both the unadjusted and adjusted models (URR=2.58, 95% CI: 1.31-5.11, p=0.006; ARR=3.34, 95% CI=1.43-7.76, p<0.01). The overall age of patients was significantly associated with the risk of developing chronic condition(s) in the first three years on ARV among HIV patients in both the unadjusted (p=0.013) and adjusted model (p=0.015).

With respect to the marital status of patients at the first visit to the ART clinic, patients who were divorced/separated constituted 66.0% (n=33/50), those cohabiting 55.6% (10/18), never married 52.5% (31/59) and married 47.4% (45/95). The unadjusted model showed that cohabiting patients were not significantly associated with developing chronic conditions but had two times increased risk of developing chronic disease complications in the adjusted model (ARR=2.14, 95% CI=1.01-4.52, p<0.05). Also, in the unadjusted model, patients who were divorced/separated had a 60% higher risk of developing chronic disease conditions during the first three years on ARVs (URR=1.60, 95% CI: 1.02-2.51, p<0.05) but was not significant for the adjusted model. Although marital status was significantly associated with the development of chronic condition(s) in the first three years on ARVs in the unadjusted model (p=0.044), it was not significant from the adjusted cox-proportional hazard model (p>0.05).

The experience of chronic condition(s) within the first three years on ARV was 64.7% (n=22/34) among patients who had no level of education, 57.1% (16/28) among those with a primary level of education, 54.7% (58/106) among patients with JSS/MSLC level of education, 50% (18/36) in respondents with secondary/technical/vocational and 27.8% (5/18) for patients with a tertiary level of education. Patients who had no level of education had about four times increased risk of developing chronic disease complications from the unadjusted model (URR=3.45, 95% CI: 1.31-9.13, $p<0.05$) and three times increased risk in the adjusted model (ARR=3.28, 95% CI=1.17-9.21, $p<0.05$). Those who had JSS/MSLC as the highest level of education were about three times at risk of developing a chronic condition from the unadjusted model (URR=2.70, 95% CI=1.08-6.74, $p<0.05$) compared to those with no formal education. The highest education level saw a significant association with chronic condition(s) in the unadjusted model ($p=0.012$), albeit it was not significant in the adjusted model (Table 5).

Table 5: Socio-demographic factors associated with chronic conditions in the first three years on ARVs

Variables	N	*Chronic conditions* n (%)	*Unadjusted cox-proportional model* URR [95% CI]	P-value	*Adjusted cox-proportional model* ARR [95% CI]	P-value
Total	222	119 (53.6)				
Age				0.013*		0.015*
<30	35	13 (37.1)	1.00 [reference]		1.00 [reference]	
30-39	76	37 (48.7)	1.40 [0.75-2.64]		1.28 [0.64-2.55]	
40-49	79	46 (58.2)	2.10 [1.14-3.90] *		2.17 [1.04-4.54] *	
>49	32	23 (71.9)	2.58 [1.31-5.11] **		3.34 [1.43-7.76] **	
Sex				0.314		
Male	77	36 (46.8)	1.00 [reference]		-	
Female	145	83 (57.2)	1.22 [0.83-1.81]		-	
Marital status				0.044*		0.236
Married	95	45 (47.4)	1.00 [reference]		1.00 [reference]	
Never married	59	31 (52.5)	1.09 [0.69-1.73]		1.17 [0.68-2.02]	
Cohabiting	18	10 (55.6)	1.45 [0.73-2.88]		2.14 [1.01-4.52] *	
Divorced/separated	50	33 (66.0)	1.60 [1.02-2.51] *		1.26 [0.75-2.10]	
Occupation				0.065		
Employed	184	94 (51.1)	1.00 [reference]		-	
Unemployed	38	25 (65.8)	1.52 [0.97-2.36]		-	
Education				0.012*		0.258
None	34	22 (64.7)	3.45 [1.31-9.13] *		3.28 [1.17-9.21] *	
Primary	28	16 (57.1)	2.57 [0.94-7.03]		2.66 [0.91-7.74]	
JSS/MSLC	106	58 (54.7)	2.70 [1.08-6.74] *		2.51 [0.98-6.44]	
SHS/TECH/VOC.	36	18 (50.0)	2.39 [0.89-6.44]		2.79 [1.00-7.77]	
Tertiary	18	5 (27.8)	1.00 [reference]		1.00 [reference]	
Religion				0.683		
Muslim	25	14 (56.0)	1.00 [reference]		-	
Christian	188	99 (52.7)	0.92 [0.53-1.62]		-	
Others	9	6 (66.7)	1.32 [0.51-3.43]		-	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval

P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

Table 5 continues

Variables	N	Chronic conditions n (%)	Unadjusted cox-proportional model URR [95% CI]	P-value	Adjusted cox-proportional model ARR [95% CI]	P-value
Dependent children				0.471		
None	106	59 (55.7)	1.00 [reference]		-	
One	55	30 (54.5)	1.06 [0.68-1.65]		-	
Two	34	13 (38.2)	0.71 [0.39-1.29]		-	
>Two	27	17 (63.0)	1.26 [0.73-2.15]		-	
Weight in kg				0.225	-	
<50	41	21 (51.2)	1.43 [0.65-3.11]		-	
50-70	149	85 (57.0)	1.76 [0.88-3.49]		-	
>70	23	9 (39.1)	1.00 [reference]		-	
Smoking status				0.847	-	
Never smoked	206	111 (53.9)	1.00 [reference]		-	
Ever smoked	16	8 (50.0)	0.93 [0.45-1.91]		-	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

4.6 Clinical related factors associated with the experience of chronic condition(s) in the first three years on ARVs

The Kaplan Meier curve (Figure 7) shows the hazard rate of developing chronic condition(s) in the first three years on ARVs by the baseline CD4 count, WHO clinical stage at baseline, ART drug combination and adherence ARV medication during the first three years on ARTs. The curve shows a higher rate of developing chronic condition(s) among HIV patients with a CD4 count below 350 cells per mm^3 compared to those with CD4 above 350 cells per mm^3 or those with unknown CD4 values at baseline. The log-rank test for equality of hazard rate of developing chronic condition(s) by baseline CD4 count level was significant (p=0.004). Likewise, the hazard rate of developing chronic condition(s) in the first three years was higher among those at WHO clinical stage III and IV compared to those at WHO clinical stage I and II or unknown stage as shown from the Kaplan Meier curve and the log-rank test (p=0.019). The log-rank test did not show a significant association between the drug combination and the hazard rate of experiencing chronic condition(s) in the first three years on ARTs. On the other hand, the hazard curve of risk of chronic disease complication was significantly higher for patients who were non-adherent to ART medication than those who were adherent, as is depicted in figure 7 and the log-rank test (p=0.018).

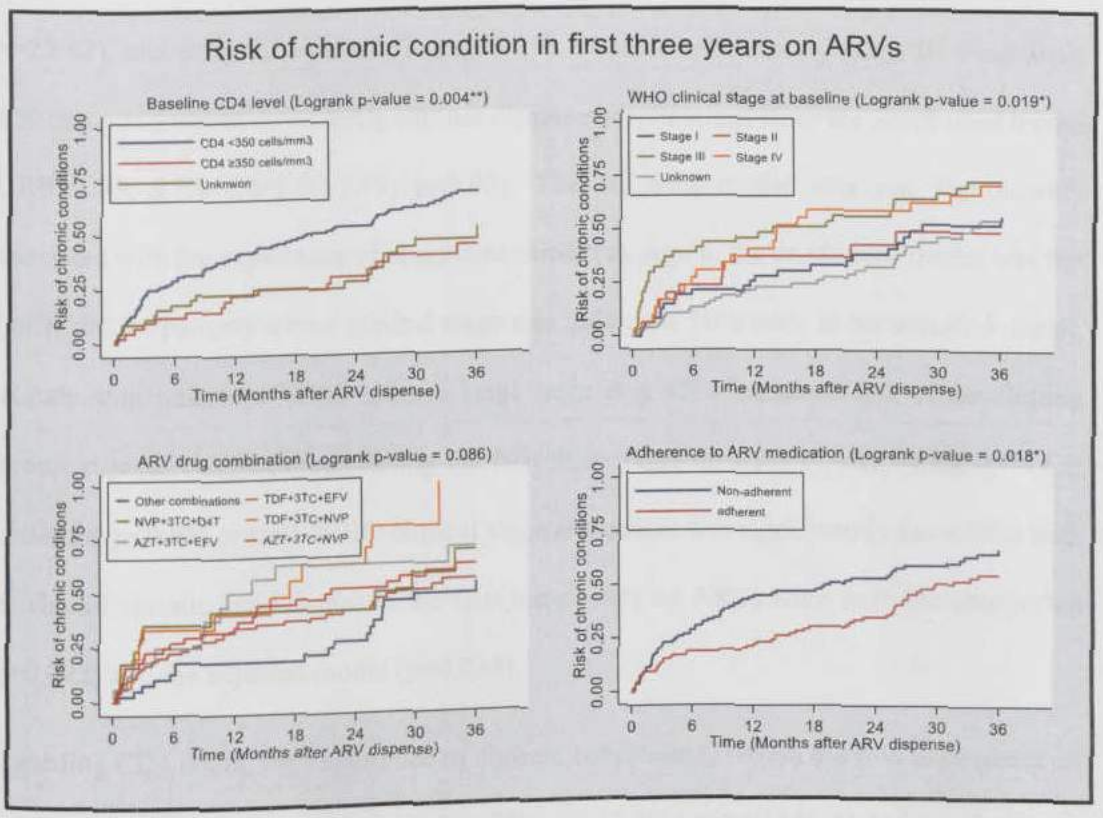

Figure 7: Kaplan Meier curve of the risk of developing a chronic condition(s) in the first three years on ARVs among HIV patients for selected clinical factors

4.7 *Association* between clinical related characteristics and experience of chronic conditions in the first three years on ARVs

The experience of chronic condition(s) within the first three years on ARV for patients who had their first visit via diagnostic HIV testing was 55.9% (n=105/188), and 41.2% (n=14/34) came in on transfer/in VCT site. Patients' first visit was not significantly associated with the experience of chronic condition(s) for both unadjusted and adjusted models (Table 6).

Within the first three years on ARVs, patients who were diagnosed to have WHO clinical stage IV HIV were 69.0% (n=20/29), stage III was 68.2% (n=30/44), stage I was 48.9%

(n=23/47), and stage II were 44.8% (n=13/29). Patients with clinical stage III were at an 85% increased risk of developing chronic disease complications from the unadjusted model (URR=1.85, 95% CI=1.07-3.19, p<0.05). The adjusted model was not significantly associated with the experience of chronic condition(s). Again, the unadjusted model was not significant for patients whose clinical stage was unknown. However, in the adjusted model, patients with unknown WHO clinical stage were at a 45% increased risk of developing chronic disease complications during the first three years on ARVs (ARR=0.55, 95% CI: 0.30-0.98, p<0.05) overall, WHO clinical stage at baseline was significantly associated with the risk of chronic condition(s) in the first three years on ARTs from both the unadjusted (p=0.023) and the adjusted model (p=0.034).

Regarding CD4 count, the experience of chronic condition(s) within the first three years on ARV for patients whose count was below 350 was 62.7% (n=84/134), 41.3% (n=19/46) for those with count unknown, and 38.1% (n=16/42) for those above 350. From the unadjusted model, patients whose CD4 count was above 350 had a 52% reduced risk of developing chronic condition(s) (URR=0.48, 95% CI: 0.28-0.83, p=0.008). The adjusted logistic regression model was not significantly associated with the experience of chronic condition(s) during the first three years on ARVs. For patients whose CD4 count was unknown, the unadjusted model showed a 44% reduced risk of experiencing chronic condition(s) (URR=0.56, 95% CI: 0.34-0.92, p=0.021). The adjusted model was not significantly associated with the experience of chronic conditions. Overall, the CD4 count level was significantly associated with experiencing chronic condition(s) in the first three years on ARV from the unadjusted model (p=0.005); however, it was not significant from the adjusted model.

The experience of chronic condition(s) within the first three years on ARV was 80% (n=12/15) among patients who were on TDF+3TC+NVP drug combination, 64.7% (11/17) among those given AZT+3TC+EFV, 58.8% (10/17) among patients given NVP+3TC+D4T, 57.8% (26/45) in respondents given AZT+3TC+NVP, 47.2% (42/89) in patients given TDF+3TC+EFV and 46.2% (18/39) in patients given other combinations. TDF+3TC+EFV was not significantly associated with the experience of chronic condition(s) for the unadjusted model. However, for the adjusted model, patients were two times at risk of developing chronic disease complications (ARR=2.15, 95% CI: 1.16-3.98, p=0.016) when given the TDF+3TC+EFV combination. For those who were given TDF+3TC+NVP, they were about three times at risk of developing a chronic condition from the unadjusted model (URR=2.80, 95% CI=1.34-5.84, p=0.006) and four times at risk of developing a chronic condition(s) from the adjusted model (ARR=4.07, 95% CI=1.64-10.08, p=0.002). For patients on AZT+3TC+EFV, the unadjusted model was not significantly associated with the experience of chronic condition(s). However, the adjusted model was significant, with patients being at three times higher risk of developing chronic disease complications (ARR=3.05, 95% CI: 1.37-6.80, p=0.006). Patients who were given drug combinations AZT+3TC+NVP had their unadjusted risk not significantly associated with the experience of a chronic condition. Yet, the adjusted model showed significance with the patients being two times at risk of developing chronic disease complications during the first three years on ARVs (ARR=2.12, 95% CI: 1.06-4.22, p=0.034). The ART drug combination was significant from both the unadjusted model (p=0.049) and the adjusted model (p=0.034).

Regarding ARV adherence, patients who were non-adherent during the first three years on ARV were 61.9% (65/105) and 46.2% (54/117) among patients who were adherent to the

prescribed drugs. ARV adherence showed a significant association with the experience of chronic conditions during the first three years using the unadjusted model. A 45% reduced risk was recorded among the ARV adherent patients (URR=0.65, 95% CI: 0.45-0.93, p=0.018), although the adjusted model showed no significance.

Table 6: Association between clinical related characteristics and experience of chronic conditions in the first three years on ARVs

Variables	N	Chronic condition n (%)	Unadjusted cox-proportional model URR [95% CI]	P-value	Adjusted cox-proportional model ARR [95% CI]	P-value
Total	222	119 (53.6)				
First visit				0.095	-	
HIV testing	188	105 (55.9)	1.00 [reference]		-	
In VCT site/transfer in	34	14 (41.2)	0.62 [0.36-1.09]		-	
Type of HIV				0.476	-	
HIV I	162	85 (52.5)	1.00 [reference]		-	
HIV I & II	7	5 (71.4)	1.73 [0.70-4.25]		-	
Unknown	53	29 (54.7)	1.10 [0.72-1.67]		-	
TB status				0.094	-	
Not screened	196	101 (51.5)	0.79 [0.32-1.95]		-	
Screened negative	18	13 (72.2)	1.50 [0.53-4.22]		-	
Screened positive	8	5 (62.5)	1.00 [reference]		-	
Drug allergies				0.640	-	
Yes	9	5 (55.6)	1.00 [reference]		-	
No	213	114 (53.5)	0.81 [0.33-1.98]		-	
HIV disclosure				0.120	-	
Disclosed	96	58 (60.4)	1.00 [reference]		-	
Not disclosed	126	61 (48.4)	0.75 [0.52-1.08]		-	
Sexually active				0.258	-	
Yes	101	49 (48.5)	1.00 [reference]		-	
No	117	68 (58.1)	1.36 [0.94-1.96]		-	
Unknown	4	2 (50.0)	1.01 [0.25-4.17]		-	
Regular condom use				0.189	-	
Yes	24	9 (37.5)	1.00 [reference]		-	
No	177	100 (56.5)	1.71 [0.86-3.38]		-	
Unknown	21	10 (47.6)	1.18 [0.48-2.91]		-	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval

*P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001*

Table 6 continues

Variables	N	Chronic condition n (%)	Unadjusted cox-proportional model URR [95% CI]	P-value	Adjusted cox-proportional model ARR [95% CI]	P-value
WHO clinical stage				0.023*		0.034*
Stage I	47	23 (48.9)	1.00 [reference]		1.00 [reference]	
Stage II	29	13 (44.8)	1.04 [0.52-2.05]		0.66 [0.31-1.43]	
Stage III	44	30 (68.2)	1.85 [1.07-3.19] *		1.34 [0.69-2.64]	
Stage IV	29	20 (69.0)	1.57 [0.86-2.86]		0.95 [0.46-1.96]	
Unknown	73	33 (45.2)	0.87 [0.51-1.49]		0.55 [0.30-0.98] *	
CD4 below 350				0.005**		0.322
<350	134	84 (62.7)	1.00 [reference]		1.00 [reference]	
≥350	42	16 (38.1)	0.48 [0.28-0.83] **		0.68 [0.37-1.26]	
Unknown	46	19 (41.3)	0.56 [0.34-0.92] *		0.69 [0.37-1.27]	
Prescribed drug regime				0.819	-	
1st line 1st choice	143	77 (53.8)	1.00 [reference]		-	
2nd line 2nd choice	79	42 (53.2)	0.96 [0.66-1.39]		-	
Drug combinations				0.049*		0.034*
Other combination	39	18 (46.2)	1.00 [reference]		1.00 [reference]	
TDF+3TC+EFV	89	42 (47.2)	1.29 [0.74-2.25]		2.15 [1.16-3.98] *	
NVP+3TC+D4T	17	10 (58.8)	1.67 [0.77-3.61]		1.85 [0.79-4.32]	
TDF+3TC+NVP	15	12 (80.0)	2.80 [1.34-5.84] **		4.07 [1.64-10.08] **	
AZT+3TC+EFV	17	11 (64.7)	1.93 [0.91-4.08]		3.05 [1.37-6.80] **	
AZT+3TC+NVP	45	26 (57.8)	1.53 [0.84-2.78]		2.12 [1.06-4.22] *	
Adherence to ARV medication				0.018*		0.099
Non-adherent	105	65 (61.9)	1.00 [reference]		1.00 [reference]	
Adherent	117	54 (46.2)	0.65 [0.45-0.93] *		0.70 [0.46-1.07]	
Change in ART medication				0.658		
Yes	71	39 (54.9)	1.00 [reference]		-	
No	151	80 (53.0)	1.09 [0.74-1.60]		-	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

4.8 Association between conditions screened at first ARV dispense and the experience of chronic conditions among study participants

The frequency and percentage distributions of conditions screened at first ARV dispense and their association with the experience of chronic condition(s) during the first three years on ARVs are shown in Table 7. The cox-proportional hazard model was used to estimate both the crude (unadjusted) and adjusted odds of experience of chronic disease condition(s) among patients visiting the ART clinic within the first three years on ARVs.

Chronic conditions among patients who did not have jaundice at first ARV dispense was 53.9% (n=118/219) and 33.33% (n=1/3) among those who had jaundice. The experience of jaundice was not significantly associated with the experience of a chronic disease condition in the first three years on ARV.

Chronic condition(s) among patients in the study was 68.5% (n=37/54) among those who had chills and 48.8% (n=82/168) among patients who did not have chills at first ARV dispense. For those who had chills at first ARV dispense, the unadjusted model showed a 65% higher risk of developing chronic condition(s) during the first three years on ARVs (URR=1.65, 95% CI: 1.21-2.44, p=0.011). However, the adjusted model showed no significance.

Chronic condition(s) among patients who experienced severe weight loss constituted 65.9% (n=56/85) and 46.0% (n=63/137) among those who did not experience severe weight loss at first ARV dispense. The unadjusted model for patients who experienced severe weight loss at first ARV dispense showed a 75% higher risk of developing chronic disease conditions during the first three years on ARVs (URR=1.75, 95% CI: 1.22-2.51, p=0.002). The adjusted

model was not significantly associated with the experience of chronic condition(s) during the first three years on ARVs.

Chronic condition(s) was prevalent among 85.0% (n=17/20) of patients who experienced vomiting at first ARV dispense and 50.5% (n=102/202) among those who did not experience vomiting. The unadjusted model for patients who experienced vomiting showed about three times increased risk of developing chronic condition(s) during the first three years on ARVs (URR=2.55, 95% CI: 1.52-4.27, p<0.001). The adjusted model was not significantly associated with the experience of chronic conditions during the first three years on ARVs.

Prevalence of chronic condition(s) among patients who experienced oral thrush at first ARV dispense was 66.7% (n=16/24) and 52.0% (103/198) among those who did not experience oral thrush. The unadjusted model showed a 79% increased risk of developing chronic disease conditions during the first three years on ARVs (URR=1.79, 95% CI: 1.06-3.04, p=0.031); the adjusted model was, however, not significantly associated with the experience of chronic condition(s) during the first three years on ARVs.

Table 7: Association between conditions screened at first ARV dispense and the experience of chronic conditions among study participants

Variables	N	Chronic condition	Unadjusted cox-proportional model		Adjusted cox-proportional model	
		n (%)	URR [95% CI]	P-value	ARR [95% CI]	P-value
Total	**222**	119 (53.6)				
Jaundice				0.737		
No	219	118 (53.9)	1.00 [reference]		-	
Yes	3	1 (33.3)	0.71 [0.10-5.11]		-	
Chronic cough				0.936	-	
No	167	88 (52.7)	1.00 [reference]		-	
Yes	55	31 (56.4)	1.02 [0.68-1.53]		-	
Difficulty in swallowing				0.999	-	
No	199	107 (53.8)	1.00 [reference]		-	
Yes	23	12 (52.2)	1.00 [0.55-1.82]		-	
Skin rash				0.357	-	
No	168	86 (51.2)	1.00 [reference]		-	
Yes	54	33 (61.1)	1.21 [0.81-1.80]		-	
Chills				0.011*		0.886
No	168	82 (48.8)	1.00 [reference]		1.00 [reference]	
Yes	54	37 (68.5)	1.65 [1.12-2.44] *		0.96 [0.58-1.60]	
Fever				0.075		
No	164	83 (50.6)	1.00 [reference]		-	
Yes	58	36 (62.1)	1.43 [0.97-2.12]		-	
Severe weight loss				0.002**		0.351
No	137	63 (46.0)	1.00 [reference]		1.00 [reference]	
Yes	85	56 (65.9)	1.75 [1.22-2.51] **		1.24 [0.79-1.93]	
Vomiting				*<0.001***		*0.248*
No	202	102 (50.5)	1.00 [reference]		1.00 [reference]	
Yes	20	17 (85.0)	2.55 [1.52-4.27] ***		1.46 [0.77-2.78]	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

Table 7 continues

Variables	N	Chronic condition n (%)	Unadjusted cox-proportional model URR [95% CI]	P-value	Adjusted cox-proportional model ARR [95% CI]	P-value
Sexually transmitted infections				0.354	-	
No	200	105 (52.5)	1.00 [reference]		-	
Yes	22	14 (63.6)	1.30 [0.74-2.28]		-	
Persistent headaches				0.058	-	
No	173	87 (50.3)	1.00 [reference]		-	
Yes	49	32 (65.3)	1.48 [0.99-2.22]		-	
Visual changes				0.710	-	
No	195	103 (52.8)	1.00 [reference]		-	
Yes	27	16 (59.3)	1.11 [0.65-1.87]		-	
Body pains				0.475	-	
No	201	106 (52.7)	1.00 [reference]		-	
Yes	21	13 (61.9)	1.23 [0.69-2.20]		-	
Abnormal menses				0.285	-	
No	199	103 (51.8)	1.00 [reference]		-	
Yes	23	16 (69.6)	1.33 [0.79-2.26]		-	
Oral thrush				0.031*		0.336
No	198	103 (52.0)	1.00 [reference]		1.00 [reference]	
Yes	24	16 (66.7)	1.79 [1.06-3.04] *		1.36 [0.73-2.52]	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

4.9 Factors associated with cardiovascular diseases in the first three years on ARV

The frequency and percentage distribution of factors associated with cardiovascular disease experience during the first three years on ARVs are shown in Table 8. The cox-proportional hazard model was used to estimate both the crude (unadjusted) and adjusted odds of cardiovascular disease experience among patients visiting the ART clinic within the first three years on ARVs.

The experience of cardiovascular disease within the first three years on ARV was 13.33% (n=2/15) among patients who were on TDF+3TC+NVP drug combination, 11.76% (n=2/17) among those given NVP+3TC+D4T, 11.24% (n=10/89) among patients given TDF+3TC+EFV, 11.11% (n=5/45) in respondents given AZT+3TC+NVP, 10.26% (n=4/39) in patients given other combinations and 5.88% (n=1/17) in patients given AZT+3TC+EFV. Both the unadjusted and adjusted cox-proportional models of the drug combinations were not significantly associated with the experience of cardiovascular diseases during the period.

For ARV adherence, chronic conditions were prevalent among 16.24% (n=19/117) of the adherent patients during the first three years on ARV, and 4.76% (n=5/105) were non-adherent to the prescribed drugs. ARV adherence showed a significant association with the experience of cardiovascular diseases during the first three years on ARV using the unadjusted model with about four times the risk recorded among the patients (URR=3.90, 95% CI: 1.45-10.44, p=0.007). The adjusted model also showed about four times the risk of developing cardiovascular disease during the period (ARR=3.86, 95% CI: 1.42-10.51, p=0.008).

Table 8: Factors associated with cardiovascular diseases in the first three years on ARV

		Cardiovascular disease (CVD)				
		CVD (%)	Unadjusted cox-proportional model		Adjusted cox-proportional model	
Variables	**N**	**n (%)**	**URR [95% CI]**	**P-value**	**ARR [95% CI]**	**P-value**
Total	**222**	**24 (10.81)**				
Drug combination				0.976		0.980
Other combinations	39	4 (10.26)	1.00 [reference]		1.00 [reference]	
TDF+3TC+EFV	89	10 (11.24)	1.32 [0.41-4.21]		1.21 [0.37-3.99]	
NVP+3TC+D4T	17	2 (11.76)	1.14 [0.21-6.24]		1.24 [0.23-6.77]	
TDF+3TC+NVP	15	2 (13.33)	1.29 [0.24-7.07]		1.31 [0.22-7.60]	
AZT+3TC+EFV	17	1 (5.88)	0.56 [0.06-5.05]		0.59 [0.07-5.39]	
AZT+3TC+NVP	45	5 (11.11)	1.08 [0.29-4.03]		1.30 [0.35-4.91]	
Adherence to ARV medication				0.007		0.008*
Non-adherent	105	5 (4.76)	1.00 [reference]		1.00 [reference]	
Adherent	117	19 (16.24)	3.90 [1.45-10.44] **		3.86 [1.42-10.51] **	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

4.10 Factors associated with respiratory tract infection in the first three years on ARV

Table 9 shows the frequency and percentage distribution of developing respiratory tract infection (RTI) factors during the first three years on ARVs. The cox-proportional hazard model was used to estimate both the crude (unadjusted) and adjusted odds of experiencing respiratory tract infection among patients visiting the ART clinic within the first three years on ARVs.

The experience of RTI within the first three years on ARV for patients whose CD4 count was below 350 was 22.39% (n=30/134), 14.29% (n=6/42) for those above 350, and 6.52% (n=3/46) for those with count unknown. For patients whose CD4 count was above 350, both the unadjusted and adjusted models showed no significance. Patients whose CD4 values were unknown had a 72% reduced risk of developing RTI during the period for the unadjusted model (URR=0.28, 95% CI=0.09-0.93, p=0.037). However, the adjusted model was not significantly associated with the development of RTI during the first three years on ARV.

The experience of RTI within the first three years on ARV was 35.29% (n=6/17) among patients who were on NVP+3TC+D4T drug combination, 26.67% (n=4/15) among those given TDF+3TC+NVP, 23.53% (n=4/17) among patients given AZT+3TC+EFV, 17.78% (n=8/45) among patients given AZT+3TC+NVP, 15.73% (n=14/89) among patients given TDF+3TC+EFV and 7.69% (n=3/39) among patients given other combinations. All the combinations but NVP+3TC+D4T were not significantly associated with developing RTI during the first three years on ARV. For NVP+3TC+D4T, the unadjusted model showed six

times increased risk of experiencing RTI (URR=6.16, 95% CI: 1.54-24.67, p<0.05). The adjusted model showed that the risk of developing RTI within the first three years on ARV was about seven times higher among the patients (ARR=6.66, 95% CI: 1.51-29.25, p<0.05).

With ARV adherence, patients who were non-adherent during the first three years on ARV were 25.71% (n=27/105) and 10.26% (n=12/117) among adherent patients to the prescribed drugs. ARV adherence showed a significant association with the experience of RTI during the first three years on ARV using both the unadjusted and adjusted models. A 62% reduced risk of developing RTI was recorded among the patients (URR=0.38, 95% CI: 0.19-0.74, p=0.005). For the adjusted model, a 57% reduced risk of RTI was recorded among patients (ARR=0.43, 95% CI: 0.21-0.90, p=0.025).

Patients who had a fever at first ARV dispense and developed RTI was 29.31% (n=17/58) and 13.41% (n=22/64) for those who did not have a fever but developed RTI during the three years on ARV. For those who had a fever at first ARV dispense, the unadjusted model showed two times increased risk of developing RTI during the period (URR=2.43, 95% CI: 1.29-4.58, p=0.006). The adjusted model showed no significance of developing RTI during the first three years on ARV for patients who had a fever at first ARV dispense.

Patients who experienced severe weight loss at first ARV dispense and developed RTI were 24.71% (n=21/85) and 13.14% (n=18/137) for those who did not experience weight loss at first ARV dispense but developed RTI. The unadjusted model for patients who experienced severe weight loss at first ARV dispense had two times increased risk of developing RTI during the first three years (URR=2.05, 95% CI: 1.09-3.85, p=0.025). The adjusted model was, however, not significantly associated with the development of RTI.

Patients who had sexually transmitted infection (STI) and developed RTI were 31.82% (n=7/22) and 16.00% (n=32/200) for patients who were not diagnosed with STI at first ARV dispense but developed RTI during the first three years on ARV. The unadjusted model for patients with STI at first ARV dispense had two times increased risk of developing RTI during the first three years (URR=2.29, 95% CI: 1.01-5.18, p=0.048). However, the adjusted model was not significantly associated with experiencing RTI during the period.

Patients who experienced visual changes at first ARV dispense and developed RTI during the first three years on ARV were 33.33% (n=9/27), and 15.38% (n=30/195) were not diagnosed with visual changes at first ARV dispense but developed RTI during the first three years on ARV. The unadjusted model for patients who experienced visual changes at first ARV dispense had two times increased risk of developing RTI during the first three years (URR=2.35, 95% CI: 1.11-4.95, p=0.025). The adjusted model showed three times the increased risk of developing RTI among patients who experienced visual changes during the period.

Table 9: Factors associated with respiratory tract infection in the first three years on ARV

		Respiratory tract infections (RTI)				
		RTI	*Unadjusted cox-proportional model*		*Adjusted cox-proportional model*	
Variables	**N**	**n (%)**	**URR [95% CI]**	**P-value**	**ARR [95% CI]**	**P-value**
Total	**222**	**39 (17.57)**				
CD4 below 350				0.078		0.383
Yes	134	30 (22.39)	1.00 [reference]		1.00 [reference]	
No	42	6 (14.29)	0.60 [0.25-1.45]		0.99 [0.38-2.56]	
Unknown	46	3 (6.52)	0.28 [0.09-0.93] *		0.41 [0.11-1.47]	
Drug combinations				0.152		0.155
Other combination	39	3 (7.69)	1.00 [reference]		1.00 [reference]	
TDF+3TC+EFV	89	14 (15.73)	2.32 [0.67-8.07]		3.51 [0.96-12.79]	
NVP+3TC+D4T	17	6 (35.29)	6.16 [1.54-24.67] *		6.66 [1.51-29.25] *	
TDF+3TC+NVP	15	4 (26.67)	3.72 [0.83-16.62]		4.58 [0.96-21.93]	
AZT+3TC+EFV	17	4 (23.53)	3.64 [0.82-16.28]		4.55 [0.97-21.44]	
AZT+3TC+NVP	45	8 (17.78)	2.55 [0.68-9.60]		2.22 [0.58-8.57]	
Adherence to ARV medication				0.005		0.025*
Non-adherent	105	27 (25.71)	1.00 [reference]		1.00 [reference]	
Adherent	117	12 (10.26)	0.38 [0.19-0.74] **		0.43 [0.21-0.90] *	
Fever				0.006		0.351
No	164	22 (13.41)	1.00 [reference]		1.00 [reference]	
Yes	58	17 (29.31)	2.43 [1.29-4.58] **		1.45 [0.66-3.19]	
Severe weight loss				0.025		0.810
No	137	18 (13.14)	1.00 [reference]		1.00 [reference]	
Yes	85	21 (24.71)	2.05 [1.09-3.85] *		1.10 [0.50-2.44]	
Sexually transmitted infections				*0.048*		*0.672*
No	200	32 (16.00)	1.00 [reference]		1.00 [reference]	
Yes	22	7 (31.82)	2.29 [1.01-5.18] *		1.23 [0.48-3.17]	
Visual changes				0.025		0.033*
No	195	30 (15.38)	1.00 [reference]		1.00 [reference]	
Yes	27	9 (33.33)	2.35 [1.11-4.95] *		2.64 [1.08-6.45] *	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

4.11 Factors associated with peripheral neuropathy in the first three years on ARV

Table 10 shows the frequency and percentage distribution of the factors related to developing peripheral neuropathy during the first three years on ARVs. The cox-proportional hazard model was used to estimate both the unadjusted and adjusted odds of experiencing peripheral neuropathy among patients visiting the ART clinic within the first three years on ARVs.

For WHO clinical stages, the experience of peripheral neuropathy within the first three years on ARV for patients with stage II was 20.69% (n=6/29), 15.91% (n=7/44) for those with stage III, 13.79% (n=4/29) for those with stage IV, 5.48% (n=4/73) for stage those whose clinical stage was unknown and 2.13% (n=1/47) for those with stage I. Both the unadjusted and adjusted models showed significance for patients diagnosed with WHO stage II HIV/AIDS. There were about 11 times increased risk of developing peripheral neuropathy for the unadjusted model (URR=10.63, 95% CI=1.28-88.35, $p<0.05$) and 13 times increase in risk for the adjusted model (URR=13.36, 95% CI=1.54-115.63, $p<0.05$). Patients with WHO stage III diagnosis had eight times increased risk of developing peripheral neuropathy during the period for the unadjusted model (URR=8.33, 95% CI=1.02-67.71, $p<0.05$). The adjusted model showed about 12 times increased risk of developing peripheral neuropathy during the first three years on ARV (ARR=11.71, 95% CI=1.41-97.26, $p<0.05$).

The experience of peripheral neuropathy within the first three years on ARV was 23.53% (n=4/17) among patients who were on NVP+3TC+D4T drug combination, 13.33% (n=2/15 and n=6/45) among those given TDF+3TC+NVP and AZT+3TC+NVP respectively, 7.87% (n=7/89) among patients given TDF+3TC+EFV, 7.69% (n=3/39) in respondents given other

drug combinations, and 0.00% (n=0/17) in patients given AZT+3TC+EFV. All the drug combinations were not significantly associated with developing peripheral neuropathy during the first three years on ARV for both models.

With ARV adherence, patients who were non-adherent during the first three years on ARV were 14.29% (n=15/105) and 5.98% (n=7/117) among adherent patients to prescribed drugs. ARV adherence showed no significant association with peripheral neuropathy experience during the first three years on ARV using both the unadjusted and adjusted models.

Table 10: Factors associated with peripheral neuropathy in the first three years on ARV

		Peripheral Neuropathy (PN)				
		PN	Unadjusted cox-proportional model		Adjusted cox-proportional model	
Variables	N	n (%)	URR [95% CI]	P-value	ARR [95% CI]	P-value
Total	222	22 (9.91)				
WHO clinical stage				0.074		0.055
Stage I	47	1 (2.13)	1.00 [reference]		1.00 [reference]	
Stage II	29	6 (20.69)	10.63 [1.28-88.35] *		13.36 [1.54-115.63] *	
Stage III	44	7 (15.91)	8.33 [1.02-67.71] *		11.71 [1.41-97.26] *	
Stage IV	29	4 (13.79)	6.32 [0.71-56.58]		6.89 [0.76-62.70]	
Unknown	73	4 (5.48)	2.67 [0.30-23.91]		3.43 [0.38-31.08]	
Drug combinations				0.444		0.449
Other combination	39	3 (7.69)	1.00 [reference]		1.00 [reference]	
TDF+3TC+EFV	89	7 (7.87)	1.15 [0.30-4.46]		1.41 [0.35-5.69]	
NVP+3TC+D4T	17	4 (23.53)	3.35 [0.75-14.99]		3.40 [0.72-16.01]	
TDF+3TC+NVP	15	2 (13.33)	1.80 [0.30-10.77]		3.23 [0.50-20.76]	
AZT+3TC+EFV	17	0 (0.00)	(empty)	.	(empty)	.
AZT+3TC+NVP	45	6 (13.33)	1.81 [0.45-7.24]		2.18 [0.53-8.89]	0.278
Adherence to ARV medication				0.058		0.097
Non-adherent	105	15 (14.29)	1.00 [reference]		1.00 [reference]	
Adherent	117	7 (5.98)	0.42 [0.17-1.03]		0.46 [0.18-1.15]	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

4.12 Factors associated with hypertension in the first three years on ARV

The frequency and percentage distribution of the factors related to hypertension experience during the first three years on ARVs are shown in Table 11. The cox-proportional hazard model was used to estimate both the crude (unadjusted) and adjusted odds of hypertension experience among patients visiting the ART clinic within the first three years on ARVs.

The experience of chronic disease conditions within the first three years on ARV was 25.00% (n=8/32) among patients >49 years, 16.46% (n=13/79) among patients aged 40-49, 6.58% (n=5/76) among patient aged 30-39, and 2.86% (n=1/35) among patient <29 years. From the unadjusted model, patients aged >49 years had nine times increased risk of developing hypertension (URR=9.37, 95% CI: 1.17-74.99, p<0.05). For the adjusted logistic regression model, patients aged >49 had ten times increased risk of having hypertension within the first three years on ARVs (ARR=10.03, 95% CI: 1.22-82.37, p<0.05).

The experience of hypertension within the first three years on ART was 20.00% (n=3/15) among patients who were on TDF+3TC+NVP drug combination, 17.65% (n=3/17) among those given AZT+3TC+EFV, 12.36% (n=11/89) among patients given TDF+3TC+EFV, 11.11% (n=5/45) in respondents given AZT+3TC+NVP, 10.6% (n=4/39) in patients given other combinations and 5.88% (n=1/17) in patients given NVP+3TC+D4T. All the combinations were not significantly associated with developing hypertension during the first three years on ARV for both models.

With ARV adherence, the experience of hypertension within the first three years on ART among patients' adherent during the first three years on ART was 13.68% (n=16/117) and 10.48% (n=11/105) among patients who were non-adherent to the prescribed drugs. ARV

adherence showed no significant association with experience hypertension during the first three years on ARV using both the unadjusted and adjusted models.

Table 11: Factors associated with hypertension in the first three years on ARV

		Hypertension				
		Hypertension	Unadjusted cox-proportional model		Adjusted cox-proportional model	
Variables	**N**	**n (%)**	**URR [95% CI]**	**P-value**	**ARR [95% CI]**	**P-value**
Total	222	27 (12.16)				
Age group				0.022*		0.026*
<29	35	1 (2.86)	1.00 [reference]		1.00 [reference]	
30-39	76	5 (6.58)	2.20 [0.26-18.81]		2.40 [0.27-20.99]	
40-49	79	13 (16.46)	6.36 [0.83-48.61]		7.10 [0.92-55.01]	
>49	32	8 (25.00)	9.37 [1.17-74.99] *		10.03 [1.22-82.37] *	
Drug combinations				0.799		0.661
Other combination	39	4 (10.26)	1.00 [reference]		1.00 [reference]	
TDF+3TC+EFV	89	11 (12.36)	1.43 [0.45-4.49]		1.68 [0.53-5.37]	
NVP+3TC+D4T	17	1 (5.88)	0.55 [0.06-4.96]		0.72 [0.08-6.63]	
TDF+3TC+NVP	15	3 (20.00)	2.12 [0.47-9.47]		3.39 [0.74-15.62]	
AZT+3TC+EFV	17	3 (17.65)	1.77 [0.40-7.92]		1.62 [0.36-7.34]	
AZT+3TC+NVP	45	5 (11.11)	1.03 [0.28-3.85]		1.40 [0.36-5.37]	
Adherence to ARV medication				0.299		0.552
Non-adherent	105	11 (10.48)	1.00 [reference]		1.00 [reference]	
Adherent	*117*	*16 (13.68)*	*1.50 [0.70-3.24]*		*1.27 [0.57-2.83]*	

URR: unadjusted relative risk. ARR: adjusted relative risk. CI: confidence interval
P-value notation: *: p<0.05. **: p<0.01. ***: p<0.001

CHAPTER FIVE

5.0 DISCUSSIONS

This study sought to investigate the chronic conditions among HIV/AIDS infected patients receiving antiretroviral therapy at the Pantang and relate the chronic disease conditions to socio-demographic factors and the line of antiretroviral drug they use. Records of patients who had been on antiretroviral therapy for a mean duration of 36 months (3 years) were reviewed.

More than half (53.6%) of patients on ARVs developed chronic disease conditions from the study within the first three years. Some of the chronic conditions developed were RTI (39, 17.6%), anaemia (27, 12.2%), hypertension (27, 12.2%), CVD (24, 10.8%), and peripheral neuropathy (22, 9.9%). Patients in older age groups who were cohabiting and had no level of education were significantly associated with experiencing chronic conditions. Also, before administering ARVs, patients who experienced chills, severe weight loss, vomiting and oral thrush had an increased risk of experiencing chronic disease conditions. Regarding the clinical characteristics of patients, WHO clinical stage, CD4 count, drug combination and adherence to ARV were positively associated with developing chronic conditions within the first three years on ARVs.

Regarding the various chronic conditions developed, patients who were adherent to ARVs had an increased risk of developing cardiovascular disease. Also, patients given NVP+3TC+D4T drug combinations and experienced visual change before ARV administration increased the risk of developing RTI. Again, patients who were adherent to ARV medication had a reduced risk of developing RTI. WHO clinical stages II and III were

positively associated with developing peripheral neuropathy. Patients in older age groups had an increased risk of developing hypertension within the first three years on ARVs.

5.1 Socio-demographic characteristics of patients

The study results clearly show that age, marital status, and educational level were significantly associated with chronic disease conditions among patients during the first three years on ARV for both models. The risk of developing at least one chronic condition was higher among older age groups. The experience of chronic conditions was lower among those who were married at baseline compared to those who were not married. Again, the risk of developing a chronic condition was higher among those without formal education than those with a tertiary education level.

5.1.1 Age

The mean age of patients in the study was 39.01± 9.64. This is consistent with findings from an observational cohort study by Hyle et al. (2019) and Mayanja et al. (2017), where it was reported that the average age for patients who developed CVD while on ART was 38 years. The mean age for a prospective clinical cohort study in Uganda on the complications of long-term ART was 35 years and above. Both results fall within the age range recorded for this present study. Patients infected by HIV have early onset of chronic condition(s) compared to those not infected. A comparison of HIV infected individuals to those not infected in the same age category reveals that HIV infected patients on long term ARVs commonly experience hypertension, bone diseases, neurological diseases as well as gastrointestinal infections (Deeks et al., 2014; Deeks & Phillips, 2009; Worm et al., 2010; Yang et al., 2019). PLWHA have been reported by Alonso et al. (2019) to have an increased

CVD risk compared to those uninfected in the same age group. For HIV-infected adults, their incidence rate of experiencing CVD was 10.8 compared to 5.9 for those uninfected

From the current study, patients in the older age group (40 to >49) were associated with developing at least one chronic condition during the first three years on ARVs. This is similar to a study done on HIV infected veterans, where sex and age, when matched with uninfected veterans, found that those infected had an increased likelihood of developing comorbid conditions (Deeks & Phillips, 2009). Generally, this could be because people are more prone to developing health conditions as they advance in age. This can also be attributed to ARV toxicity (Deeks et al., 2014).

It is no secret that as PLWHA advance in age, their care will become more complicated. As the years of survival of PLWHA increases, more patients will move to age groups with higher incidence and prevalence of some health conditions; thus, specialists (gastroenterologists, cardiologists, and oncologists, among others) would have to be present to help manage these patients. As ART coverage is increasing, more people will have access to treatment options. They then will live longer with this infection than the short life lived in the pre-ART era. Due to this paradigm shift, PLWHA are faced with a greater risk of developing chronic disease complications/conditions. It may be unrealistic to expect that HIV patients on ARVs have a 'normal' lifespan that is devoid of other chronic conditions as they deal with age-related complications.

5.1.2 Sex

From the study, the number of people who developed chronic conditions while on ART was higher in females (57.2%) than in males (46.8%). This was significant for the unadjusted model. Masenga et al. (2019) report the opposite in a systematic review among PLWHA in

Africa, where they reported that the prevalence of hypertension was higher in men than in women. The higher number of females who developed chronic conditions from the current study could be attributed to the fact that females accessing ART at the hospital were far more than males. Again, studies show that women visit health centres more often than men; thus, women with HIV are easily detected. This could be why higher numbers were recorded for females who developed chronic conditions while on ART at the hospital during the study period. A study by Karamchand et al. (2016) also stated that males on NNRTIs have an increased risk of developing diabetes. However, a systematic review study by Widyadharma et al. (2019) reported that females had about ten times increased risk of developing chronic conditions in less than three years on ART compared to men.

5.2 Clinical characteristics of patients

5.2.1 WHO Clinical stage

Compared to those with WHO clinical stage I, the risk of developing a chronic condition was higher among those with stage III HIV before ARV initiation. At HIV stage III, the person's immune system is severely damaged and cannot fight chronic infections (National Centre for AIDS & STD Control (NCASC), 2009; Rastogi et al., 2011). Again, most people do not know their HIV status until they get to stage III (advanced stage), where adverse symptoms persist. At this stage, the immune system is weakened, opportunistic infections are evident, and the individual becomes more prone to other chronic conditions. This is consistent with findings from Rastogi et al. (2011), where it was reported that stage III is characterized by severe weight loss, chronic diarrhoea, fever, oral candidiasis, and CD4+ cell count <200 cells/mm^3. People with HIV Stage I infection are generally asymptomatic.

Stage II is characterized by herpes zoster, recurrent respiratory tract infection, and papular pruritic eruptions, to mention a few (National Centre for AIDS & STD Control (NCASC), 2009; Rastogi et al., 2011; World Health Organisation (WHO), 2015). With stages III and IV, the symptoms are adverse, and people in these stages have moved from HIV to AIDS; thus, they face several chronic disease conditions (Rastogi et al., 2011).

5.2.2 Adherence to medication

The patient's adherence to ART from the study was associated with a reduced risk of developing a chronic condition during the first three years on ARVs from the unadjusted model. A 45% reduced risk was recorded. According to Siedner (2016), from the SMART study in which approximately 5000 HIV patients were randomized, patients who were non-adherent to ART had about 70% increased risk of CVD complications. Thus CVD events had a probability of occurring five times more often than other opportunistic infections.

The SMART study also reported that HIV patients who were non-adherent to ARVs had a significantly higher risk of developing kidney failure than those who were adherent (Deeks & Phillips (2009). The use of ARVs suppresses viral load in HIV patients to undetectable levels. For this to be achieved, patients need about 95% adherence level to ART (Iacob et al., 2017). The factors that influence medication adherence are the type of ARV drug (their side effects), the devotion of the doctor (counselling and confidentiality), and the patient (accepting to take the medication). Iacob et al. (2017) reported that non-adherence in about 5% of HIV infected people is due to nightmares and insomnia they experience while on NNRTIs and may lead to chronic conditions.

The World Health Organisation (WHO) (2015) adduced that about 25% of HIV-infected patients discontinue their ART regimen due to non-compliance, treatment failure, or toxic effects of the drug, typically within the first eight months of the start of ART.

Again, low-level adherence is most common in patients with other chronic diseases because they have to take multiple drugs and sometimes 'trade-off.'

5.2.3 CD4 + T-cells

The mean CD4+ T-cells screened at the first ARV dispense was 244.56 ± 197.61, with about 61% of the patients having CD4 count below 350cells/mm^3. CD4 cells below 350 were significantly associated (about 52% increased risk) with the experience of a chronic condition(s) during the first three years on ARVs for the unadjusted model. HIV patients with a CD4 count below 350 at first ARV dispense were at a higher risk of having a chronic condition within the first three years on ARVs than those with CD4 above 350.

From their study, Deeks & Phillips (2009) stated that HIV-infected patients had an increased risk of developing several 'non-AIDS' complications. This was higher in patients whose CD4+ T-cells were below 350; this is similar to the results from the current study. Also, from the FIRST study (as cited in Deeks & Phillips, 2009), among HIV patients on ARVs, it was reported that those whose CD4 T-cells fell below 350 were associated with a higher risk of dying from CVD renal disorder, liver diseases, and cancer. A reduction in CD4 count increases the risk of CVD and MI (Feinstein et al., 2019). Again, from a study by Fahme, Bloomfield, & Peck (2018), low CD4+ cell count is associated with hypertension after ART initiation due to immune suppression.

5.3 Conditions screened at first ARV dispense

The risk of developing at least one chronic condition was higher among patients with chills, severe weight loss, and vomiting at first ARV dispense from the unadjusted model. These symptoms were common and were recorded in more than 10% of HIV patients on ARVs within the first three years.

The Centres for Disease Control describes weight loss as an AIDS-defining condition. Some early symptoms of HIV infection may be associated with fever, chills, headaches, weight loss, and diarrhoea (Centre for Disease Control (CDC), 2018; Max & Sherer, 2000; Weinberg & Kovarik, 2010). The Centre for Disease Control (CDC) (2018) reported that HIV infections tend to compromise with the immune system; thus, opportunistic infections results, which causes many symptoms. Once these conditions are present, it means the immune system has been compromised; thus, the body is likely to be 'attacked' by other chronic conditions, this was consistent with findings from this study where patients before the start of ART experienced several symptoms. Mangili, Murman, Zampini, & Wanke (2006) indicated that for a 5% weight loss in HIV patients, there is a positive association with an increased risk of disease progression.

Again, low CD4+ cell counts may account for severe weight loss. In a large cohort study by Mangili et al. (2006), it was reported that both HIV infected patients on ART and those ART-naïve all experienced weight loss and wasting.

5.4 The prevalence of chronic conditions among HIV patients receiving ART at the Pantang hospital

The study showed that the proportion of patients on ARVs at the Pantang ART clinic, who developed at least one chronic condition, was 53.6% (119/222). The proportion of HIV patients who have been on ART for the first three years who experienced RTIs was 17.5% (39/222), 12.16% (27/222) for those who developed hypertension, 10.81% (24/222) for patients who developed cardiovascular disease, and 9.9% (22/222) for patients who experienced peripheral neuropathy. A systematic and thematic review paper by Masenga et al. (2019) estimated that the prevalence of hypertension in PLWHA and ART in an African study was 2-50.2% compared to 13.7-44% uninfected people. Results from this current study fall within this range. Also, in a prospective cross-sectional survey by Jericó et al. (2005), they reported a 13.8% prevalence of developing hypertension while on ARV. This is slightly higher than what was recorded in the current study. Again, from a cohort study done in Uganda, the prevalence of hypertension was among HIV infected patients on ART was 14.50% (Mayanja et al., 2017), which is about 2.5% higher than what was recorded in the present study.

In a study by Schütz & Robinson-papp (2013), the prevalence of peripheral neuropathy was estimated at 21%. Another survey by So-Armah & Freiberg (2019) also reported the prevalence of peripheral neuropathy among PLWHA on ART to be 27%. Both values are higher than the 9.9% prevalence recorded in the current study.

According to Ray et al. (2008), the prevalence of respiratory tract infections among HIV-infected women with an ARV was 24.3%. This value is about 6.8% higher compared to the prevalence recorded in this current study.

5.5 Drug combinations associated with the experience of chronic conditions

It is an undeniable fact that all drugs have side effects. The risk of experiencing chronic disease in the first three years was two times higher among those on TDF+3TC+EFV, four times higher for those on TDF+3TC+NVP, three times higher for those on AZT+3TC+EFV, and two times higher for those on AZT+3TC+NVP. The adverse effect from ARVs may be attributable to active compounds present in the drugs, the patient's genetic factors, and lifestyle factors (Smith et al., 2015).

A study by May et al. (2014) indicated that for 444 infected adults who did not have hypertension at baseline, antiretroviral therapy drug combination with 3TC and TDF as compared to 3TC and AZT was associated with two times increased risk of developing hypertension (OR=2.3; 95% CI=1.0-5.2, p=0.046). Again, AZT therapy was reported to be positively associated with the experience of myopathy. In a sub-analysis of a prospective cohort study of 527 HIV patients, stavudine (D4T) was associated with a 54% increased odds with hypertension (OR=1.54; 95% CI=1.04-2.30) (May et al., 2014).

In another study done by Golrokhy in 2017 (as cited by Jugulete et al., 2017), it was reported that about 94% of HIV patients on ART experience chronic conditions. This affects adherence to drugs, as some may even stop taking medications. From the current study, all the drugs associated with developing chronic conditions were NNRTIs and NRTIs. For NRTIs, patients who have been on these groups of drugs for at least two years tend to experience lipodystrophy (De Wit et al., 2011; Langs-Barlow et al., 2013; National Centre for AIDS & STD Control (NCASC), 2009; White, 2001). Again, the development of CVD

events, peripheral neuropathy, myopathy, hypersensitive reactions, renal toxicity, and osteoporosis have been linked to NRTIs (Iacob et al., 2017). Diabetes, stroke, CVD, and hypertension have been reported by Yang et al. (2019) to be found in patients on NNRTIs. These chronic disease conditions are evident after the long-term use of these drugs.

In a cross-sectional study carried out by Mauss, Berger, & Schmutz (2005), tenofovir (TDF), an NNRTI, was associated with renal toxicity. It reduces the estimated glomerular filtrate (eGFR), thereby causing acute renal failure and dysfunction of the proximal kidney (Zimmermann et al., 2016).

Tenofovir (TDF) has also been reported by Iacob et al. (2017) to be associated with neurological effects. Peripheral neuropathy has been reported to have a high incidence and prevalence since the advent of ART (Widyadharma et al., 2019). Stavudine (D4T) has also been reported to have a significant association with the onset of peripheral neuropathy (damage of nerves in hands and feet) and lipoatrophy (Aberg, 2009). A study by Gunasekaran & Sivakumar (2018) estimated that about 47.1% of all HIV patients on D4T developed peripheral neuropathy.

Serrano-villar et al. (2016), in a systematic review, reported that ART use, low CD4+ cell counts, and high viral load might contribute to the experience of stroke in HIV-infected patients. Again, from this same study, it was mentioned that the incidence of lung cancer is increasing at an exponential rate in the post-ART era.

Nevirapine (NVP) is associated with hypersensitivity reactions such as rash, Steven-Johnson syndrome, hepatotoxicity, drug-induced hepatitis, pancreatitis, and lactic acidosis (Jantarapakde et al., 2014). The WHO (2010) reported a significant association between

Nevirapine's use and the experience of hepatotoxicity in pregnant women whose CD4 count is between 250-350 cells/mm^3.

Lamivudine (3TC) has been found to cause lactic acidosis. It acts to inhibit DNA polymerase gamma, thereby interfering with mitochondrial DNA replication (Anderson & Rower, 2010). This problem is one of non-specificity, thus reducing mitochondrial DNA and lowering protein and RNA output, which causes a dysfunction of the mitochondria in response to anaerobic respiration, hence causing oxidative damage and lactic acid production. Lamivudine is also associated positively with the experience of hepatosteatosis. Even though this disease is rare, it is significantly life-threatening. Peripheral neuropathy, anaemia, and neutropenia have also been associated with 3TC (Campbell et al., 2005).

D4T has been found to elevate the levels of lactate and increase mitochondrial toxicity. D4T has also been reported to raise blood cholesterol triglyceride as well as lactic acidosis. The muscles tend to lose their control. Again, D4T tends to cause fat wasting.

5.6 Chronic conditions developed among patients during the first three years on antiretroviral drugs

5.6.1 Cardiovascular disease

For cardiovascular disease, the risk of developing CVD was higher among patients who were adherent to ARVs. HIV-infected adults tend to have an increased risk of CVD and other comorbidities (Alonso et al., 2019; Masenga et al., 2019). Again, a causal association between ARV treatment and the early advent of heart disease has been established despite controlling CVD's traditional risk factors and age (Deeks et al., 2014; Deeks & Phillips,

2009), similar to findings in the current study. The more patients adhere to ARV drugs, the more they are likely to develop cardiovascular disease.

Certain ARVs have been found to affect the onset of CVD directly. Recent data from Siedner (2016) suggest that as infected individuals experience a decrease in AIDS-related mortality, CVDs have become the most common cause of death after cancer with those whose viral load is undetected while on ARV. Also, in a prospective cross-sectional study among PLWHA on ART in South Africa, the study reported that more than 50% of the study participants on ART had one or more *CVD* risk factor(s) (*Hyle et al., 2019*).

5.6.2 Respiratory Tract Infection

Patients on nevaripine+lamivudine+stavudine had about seven times increased risk of developing RTI. Adherence to ARV, however, was associated with a reduced risk of developing RTI. At the first ARV dispense, patients who screened positive for visual changes increased the risk of developing respiratory tract infection during the first three years on ARV. Patients whose CD4 count was unknown, had a fever, severe weight loss, sexually transmitted infections were associated with the experience of RTI from the study in the unadjusted model. A survey by Weinfurt, Willke, Glick, & Freimuth (2000) showed similar results. Their study indicated that as CD4 count falls below 500 cells/mm^3, morbidity and mortality among HIV-infected individuals increases. Again, as CD4 levels reduce to 200 cells/mm^3, lower respiratory tract infection risk remains high (Fitzpatrick, Kunisaki, & Morris, 2019). This can be prevented by raising the CD4 count of patients by encouraging adherence to ART.

According to Lamas, Coelho, Grinsztejn, & Veloso (2018), an increase in CD4 count due to antiretroviral drugs reduces the risk of developing chronic conditions by 14% (AHR=0.86, 95% CI=0.82-0.91). Other studies also indicated that pulmonary infection is significantly associated with health burden among PLWHA and is recognized as one reason for hospitalization (Fitzpatrick et al., 2019; Hunt, 2012). This study also states that about 65% of patients infected with HIV present with pulmonary infection as one of the first clinical manifestations, and over 80% develop the pulmonary disease.

5.6.3 Peripheral Neuropathy

The proportion of patients who developed peripheral neuropathy was 9.91%. There was an increased risk for patients at WHO clinical stages II and III compared to those at the other stages for patients who developed peripheral neuropathy during the first three years on ARV. Schütz & Robinson-Papp (2013) reported that one of the most frequent neurological complications among PLWHA is distal symmetry polyneuropathy, which affects about 50% of all HIV infected population. This prevalence is extremely higher than that recorded in the present study. Schütz & Robinson-papp (2013) again estimate that the prevalence of peripheral neuropathy among patients on ART is about 21%, affecting 12-25 per person-years. Again, this prevalence was higher than what was reported in this study.

Tumusiime et al. (2014) reported that low CD4 count does not have any association with experiencing peripheral neuropathy; this is similar to results from this study where CD4 count was not associated with the onset of peripheral neuropathy. This, however, contrasts with a study done by Max & Sherer (2000), where they reported that low CD4+ T-cells <500cells/mm^3 is associated with an increased risk of developing peripheral neuropathy. Patients on long-term HIV combination treatment (who are adherent) and advanced stages

of HIV have been found to have an association with progressive neurological diseases (Saylor et al., 2017; Schifitto et al., 2012; Tumusiime et al., 2014). These results are consistent with findings from the present study.

Some NRTIs (especially D4T) has been found to have a more significant association with the experience of peripheral neuropathy in low resource countries. Age was also a major contributing factor to peripheral neuropathy experience for people on ART (Schütz & Robinson-papp, 2013).

5.6.4 Hypertension

From this study, the prevalence of those who developed chronic conditions while on ART for the first three years was 12.16%. This prevalence is low compared to a study by Amusa et al. (2016), where the prevalence of hypertension in a cross-sectional analytical study was 46%. They concluded that using ART was associated with a much higher prevalence of experiencing hypertension.

From the current study, patients who were above 49 years at baseline had nine times increased risk of developing hypertension during the first three years on ARV. According to emerging data, pulmonary artery disease is common in HIV-infected individuals compared to uninfected people in the same age range (Deeks & Phillips, 2009). These findings are in agreement with what was found in this present study.

Adults who have HIV and on ART have been reported by Fahme, Bloomfield, & Peck (2018) to have a higher hypertension prevalence than adults in the same age group who are uninfected. This is consistent with the findings of this study. Hyle et al. (2019) also assert

that there was a 4% increase in relative risk of developing hypertension for every increase in age.

Again, in a meta-analysis done by Fiseha, Belete, Dereje, & Dires (2019), it was reported that globally, about 35% of all HIV-infected adults on ART have hypertension compared to 30% of all HIV uninfected adults. The study also asserted that 50% of all HIV infected people who are more than 50 years have hypertension. The same results were reported in the current study. In a prospective cohort study by Fahme et al. (2018), they reported that more than 80,000 American veterans who have HIV and were followed for about six years found that these patients were two times more likely to develop myocardial infarction while on ART compared to the average population with hypertension.

From several published studies on hypertension in HIV-infected adults on ART, age was significantly associated with developing hypertension; this is consistent with findings from this study. A prospective cohort study by Fahme et al. (2018) found that out of 17,179 HIV infected people followed in 21 countries in Europe, the USA, and Australia, 84% develop hypertension while on ART. A similar study by May et al. (2014) in the US and Spain reported similar results, where among 444 and 95 HIV-infected adults on ART, respectively, 100% developed hypertension in both studies.

There is a need to assess patients before dispensing ARVs. This must be followed by recurrent monitoring during treatment.

CHAPTER SIX

6.0 CONCLUSION, RECOMMENDATIONS, AND LIMITATIONS

6.1 Conclusion

This study has clearly shown that more than half (53.6%) of HIV patients on ART at the Pantang hospital developed chronic disease conditions during the first three years. Baseline sociodemographic factors such as age, sex, marital status, and education were associated with experiencing at least one chronic condition while on ART. Clinical characteristics, which included the WHO clinical stages, medication adherence, drug combinations given, and the CD4 counts of the patients studied, confirmed their association to the onset of chronic conditions. Before the first ARV administration, symptoms screened, such as severe weight loss, fever, cough, chills, headache, and diarrhoea, were also associated with developing chronic conditions. Out of the 64.41% of patients that were on the first line, first-choice drugs, 40.09% were given tenofovir, lamivudine, and efavirenz combination. Tenofovir, lamivudine, and nevirapine were the drug combinations with the highest association (80%) of experiencing chronic conditions.

The study has provided vital data on the association between the various antiretroviral drugs and experiencing chronic disease conditions. This will help in HIV treatment policies and clinical guidelines.

The study's findings further highlight the essence of aggressively managing HIV/AIDS and chronic disease complications associated with ART. The NACP can address this by ensuring that ARVs available to patients have no association with the onset of chronic disease

complications. Again, clinicians must ensure that drugs administered to patients do not tend to cause other chronic disease complications in HIV-infected patients.

6.2 Recommendations

Several recommendations can be made based on this study. They include:

- Patients' symptoms before administering ARV must be well considered before dispensing ARV drugs. This will inform the HIV stage of patients and the presence of other comorbidities; hence the most appropriate regimen can be administered.
- The National AIDS Control Program (NACP) and its partners must ensure that ART administered to patients does not positively associate with the onset of chronic conditions.
- Regarding the high proportion of patients who developed chronic disease conditions during their first three years on ART, further studies must be carried out to find the active ingredients in ARVs that trigger the onset of chronic conditions and to investigate effective alternatives.
- Clinicians should thoroughly consider likely adverse effects, prior history of intolerance to drugs, comorbidities of patients, and other related medications before administering ARVs.

6.3 LIMITATIONS

- The follow-up interval was not consistent for all patients, so assessing the chronic disease conditions could not be done for patients within longer follow-up intervals.

- Due to missing data from medical records, a 20% upward adjustment was used; thus, more data collection had to be done as records with missingness were omitted.
- Some patients did not regularly visit the hospital; therefore, dates for visits were not compatible with their scheduled visit date. This could account for some chronic disease conditions recorded as patients may only visit the hospital when they feel unwell.

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APPENDIX

Appendix I: ETHICAL CLEARANCE

The ethical clearance certificate received from the Ghana health service ethics review committee is found on the Page below. The study received its ethical approval in June 2020.

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

In case of reply the number and date of this Letter should be quoted

Research & Development Division
Ghana Health Service
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MyRef: GHS/RDD/ERC/Admin/App/20/192
Your Ref. No.

18th June, 2020

Martha Kotey
University of Ghana
School of Public Health
Legon, Accra

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol

GHS-ERC Number	**GHS-ERC 017/02/20**
Project Title	Chronic Complications Associated with HIV/AIDS Infected Patients receiving Active Antiretroviral Therapy at the Pantang Hospital
Approval Date	18th June, 2020
Expiry Date	17th June, 2021
GHS-ERC Decision	**Approved**

This approval requires the following from the Principal Investigator

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months.
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report after completion of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.
- Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED .....
Dr. James Akazili
(Head, Ethics & Research Management Department)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra

APPENDIX II: DATA ABSTRACTION TOOL

PATIENTS IDENTIFICATION AND BASIC INFORMATION

1. Unique Identification (ID).....
2. Date of entry..... /..... /..... (DD/MM/YYYY)
3. Date of registration: ..... /..... /..... (DD/MM/YYYY)
4. Date of birth: ..... /...../..... (DD/MM/YYYY)
5. Age.....
6. Sex of patient
   [1] Male [2] female
7. Marital status
   [1] Married [2] Single [3] Divorced [4] Separated [5] Widow(er) [6] Cohabitating
8. Occupational status
   [1] Full time [2] Part-time [3] On leave [4] Unemployed
9. Education.
   [1] None [2] Primary [3] JSS /MSLC [5] SEC/Tech [6] Tertiary
10. Religion .
    [1] Muslim [2] Christian [3] Traditional [4] None [5] Others (specify) .....
11. Number of dependents (children <18years, zero if none)
    .....
12. Referrals
    [1] Diagnostic HIV testing [2] Walk-in VCT site [3] PMTCT program [4] Old patient
    [5] Transfer in ON OI [6] Transfer in ON ART [7] Transfer in from Paediatric [8] TB [9] STI
    [10] Others (specify).....

INITIAL CLINICAL CARE ASSESSMENT AT FIRST ART DISPENSE

13. Date first given ART medication ..... /...../..... (DD/MM/YYYY)
14. Type of HIV
    [1] HIV I [2] HIV II [3] both HIV I & HIV II
15. Height (cm): .....
16. Weight (kg): .....
17. Temp (°C): .....
18. Pulse (bpm): .....
19. Systolic blood pressure (SBP): .....
20. Diastolic blood pressure (DBP): .....
21. TB status:

[1] Not screened [2] Screened negative [3] Screened positive

22. If TB positive, treatment initiated? [1] Yes[2] No [3] Deferred
23. Drug allergies? [1] Yes[2] No
24. Past ARV experience? [1] Yes [2] No
25. If past ARV experience, drugs

[1] Drug 1 ..... Duration (months)
[1] Drug 2 ..... Duration (months)
[1] Drug 3 ..... Duration (months)

26.

No	Conditions	Current	Past	Never	Date (DD-MM-YY)
i.	Jaundice	[1]	[2]	[3]	
ii.	Chronic Cough	[1]	[2]	[3]	
iii.	Skin rash	[1]	[2]	[3]	
iv.	Difficulty in swallowing	[1]	[2]	[3]	
v.	Fever/chills	[1]	[2]	[3]	
vi.	vomiting	[1]	[2]	[3]	
vii.	Severe weight loss (>10%)	[1]	[2]	[3]	
viii.	STIs	[1]	[2]	[3]	
ix.	Blood in urine	[1]	[2]	[3]	
x.	Fatigue	[1]	[2]	[3]	
xi.	Nausea	[1]	[2]	[3]	
xii.	Vomiting	[1]	[2]	[3]	
xiii.	Diarrhoea	[1]	[2]	[3]	
xiv.	Abdominal discomfort	[1]	[2]	[3]	
xv.	Persistent Headache	[1]	[2]	[3]	
xvi.	Dizziness	[1]	[2]	[3]	
xvii.	Insomnia	[1]	[2]	[3]	

xviii.	Anxiety/Depression	[1]	[2]	[3]	
xix.	Visual changes	[1]	[2]	[3]	
xx.	Abnormal menses	[1]	[2]	[3]	
xxi.	Oral thrush	[1]	[2]	[3]	
xxii.	Body pains	[1]	[2]	[3]	

27. Smoking status [1] Yes[2] No [3] Ex-smoker
28. Alcohol intake[1] Yes[2] No [3] Ex-alcoholic
29. HIV disclosure [1] Disclosed [2] Not disclosed
30. If disclosed, to whom? [1] Family [2] Friends
31. Is patient sexually active? [1] Yes [2] No
32. Disclosure to sexual partner? [1] Yes [2] No
33. Regular condom use? [1] Yes [2] No

34. Physical examination

No	Conditions	Yes	No	Date (DD-MM-YY)
I.	General appearance	[1]	[2]	
II.	Lymphatic system	[1]	[2]	
III.	Oral	[1]	[2]	
IV.	Respiratory	[1]	[2]	
V.	Cardiac	[1]	[2]	
VI.	Breasts	[1]	[2]	
VII.	Skin	[1]	[2]	
VIII.	Gastrointestinal	[1]	[2]	
IX.	Neurological	[1]	[2]	
X.	Mental status	[1]	[2]	
XI.	Others	[1]	[2]	

35. WHO clinical stage? [1] Stage I [2] Stage II [3] Stage III [4] Stage IV

36. Other acute/chronic conditions

[1] Malaria date ..... (DD-MM-YY)
[2] STI date ..... (DD-MM-YY)
[3] Diabetes date ..... (DD-MM-YY)
[4] Hypertension date ..... (DD-MM-YY)
[5] Pregnancy date ..... (DD-MM-YY)
[6] Others ..... date ..... (DD-MM-YY)
..... date ..... (DD-MM-YY)
..... date ..... (DD-MM-YY)
..... date ..... (DD-MM-YY)
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..... date ..... (DD-MM-YY)
..... date ..... (DD-MM-YY)

37. Baseline CD4 value: .....

38. CD4 below 350? [1] Yes [2] No

39. Prescribed drug regime [1] 1st line 1st choice [2] 1st line 2nd choice [3] 2nd line first choice [4] 2nd line 2nd choice

40. The component of the ART drug regime

[1] AZT (Zidovudine) 300mg [2] 3TC (Lamivudine) 150mg
[3] NVP (Nevaripine) 200mg [4] EFV (Efavirenz) 600mg
[5] EFV (Efavirenz) 800mg [6] D4T (Stavudine) 300mg
[7] TDF (Tenofovir) 300mg [8] FTC (Emtricitabine) 200mg
[10] ABC (Abacavir) 300mg [11] ATV/r (Atazanavir/r) 300mg/100mg

FOLLOW-UP INFORMATION DURING FIRST THREE YEARS ON ART

41. Weight (kg): .....

42. Temp (°C): .....

43. Pulse (bpm): .....

44. Systolic blood pressure (SBP): .....

45. Diastolic blood pressure (DBP): .....

46. Client on ART? [1] Yes [2] No

47. TB status:

[1] Not screened [2] Screened negative [3] Screened positive

48. If TB positive, treatment initiated? [1] Yes [2] No [3] Deferred

49. Patient complaints

No	Symptoms	Yes	No	Date
i.	Cough	[1]	[2]	
ii.	Skin rash	[1]	[2]	
iii.	Difficulty in swallowing	[1]	[2]	
iv.	Fever/chills	[1]	[2]	
v.	Blood in urine	[1]	[2]	
vi.	Fatigue	[1]	[2]	
vii.	Nausea	[1]	[2]	
viii.	Vomiting	[1]	[2]	
ix.	Diarrhoea	[1]	[2]	
x.	Abdominal discomfort	[1]	[2]	
xi.	Headache	[1]	[2]	
xii.	Dizziness	[1]	[2]	
xiii.	Insomnia	[1]	[2]	
xiv.	Anxiety/Depression	[1]	[2]	
xv.	Others (specify)			

50. Physical examination

No	Symptoms	Yes	No	Date
i.	General appearance	[1]	[2]	

ii.	Lymphatic system	[1]	[2]	
iii.	Oral	[1]	[2]	
iv.	Respiratory	[1]	[2]	
v.	Cardiac	[1]	[2]	
vi.	Breasts	[1]	[2]	
vii.	Skin	[1]	[2]	
viii.	Gastrointestinal	[1]	[2]	
ix.	Neurological	[1]	[2]	
x.	Mental status	[1]	[2]	
xi.	Others (specify)			

51. Is patient sexually active? [1] Yes [2] No
52. Disclosure to sexual partner? [1] Yes [2] No
53. Regular condom use? [1] Yes [2] No
54. ARV adherence
    [1] 0 pills missed [2] 1-2 pills missed [3] 3-4 pills missed [4] >5 pills missed
55. CTX adherence
    [1] 0 pills missed [2] 1-2 pills missed [3] 3-4 pills missed [4] >5 pills missed
56. Change in ART combination [1] Yes [2] No
57. Diagnostic findings
    [1] Malaria date ..... (DD-MM-YY)
    [2] STI date ..... (DD-MM-YY)
    [3] Diabetes date ..... (DD-MM-YY)
    [4] Hypertension date ..... (DD-MM-YY)
    [5] Pregnancy date ..... (DD-MM-YY)
    [6] Others ..... date ..... (DD-MM-YY)
    ..... date ..... (DD-MM-YY)
    ..... date ..... (DD-MM-YY)
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..... date ..... (DD-MM-YY)

58. Last follow-up visit date ..... (DD-MM-YY)

THANK YOU