ADHERENCE TO ANTI-RETROVIRAL THERAPY IN THE FEDERAL CAPITAL TERRITORY, ABUJA, NIGERIA

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KEY WORDS

Adherence

Anti-retroviral Therapy

Combination

Barriers

Facilitators

Suboptimal

Optimal

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HIV

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ABSTRACT

Background

Nigeria accounted for 2.95 million of the 22 million people globally living with HIV in 2008. In 2010, the HIV prevalence increased to 3.1 million, with 1.5 million people requiring anti-retroviral treatment (ART). ART is effective if patients adhere to treatment (taking 95% or more of drugs as prescribed) over a sustained period. Taking less than 95% of the medication can lead to drug resistance and treatment failure, which have dire individual and public health consequences. This study described adherence to ART and the factors that constrain and motivate adherence among patients on ART at the University of Abuja Teaching Hospital in the Federal Capital Territory (FCT), Nigeria.

Methodology

An observational, descriptive and analytical, cross-sectional survey of adherence among 502 adult ART patients (254 women and 248 men) from the University of Abuja Teaching Hospital was conducted. I collected sociodemographic and clinical characteristics of participants, and barriers and facilitators to adherence. For the prescription refill data, I utilized the updated pharmacy refill records from the ART dispensary. Bivariate and multivariate analysis was performed to analyse the factors that influence adherence to ART.

Results

Participants in this study had been on therapy for a mean of 43±27 months. Total optimal self-reported adherence over the previous three days (not missing a dose, taking correct doses in the correct frequency and correct schedule) was 53.6%, compared with 62.5% adherence calculated by prescription refill. However, most (80.3%) participants achieved virologic suppression at a level of <400 copies/µl^3. Reported barriers to adherence were: forgot (43%); travelled away from home (21%); ran out of medication (16%); busy at work (13%); lack of food (5%) and medication snatched by armed robbers (2%). Self-reported adherence over the previous three days was positively associated with age and viral load. Younger respondents (under 30 years) were 3 times more likely to adhere to their regimen

compared with those older than 30 years (OR = 2.5; 95% CI = 1.26-4.61; p = 0.023). As expected, participants who had adequate viral suppression (<400 copies/µl^3) were 7 times more likely to report optimal total adherence to their medications over the previous three days compared to those who did not have adequate viral suppression (>400 copies/µl^3) (OR = 6.6; 95% CI = 1.6- 11.07).

Conclusion

Most participants (above 90%) continued on ART and majority (80.3%) achieved satisfactory viral suppression. However, 53.6% had suboptimal adherence to ART because participants were not taking their medications as prescribed. Strategies to address adherence to ART must emphasize taking medication at the correct times and on schedule.

DECLARATION

I declare that **Adherence to antiretroviral therapy in the Federal Capital Territory, Abuja, Nigeria** is my own work, that it has not been submitted before for any degree or examination in any University or College, and that all the sources I have quoted or used have been indicated and acknowledged as complete references.

Yohanna K. Avong **24 August 2012**

DISCLAIMER

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ACRONYMS

AIDS: Acquired Immunodeficiency Syndrome

ART: Antiretroviral Therapy

ARV: Antiretroviral

ACTION: AIDS Care and Treatment in Nigeria

HAART: Highly Active Antiretroviral Therapy

HIV: Human Immunodeficiency Virus

CD4: Cluster of Differentiation at level 4

FMOH: Federal Ministry of Health

PLWHA: People Living with HIV and AIDS

PEPFAR: United States Presidential Emergency Plan for AIDS Relief

IHVN: Institute of Human Virology, Nigeria

STI: Sexual Transmitted Infections

WHO: World Health Organization

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It is very easy to appreciate people that have done you a favor with a "thank you". It is not that easy when you have to appreciate people who put down their lives, sacrifice their time and went the Biblical "extra mile" to ensure that you have succeeded in your work. You will not have the word to appreciate them – this is the difficulty I have appreciating the innumerable number of people that contributed to this work.

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I wish my mother could still see; she would have been overwhelmed with joy seeing the beautiful MPH certificate. What should I do? I will place her frail hands on the certificate to appreciate her for rising every morning to cook my delicious "Tuck". It was this local Kataf (Atyap) meal that gave me the strength to cross the river Wonderful and trek the long distance to my local primary school for six years. As for Dad, when I do join him in Heaven someday, I will show him the certificate and tell him, "I made it dad".

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CHAPTER ONE

INTRODUCTION

1.1 Background

The United Nations Agency for AIDS (UNAIDS) described AIDS as an epidemic ravaging lives at unprecedented levels (UNAIDS, 2008). According to UNAIDS, 22 million out of the 33 million people living with the HIV globally, were from sub-Saharan Africa in 2007. In 2008, Nigeria had the third highest population of people living with HIV in the world with 2.95 million people being aware that they were infected with the HIV [Federal Ministry of Health (FMOH), 2009]. In 2010, AIDS killed 280,000 people out of an estimated population of 3.1 million people living with the HIV (FMOH, 2009).

In the Federal Capital Territory (FCT) where this study was conducted, 45,000 people out of a population of 1.18 million were infected in 2009 (FMOH, 2010). HIV sero-prevalence rate was estimated at 9.9%; HIV and AIDS patients occupy 60% of hospital beds in public health institutions in the FCT (Federal Capital Territory [FCT], 2006).

1.2 Country profile

Geography, population and socio-demographic characteristics

Nigeria has 36 states and the Federal Capital Territory (FCT) spread across a land area of approximately 923,768 square kilometres (Fig 1.1). It is Africa's 15th largest country in land

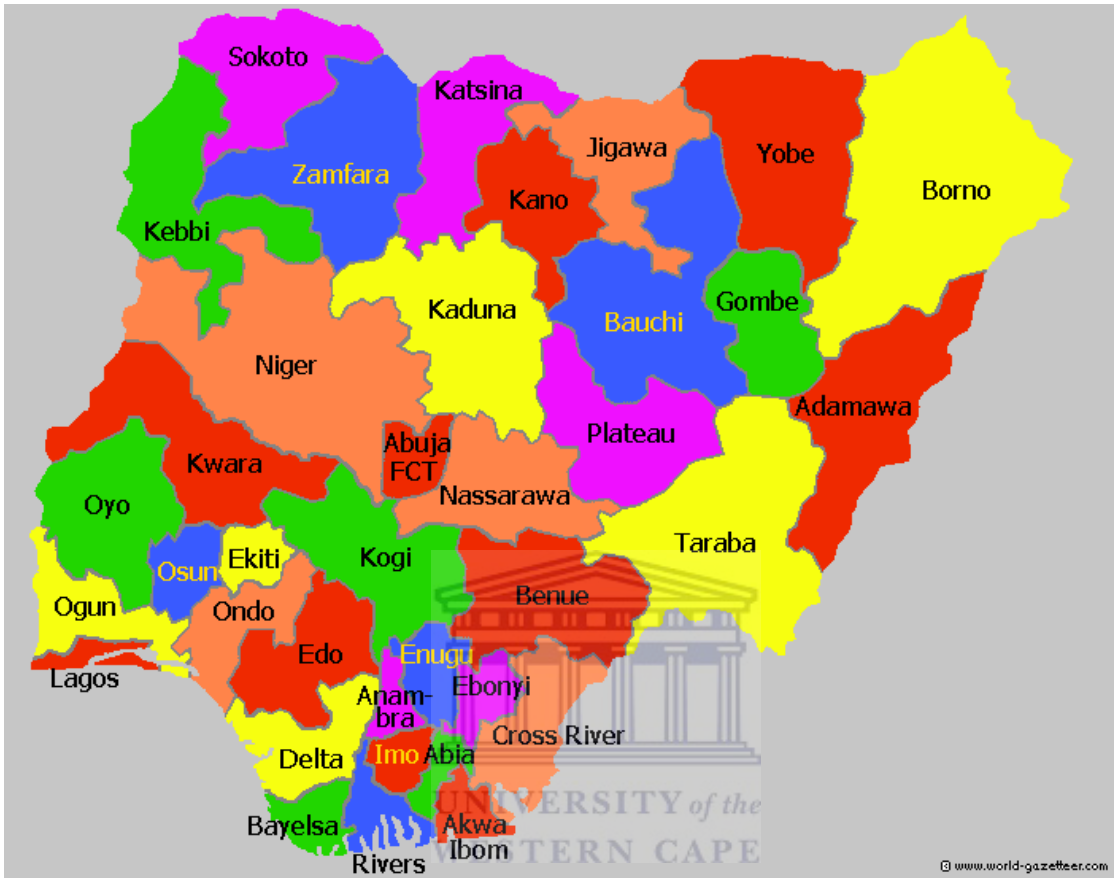
mass, the 10th most populous country in the world and the most populous country in sub-Saharan Africa. The total population had grown to an estimated 170 million people in July 2012 but the population growth rate has decreased from 3.2% in 2006 to 2.6% in 2012 (CIA, 2012). Current statistics show that approximately 50% of the total population live in urban areas; the rate of urbanization has increased from 2.2% in 2006 to 3.5% in 2012 (CIA, 2012). The population age structure indicates that Nigeria has a young population. According to the National Bureau of Statistics (NBS) (2011), persons aged 0 to14 years constituted 39.6 %, those aged between 15 and 64 years (the economically active population), constituted 56.3 %, while those aged 65 years and above constituted 4.2 % (National Bureau of Statistics [NBS], 2011). The gross domestic product (GDP) report showed that the Nigerian economy grew by 7.40 % in the third-quarter of 2011 as against 7.86 % in the corresponding quarter of 2010 (NBS, 2011). Nigeria's unemployment rate increased to 23.9 % in 2011 compared with 21.1 % in 2010 and 19.7 % in 2009 (NBS, 2011). The rate is higher in the rural areas (25.6 %) than in the urban areas (17.1 %) according to the NBS (2011). The NBS (2011) report also shows that 70% of the population is living below the poverty line (NBS, 2011).

Health care delivery services are poor in Nigeria; this is demonstrated by the health and socioeconomic indicators presented in Table 1.1. The situation may worsen with the HIV/AIDS epidemic unless current effort at controlling the epidemic leads to a reduction in the public health problems (like tuberculosis) that are driven by HIV/AIDS.

Table 1.1 Nigeria's health and socioeconomic indicators, 2010

Indicators	**Estimates**
Life Expectancy at birth: total population (in years)-2012	52
Total fertility rate (children born per woman)-2012	5
Total infant mortality rate (per 1,000 live births)-2012	74
Adult Literacy (15 years & above)- 2003	
Total population	68%
Female (%)	60.6%
Male (%)	75.7%

Source: *2012 CIA World Factbook.*



Legend

	Borno	Kaduna	Taraba	Ekiti	Delta	Ogun				
	Yobe	Kano	Adamawa	Kwara	Edo	Benue	Abuja FCT	Akwa Ibom	Lagos	Imo
	Kebbi	Oyo	Kogi	Gombe	Abia	Bayelsa				
	Zamfara	Bauchi	Rivers	Osun	Enugu					
	Sokoto	Katsina	Plateau	Anambra	Eboyi					
	Jigawa	Niger	Nassarawa	Cross River	Ondo					

Fig. 1.1 Map of Nigeria showing the 36 states and Abuja, FCT

Source: *National Bureau of Statistics, 2011*

1.3 HIV/AIDS in Nigeria

The first case of HIV patient was reported in Nigeria in 1986 (FMOH, 2007). The national HIV sero-prevalence level which is obtained through sentinel survey of antenatal care attendees, increased from an initial 1.8% in 1991 to 5.8% in 2001. A slight drop to 5% was recorded in 2003; which stabilized in 2005 with a sero-prevalence rate of 4.4%. In 2008, the prevalence rate increased to 4.6%, but dropped to 4.1% in 2010 (FMOH, 2010).

The epidemic is unequally distributed across the 36 states; from 1% in Ekiti State to 10.6% in Benue State (FMOH, 2009). The 2008 survey showed that 17 states and the FCT recorded sero-prevalence of 5% or more. In seven states and the FCT, sero-prevalence was 7% or higher. There are also HIV "hot spots", with prevalence rates higher than the national prevalence rate of 4.1% (FMOH, 2010). Wannune, for instance, is a hot spot in Benue State; the HIV prevalence was estimated at 21.3% in 2010.

Women are most affected by HIV/AIDS: 58.3% of the infected people (which is a total of 1.72 million people) living with HIV in 2008 were females. The HIV prevalence peaks at age group 25-29 years with a sero-prevalence level of 5.6% (FMOH, 2009). The result of mode of transmission analysis carried out by the National Agency for the Control of AIDS (NACA) in 2008, showed that about 62% of new infections occur among persons perceived as practicing "low risk sex" in the general population including married sexual partners. The rest of the new infections (38 %) are attributable to injecting drug users (IDU), female sex workers (FSW), men having sex with men (MSM) who constitute about 3.5% of the adult population (FMOH, 2009).

The leading route of HIV transmission in Nigeria is hetero-sexual intercourse, which accounts for 80% of all infections. Other routes of transmission include mother-to-child-transmission, transfusion of infected blood and blood products, accounting for 10% each (FMOH, 2009).

Few studies have been conducted in Nigeria to evaluate the economic impact of AIDS. Bollinger, Stover and Nwaorgu (1999) reported a reduction in labor supply and increased in cost among families that are affected by AIDS (Bollinger, Stover and Nwaorgu, 1999). They also argued that the epidemic has had large macroeconomic repercussions due to the loss of lives of many individuals during their productive years (Bollinger, Stover and Nwaorgu,1999). Another study assessed the economic impact of AIDS on Nigerian households and reported that in affected households, a direct private healthcare costs and indirect income loss per HIV-positive individual were 36,065 Naira, approximately 56% of annual income per capita. Approximately 40% of these costs were income losses associated with sickness and care-giving. This study also reported that 10% of the cost of HIV is accounted for public subsidies for health and the largest single cost, representing 54% of the total economic burden of HIV, is for out-of-pocket expenses for healthcare (Mahal, Canning, Odumosu and Okonkwo, 2008). According to the United Nations Development Program Human Development (UNDP), life expectancy in Nigeria increased from 45 years in 1963 to 51 years in 1991 in the absence of HIV/AIDS but dropped to 48.4 years in 2010 as a result of the HIV/AIDS epidemic (UNDP HDR, 2010).

1.4 The national response to the HIV/AIDs epidemic in Nigeria

Nigeria initiated the antiretroviral treatment (ART) program in January 2002 in 25 health facilities across the country (FMOH, 2007). The facilities enrolled 25 patients each between February and June 2002, but the National Institute for Medical Research (NIMR) registered 50 patients. The program was later expanded to accommodate more patients (an additional 100 to 500) based on the capacity of the individual centers to care for people living with HIV. The Federal Government negotiated with Cipla Pharmaceuticals and obtained a flat price of $350.00 for a standard triple regimen of Stavudine, Lamivudine and Nevirapine. Personnel including doctors, pharmacists, nurses and laboratory staff were trained to treat 10,000 adults and 5,000 children yearly. An ART committee to guide the implementation of the ART program was set up in 2004 to provide technical support for the development of ART guidelines at the national level (FMOH/WHO, 2003). The committee consisted of clinicians, pharmacists and other health workers.

In January 2006, the Federal Government commenced the free ART program. Records indicated that 166,374 patients received free antiretroviral drugs and treatment in 2007, and in 2008, the number increased to 247,815. A further scale up to 309,800 patients was reported in 2009; which was increased to 380,182 patients in 2010 (Supply Chain Management System [SCMS]/FMOH, 2011). It is estimated that about 1.5 million people still require ART from an estimated 3.1 million Nigerians living with the HIV in 2010 (FMOH, 2010).

In the FCT, 30,000 AIDS patients out of the 45,000 people living with the HIV in 2009 were on ART. According to the FCT HIV/AIDS Control Program, about 60 health facilities are involved

in ART but only 19 of them provide comprehensive ART services including treatment and care, laboratory services, HIV prevention, prevention of mother- to- child transmission and home-based care (FCT HIV/AIDS Control Program, 2009). The other facilities provide only the treatment and care and laboratory services. Among the HIV/AIDS treatment centers in the FCT, the University of Abuja Teaching Hospital is the largest treatment center. It was treating over 9,000 AIDS patients in April, 2010 followed by the National Hospital, Abuja and the Asokoro District Hospital, which were treating 7000 and 5000 AIDS patients respectively.

Despite the enormous challenges controlling the epidemic pose, notable achievements have been recorded in the fight against HIV/AIDS. International donors and developmental partners such as the United States President's Emergency Plan for AIDS Relief (PEPFAR), World Bank, Clinton HIV/AIDS Initiative (CHAI) and Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) financially supported ART services at over 150 sites across the nation (FMOH, 2007). In addition, faith based and private organizations are also providing ART services under the public-partnership scheme. The Clinton HIV/AIDS initiative (CHAI) donated free anti-retroviral drugs (adult 2nd line and pediatric 1st and 2nd line) and drugs for treating a wide range of opportunistic infections. The PEPFAR is the leading funder of ART activities in Nigeria; in the first 4 years of the project (2004 to 2008), PEPFAR had planned to treat 350,000 patients, prevent 1.7 million new infections and provide care to 1.15 million patients and AIDS orphans (FMOH, 2007). As PEPFAR enters into the 2nd phase of collaborating with the government with a focus on quality care, the 4.1% reported national prevalence rate might reduce further. Also, the Federal Government budgeted 24,307,729.00 US Dollars for the procurement of anti-

retroviral dugs in 2010 (SCMS/FMOH, 2011), and this may further strengthen the ART program in Nigeria and reduce both the morbidity and mortality of the epidemic.

1.5 Problem Statement

As indicated earlier, ART has been available at both private and public health centers in Nigeria since 2002. In 2010, the Federal Government expanded ART services to remote areas that were otherwise neglected. The President, Dr. Goodluck Ebele Jonathan directed that: "all relevant government ministries, department, and agencies (MDAs) to accelerate the implementation of the decentralization of HIV treatment, care and support services to the primary health care levels in all parts of the country" (FMOH, 2010: i). But to maximize the benefits of ART at the primary health care levels, sufficient information is required on the factors that constrain or motivate adherence to ART. However, only a few adherence studies have been conducted in Nigeria and the factors that constrain and motivate adherence in this setting has not been systematically investigated. Furthermore, previous adherence studies in Nigeria did not measure adherence in a comprehensive way; the investigators used the number of pills taken versus the number prescribed criterion to evaluate adherence without taking into consideration whether medications were taken at the correct times and on schedule. There is need to conduct a quantitative study to describe adherence as well as the factors that constrain or motivate it. The current study therefore set out to determine the level of adherence to ART in a comprehensive way (considering the pills taken and whether drugs were taken at the correct frequencies and on schedule); the factors that are associated with adherence to ART were also evaluated.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

The chapter is structured into themes which include: definition of terms, key concepts in anti-retroviral therapy, adherence studies in different settings and the conceptual framework of factors associated with adherence to ART.

2.2 Definition of Concepts

Adherence to Antiretroviral Therapy

Adherence generally refers to the "*extent to which a person's behaviour - taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health provider*" (WHO, 2003a: 3). In the context of the ART, it is defined as taking all the prescribed doses at the correct time, in the correct doses and in the correct way (Kgatlwane *et al.*, 2006; Roux, 2004; Aspeling, 2006). It involves a change in the patient behaviour base on a decision-making process between the patient and health care provider (WHO, 2003a; Bader *et al.*, 2006)**.** It also involves the following elements:

♦ that the medication is taken with or without food, according to the instructions. Some medicines need to be taken with food to ensure that the body absorbs them properly while others need to be taken on an empty stomach, a certain amount of time before or after eating. It can also be important that the patient eats the right kind of food; for example, the amount of fat eaten can make a difference to how well some drugs are absorbed.

♦ that drug interactions with any other medication is checked. This includes medicines that have been prescribed for the patient, or bought at a pharmacy, supermarket or health store, including complementary or alternative therapies. Some recreational and illegal drugs can have potentially dangerous interactions with ARVs.

Highly Active Antiretroviral Therapy

The clinical management of AIDS depends on the use of Highly Active Anti-retroviral Therapy (HAART**)** which is defined as a treatment regimen with 3 or more combination of anti-retroviral drugs (WHO, 2006a). According to the Nigerian guideline (FMOH, 2009), the basic first line HAART regimens include the following options:

- Stavudine (d4T) + Lamivudine (3TC) + Nevirapine (NVP) or Efavirenz (EFV)
- Zidovudine (ZDV) + Lamivudine (3TC) + Nevirapine (NVP) or Efavirenz (EFV)
- Tenofovir (TDF) or Abacavir (ABC) + Emtricitabine (FTC) or Lamivudine (3TC) + Nevirapine (NVP) or Efavirenz (EFV)
- Didanosine (ddI) + Lamivudine (3TC) or Emtricitabine (FTC) + Nevirapine (NVP) or Efavirenz (EFV) (FMOH, 2007).

The World Health Organization (WHO) recommends 4 regimens for starting ART in ART-naïve individuals (WHO, 2009). These are:

- AZT+3TC+EFV;
- AZT+3TC+NVP;
- TDF+ FTC+EFV and

- TDF+3TC +NVP

However, when treatment fails, a wide range of regimens could be used with the Protease Inhibitors included in the regimen mix (WHO, 2009).

Non-adherence

Non-adherence refers to situations when patients fail to take medication as prescribed, take medication at the wrong time, skips doses, interrupts treatment for a period or abandons treatment altogether (WHO, 2003a). It aslo includes: consistent underdosing, chronic overdosing, abrupt overdosing, drug holidays and random drug administration.

Poor adherence

According to the WHO (2001; 2003a), poor adherence refers to situations when patients take antiretroviral medications without compliance to time, schedule and dietary recommendations. In this study, non-adherence, poor adherence and suboptimal adherence are used interchangeably.

Fixed Dose Combination (FDC)

A Fixed Dose Combination (FDC) describes the drug formulation. It is combining many drug constituents at fixed strengths in one tablet. For example, the medicine call Truvada has two drugs – Tenofovir and Emtricitabine combined at the fixed strengths of 300mg and 200mg

respectively. With FDCs, many drugs can be taken in one tablet; which reduces both the pill burden as well as the dosing frequency.

Side Effects of Antiretroviral Drugs

A side effect of a drug is defined as "*any unintended effect of a pharmaceutical product occurring at doses normally used in humans, which is related to the pharmacological properties of the drug*" (National Agency for Food and Drug Administration Control- National Pharmacocovigilance Centre, (NAFDAC-NPC), 2004: 4). In the context of this study, the side effects of the medications are the unpleasant effects patients experienced with those medications. For example, Zidovudine may cause anaemia while Nevirapine may cause a fatal condition known as Stephen Johnson's syndrome (Flexner, 2006). These side effects may hinder adherence to the prescribed regimen leading to suboptimal adherence to the regimen.

Undetectable Viral Load Level (UDVL)

The *Undetectable Viral Load Level is a* level the HIV virus cannot be detected in the blood through quantitative laboratory test (Bangsberg *et al.,* 2000; Bangsberg *et al.*, 2003; Bangsberg *et al.*, 2001; Paterson *et al.,* 2000; Wood *et al*., 2003a). In the Nigerian treatment guideline, the UDVL is 400 copies/μl^3 (FMOH, 2007).

CD4

CD4 (cell differentiation at level four) is a type of white blood cells which protect the body against infection. When a person has been infected with the HIV for a long time, the number of CD4 cells they have goes down, resulting in acquired immune deficiency syndrome (AIDS), in which the person's immune system no longer functions effectively. Consequently, the victim is exposed to more attacks by other infections, which further weakens the immunity.

2.3 Adherence to combination anti-retroviral therapy

Antiretroviral therapy has proved effective at minimizing both the morbidity and mortality of AIDS (Mannheimer *et al*., 2005; Altice, Mostashari and Friedland, 2001), but the success of ART relies almost entirely on adherence to ART. Studies found that consistently high levels of adherence (95% or more) to a combination of highly active anti-retroviral medications is necessary for effective viral suppression, prevention of resistance, disease progression and death (Paterson *et al*., 2000; Bangsberg *et al*., 2000; Bangsberg *et al*., 2003; Bangsberg *et al*., 2001; Wood *et al*., 2003b). According to Wei *et al*. (1995), using only a single anti-retroviral drug inevitably provokes the emergence of drug-resistant virus - in some cases within a few weeks. Several prospective comparative trials found that two regimens were more effective than single–drug regimens (Fischl *et al.*, 1995; Hammer *et al.*, 1996; Saag *et al.*, 1998), and three–drug regimens were more effective still (Collier *et al*., 1996; Gulick *et al*., 1997; Hammer *et al*., 1997). Mathematical models of HIV replication suggest that three is the minimum number of drugs required to guarantee effective long-term suppression of HIV replication (Collier *et al*., 1996; Gulick *et al*., 1997; Hammer *et al*., 1997). The current standard of care is to use at least

three drugs simultaneously for the entire duration of treatment. Four or more drugs are often used simultaneously in pretreated patients harboring drug-resistant virus, but the number of drugs a patient can take is limited by toxicity and inconvenience (Piketty *et al*., 1999).

Some studies have argued that viral suppression may depend on other factors other than the regimented 95% adherence rate. The drug regimen, for instance, has been shown to affect the level of adherence (Weiser *et al.*, 2004; Maggiolo *et al.*, 2005; Bangsberg *et al.*, 2007; Wainberg *et al.*, 2007; Bangsberg *et al.*, 2003; Harrigan *et al.*, 2005; King *et al.*, 2005). The un-boosted Protease Inhibitors-based combination antiretroviral therapy (cART) requires more than 95% adherence to be consistently effective (Friedland, 2006), but the non-nucleoside reverse transcriptase inhibitors (NNRTIs) and boosted protease inhibitor-based cART can achieve virologic suppression at a moderate adherence of 70 – 90% (Nachega *et al*., 2007; Shutter *et al*., 2007; Martin *et al*., 2008). Nevertheless, optimal outcomes require optimum adherence (95% or more) particularly in the first four to six months of treatment (Gardner *et al.*, 2006; Wainberg *et al.*, 2007). This means that:

- If a patient is taking once-daily treatment, optimal adherence requires not missing more than one dose a month
- If a patient is taking twice a day treatment, optimal adherence requires not missing more than three doses a month
- If a patient is taking three times a day treatment, optimal adherence requires not missing more than four doses a month

In this study, the 95% adherence rate was adopted as the cut-off level for measuring optimal adherence to ART, i.e. patients who took at least 95% of their medications in the past 3 days were assumed adherent to the ART.

2.4 Poor adherence in Sub-Saharan Africa

Optimal adherence rates have been reported in some countries in Africa. Orrell and his colleaques (2003) reported a 99% rate in South Africa (Orrell *et al.*, 2003); Nachega and his team also reportd 95 % in South Africa (Nachega *et al.*, 2009b) and Jean Baptiste reported more than 90% rate in Bostwana (Jean, 2010). On the basis of these studies and others, it was argued that adherence to ART is not a problem in Africa. The *New York Times* reported this great achievement with the headline "Africans Outdo US Patients in Following AIDS Therapy" (McNeil, 2003). However, suboptimal adherence levels have been reported in some countries in Africa: In Cameroon and Senegal, 86% and 80% over-all adherence rates were reported respectively (Akam, 2004; Laurent *et al.*, 2002); in Botswana, a 54% over-all adherence rate was reported (Weiser *et al*., 2003) and in South Africa, 80% over-all adherence rate was documented (Darder *et al*., 2004). Furthermore, Gills *et al.* (2005) commented that the high adherence rates reported in most studies in Africa were exerggerated (Gill *et al.*, 2005), suggesting that the actual adherence rates in most African countries is unknown. Thus, researchers are concerned that Africa may be facing suboptimal adherence as the western countries where studies reported that between 100% - 28% of HIV/AIDS patients on ART could not achieve the 95% adherence threshold required for viral suppression (Haubrich *et al.*, 1999; Paterson *et al*., 2000; Bangsberg *et al*., 2000; Gordillo *et al*., 1999; Gifford *et al*., 2000).

There are four possible explanations of the poor adherence rates in Africa. Firstly, adherence to drugs in the management of chronic conditions such as hypertension, diabetes and cancer has generally been a great challenge even in rich western nations (DiMatteo, 2004). HIV/AIDS is

also a chronic condition and therefore adherence to the combination ART is a great challenge. Secondly, the ART regimens are often complicated and can include varying dosing schedules, dietary restrictions and adverse effects (Ferguson *et al.*, 2002).Thirdly, adherence barriers (e.g. lack of drugs, forgetfulness and side effects of drugs) have also been reported in many African countries (Pinheiro *et al.*, 2002; Fong *et al.*, 2003; Orrell *et al.*, 2003; Weiser *et al.*, 2003; Nemes *et al.*, 2004; Stout *et al.*, 2004). These barriers decrease adherence to ART according to studies (Ammassari *et al.*, 2004b; Cederfjall *et al.*, 2002; da Silveira *et al.*, 2003; Weber *et al.*, 2004; Chesney, 2006; Simoni *et al.*, 2006). Fourthly, studies show that adherence wane over time (Byakika-Tusiime *et al.*, 2009; Carrieri *et al*., 2003). Laurent and his colleagues (2012), for instance, found that after 1 month of therapy, 95% of their patients had adherence exceeding 80% but after 18 months, only 80% of the patients remained adherent above that level (Laurent *et al*., 2002). The implication of this is that assessing adherence among patients who have been on therapy for shorter periods may generate exaggerated adherence rates, since patients may not have been on therapy long enough for adherence to start waning (Gill *et al*., 2005). For this reason, only patients who have been on therapy for 12 months and above were included for adherence evaluation in the current study.

2.5 Poor adherence in Nigeria

Nigeria is ranked third among the countries that are worst affected by the HIV/AIDS epidemic, yet poor adherence has been reported by the few studies that evaluateed the level of adherence to anti-retroviral therapy in Nigeria (Idigbe *et al.*, 2005; Adebayo, Modupeola and Timothy, 2005; Daniel *et al*., 2004; (Uzochukwu *et al*., 2009); Iliyasu *et al*., 2005; Farley *et al.*, 2007). The

significant studies were conducted in the South-West, North-Central and South-East geopolitical regions of Nigeria. In the South-West, Daniel and his team (2004) measured the level of adherence through a cross sectional study in two subsets of HIV infected patients in Sagamu: those who were on self-purchased drugs and those on free medications. They included only 53 participants (40 receiving free medications and 13 on self purchased drugs) who had been on ART between 1st Septemeber and 30th November, 2003. They found an overall 79.2% adherence rate; the adherence rate was higher among those on free medication compared with those on purchased medication but the difference was not statistically significant (Daniel *et al*., 2004). In the North-Central, Farley *et al.* (2007) assessed adherence using pharmacy refill records and patient self-report at the University of Abuja Teaching Hospital. They recruited 529 adults' patients newly initiating ART and evaluated their adherence over six months. They found that only 305 (58%) had a refill rate of ≥95% (Farley *et al*., 2007). In the South-East, an adherence rate of 27% was reported by Uzochukwu *et al.* (2009). They had assessed the adherence rate among 174 patients for 12 months through a cross sectional descriptive study (Uzochukwu *et al*., 2009).

Although the above studies were limited by sample size, they all reported suboptimal adherence rates in the three geopolitical regions of Nigeria; suggesting that Nigeria is struggling with adherence to ART. Adherence barriers were also reported by these studies and this has compounded the problem of adherence to ART in Nigeria. For instances, psychosocial (e.g. forgetting to take drugs), structural (e.g. lack of drugs at treatment centres) and socioeconomic factors (e.g. poverty) have been found to be the cause of poor adherence to ART in Nigeria (Uzochukwu *et al*., 2009). The structural factors were considered the major cause of poor

adherence before the introduction of the free drug scheme by the Federal government but with the introduction of the free drug scheme, the psychosocial and the socioeconomic factors are now the leading cause of poor adherence to ART (Uzochukwu *et al*., 2009).

2.6 ART failure

The Nigerian national treatment guideline defines treatment failure based on three parameters: virological, immunological, and clinical (FMOH, 2007). Virological failure means any of the following conditions: when the viral load is not suppressed to undetectable levels after 6 months on ART or viral load is not reduced by at least 2 to 2.5 $\log_{10}$ in HIV RNA level after 24 weeks on the ART or a persistent increase in viral load following a period of adequate suppression. Immunological treatment failure refers to situations when immunogical test shows a return of CD4 cell count to pre-therapy baseline level or 50% decline from on-therapy CD4 cell peak level or a failure to achieve a CD4 cell count increase of 50 to 100 cells/μl^3 per year. Treatmnt fails clinically when new opportunistic infections occur or malignancy (signifying clinical disease progression) is reported or recurrence of WHO Stage 3 defining conditions (e.g. Kaposi's sarcoma) (FMOH, 2007). The virological and immunological parameters provided the theoretical basis for the collection of the clinical data (CD4 and Viral load) in the current study.

2.7 Measuring adherence to ART

There is no gold standard for the measurement of adherence to ART; thus the use of surrogate measures has been adopted for measuring adherence to ART (Chesney, 2006; Fogarty *et al.*, 2002; Wagner, 2002; da Salviera *et al.*, 2003; Roux, 2004; Levine *et al.*, 2006; Liu *et al.*, 2006;

Marias, 2006; Simoni *et al.,* 2006; Dzinza, 2007). The commonly used methods in research and clinical settings include pill counts, pharmacy refill records, drug level monitoring, electronic drug monitors (EDM) and various self-reporting tools, such as questionnaires and visual analogue scales. Chesney (2006) classified these methods into two main groups: observation and patient self-report.

Observational methods

Observational methods include pill counts, pharmacy refill records, medication event monitoring systems (MEMS), and biological and therapeutic drug monitoring and directly observed therapy (Chesney, 2006).

Pill counts

The pill count method entails counting the remaining doses of medication that were dispensed to the patient in the previous visit. It can be done at the pharmacy when patient come for prescription or at home during unannounced visits (Chesney, 2000). According to Chesney (2000), a pill count may provide tangible evidence of poor adherence to the ART, because returned pills that were left in the container give an indication of the quantities of drugs taken. The method is easy, but it has some limitations. Patients could dump pills before visiting the clinic and create the false impression that they have been adhering to the prescribed regimen. Also, patients tend to forget drug packages or discard them for the fear of stigmatization, it is

difficult to accurately determine adherence with this method. The method also consumes the health workers' time (Liu *et al.,* 2006).

Pharmacy Refill

This is a dispensing-based method which relies on the use of pharmacy dispensing records (Chesney, 2006). The number of days a patient has medication over a period of time is counted and divided by the number of days within the review period to get the proportion of days covered by drugs. For example, if the patient was dispensed medicine for 145 out of 180 treatment days, then the patient's maximum adherence rate could only be 81%. The greatest advantage of pharmacy refill is that the method can be used to measure long-term adherence. However, because dispensing data are used, it is impossible to reliably measure if drugs are actually taken and because of this, true adherence may be overestimated (Chesney, 2000; International Network for the Rational Use of Drugs-Initiative on Adherence for Anti-retrovirals (INRUD-IAA), 2008).

Medication Electronic Monitoring Systems

This method uses an electronic pill cap that records when it is opened (Roux, 2004). Several studies conclude that MEMS is an objective and accurate measure of adherence to ART (Chesney, 2000; Liu *et al.*, 2006; WHO, 2006). It allows detailed view of non-adherence which correlates with virological outcomes. However, the MEMS are expensive and complex to implement (Liu *et al.,* 2006). The method rests on the assumption that opening the bottle equals to use.

Biological and therapeutic drug monitoring

CD4+ lymphocyte count and viral load level are regarded as clinical indicators of adherence to the ART (Chesney, 2000). A patient adhering to the prescribed regimen is expected to have high CD4 count and low viral load level. However, this method is not a reliable indicator for measuring adherence to the ART because CD4 count is affected by other factors other than adherence to the ART. Similarly, viral load may not accurately measure adherence to ART particularly if resistance to the prescribed regimen has developed.

Patient self-reporting methods

The self-reported methods involve the use of questionnaires which are either administered by the participants or administered by an interviewer. Patients may be asked to recall the number of times they correctly took their medications over the previous 3 days, 4 days, one week or one month. For shorter recall periods (3 or 4 days), patients are asked to recall the doses they took or did not take each day in the previous 3 or 4 days. There has not been any evidence to suggest a difference between the validity of using a 3 or 4-day recall, which suggests that a 3-day recall may be used (Simoni *et al.*, 2006).

As stated earlier, there is no gold standard to measure ART adherence; each measure has its advantages and disadvantages. The choice of a measure is often determined by several factors including cost and availability of resources (Chesney, 2006). It is suggested that more than one measure should be selected to accurately measure adherence to ART (Chesney, 2006). By

choosing two measures, the errors inherent in one measure are addressed by the other measure (triangulation) and a more realistic adherence rate is determined. In the current study, two adherence measures were selected: the pharmacy refill for 360 days and self-report based on a 3 day recall. For the self-report, respondents were asked to recall the number of pills that they took in a dose over the previous 3 days. The 3-day recall was selected, because it is easier for patients to recall their experiences with drug intake for shorter periods than they would for longer periods e.g., the past one month. It is also less costly and not sophisticated like the therapeutic drug monitoring. In addition, the self-report measures are highly correlated with clinical measures of viral load (Nieukerk and Oort, 2005).

2.8 Factors that affect adherence to combination ART

A number of factors have been associated with adherence to ART and are commonly divided into intersecting categories: patient level, treatment regimens, disease characteristics, patient provider relationship and clinical setting (Reiter *et al.*, 2003).

2.8.1 Patient level factors

The patient level factors are divided into socio-demographic and psychosocial factors. The socio-demographic factors include age, gender, race, socio-economic (financial income and poverty), education and HIV risk factors; while the psychosocial factors include mental health, substance abuse, socio-cultural issues and support, knowledge and attitude about

HIV and its treatment (Carrieri *et al.*, 2001; Nemes *et al.*, 2004; Murphy *et al.*, 2004; Machtinger and Bangsberg, 2005; Mills *et al.*, 2006a; Mills *et al.*, 2006b).

Socio-demographic factors

Age

Age may influence adherence to ART. A study conducted in Los Angeles among 148 HIV-infected adults between the ages 25 and 69 years to examine the effects of older age, cognitive impairment, and substance abuse found a higher mean adherence with the older subjects compared with the younger subjects (87.5% vs 78.3%; p=0.01). The older subjects were also found to be three times more likely to be good adherers than the younger subjects (OR = 3.1, 95% confidence interval: 1.40-6.76) (Hinkin *et al.*, 2004). In southern Africa, a cohort study revealed that adolescents and young adults who were on the ART had both poorer adherence and poorer virologic outcomes than do adults (Nachega *et al.*, 2009b). The reason that was given for this is that younger individuals who depend on care givers for the administration of drugs may struggle with adherence when the care givers are not committed to administering the drugs (Mehta, Moore and Graham, 1997; Gordillo, del Amo, Soriano and González-Lahoz, 1999; Chesney, 2000). Also, younger individuals may be forced by adults to keep their treatment secret because of the fear of stigmatization and this affects adherence to the ART among younger individuals (Naar-king *et al.*, 2006; Hammami, Nostlinger, Hoerée, Lefèvre, Jonckheer and Kolsteren, 2004).

Some studies, however did not find positive association between age and adherence. In Brazil, a cross-sectional quantitative study evaluated adherence among 195 patients aged 13 years and above and found that adherence to ART was not significantly associated with age (Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002). Also, Eldred and his team did not find association between adherence and age (Eldred *et al.*, 1998). Some researchers argue that clinician bias rather than patients' actual behavior is responsible for the association between age and adherence. Adherence, according to these researchers, is a behavioral issue and cannot be linked to age but clinicians often correlate patients' level of education, living standards and lifestyles, and sometimes also age and sex, with their adherence potential (Eldred *et al.*, 1998). In general however, older age has been associated with better adherence to HAART (Hinkin *et al*., 2002; Becker *et al*., 2002; Wutoh *et al.*, 2001) because cognitive status is generally associated with successful adherence (Hinkin *et al*., 2004; Ammasari *et al*., 2004a).

Gender

The role that gender plays as the predictor of adherence has been the subject of several studies. A prospective cohort study by Berg and his team examined the role of gender difference in adherence to ART among 113 AIDS patients that were current or former opiod users at the Montefiore Medical Centre's Substance Abuse Treatment Program in the Bronx, New York, USA. The authors found that women were less adherent to HAART than men, with a median adherence rate of 46% (IQR 18%- 77%) compared to 73% (IQR: 30% - 93%) (Berg *et al*., 2006). Other studies also showed that women are less adherent to ART than men (Arnsten *et al*., 2002; Turner *et al*., 2003; Altice *et al*., 2001; Delgado *et al*., 2003; Wenger *et al*., 1999; Montessori *et*

al., 2000; Abriola *et al*., 2000; Arabe *et al*., 1998; Montaner *et al*., 2000). However, a large body of researchers have failed to show a significant association between gender and adherence to ART (Eldred *et al*., 1998; Moatti *et al*., 2000; Wagner *et al*., 2002; Carrieri *et al*., 2003; Holzemer *et al*., 1999; Bouhnik *et al*., 2002; Golin *et al*., 2002; Gordilo *et al*., 1999; Chesney *et al*., 2000; Paterson *et al*., 2000).

The reasons that have been advanced for the contradictory finding on the association between gender and adherence to ART included the following:

- The use of small number of women in studies

Most studies that found no association between gender and adherence to ART were limited by small numbers of women in the studies (Berg *et al*., 2004).

- Clinician biases

As stated above, clinician bias rather than patients' actual behavior is responsible for the inconsistency in the association between gender and adherence; clinicians often correlate patients' level of education, living standards and lifestyles, and sometimes also age and sex, with their adherence potential (Eldred *et al*., 1998).

- Failure to address confounders

Another possible explanation for the inconsistency in the relationship between gender and adherence is the role of confounders. Most studies do not examine social or behavioral factors which confound the relationship between gender and adherence to ART.

Socio-economic factors

Socioeconomic factors include financial constrains (e.g. not being able to travel to study centre for treatment due to lack of money), lack of financial support and poverty. The World Health Organisation (2006) has cited economic support as directly related to the level of adherence to the ART. For example, in a cross-sectional study of 195 patients in Brazil, it was observed that there was better adherence to the ART among patients who had sustainable occupations and could support themselves economically (Gordillo *et al.,* 1999). In many studies financial constraints have frequently been cited as a barrier to adherence to ART (Kleeberger, Phair, Strathdee, Detels, Kingsley and Jacobson, 2001; da Salviera *et al.*, 2003; WHO, 2006a; Falagas *et al.*, 2008).

Poverty may prevent individuals from following treatment-related dietary advice and traveling to treatment centres to receive medications (INRUD-IAA *et al.*, 2008). Poverty has been cited as a predictor of poor adherence to ART in sub-Saharan Africa. In a multi-country adherence study in Uganda, Botswana and Tanzania, 20, 163 and 70 participants were interviewed respectively. The authors found that lack of food and transport cost (due to poverty) in Botswana respectively accounted for 2.1% and 13% of the reasons for missing medications (WHO, 2006b). However, in Uganda and Tanzania, poverty did not affect adherence to ART. Medication may induce appetite and if patients are poor and lack the food to eat, they may discontinue the medication (da Salviera *et al.*, 2003; Kalichman, Simbayi, Kagee, Toefy and Jooste, 2006; Marais, 2006; WHO, 2006b; Moratioa, 2007; Spies, 2007; Thobias, 2008). Also, four studies evaluated the relationship between poverty and adherence among poor communities in United States; they found that individuals living in poverty had suboptimal adherence in the range of 56% to 67%

(Bangsberg, Ware and Simoni, 2006). However, the role of poverty as non-adherence indicator has been contentious. Mills and colleques argued that the barriers to adherence among the impoverished individuals in the North America studies appeared to be due to poor patient-clinician relationships, untreated depression, substance abuse, and other factors that are common among poor individuals in North American settings rather than poverty itself (Mills *et al.*, 2006b). It is likely, therefore, that poverty may not be a predictor of poor adherence to ART under every circumstance. In the Brazilian study in Pelotas (Southern Brazil), no significant association was found between poverty and adherence to ART which further strengthen the argument that poverty may not be a predictor of poor adherence to ART under every circumstance (Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002).

Educational level

Some studies have found positive association between education and adherence to ART. In France, a prospective, multicentre, randomized clinical trial at three university-based hospitals, examined the impact of an educational intervention on adherence to ART, knowledge, quality of life and therapeutic response in a large cohort of chronic HIV infected patients. The study found that educational intervention increased adherence in the experimental subjects at 12 month and was maintained at 18 month. The health status improved in the 56% of the experimental subjects and 50% of the control subjects. The authors concluded that educational intervention improves adherence to ART and health status (Goujard *et al*., 2003). In Pelotas, Brazil, Pinheiro and his team found that schooling was positively associated with better adherence; with an increasing schooling level, there was an increase in rates of adherence (p=0.02) (Pinheiro, de Carvallo-

Leite, Drachler and Silveira, 2002). Van Servellen and his colleagues (2002) also found that functional health literacy was significantly associated with medication adherence. These authors argue that individuals with low level of education may have difficulties recognizing their correct current medications whereas, increased level of education provides patients with vital skills (planning, organizing and integration), which promote adherence to ART (Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002). However, Uzochuwu and team, found formal education to be negatively and statistically significantly associated with adherence to ART (Uzochukwu *et al.*, 2008). Eldred and his team did not find higher education as predictor of optimum adherence (Eldred *et al.*, 1998).

The psychosocial factors

Patient knowledge of treatment and medicines

Knowledge of the importance of ART adherence and ability to take antiretroviral medications as directed (adherence self-efficacy) have a positive effect on adherence. A multi-center study among 980 treatment naïve patients found that less-positive beliefs about ART adherence were associated with greater stress, depression, and symptom distress but more-positive beliefs about ART adherence were associated with better scores on health perception and functional health (Reynolds *et al*., 2004). Lack of knowledge of drugs (correct doses, frequency of administration and schedule) are barriers to adherence to ART (Mehta, Moore and Graham, 1997). The ART regimens are very complex and may be confusing; as a result, when patients have not been sufficiently counselled to know how to use the drugs, adherence becomes a challenge.

Social support

In Rwanda, a multi-site adherence study involving 653 patients on ART found that significantly greater proportion of patients who took at least 95% of prescribed antiretroviral drugs had good social support compared to those who did not (64% vs 48%, p= 0.03) (Jean-Baptiste, 2008). HIV/AIDS is a chronic condition requiring chronic care as such, consistent support from the family facilitates adherence to the ART (Chesney *et al.*, 2000; Bearman and La Greca, 2002; Simoni, Frick, Lochkart and Liebovitz, 2002; Attawell and Mundy, 2003; Hofer, Schechter and Harrison, 2004; Skhosana, 2006; Kagee, Le Roux and Dick, 2007). According to Attawell and Mundy (2003), support from a spouse and support groups play a crucial role in HIV medication adherence, but social support could be negatively applied when family members choose to stigmatize and discriminate against the sufferers. As stigmatization itself has been shown to be a barrier to adherence to the ART (Nachega *et al.*, 2004; 2006a), it is argued that social support could be used negatively or positively (Van Dyk, 2001; Timmons and Lynch, 2004).

Disclosure of HIV status

Disclosure of HIV status could either facilitate or compromise adherence to the ART. When patients are stigmatized after disclosing their status, they may suffer psychological depression and be discouraged from taking drugs. Under this condition, disclosure of HIV status becomes a barrier to the ART (Ormazu, 2000; Klitzman *et al.*, 2004; Zea *et al.*, 2005). In the Botswana adherence study, 15% of patients claimed stigma (arising from disclosure of HIV status) interfered with their ability to take treatment (Weiser *et al.*, 2003). Some studies claimed that disclosure of HIV status promoted adherence to the ART and this was when disclosure attracted

family support or assistance from the community or other well-wishers (Nachega *et al.*, 2004; 2006b).

Attitudes and beliefs

According to the World Health Organisation (2001) and Mills *et al.* (2006a), patients' beliefs about their illness and effectiveness of medication are predictive of adherence. For instance, the beliefs that anti-retroviral therapy is effective and prolongs life and that poor adherence may result in viral resistance and treatment failure can impact positively upon a patient's ability to adhere to the ART (Montgomery *et al.*, 1989; Mehta, Moore and Graham, 1997; WHO, 2001; 2006b). It is also argued that beliefs in personal abilities to adhere to medication affect adherence to anti-retroviral therapy according to Becker (1974) and Pinheiro *et al.* (2002).

Patient forgetfulness

In Hong Kong, a retrospective survey of 161 Chinese patients on ART for 1 year found forgetfulness to be negatively associated with optimum adherence (Fong *et al.*, 2003). Forgetfulness was also shown to be a barrier to ART adherence in many studies (Roberts, 2000; Reynolds *et al.*, 2004; Marais, 2006; Mills *et al.*, 2006a; WHO, 2006b; Dieckhaus and Odesina, 2007; Wang and Wu, 2007; Amberir *et al.*, 2008; Thobias, 2008; Malangu, 2008). Forgetfulness could be due to patients' being over busy, not using adherence reminders or being away or attending important social events such as night vigil, funerals, weddings and parties. Whatever is the cause of forgetfulness, adherence to the ART suffers if patients forget to take their drugs (Stout *et al.*, 2004).

Alcohol and drug abuse

Studies conducted in Brazil by Chesney *et al.* (2000) and Palmira *et al.* (2005) found a positive association between alcohol abuse and poor adherence. Another study conducted in Botswana also showed that alcohol abuse was one of the reasons patients on the ART was missing doses of their medication (WHO, 2006b). Alcohol is thought to induce forgetfulness, which might cause patients not to take their medication or take them incorrectly.

Substance (drug) abuse is also associated with poor adherence. The study by Hinkin and team which was discussed above also examined the impact of substance abuse on adherence to ART. They authors found that drug abuse was positively associated with poor adherence to ART; 13 of the 14 HIV-positive participants who met the diagnostic criteria for drug abuse or dependence were classified as poor adherers.

The mechanism through which active drug abuse causes poor adherence is unclear. One possibility is that drug abuse potentiates HIV-associated neuropsychological compromise, which then results in difficulties with adherence (Hinkin *et al*., 2004). Another explanation would argue that the often chaotic lifestyle associated with illicit drug abuse cannot accommodate the structure necessary to adhere to a complex medication regimen (Hinkin *et al*., 2004). But Golin *et al*. (2002) argued that the relationship between substance abuse and adherence is very complex. A study by Fogarty *et al.* (2002) actually found that patients on the ART with a history

of substance abuse had better adherence. The reason given for this is that, the discipline drug abusers gained from the methadone control programs invariably help them to adhere to the ART regimen.

Traveling/busy with work

Poor adherence has been associated with traveling or being busy (Stout *et al.,* 2004). Over busy patients are likely to forget their medication or they may carry them along but forget to take them. In the Hong Kong study quoted above, being busy with work was found to be significantly associated with poor adherence (Fong *et al*., 2003).

2.8.2 Treatment regimen factors

The number of pills prescribed, formulation, complexity of the regimen (dosing frequency and food restriction) and the specific type of the ART and medication side effects are factors related to the treatment regimens.

Number of pills (Pill burden)

Taking a greater number of anti-retroviral medications and frequent dosing were found to be positively associated with non-adherence (Kleeberger, Phair, Strathdee, Detels, Kingsley and Jacobson, 2001; Eldred, Wu, Chaisson and Moore, 1998). Patients with prescriptions of three to four daily doses were 53% less likely to comply with treatment than patients who had been

prescribed a two-dose regimen (da Salviera *et al.*, 2003). This is because with complex regimen, patients commonly misunderstand their health care provider's instruction on how to take medication. In South Africa, a study found that 13% of patients prescribed ARVs were not taking their medication correctly, despite believing that they were (Bangsberg, 2000). However, in the Hong Kong study, pill burden, dosing frequency and the need for dietary restriction did not predict a poorer drug adherence among Chinese patients who took more than 10 pills per day and thrice-a-day (Fong *et al.,* 2003). The authors argued that the counselling program deployed to prepare patients for the HAART initiation and the willingness of Chinese patients to follow treatment prescribed by the doctors were responsible for the high adherence despite the complexity of regimen and high pill burden (Fong *et al.*, 2003).

Formulation of ARV drugs

The formulation of a drug regimen (i.e. whether it is a fixed dose combination (FDC) or multiple single drugs) may also affect adherence. In the Rwanda study discussed above, Jean-Baptiste reported a higher rate of adherence among patients taking fixed dose combinations (FDC) than patients on multiple drug regimens (Jean-Baptiste, 2008). The fixed dose regimens usually require lesser frequent dosing and pill burden than the multiple drug regimens, which explain the reason for good adherence with the FDCs.

Side effects

The Hong Kong, Botswana and Rwanda adherence studies found the side effects of medication as predictors of non-adherence (Fong *et al*., 2003; Weiser *et al*., 2003; Jean-Baptiste, 2008). Other studies also cited the side effects of medication as predictors of non-adherence (Ammassari *et al*., 2001; Weiser *et al.*, 2003; Machtinger and Bangsberg, 2005; Weiser *et al.*, 2003; Roberts, 2000; Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002; Popa-Lissenanu *et al.*, 2005; Mills *et al.*, 2006a; Uzochukwu *et al*, 2008). However, the experience of symptoms and patients' view about medication side effect may be complex and may vary according to the type of regimen (Chesney, 2000; Carr and Cooper, 2000; Ammassari *et al.*, 2001; Carr, 2002; Murphy *et al.*, 2004). For instance, symptoms could stimulate the use of medication by acting as reminders or reinforcing beliefs about the necessity for treatment but the perception of side effects as harmful may constrain the use of medication (Ammassari *et al.*, 2001). It is generally believed that treatment burden of long duration, with serious side effects, and potential drug interactions, such as the one found with the HAART, manifests significant adherence problems (Van Servellen *et al.*, 2002). Horne and his colleagues had argued that missed doses of medication may be a logical attempt by the patient to moderate the risk of side effects by taking few medications (Horne, 2001).

2.8.3 Patient-provider relationship

Patient-provider relationship includes the patient's overall dissatisfaction and distrust in the provider and clinic staff, the patients' negative opinion of the provider's competency, the provider's unwillingness to include the patient in the decision-making process and the lack of

friendliness (e.g. warmth, openness and cooperation) (Chesney, 2000; WHO, 2006 and Marais, 2006).

A cross-sectional survey of 205 HIV-infected prisoners (most of whom were injection drug users) in four prison HIV clinics in Connecticut, USA found that, trust in physician and in HIV medications motivated the rate of adherence to the ART (Altice, Montashari and Friedland, 2001). In another study, Johnston (2004) examined physician-patient relationships, patient satisfaction and antiretroviral adherence among 28 HIV-infected adults in a qualitative study. The study found that good quality physician–patient relationships tended to promote adherence while lesser quality relationships impeded it. However, in the Rwandan study, patients who were non-adherent reported slightly greater satisfaction with their provider than those who were adherent (Jean-Baptiste, 2008).

Involvement of patients in decision-making makes the patient to have trust in the health provider and clinic staff and increases patient-satisfaction (Barker *et al.,* 2004). Studies have shown increase in adherence when patients are involved as active members in the decision-making process (Cassidy 1999; Bader *et al.*, 2006). The incompatibility of race/ethnicity between patient and provider and the inadequacy of referral have also been cited as determinants of non-adherence.

2.8.4 Clinic setting/health facility factors

Health facility factors that affect adherence to antiretroviral therapy include quality care, lengthy waiting times and distances to health facilities, availability of drugs and follow-up schedules (WHO, 2006a).

Availability of drugs and structural barriers

It is argued that in resource-limited settings, structural barriers are emerging as perhaps the most important barriers to the cART (Nachega *et al.,* 2010). A study that surveyed adherence among 174 patients on ART in South-East Nigeria found that non-availability of drugs in a University Teaching Hospital accounted for 65.6% of the reasons patients' were not adhering to their medications. The authors argued that the sustainability of the Nigerian ART program was in grave danger unless the government instituted an effective mechanism that would ensure consistent supply of medicines (Uzochukwu *et al.,* 2008). In Uganda, a cohort analysis found that initially excellent adherence declined over 1 year as patients experienced pharmacy stock-outs and excess/transportation difficulties (Oyugi *et al*., 2007). A systematic review of African studies also indicated that the most important and frequent factors reported to negatively impact adherence in developing countries are cost of drugs and structural barriers such as lack of transportation and pharmacy stock-outs (Mills *et al.,* 2006b). The Botswana study by Weiser and team reported that 17% of the patients missed their medications due to running out of medication (Weiser *et al,* 2003). Patients in rural areas have great difficulties accessing health facilities located in townships because of bad roads, long distances and the cost of the transport

(Jaffar *et al.*, 2005; Popa-Lissenanu *et al.*, 2005). In the Botswana study, the patients lived 800 to 1000km away from the clinic and had to travel that distance on monthly basis to access treatment (Weiser *et al.*, 2003). Perceived lack of confidentiality and dissatisfaction with past experiences with the health care system are also barriers that are related to the clinic. Chesney (2003) found that dissatisfaction with the health services is a predictor of non-adherence.

Quality of care

Patients' perception of the quality of care they receive affects their behaviour and ultimately affect adherence to the ART. Shortage of staff is one major area where quality of care is easily affected. It results in overworking of the available staff and overworked staff may be unwilling to engage the patients in the planning and management of care, which negatively affect adherence to the ART (WHO, 2006b; Attawel and Mundy, 2003). According to Aspeling (2006), patients may stop consulting with the clinics temporarily and interrupt treatment when treated disrespectfully by health care providers.

Waiting times in health facilities

In Botswana, Tanzania and Uganda, long waiting time was identified as a major challenge to adherence among patients who were on the ART (WHO, 2006b). Dehab *et al.* (2008) also found that prolonged waiting times have negative effects on complying with follow-up appointments and medication adherence. The World Health Organization recommended that health facilities

should avoid keeping patients waiting for longer periods when they come for consultation and medication to maintain high adherence levels over a long period.

2.8.5 Diseases characteristics

The stage and duration of HIV infection, associated opportunistic infections, and HIV-related symptoms are barriers in this category. The severity of the illness could impact negatively on adherence particularly, when severely ill patients do not have treatment supporters to assist them with drug medication (WHO, 2003a).

Illness-related factors that influence adherence to anti-retroviral therapy such as depression, stress and anxiety were reported to be associated with poor adherence in several studies (Mehta, Moore and Graham, 1997; Thobias, 2008). Research shows that there is a strong relationship between adherence and depression (Ciechanowski, Katon and Russo, 2000; Mills *et al.*, 2006a). In an Italian adherence study involving 135 patients on ART, non-adherence to ART was independently associated with worse depressive symptoms (Ammasari *et al.*, 2004a). Studies had also shown that depressive syndromes are the most prevalent mental disorders related to HIV infection (Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002; Starace *et al.*, 2002); also, it has been cited to be having negative effect on the quality of life of people living with HIV/AIDS and is associated with poor adherence to HIV treatment (Reynolds *et al.*, 2004; WHO, 2006b).

2.9 Study designs and methodologies in previous adherence studies

The review of studies on adherence to anti-retroviral therapy in sub-Saharan Africa revealed that most studies used the cross-sectional or longitudinal design over other designs (Gill *et al*., 2005). In Nigeria, all the adherence studies conducted in the past 5 to 10 years used the cross-sectional design (Mills *et al*., 2006b) to describe the scope of adherence to the ART. The cross-sectional design is the best design for describing the scope of problems according to Grimes and Schuz (2002).

The patient self-reporting measure has frequently been employed in anti-retroviral research (Gifford, Bormann, Shively, Wright, Richman and Bozzette, 2000; Eldred, Chaisson and Moore, 1998; Haubrich *et al*., 1999; Chesney *et al.*, 2000; Gordillo, DelAmo, Soriano and Gonzalez-Lahoz, 1999). A meta-analysis of adherence studies conducted in sub-Saharan Africa and North America by Mills *et al*. (2006b) indicated that 71% of the North American studies used patient self-report to assess adherence and 66% of the African assessments used the same method. According to Pinheiro, de-Carvalho-Leitre, Drachler and Silveira (2002), researchers prefer the patient self-reporting measure, because of its practicality, low cost and the fact that adherence detected by it has proved to be related to viremia below detection limits (Bangsberg *et al.*, 2000; Gifford, Bormann, Shively, Wright, Richman and Bozzette, 2000; Haubrich *et al*., 1999; Chesney *et al.*, 2000) and to serum levels of protease inhibitors. However, studies conducted in developed countries to measure the comparative accuracy of the measures of adherence have shown a poor association between self-report or pill counts and undetectable viral load (UDVL) compared with the association between electronic drug monitoring (EDM) and UDVL. For

instance, Arnsten *et al*. (2001) found that mean HAART adherence rates was 79% by self-reporting but only 53% by EDM. Moreover, patients whose EDM data indicated high adherence (above 90%) was far more likely to achieve UDVL than patients with the same level of adherence by self-report. In another study, Liu *et al*. (2006) concurrently compared several measures against patient UDVL rates. He found mean adherence using EDM to be 63% while pill count was 83% and self-report to be 93%. Among patients who failed to achieve UDVL at 8 weeks, the mean adherence was 87% for self-report, 74% for pill count, but only 59% for EDM – indicating that pill counts and self-reporting greatly overestimate adherence. Therefore, researchers suggest that more than one adherence measure should be used in assessing adherence to the ART (Chesney, 2006). By choosing two measures, it is argued that the errors inherent in one measure are addressed by the other measure (triangulation) and a more realistic adherence rate is determined.

2.10 Adherence in different settings

Gill and his colleagues enumerated some of the gaps in previous adherence studies conducted in sub-Saharan Africa (Gill *et al*., 2005). According to these authors, some of the studies were part of clinical trials or other highly controlled patient environments such as the Khayelitsha study in South Africa (WHO, 2003b). They argued that the studied patients may have benefitted from the structural supports provided by the trial and as such, adherence rates cannot be generalized to normal settings (Gill *et al*., 2005). Furthermore, longitudinal studies that used self-report measure, according to the authors, took smaller sample sizes of patients who have been on the HAART for short periods. The median

sample size in a meta-analysis of African studies was barely 100 (Gill *et al.*, 2005). Also, most of the studies (66%) used the recall measure to assess adherence, but could not validate adherence, because viral load tests were either not available and where available were too expensive to be incorporated into routine clinical care. The authors concluded these short comings had exaggerated adherence levels in Africa and accurate adherence rates remain unknown (Berg and Arstein, 2006; Gill *et al*., 2005).

2.11 Summary

The factors that influence adherence to anti-retroviral therapy (patient, socio-economic, health service, therapy, illness and the community factors) identified in the preceding literature review can be summarised by a conceptual framework (Figure 2). These factors interact, resulting in poor adherence to anti-retroviral therapy among patients, and form the conceptual basis for the current study (WHO, 2004).

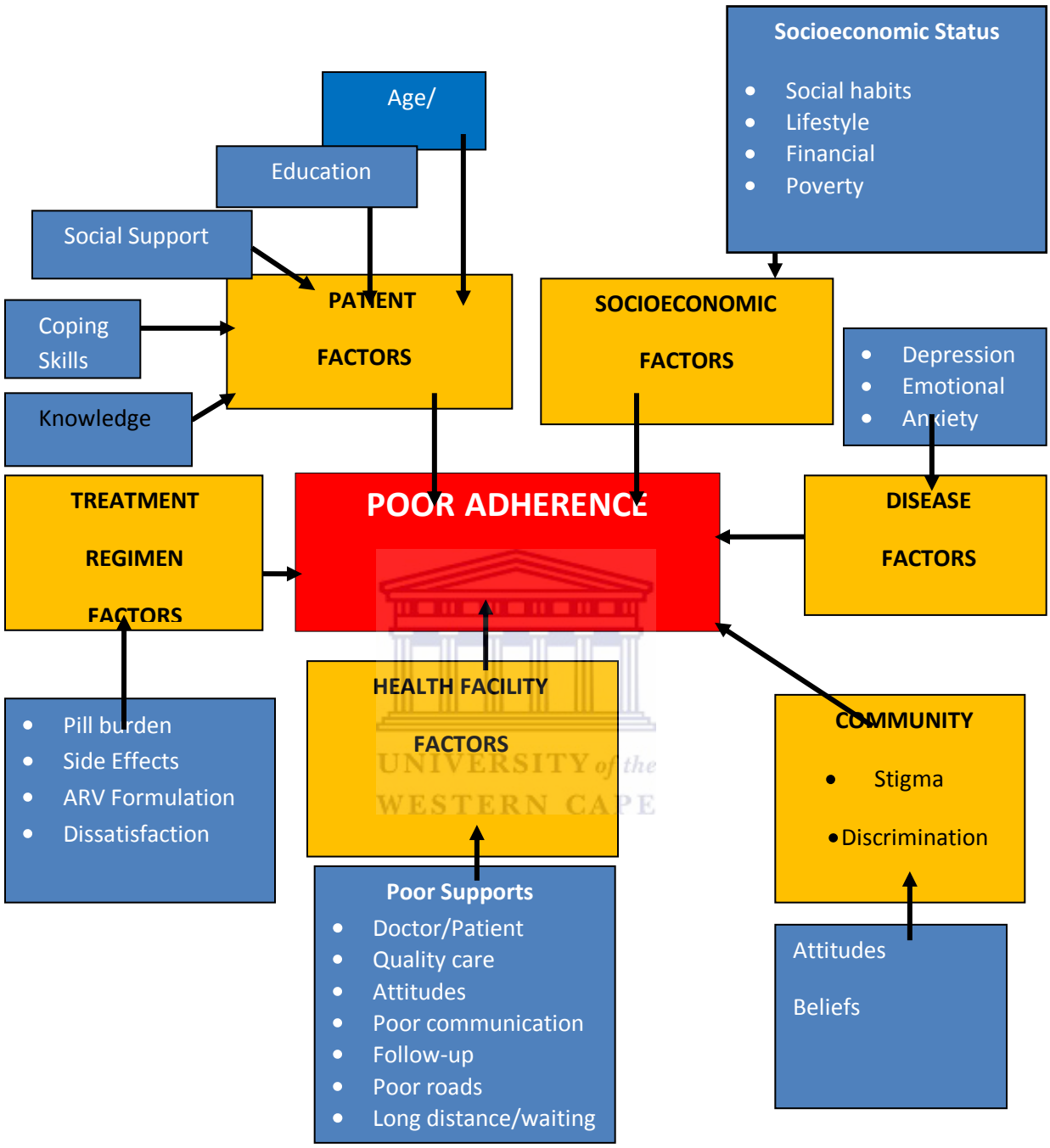


Figure 2:1. Factors leading to poor adherence to ART

CHAPTER THREE

METHODOLOGY

This section describes the aim and objectives of the study, the study design, how the study was conducted and the strategies that were adopted to improve validity, reliability and generalizability of the study as well as the ethical considerations.

3.1 Aim of the study

The current study aimed to describe adherence to anti-retroviral therapy among adult AIDS patients (aged 18 years and older) who had been on HAART at the University of Abuja Teaching Hospital, over the period of 2005 - 2010, and analyze the factors that constrain (barriers) and motivate (facilitators) adherence to ART.

3.2 Objectives

The specific objectives of the study were:

- to measure the level of adherence to ART in the FCT
- to describe socio-demographic characteristics of adult ART patients on the HAART
- to describe clinical characteristics of adult ART patients
- to analyze the determinants of adherence to antiretroviral therapy.

3.3 Study setting

The current study was conducted at the ART clinic of the University of Abuja Teaching Hospital, Gwagwalada - otherwise called the Special Treatment Clinic (STC), in order to mask

its identity and minimize stigmatization of the patients (Figure 3.1). The STC was created in 2005 through the PEPFAR collaboration with the Federal Government of Nigeria (FGN). It is managed by the AIDS Care and Treatment in Nigeria project (ACTION) – a joint initiative between the Institute of Human Virology of the University of Maryland School of Medicine (USA), Institute of Human Virology Nigeria, Federal Ministry of Health and the University of Abuja Teaching Hospital. The clinic has fully established counseling, pharmacy, laboratory and treatment units.

In May 2010, over 9,000 AIDS patients were registered for ART at STC. The records of clinic attendees as at 2010 show that 38% of patients were from the FCT region, 8% from Gwagwalada town, 34% from states that are at least five hours drive from the FCT region, and 18% from the neighboring states that are one to two hours from the FCT.

Figure 3.1: A cross section of the University of Abuja Teaching Hospital, Gwagwalada, FCT, Nigeria

Source: The Department of Administration, University of Abuja Teaching Hospital, Gwagwalada, Abuja, Nigeria.

The clinic provides services daily excluding weekends; to an average of 100 patients. There are between 5 and 8 doctors, 4 pharmacists, 3 adherence counselors and 10 nurses in the clinic. At ART enrollment, patient's history is taken by the nurses and physical examination conducted by the doctors in order to complete an intake record which included demographic data. Adherence counseling is routinely provided to patients and a regimented intensive HIV treatment preparation program is offered as part of routine clinical care. The *National Guideline for HIV and AIDS Treatment and Care in Adolescents and Adult* is used and five different anti-retroviral treatment regimens were prescribed during the study. Cotrimoxazole and other opportunistic infection drugs were also used to manage co-infections. The choice of regimen is at the discretion of the physician which is based on the national treatment guide line.

Patients are scheduled for a follow-up visit one month after ART was dispensed for the first time, and then every two or three months at the discretion of the physician. A sufficient supply of medication is dispensed to last until the next scheduled visit and at each follow-up visit, patients are given a health talk, their history taken and physical examination conducted. In addition, any side effects reported are recorded by the physician/pharmacist /nurses on a clinical encounter form called the Pharmacovigilance form. A pharmacy order form (prescription), which includes date the medication was dispensed, formulations dispensed, and quantity of formulation dispensed, is completed by the physician or nurse at each visit and presented to the pharmacist for dispensing. Clinicians review patients for treatment failure using the treatment failure algorithm. Patients who have been on therapy for six months and more, and are showing evidence of treatment failure (predicted through the viral load level, CD4 count and opportunistic

infections) are sent to the laboratory to have a fresh viral load test conducted. Physicians use the viral load order form (Appendix 8) to request for such tests.

3.4 Study design

The study used an observational, descriptive and analytical, cross-sectional survey design. This design was selected for four reasons. First, it is the recommended design for studies that describe the scope or the extent of research problems (Grimes and Schuz, 2002; Beaglehole, Bonita and Kjellstrom, 2006). Since the aim of this study is to describe the scope of adherence and its determinants, the cross sectional survey design was adopted. Second, literature review showed that similar adherence studies have used this design with outstanding results (Weiser *et al.*, 2003; Bangsberg *et al.*, 2000; Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002). Third, generalization of findings to the study population is feasible, because the design allows a cross section of the study population to be examined at a given time (Durrheim and Painter, 2006; Park, 2007). Fourth, very few ethical difficulties are associated with it. However, the causes of problems cannot be identified because causal relationships cannot be established with the cross sectional design (Grimes and Schuz, 2002).

3.5 Study population and sampling

The study population comprised of all adults (18 years and older) who have been treated with the HAART medications for at least 12 months as at May 2010. The criterion of a minimum 12 months treatment was chosen for three reasons. Firstly, it may take 6 months or more for some

patients to achieve undetectable viral load after treatment initiation or switch (Paterson *et al*., 2000; Pradier *et al*., 2001; Clay, 2005) and the study relied on patients' viral load to validate self-reported adherence. Secondly, HAART is a life-long treatment; it is therefore more meaningful to evaluate longer term, rather than short-term adherence to the HAART. Thirdly, patients who have been on therapy for short term are likely to have very high rates of adherence, because adherence falters after patients have been on therapy for longer terms (Akam, 2004; Carrieri *et al*., 2001; Laurent *et al*., 2002). Patients who were critically ill or hospitalized as well as those who were not currently taking ARVs or had defaulted for 4 months within the 360 days were excluded from the study.

Participants' preparation for sampling

The participants were prepared for sampling at the "health talk hour". As part of routine care, the facility conducts a compulsory one-hour health talk (8-9am) for all HIV positive patients visiting the ART clinic to refill their medication prescriptions. During the health talk (Figure 3.3), the study's aim, eligibility criteria, viral load test, confidentiality and benefits of the study were presented to the patients by the nurses and adherence counselors who were responsible for coordinating the health talk. Participants were allowed to ask questions on the study after the presentation.

Figure 3:2. An interactive session

Sampling strategy

Prior to going to the dispensary to refill prescriptions, nurses arranged patients in rows on the basis of "first-come-first-serve" and they waited patiently to be called to refill their prescriptions by the pharmacists. It took about 10 minutes for pharmacists to attend to a patient; therefore, 10 minutes was used as the sampling interval for the selection of the participants.

The first patient that was selected to be included in the study was called to the dispensary after she met the criteria and gave consent. After that, every person was selected at every 10th minute interval. Dispensing pharmacists checked the pharmacy records and patients who were 18 years and above who had been taking their ARVs for at least 12 months as at May 2010 were further informed of the study's aim, benefits and risks and if they were willing to be interviewed, were directed to the interview center, which was opposite the dispensary. If the patient declined, the next patient was invited at the 10th minute interval and his consent requested. The same

procedure was repeated until the sample size was realized.

A systematic sampling was adopted for the recruitment of respondents, as used by Bangsberg (2000). Systematic sampling was convenient both for the patients and the data collectors; it did not have the rigor of simple random sampling (Durrheim and Painter, 2006).

Sample size determination

A non-adherence rate of 42% from a study conducted at the study center by Farley *et al. (*2007), and an error margin of 5% and 95% confidence level were applied as parameters for sample size calculation. These figures were built into a statistical formula (Joubert and Katzenellenbogen, 2007) and a minimum sample size of 374 was derived. However, a larger sample size was chosen to increase its power (Durrheim and Painter, 2006; Hedges, 1978). Therefore, the minimum sample size derived from the calculation (374) was raised to 502.

3.6 Data collection

Pretesting of questionnaire and pilot study

The questionnaires were pre-tested in two phases. During the first phase, its content was evaluated for content validity using current literature and one HIV/AIDS clinical expert at the study centre. Suggestions were discussed and incorporated where necessary. During the second phase, the proposed process for identifying and interviewing patients was evaluated. Two health providers identified ten eligible patients who were approached by the data collectors for interviews. Three key lessons were learnt during the exercise: the questionnaire was too long to be administered in 3 to 5 minutes, some important questions that should have been included in

the questionnaire were omitted and some of the participants were upset for the fact that their occupations/professions were not specifically listed in the questionnaire. For instance, the pastors were not happy to be classified as "civil servants". Based on the lessons taken from this exercise, the questionnaire and the data collection process were modified. The revised questionnaire (Appendix 12) and data collection process were used in subsequent data collection efforts as described.

Logistics of data collection

Prior to data collection, several meetings with individuals and groups of health workers at the study center were held. The ART Coordinator, ART Facility Manager, Clinical Associate (CA) and the heads of Pharmacy, Treatment Support Specialist (TSS), Monitoring and Evaluation, Records and Laboratory Services were presented with the research approval letters from the University of Abuja Teaching Hospital (Appendix 1) and the Institute of Human Virology, Nigeria (Appendix 3). The roles the different health workers performed to ensure smooth data collection were fully discussed and agreed upon during the meetings. In Table 3.1, the specific responsibilities of the workers are presented.

Table 3.1: Facility staff and the responsibility they carried out during the data collection

Health Staff	**Specialty**	**Responsibility**
ART Coordinator	Physician	Coordinated the data collection
Clinical Associate	Physician	Ordered the viral load tests
Facility Manager	Nurse	Coordinated the data collection.
Phlebotomists	Medical Laboratory	Collected blood for viral load assay
Medical Laboratory Scientists	Medical Laboratory Science	Performed the Viral Load Assay
Pharmacists	Pharmacy	Screened patients for inclusion
Nurses	Nursing	Introduced the study at the health interactive session
Monitoring and Evaluation Staff	Statistician	Extracted patients' prescription refill record from CAREWare
Record Staff	Sociologist	Extracted patients' CD4 from folders
Treatment Support Specialists	Community health workers	Motivated respondents to participate in the study

On the days of data collection, data collectors arrived at the study center one hour (7am) before the clinic opens with the health interactive session. The principal investigator went round and thanked the health workers for assisting with the data collection and solicited for continued support. Emerging problems or challenges reported the previous day by the data collectors were raised and resolved with the workers during the thank-you visits. The lady who was contracted to

provide snacks was also visited routinely to ensure that the quality of snacks recommended by the ART Coordinator was what was presented. Interviews started around 10: 00 am and ended by 3:00 pm daily except on Mondays when it started late because of the clinical meetings. The types of data collected, sources of the data, the measurement instruments and the purpose of the data are out-lined in Table 3.2. A description of how the data were collected is presented under the ethical consideration section.

Table 3.2 Type of data, source of data, measurement instrument and purpose of the data

Type of data	**Source of data**	**Measurement Instrument**	**Purpose of data**
Socio-demographic and Adherence (patients' experience with use of ARVs)	Adult patients on ART for at least 12 months	Exit questionnaire	To measure short term adherence ; To measure adherence barriers and socio-demographics of patients
Viral load	Consented respondents who were interviewed	Amplicor HIV-1 Monitor Test, Version 1.5	To validate adherence information
Patients' Prescription |Refill	CAREWare (software)	Retrospective pharmacy form	To measure long term adherence
Patients' clinical characteristics (CD4)	Patients folders	Patients clinical characteristics form	To measure clinical characteristics and validate adherence information

Procedures/processes for data collection

The socio-demographic and adherence data using the exit questionnaire

Data collectors asked questions in English but for patients who could not understand English, Hausa was used and for this reason, the consent and participants' information sheet were translated into Hausa by a certified Hausa translator (Appendixes 5 and 7). Participants were permitted to voice any questions and whether or not he/she would consent to participate and those who consented were asked to sign or thump print informed consent forms (Appendixes 4 and 6) before the interview commenced using the exit questionnaire. Data collectors signed

confidentiality forms to maintain confidentiality on patients' information. Anonymity was maintained throughout the study – patients' names did not appear on interview forms. Participation was completely voluntary and those who chose to withdraw at any stage from the study were allowed to freely do so.

The questionnaire was a structured interviewer-administered questionnaire; built on work done by the INRUD-IAA, and modified to fit the study objectives and local situation in the FCT. Items on the questionnaire included: socio-demographics and adherence information. For instance, participants were asked how long they waited at the clinic, how long it took to travel to the clinic, how many of their prescribed ARVs and other drugs were actually dispensed, whether the medicines were correctly labeled, whether they experienced any adverse drug events. The questionnaire also evaluated patients' knowledge of drug regimen, e.g., whether participants knew how to take their medicine correctly with respect to dosage, frequency of administration, compliance with food restrictions and whether medicines were taken on schedule. Adherence determinants classified into five groups: patient variables, treatment regimens, disease characteristics, patient provider relationship and clinical setting were examined using the questionnaire. These variables were evaluated because studies have shown that they might potentially have an impact on adherence to ART in resource limited settings (Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002; Fong *et al.*, 2003; Orrell *et al.*, 2003; Weiser *et al.*, 2003; Nachega *et al.*, 2004; Nemes *et al.*, 2004; Stout *et al.*, 2004; Byakika-Tusiime *et al.*, 2005; Safren *et al.*, 2005).

Viral load data using the Amplicor HIV-1 Monitor Test, Version 1.5

The Clinical Associate (CA) requested for the viral load test to be conducted by signing the viral load order form (Appendix 8). After the participants were interviewed by the data collectors (Figure 3.3), they presented the signed form to the facility's Phlebotomist who took blood samples. The Phlebotomists used a standard protocol approved by the ACTION project to collect process and transport blood samples for the viral load assay (Appendixes 9 and 10). Processed blood samples were shipped to the PEPFAR laboratory for the viral load assay according to the standard protocol (Appendix 11).

Figure 3.3 A Phlebotomist taking blood sample from a participant

Viral load assay

The PEPFAR trained medical laboratory scientists used the approved ACTIONs' viral load assay protocol (Appendix 11) for the assay (Figure 3.4). Viral load results were recorded in the viral load template and then extracted into the viral load form (Appendix 8) for the data analysis.

Figure 3.4 A PEPFAR trained medical laboratory scientist performing viral assay

The Amplicor HIV-1 Monitor Test, Version 1.5 was used for the assay. The instrument measures the plasma HIV-1 viral load using the Polymerase Chain Reaction (PCR) and could detect up to 200 copies of viral RNA and is used to monitor the effects of anti-retroviral therapy by measuring changes in plasma HIV-1 RNA levels during the course of anti-retroviral treatment. However, the base line for viral undetectability according to the Nigerian treatment guideline is <400 copies/µl^3. Participants with viral loads above this level were reviewed by clinicians and treatment regimen switched. In the data analysis, <400 copies/µl^3 was used as the base line for validating adherence information provided by the participants.

Patients' prescription refill data using CAREWare

Data generated by pharmacists during routine dispensing are entered in real-time into CAREWare – computer software for health management information system. The data include the identity of the patient (name, hospital number and PEPFAR ID), date ART was initiated, date medications were dispensed, the formulations dispensed and the quantity of each formulation dispensed.

During the data collection, the facility CAREWare specialist was given a list with hospital numbers and PEPFAR IDs of participants who were interviewed. The prescription refill records of each participant for 360 days, starting from May 2009 to April 2010 were collected and entered into the retrospective pharmacy record form for analysis. To maintain participants' confidentiality, prescription refill data did not reflect their names and the captured data were destroyed immediately the relevant ones were extracted into retrospective pharmacy record form.

Patient CD4 data using the patient folders

As part of routine clinical care, physicians conduct physical examination and order for laboratory tests, CD4 counts as well as other tests vital for both managing and reviewing the progress of treatment. Data generated from the laboratory tests and physical examinations are entered into the patient's folders and are retained in the record department. During the data collection, the facility record staff in charge of the folders was given a list containing the hospital numbers and PEPFAR IDs of the 502 participants who were interviewed. He extracted the participants' latest CD4 and entered them into the patient clinical characteristic form for data analysis.

3.7 Data Management

To ensure data integrity during the data collection phase, efforts were made to streamline the process and maintain confidentiality. All forms necessary for a particular interview (i.e., participant's identification, consent form, data collection tools and viral load form) were collated and placed in plastic bags so that interviewers could easily pick up full and complete interviewing packages. Interviewers asked every question in the questionnaire; before leaving each interview, they double-checked the questionnaire for any accidental omissions. Whenever possible, an attempt was made to obtain any data omitted during the interview from the relevant participants. The principal investigator periodically (every two or three days) reviewed data tools from interviews for completion. The data were entered into an ACCESS base template and later uploaded into secured SPSS master files. To ensure accuracy, the data were double-entered and hand-checked. In addition, the data were closely monitored for missing lines, blanks, outliers, inappropriate or impossible values, and illogical values for logical combinations of variables by evaluating frequency distributions. Data entry was concurrent with data collection, so that to the extent possible and necessary, interviewers could be briefed on any noted patterns of data collection errors.

3.8 Data Analysis

Data were captured on Microsoft Excel 2007 and imported in SPSS Version 16 for Windows. Descriptive statistics including sum, frequency, mean, mode, median, proportion, range and percentage distribution were applied in the analysis of data variables. Measures of association were tested by cross-tabulation of variables of interest using Chi-square. A *p*-value of less than

0.05 was considered statistically significant. All co-variables (e.g. age) with $p<0.05$ were described as having significant effect, difference or influence on the variable of interest (missed dose adherence or prescription refill adherence). Both sets of criteria for measuring adherence (not missing dose, correct dose, frequency and schedule) were analyzed using descriptive statistics.

Analysis of adherence to ART

Five criteria, namely not missing a dose, correct dose, correct frequency, correct schedule and total adherence, were used to assess adherence by self-report

a) "Not missing a dose" criterion

To assess adherence by not missing dose criterion, participants were asked, "How many of the doses did you miss in the last 3 days?" The responses they gave were cross checked against a set of options: 0, 1, 2, 3, 4, 5 and 6; representing the possible doses a participant could missed in 3 days. For a medication that is taken twelve hourly (most of the ARV drugs are taken twelve hourly), a maximum of 6 doses are taken in 3 days (2 x 3). To achieve ≥95 adherence, a patient can only miss 0.3 doses in three days (5.7 x 100/6). A participant was considered adherent under this criterion if he/she missed 0.3 doses but since missing 0.3 doses is equivalent to not missing a dose, patients that did not miss a dose in the past 3 days were considered adherent.

b) Correct dose adherence criterion

To assess adherence by correct dose, participants were asked, "In the last 3 days, how many

tablets of this medicine did you take in one dose?" The responses they gave were compared with the officially approved doses to determine whether the correct dose was taken or not. If the correct dose was taken, the interviewer ticked the option, "Yes" and "No" if the wrong dose was taken. A participant was considered adherent under this criterion if he/she reported taking 95 – 100% of the correct doses in the past 3 days.

c) Correct frequency adherence criterion

To measure adherence by this criterion, participants were asked, "In the last 3 days, how many times in a day did you take this medicine?" The responses they gave were compared with the officially approved frequencies to determine whether the correct frequency was complied with or not. If there was compliance with the correct frequency, the interviewer ticked the option, "Yes" otherwise, "No" if there was no compliance. A participant was considered adherent under this criterion if he/she reported complying with the correct frequencies at a level of 95 – 100% in the past 3 days.

d) Correct schedule adherence criterion

A schedule refers to the time interval between doses. For instance, a drug regimen that is taken two times daily will require a twelve-hour time interval; the first dose taken at 7am and the second dose taken at 7pm to maintain the twelve-hourly interval. To measure adherence by this criterion, participants were asked: "At what times were you taking this medicine in a day for the past 3 days (specify the hours e.g. 8am and 8pm)?" The response they gave was compared with the officially approved schedule to determine whether the correct schedule was complied with or not. If drugs were taken on schedule, the interviewer ticked, "Yes" otherwise, "No," if outside

schedule. A participant was considered adherent under this criterion if he/she reported complying with the correct schedule at a level of 95 – 100% in the past 3 days.

e) Total adherence

Total adherence was measured on the basis of taking 95–100% of prescribed drugs in correct doses, correct frequencies and correct schedule during the previous three days.

Prescription refill adherence

Adherence by prescription refill is defined as having medication for 95% of the review period – the review period was 360 days (May 2009 to April, 2010). A patient who had 95% of review period covered by the ART medications is considered adherent by prescription refill. It is calculated using the formula:

$$\text{Adherence Rate} = \frac{\text{Number of days covered by drugs} \times 100}{\text{Review Period (in days).}}$$

3.9 Validity

The validity of the study was enhanced by minimizing selection and information biases (Myer and Karim, 2007).

a) Selection bias

Selection bias was minimized by adopting inclusion criteria that ensured the sample has the same characteristics with the target population. Furthermore, each respondent had an equal and independent chance of being selected by the systematic sampling strategy applied.

b) Information bias

Validation of self-reported adherence with viral load testing

Social desirability bias, in which participants respond to particular questions with the answers that they consider to be most socially desirable (or least stigmatizing), rather than answering with complete honesty, is a significant bias with the self-reported adherence (Chesney, 2006; Myer and Karim, 2007). To control for information bias, viral load test was requested from respondents who consented to the interview. As optimum adherence correlates with undetectable viral load level (UDVL) (Paterson *et al.*, 2000; Arnsten *et al.*, 2001), it is argued that respondents who have been taking their medications as prescribed for a long period should have undetectable viral load level. So, by measuring both validated viral load adherence and non-viral load adherence, social desirability bias was largely accounted for.

Exit interviews

Asking questions in a consistent way minimizes information bias (WHO, 2008). Hence, questions were asked in a consistent way using the structured exit questionnaire. For instance, "In the last 3 days, how many tablets of this medicine did you take in one dose?" and "How many of the doses did you miss in the last 3 days?" were consistently asked to all the

participants. Additionally, data collectors were friendly and non-judgmental as they asked critical questions on adherence (Fig. 3.5).

Figure 3.5 A data collector being friendly during an interview with a participant

.

Training of data collectors

Four Pharmacy graduates (two males and two females) were recruited for the data collection. They were fluent in Hausa and English and could use either of the languages depending on which one the respondents could understand. Additionally, they were indigenes of local communities who share similar culture and traditions with majority of the respondents so that cultural differences did not inhibit data collection.

Training slides on the basic concepts of ART and adherence to ART were developed using the Nigerian treatment guideline and the most current literatures on the subject. The International Network for the Rational Use of Drugs-Initiative on Adherence for Anti-retrovirals (INRUD-

IAA) was contacted through Professor Richard Laing and John Chalker and additional training slides on data collection were provided. These slides were utilized throughout the duration of the training which lasted for three days consecutively.

During the training, data collectors were instructed to ask questions in simple English. However, for patients who could not understand English, Hausa was to be used. Collectors were further instructed to ask questions in a unified way and to be pleasant and polite rather than being officious or speak with technical words. They were also to dress casually so as to make the participants to feel at home in giving real information. Practical demonstration on how the data would be collected was presented using the collectors as the participants. The data collectors were allowed to ask questions and made in-puts on the logistics of data collection during the training. The cost of transportation and the little financial assistance for the collectors were discussed and agreed upon. From the financial support provided by the UMD Fogarty AITRP (UMD AITRP 5-D43 TW 01041) (Appendix 2) for the study, each data collector was paid ₦10, 000.00 ($67.00) at the end of the data collection period, which lasted for two and a half months. Also, data collectors were trained to conduct interview with a deep sense of concern, care and friendliness so as to get real information from the participants

Anonymity of data collectors

The data collectors had no knowledge of the participants and their past experiences with the use of the ART medications. Furthermore, they were not health staff of the study center as a result, the respondents were free to speak about their experiences with the use of the medications because they knew that any information they provided would be kept confidential. Thus, the

information they provided was likely to be honest.

3.10 Reliability

According to studies, the reliability of a study can be enhanced by addressing two factors: random sampling error and random measurement error (Myer and Karim, 2007).

Random sampling error

To minimize random sampling error, a large sample of 502 respondents was taken. It is argued that a large sample is similar to the target population than a smaller sample and similarity of the sample to the target population minimizes random sampling error (Myer and Karim, 2007; Grimes and Schuz, 2002; Beaglehole, Bonita and Kjellstrom, 2006).

Random measurement error

The use of standardized, tested and precise measurement instruments has been recommended for minimizing random measurement error (Myer and Karim, 2007). As a result, the measurement instruments that were used namely, the exit interview questionnaire, Amplicor Monitor Test Version 5.1 and CAREWare, were tested before they were deployed for the data collection.

The exit interview questionnaire had been pretested in Uganda, Ethiopia, Rwanda and Kenya by the INRUD-IAA. As Nigeria is also a resource limited nation as these nations, the tools were adopted and pretested twice. First, on the data collectors outside the study center and second, on 10 respondents randomly selected at the study center. After the pretesting, the tools were modified to match the local standard. Modification of the tools with the data collectors improved the reliability of the tools and the confidence of the data collectors to use the tools effectively.

The Amplicor Test machine was in a functional state before it was deployed for the viral load test. Additionally, its precision was tested against a standard test specified in the approved protocol. Tests were repeated if the viral load result varied with the result of the standard test.

3.11 Generalizability

The result of this study could only apply to this study population. However, a large sample size, systematic random sampling and appropriate inclusion criteria were adopted to improve the generalization of the findings in adult HIV/AIDS patients in the FCT.

3.12 Ethical considerations

To meet the legal requirements, the study was approved by the human research ethical committees of the University of Western Cape (UWC), Institute of Human Virology, Nigeria and University of Abuja Teaching Hospital. Furthermore, blood samples were collected in accordance with the ethical standards prescribed by the University of Abuja Teaching Hospital committee on human experimentation and with the Helsinki Declaration. Also, socio-demographic and adherence data, viral load, patient's prescription refill and patients' clinical characteristics data were collected from participants who consented. Facility Manager, data collectors and participants authorized the taking of photographs by a certified photographer.

CHAPTER FOUR

RESULTS

4.1 Introduction

A total of 537 patients consented to be interviewed; 6 did not have viral load test data. During the data cleaning, it was found that 28 participants had incomplete prescription refill data and one (1) was younger than 18 years. Thus, 35 participants were excluded leaving a total of 502 subjects entered into the analysis (Figure 4.1).

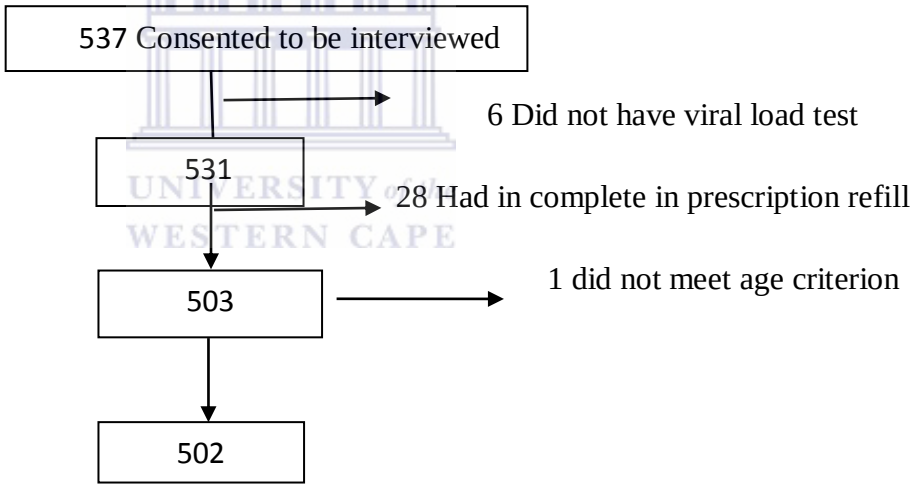


Figure 4.1 Recruitment of patients to the study

4.2 Socio-demographic characteristics of participants

Equal proportions of females (n=254; 50.6%) and males (n=248; 49.4%) participated in the study. Male participants were on average older (p <0.001) than the females; with the median age for males being 42 years (IQR: 38 – 44 years) and the females 36 years (IQR: 30-40 years) (Table 4.1). Most men were in monogamous married relationships (68.1% vs. 37.8%).

Significantly (p <0.001) more female than male participants were single (24.8% vs. 15.3%) or widowed (25.6% vs. 7.7 %). More male participants had higher education (71% and 9% had secondary and tertiary education, respectively) compared to female participants (63.4% and 4.7%) (p =0.017). Also, significantly more females than males in the study (13% vs. 5.2%) had none or informal education (Quranic education). More men had formal employment (private business which includes, artisans (automobile mechanic, furniture makers), business/traders, civil servants and professional executives) compared to females in the study (84.2% vs. 68.9%); female participants, on the other hand, were significantly more in the informal employment sector (household/domestic work, housekeeping and farming) (p <0.001) (18.9% vs. 9.7%), or unemployed (12.2% vs. 6.0% for men, p <0.001) than the males. Most participants were Christians (77%); with some Muslims (23%).

Table 4.1 Socio-demographic characteristics of respondents

Socio-demographic characteristics	TOTAL		Male		Female		p
	n	%	n	%	n	%	
Age (in Years)							< 0.001
< 21	2	0.40	1	0.4	1	0.4	
21 – 30	84	16.7	16	6.5	68	26.8	
31 – 40	216	43.1	88	35.5	128	50.4	
41 – 50	148	29.5	104	41.9	44	17.3	
51 – 60	49	9.8	38	15.3	11	4.3	
>60	3	0.60	1	0.4	2	0.4	
Marital status							< 0.001
Single	101	20.1	38	53.3	63	24.8	
Married, monogamous	265	52.8	169	68.1	96	37.8	
Married, polygamous	38	7.6	18	7.3	20	7.9	
Widow	98	19.5	23	9.3	75	29.5	
Education							0.017
None/Informal	46	9.2	13	5.2	33	13.0	
Primary	84	16.7	36	14.6	48	18.9	
Secondary	337	67.1	176	71.0	161	63.4	
Tertiary	35	6.9	23	9.2	12	4.7	
Occupation							<0.001
Formal Employment	384	76.5	209	84.2	175	68.9	
Informal Employment	72	14.3	24	9.7	48	18.9	
Unemployed	46	9.2	15	6.0	31	12.2	
Religion							0.597
Christianity	388	77.3	191	77.0	197	77.6	
Islam	113	22.5	56	22.6	57	22.4	
Traditional	1	0.0004	1	0.4	0	0	

4.3 Clinical characteristics of participants

Participants were on therapy for an average of 43±27 months but the females' had been on therapy for a longer period (46.8±10.4) compared with the males (38.9±18.6) (Table) 4.1. Most respondents were on Combipak^{R} (40.8%) or Truvada^{R} regimens (32.3%); using a twice-daily-regimen (85.9%) with 2-4 pills daily (80.5%). Less than half of all participants (48%) experienced side effects with their medications. Most participants (80.3%) had undetectable viral load (<400 copies/μl^{3}); significantly more female (66.5%) than male (43.5%) participants' achieved a CD4 count above 350 copies/μl^{3} (p=<0.001).

Table 4.2 Clinical characteristics of participants

Clinical characteristics	TOTAL		Female		Male		*P*
	n	%	n	%	n	%	
Months on therapy							0.03*
12 - 24	61	12.2	45	17.8	16	24.7	
25 - 36	98	19.5	42	16.6	56	22.7	
37 - 48	118	23.5	69	27.3	49	19.8	
>48	178	35.4	97	38.3	81	32.8	
Regimen							0.200
Combivir^{R}	56	11.4	17	6.7	39	15.7	
Combipak^{R}	201	40.8	116	45.7	85	34.3	
Triomune^{R}	31	6.3	18	7.1	13	5.2	
Truvada^{R}	159	32.3	80	31.5	79	31.9	
TDF/3TC/LPV/r	46	9.2	19	7.5	27	10.9	
Frequency of dosing							<0.001*
Once daily	71	14.1	10	3.9	61	24.6	
Twice daily	431	85.9	244	96.1	187	75.4	
Daily pill burden							<0.044*
2 - 4	404	80.5	207	81.5	197	79.4	
5 -7	93	18.5	44	17.3	49	19.8	
>8	5	1.0	3	1.2	2	0.8	
Experienced side effects	241	48	119	46.7	132	53.6	0.72
CD4 - count							<0.001*
<350	225	44.8	85	33.5	140	56.5	
>350	277	55.2	169	66.5	108	43.5	
Viral load							0.126
<400	403	80.3	196	77.2	207	83.5	
400 - 999	26	5.2	12	4.7	14	5.6	
1000-3000	22	4.3	15	5.9	7	2.8	
>3000	51	10.2	31	12.2	20	8.1	

***** ***Statistically significant***

4.4 Behavioral characteristics of participants

Most participants (95%) have disclosed their HIV status to family members (spouse, children or close relative) (90.4%), close friends (8.8%) or a religious leader (0.8%) (Fig 4.2). Almost all the participants (99.6%) knew the correct doses of prescribed medications. Similarly, 99.6% knew

the correct frequencies of administration (p=0.324) and 95.0 % knew the correct schedules of administration (p=0.236) (Table 4.3).

Table 4.3: Behavioral characteristics of participants

Behavioural Characteristic	**Total**		**Female**		**Male**		***p***
	n	**%**	**n**	**%**	**n**	**%**	
HIV disclosure	477	95.0	248	97.6	239	96.4	0.258
Knowledge of correct dose	500	99.6	253	99.6	247	99.6	0.37
Knowledge of correct frequency	500	99.6	253	99.6	247	99.6	0.324
Knowledge of correct schedule	477	95.0	239	94.1	238	96.0	0.236

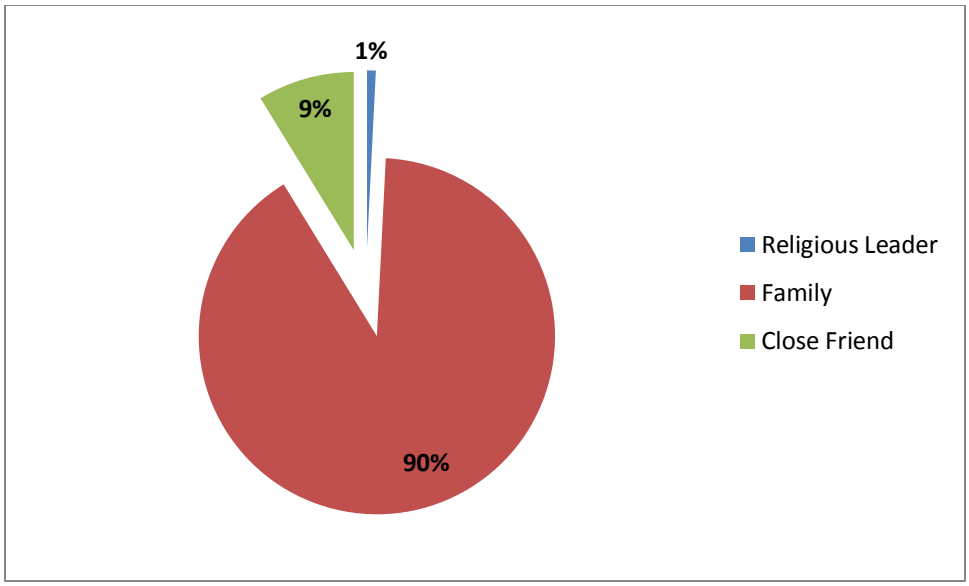


Figure 4.2 Targets of HIV disclosure

4.5 Adherence

The current study found that 95.0% of participants did not a miss a dose of their medication in the past 3 days while 99.6% took the correct doses of medication in the past 3 days. Also, 99.6% and 95.0% took their medications at the correct frequencies and on schedule in the past 3 days respectively. Total adherence – defined as taking 95–100% of prescribed medication in correct doses, at the correct frequencies and correct schedule during the previous three days - was only 53.6% (p=<0.001). Significantly more male than female participants had total correct adherence over the previous three days (56.9% vs 43.1%; p=<0.001). Correct adherence based on prescription refill count over a period of 360 days was 62.5% (Table 4.3).

Table 4.4: Self-reported and prescription adherence

Adherence	Total		Female		Male		*P*
	n	%	n	%	n	%	
Self-report over past 3 days							
Not missing a dose	477	95.0	238	93.7	239	96.4	0.169
Correct dose	500	99.6	253	99.6	247	99.6	0.37
Correct frequency	500	99.6	253	99.6	247	99.6	0.324
Correct schedule	477	95.0	239	94.1	238	96.0	0.236
Total correct adherence	269	53.6	116	45.7	153	61.7	<0.001
Prescription refill count over 360 days	314	62.5	163	64.2	151	60.9	0.447

Barriers to adherence to ART

The reasons for not adhering to prescribed medication among the participants (n= 25) that missed a dose of prescribed medication in the past 3 days were assessed. The study found that, 43% of participants missed a dose because they forgot to take their medication and, 21% said they travelled away from their homes, which was the reason for missing their medications. Similarly, 16% of participants said they ran out of medication, 13% were busy at work, 5% lacked food and 2% had their medication snatched by armed robbers (Figure 4.3). Thus, the psychosocial factors of forgetfulness, and travelling away from home and the structural problem of running out of medication were the common barriers to ART.

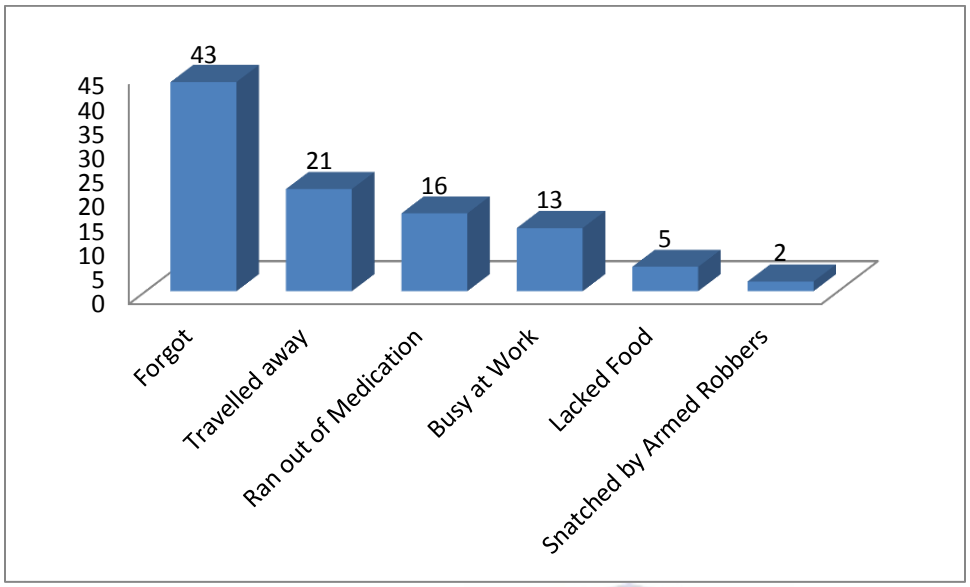


Figure 4.3 Reasons for missing doses

Facilitators of adherence to ART

The reasons for adhering to the prescribed medication were evaluated among the participants (n=477) who did not miss a dose of their medication in the past 3 days. The participants said they were motivated to take their medication because their "health condition improved (40%)"; and they "desired to live" (30.0%), had "family support" (22.0%) and "support group" (8.0%) (Figures 4.4).

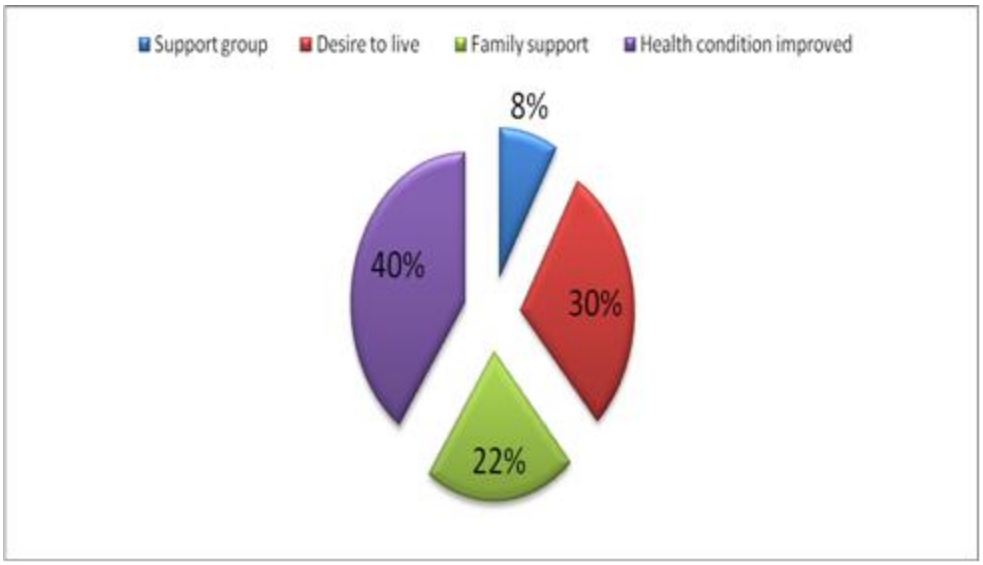


Figure 4.4 Reasons for not missing doses

4.6 Health system factors

Drug availability

Most participants (99.6%) were given all the prescribed ARV medication.

Distance travelled, travel cost and time spent in the clinic

Participants spent on average 100 minutes (IQR: 40 – 180 minutes) to travel to the study center (Figure 4.5). The median traveling cost to the clinic was ₦500 (IQR: ₦250- 900 for females and ₦250- ₦1000 for males; corresponding to a total IQR of 250-1000) (Figure 4.6). Female respondents spend a median of 260 minutes (IQR = 200-340) in the clinic while the males spend a median of 300 minutes (IQR: 240-380) (Figure 4.7).

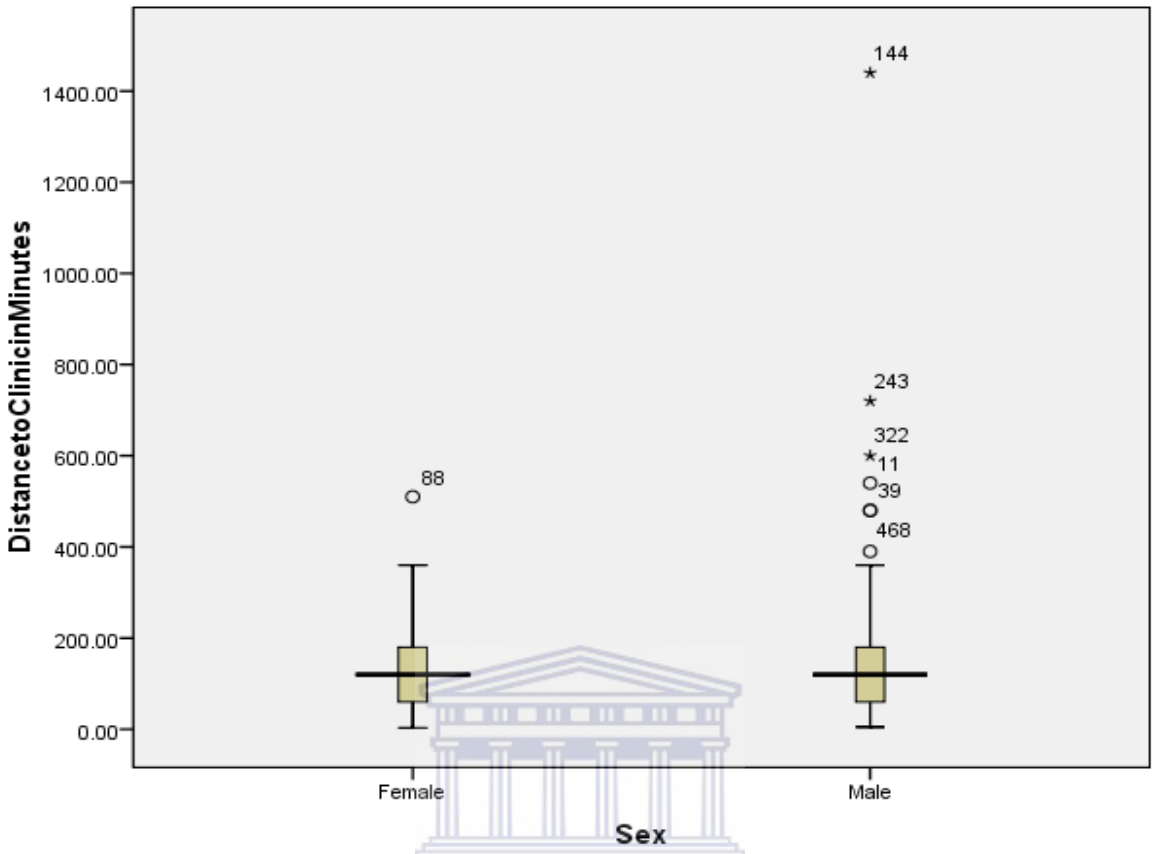


Figure 4.5 Distance travelled to ART clinic

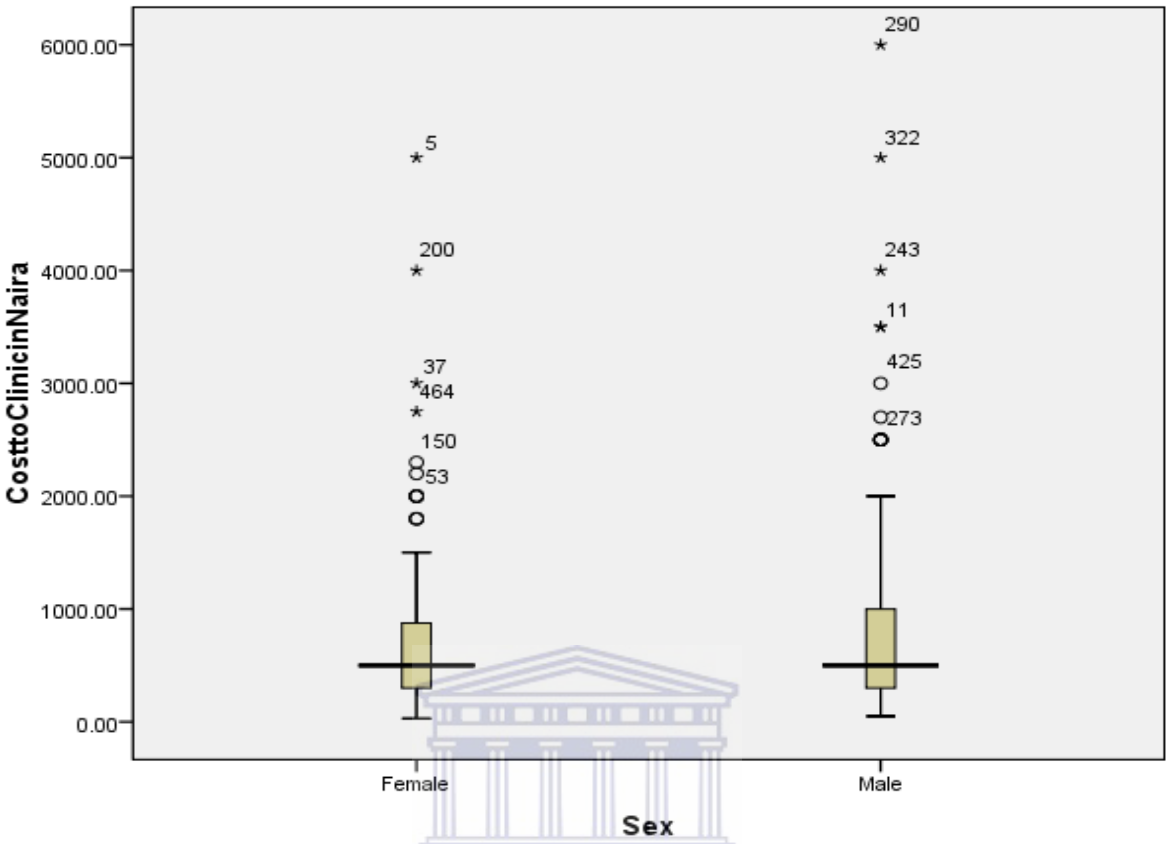


Figure 4.6 Travel cost to ART clinic

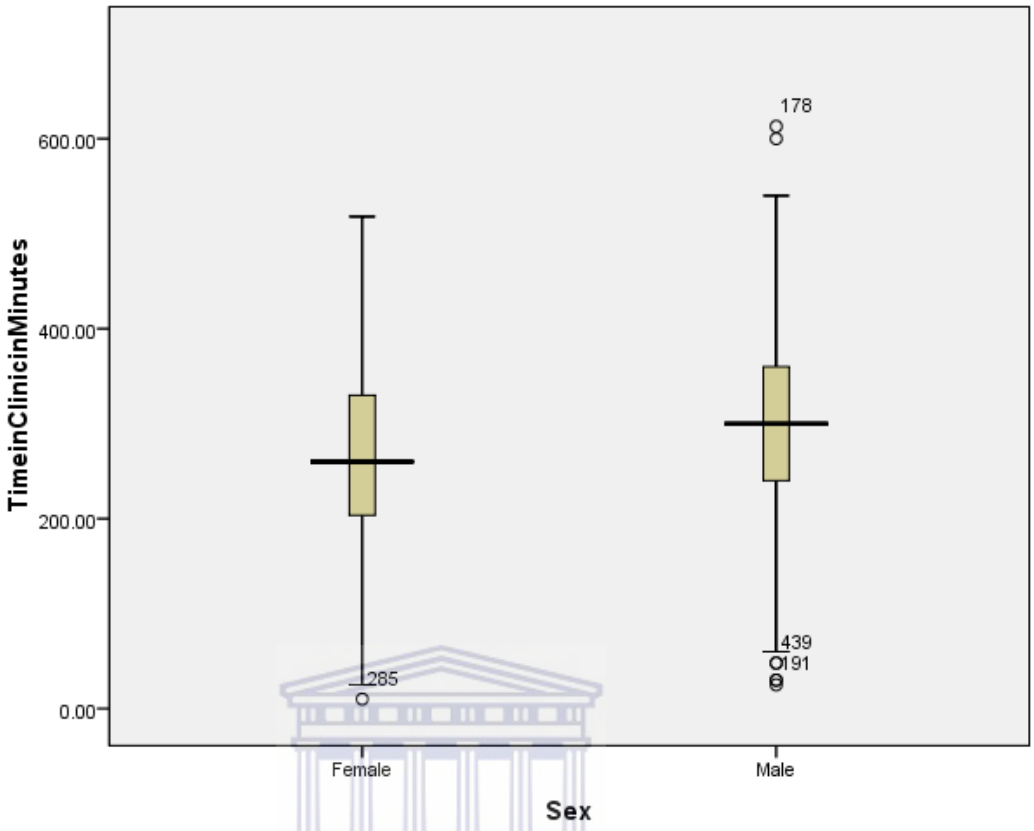


Figure 4.7 Time spent in ART clinic

4.7 Factors associated with adherence

A positively statistically significant association was found between adherence and age; adults that were 30 years or less were 2.5 times more likely to adhere to their medications compared with those that were more than 30 years (OR = 2.5; 95% CI = 1.26-4.61; p = 0.023). The study also found a strong statistically significant positive association between adherence and viral load. Participants with viral loads of <400 copies/μl^3 were 7 times more likely to adhere to their medication than those with a viral load >400 copies/μl^3 (OR = 6.6; 95% CI = 1.6- 11.07; p = 0.001). However, no statically significant association was found between adherence and marital status (p = 0.111); education (p = 0.331) and occupation (p= 0.147). Similarly, no significant

association was between adherence and CD4 count (p=0.281), second line regimen (p=0.466) and pill burden (p=0.320) as well as experiencing side effects (p=0.372). Also, the distance that participants travelled to the ART Clinic to access treatment (p=0.460), the cost of travel to the clinic (p=0.102) as well as the time they spend in the clinic (p=0.210) to receive drugs were not significantly associated with adherence (Table 4.5).

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Table 4.5 Factors associated with adherence over previous 3 days

Variable	Optimal Adherence	Suboptimal Adherence	Odd ratio (95% CI)	P-value
Age (in years)				
> 30	239	177	Ref	
≤30	30	56	2.5 (1.26-4.61)	0.023*
Marital Status				
Ever Married	214	187	Ref	
Single (Widow/Divorce/Separated	55	46	0.9 (0.26-2.19)	0.111
Education				
None/Informal	28	22	Ref	
Formal	241	211	1.1 (0.31-5.14)	0.331
Occupation				
Formal Employment	201	183	Ref	
Informal Employment (unemployment)	68	50	0.8 (0.28-3.84)	0.147
CD4 count				
<350 copies/μl^3	112	113	Ref	
>350 copies/μl^3	157	120	0.8 (0.13-1.62)	0.281
Viral load				
> 400	84	15	Ref	0.001*
<400	185	218	6.6 (1.6- 11.07)	
Type of regimen				
1st Line regimen	156	124	Ref	0.466
2nd Line regimen	113	109	1.2 (0.23-9.6)	
Pill Burden				
>12 pills	95	79	Ref	
<12 pills	174	154	1.0 (0.12-2.34)	0.320
Experienced side effects				
No	182	122	Ref	
Yes	87	111	1.9 (0.24-5.32)	0.372
Distance to clinic				
>100 minutes	152	119	Ref	
<100 minutes	117	114	1.2 (0.11-3.02)	0.460
Cost to clinic				
>₦500.00	164	116	Ref	
<₦500.00	105	117	1.6 (0.55-8.16)	0.102
Time in Clinic				
>260 minutes	171	143	Ref	
<260 minutes	98	90	1.1 (0.34-2.10)	0.210

**Statiscally significant*

4.8 Summary

Of the 502 participants, 254 were women and 248 men, with majority on ART for a mean of 43±27.1 months. Total adherence as measured by self-report was 53.6% (not missing dose (95.0%); correct dose (99.6%); correct frequency (99.6%), correct schedule (95.0%). However, prescription adherence was 62.5% and 80.30% of participants achieved virologic suppression at a level of <400 copies/μl^3. Factors that constituted barriers to adherence were: forgot – 43%; travelled away from home – 21%; ran out of medication – 16%; busy at work – 13%; lack of food – 5% and snatched by armed robbers – 2%. The adherence facilitators were: health condition improved – 40%; desire to live – 30%; family support – 22%; and support group – 8%.

Adherence was positively and significantly associated with age; adults ≤30 years were 2.5 more likely to adhere to their medications compared with those ≥30 years (OR = 2.5; 95% CI = 1.26-4.61; p = 0.023). Similarly, adherence was positively and significantly associated with viral load; participants with viral load of ≤400 copies/μl^3 were 7 times more likely to adhere to their regimens compared with those with viral load ≥400 copies/μl^3 (OR = 6.6; 95% CI = 1.6- 11.07; p = 0.001). No positive associations were found between adherence to ART and marital status (p= 0.111); education (p= 0.331); occupation (p = 0.147); CD4 count (p=0.281); regimen type (p=0.466); pill burden (p= 0.320); experienced side effects (p =0.372); distance to clinic (p = 0.460); cost to clinic (p= 0.102) and time spent in the clinic (p= 0.210).

CHAPTER FIVE

DISCUSSION

5.1 Introduction

Nigeria was facing HIV/AIDS crisis at the time this study was conducted in 2010. It was ranked third among the nations with the largest population of people living with HIV/AIDS in the world (FMOH, 2009). In 2010, a presidential directive to expand ART to remote areas was issued in an effort to stem the epidemic. This study set out to investigate adherence to antiretroviral therapy as well as analyse the factors that might constrain (barriers) and motivate (facilitators) adherence among adults who were on highly active anti-retroviral therapy in the Federal Capital Territory, Abuja, Nigeria, from 2005 to 2010. The specific objectives of the study were to: measure the level of adherence to the ART; describe the socio-demographic characteristics of adult ART patients on the HAART; describe the clinical characteristics of adult ART patients and analyse the factors that constrain and facilitate ART adherence.

5.2 The socio-demographic characteristics of adult ART patients on the HAART

An equal proportion of women and men (50.6% vs 49.4%) participated in the study. This does not reflect the HIV prevalence across gender in Nigeria; 1.8 million women as against 1.3 million men were living with the HIV at the end of 2010 (FMOH, 2010). The reason for the uniformity in the proportions of men and women in the current study may be due to how the participants were selected for the interview. The study devised a strategy that allowed an equal

number of men and women to be included in the study population. This was done to increase the internal validity of the study as well as enable a valid comparison between the characteristics of men and women.

A vast majority of participants (82.2%) were older adults (above 30 years) with only a few (17.1%) younger adults (30 years or less). It is difficult to use the predominance of older people in this study to argue for a generational shift in the burden of HIV in sub-Saharan Africa where, younger adults are still the worst victims of HIV/AIDS (UNAIDS, 2008). The current study excluded younger persons less than 18 years, and the proportion of younger males and females who were less than 21 years was very small (0.8%); this may explain the reason for the low proportion of younger people in the study. However, it is important to high light the fact that it is the younger adults (≤30 years) that were 2.5 times more likely to adhere to their medications compared with the older adults (OR = 2.5; 95% CI: 1.26-4.6). This finding is not consistent with the Los Angeles study that found older subjects to be three times more likely to be good adherers than the younger subjects (OR = 3.1, 95% CI: 1.40-6.76) (Hinkin *et al*., 2004). The finding is not also consistent with a South Africa study where adolescents and young adults were found to have poor adherence and poor virologic outcomes than do adults (Nachega *et al*., 2009a).

There were more married men than women among the participants (68.1% men vs. 37.8% women). More female participants were single or widowed which is consistent with the current HIV prevalence in Nigeria: lower HIV prevalence (4.9%) was reported among married women

compared with women who were single (5.6%) while women who were divorced, separated or widowed were reported to have the highest prevalence rate (6.9%) (FMOH, 2010).

Male participants had significantly higher education than the females which reflects the literacy level in Nigeria: more men than women go to school particularly in the north. The current study did not find statistically significant association between adherence and education, which agrees with the finding of Eldred and his team where higher education was not found to predict adherence to ART (Eldred *et al.*, 1998).

Most men had formal employments [private business which includes, artisans (automobile mechanic, furniture makers), business/traders, civil servants and professional executives] compared with women (84.2% vs. 68.9% for women). Female participants, on the other hand, were significantly more in the informal employment sector (household/domestic work, housekeeping and farming) (p=<0.001) compared with the men (18.9% vs. 9.7% for men). These findings are consistent with the labour market situation in Nigeria: women were higher in proportion (57%) in informal employment, but in the formal sectors, they accounted for only 39% (Ogwumike, Alaba, Alaba, Alayande and Okojie, 2005). The current study did not find occupation (formal or informal) to be associated with adherence to ART. This contradicts the claim in some studies that economic support is directly related to the level of adherence to ART (Gordillo *et al.*, 1999; WHO, 2006a). The Brazilian study (Pelotas, Southern Brazil), also found that no significant association existed between poverty and adherence which further strengthen the argument that poverty may not be a predictor of poor adherence to ART under every circumstance (Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002).

5.3 Clinical characteristics of adult ART patients

Viral load

A vast majority of participants (80.3%) who were adherent to their regimens at a level of ≥95%, achieved undetectable viral load level (< 400 copies/μl^3). This finding is similar to the finding by Paterson *et al.* (2000) where 80% of patients with ≥95% adherence had undetectable viral load level. The current study also found a statistically significant and positive association between viral load and adherence to ART. This is consistent with the overwhelming conclusion that adherence to ART is associated with viral suppression (Paterson *et al.*, 2000; Safren, Kumarasamy, Raminani, Solomon and Mayer, 2005).

The positive and significant association between the reported adherence level and the corresponding virus load in the current study lent support to the reliability of the adherence assessment used in the current study. It also provides an insight into the quality of drugs at the treatment centre; the review of literature revealed that the type of drug and quality of drug contribute to viral suppression (Weiser *et al.*, 2004; Maggiolo *et al.*, 2005; Bangsberg *et al.*, 2007; Wainberg *et al.*, 2007; Bangsberg *et al.*, 2003; Harrigan *et al.*, 2005; King *et al.*, 2005). Thus, drugs with high quality will consequently suppress the viruses to undetectable viral load level even with suboptimal adherence (< 400 copies/μl^3). Since the current study found a significant association between virologic suppression and adherence to ART despite the fact that only 53.6% of the participants had optimal adherence, it suggests that the virologic suppression reported in the curret study may be as a result of the quality of drugs or the type of drugs and other factors rather than adherence to ART itself. If this is the case, then the stocking of high

quality drugs as well as storing drugs at the recommended temperatures should be sustained at the treatment centre.

CD4

There were more participants with CD4 counts above 350 copies/μl^3 compared with those with CD4 count of less than 350 copies/μl^3 (55.2% vs 44.8%). This is a good development considering the fact achieving higher CD4 counts is one of the goals of ART. However, participants that were still having CD4 count less than 350 copies/μl^3, despite being on treatment for twelf months may be struggling with immunological treatment failure since immunological treatment failure is assumed if there is a failure to achieve a CD4 cell count increase of 50 to 100 cells/μl^3 per year (FMOH, 2007). The WHO recommends regimen switch from first line to second line regimens for participants with treatment failure (WHO, 2009) but the current study found that majority of the participants were still using first line regimens, which suggests that the treatment centre may not be reviewing and switching patients to second line regimens as it should be. The health providers must pursue with greater seriousness the review of treatment and possible regimen switch inorder to improve quality of care and adherence to ART. No statistically significant association was found between CD4 and adherence to the ART in the current study. In most studies however, adherence to ART has been found to be a predictor of high CD4 count (Paterson *et al.*, 2000; Safren, Kumarasamy, Raminani, Solomon, and Mayer, 2005). The reported lack of association between CD4 count and adherence in the current study could be as a result of several reasons including the way the study was designed, immune system, nutritional status and socio-economic status of the participants and drug resistance.

Nonetheless, achieving high CD4 count remains the goal of antiretroviral therapy which ART program implementers must strive to achieve.

HIV status disclosure

Disclosure of HIV status was very high (95%) and disclosure to the family alone accounted for 90.0% (Table 4.3). This finding contradicts the general believe that people living with the HIV are not diposed to disclosing their HIV statuses due to the fear of stigmatization. Optimum adherence to ART has also been associated with the disclosure of HIV status on the ground that it promotes a strong internal commitment to treatment which leads to ART adherence (Reynolds *et al.,* 2004). In the current study, suboptimal adherence has been reported among the participants; this questions the impact of HIV disclosure in improving adherence to ART.

Months on therapy

Majority of participants had been on therapy for a mean of 43±27.1 months. This finding supports two findings of the current study. First, it supports the high viral suppression reported in this study (80.3% participants had < 400 copies/μl^3) because studies have shown that high viral suppression minimizes both morbidity and mortality and as a result, patients may live longer (Paterson *et al.*, 2000). It also supports the participants' claim that the treatment was improving their condition – the current study found that 43.0% of the participants gave "improvement in health condition" as the principal reason for adhering to their medications.

Treatment regimens

Our study found no significant association between adherence and type of regimen (first line and second line). However, most respondents were using the Combipak^{R} (40.8%) and Truvada^{R} based regimens (32.3%) which are classified as first line regimens under the Nigerian treatment guideline. Additionally, Combipak^{R} and Truvada^{R} are fixed dose combination of drugs and as such, only few pills are taken and they have manageable side effects with no food restriction. Medications with low pill burden, less side effects and frequency of dosing have been found to promote adherence to ART (Kleeberger, Phair, Strathdee, Detels, Kingsley and Jacobson, 2001; Eldred, Wu, Chaisson and Moore, 1998). They are usually preferred by clinicians and are the first treatment of choice according to studies (Bangalore, Kamalakkannan, Parkar and Messerli, 2007). In the current study, high adherence rates were found when adherence was measured by dose taken, frequency and compliance to schedule of administration. Jean-Baptiste (2008) also found a high adherence rate when adherence was measured by dose taken among patients who were on fixed dose Triommune than among those on multiple drug regimens. It is likely therefore, that the dependence on the FDCs at the treatment centre as found out in the current study is the reason for the reported high adherence rates when adherence was measured by dose, frequency and schedule of administration. But "total adherence" was only 53.6%, suggesting a failure to comply with frequency and schedule, which indicates that as treatment failure occurs and patients are switched to second line regimens, which are much more complicated and difficult to take, maintaining high level of adherence may not be possible.

Side effects of regimen

Majority of the participants (52.0%) did not experience side effects with their drugs and no significant association was found between adherence and the side effects of the ART drugs used in the current study. This is a strange finding because some studies have found that side effects of anti-retroviral drugs are predictors of poor adherence to ART (Ammassari *et al*., 2001b; Weiser *et al.*, 2003; Machtinger and Bangsberg, 2005; Weiser *et al.*, 2003; Roberts, 2000; Pinheiro, de Carvallo-Leite, Drachler and Silveira, 2002; Popa-Lissenanu *et al.*, 2005; Mills *et al.*, 2006a; Uzochukwu *et al.*, 2008). The reason for the lack of association between adherence and side effects in the current study may be related to the drug regimen the participants were using. As shown earlier, the regimens most participants were using have less and manageable side effects that may disappear within 4 months on therapy (Flexner, 2006). Since the participants had been on therapy for at least 43 months, it is likely that the side effects they experienced at the beginning of the therapy have disappeared at the time the current study was conducted. It is also argued that patients with HIV tolerate side effects better than patients with less severe chronic diseases, such as hypertension and diabetes mellitus (Mehta, Moore and Graham, 1997), because they are more aware of the adverse outcomes associated with poor adherence (Paterson *et al*., 2000). The studied population has benefitted from the formal counseling reported in the current study and as such, they were more likely to be aware of the danger of poor adherence and have developed tolerance to the side effects.

Pill burden and frequency of administration

Most participants (80.5%) were using twice-a-day regimen with low pill burden and frequency of administration but no positive significant association was found between pill burden and adherence to ART by the current study. This is consistent with the finding of Fong *et al.* (2003); pill burden, dosing frequency and dietary restriction did not predict a poorer drug adherence among Chinese patients who took more than 10 pills per day and thrice-a-day. It is noted that Government collaboration with PEPFAR in the ART program made it possible for fixed dose combination drugs with less pill burden to be supplied to the study center.

5.4 The health system factors

Drug availability at the study center

Almost all the participants (99.6%) were given all the antiretroviral medications prescribed; suggesting that the study center was adequately stocked with drugs. The World Health Organization recommends 4 regimens (AZT+3TC+EFV; AZT+3TC+NVP; TDF+3TC or FTC+EFV and TDF+3TC or FTC+NVP) for starting ART in ART-naïve individuals (WHO, 2009) but five different regimens were physically sighted at the time of the study which further indicates that the treatment centre was adequately stocked with drugs. Ideally, the constant availability of drugs at the treatment centre should lead to high adherence among the participants as drug availability has been associated with ART adherence (Mills *et al.*, 2006b). However, suboptimal adherence has been reported in the current study which reflects the thinking that sustaining high adherence to ART goes beyond having constant availability of products. Health providers must ensure that patients are properly counselled on the use of ART drugs which are

complicated and difficult to use. But this seems to be lacking at the treatment centre with the finding that only 53.6% of the participants were taking their drugs correctly with respect to dosing, frequency and schedule of administration.

Distance to clinic

Both male and female participants spend an average of 100 minutes (IQR: 40 – 200 minutes) to get to the clinic. Since most of the participants claimed they travelled by automobiles, a journey of 100 minutes (above 1.7 hours) is definitely a long distance. In Botswana, a similar finding by Weiser *et al*. (2003) showed that patients lived 800 to 1000km away from the clinic and had to travel that distance monthly. Citing treatment centres in Hospitals located in townships while majority of patients live in rural areas many kilometres away, is one reason patients have to travel long distances to access treatment. Also, the fear of stigmatization from the community might also force individuals to select treatment centres that are far away from them. A few studies actually show that stigma and discrimination forces HIV infected patients to engage in high-risk behaviour such as unsafe sex and travelling longer distances to access treatment to hide their HIV statuses (Qwana*et al*., 2000).

Cost to clinic

Both men and women paid on average, ₦500.00 (IQR for females and males: ₦250.00- ₦900.00 and ₦ 250.00- ₦1000.00 respectively) to get to the clinic. However, 75% of male participants paid more than the females' with as much as ₦1000.00). No study has been done to establish the

personal cost of accessing ART in Nigeria, but considering the high rate of unemployment (4.9%) with 70% of the population living below the poverty line (CIA, 2008), paying ₦1000 just to go to clinic is too expensive. It is difficult to explain why the men were paying more money on transportation than the women; it is likely that stigmatization might be the reason as male participants may select to pay more money and travel longer distances to access treatment to hide their health condition. This assumption is strengthened by the fact that stigmatization was reported to be a serious problem among patients on the ART in South East, Nigeria (Uzochukwu *et al.*, 2008).

Time in the clinic

The current study found that participants spend longer times in the clinic but women spend less time than men (a median of 260 minutes for females and 300 minutes for males). Similar studies in Botswana, Tanzania and Uganda found that a patient spend on an average of up to five hours waiting for consultation and medication (WHO, 2006b). Again, it is difficult to explain why the women spend less time than the men. But if men were travelling longer distances to arrive at the clinic late when the health workers were tired, that might affect the length of time they have to wait to be attended to. The study centre keeps the "first come, first serve" rule, i.e., those who come to the clinic first are served first and those who came late are served later.

The current study did not find statistically significant positive associations between distance to clinic, cost to clinic and time in clinic with adherence to ART. However, the lack of association does not in any way under rate the vital role that these factors play in constraining or motivating

adherence to ART. Studies have recommended the suggestions below for addressing long distance, high cost and long waiting time in the clinic (INRUD-IAA *et al.*, 2008). However, it should be noted that the effectiveness of these recommendations has not been tested and as such, caution is required.

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Distance to the clinic could be reduced by:

- providing patients with drugs for longer time and arrange for better laboratory services so that patients will not have to return so frequently
- Bring services closer to the patients, and use peripheral community-based health workers for drug distribution
- Give direct economic support and/or initiate income-generating programs
- Home delivery of drugs can also reduce distance and the cost of transportation; and some studies have shown that the use of home delivery of drugs appears to be effective in increasing adherence and decreasing viral loads.

Waiting times in clinics can be reduced by:

• Arranging more efficient flow of patients between different providers and stations appointment schedule,

• Splitting appointments into two half days,

• Keeping clinics open additional days,

• Increase number of staff

• Decentralize services to the communities

A multi-centre study in Uganda and Kenya recommended the deployment of the above strategies, although there are no evidence to prove their effectiveness on reducing the waiting time in clinic and subsequently improving adherence to the ART (INRUD-IAA *et al.,* 2008).

5.5 Behavioral characteristics

Knowledge of the ARV regimen

Most participants had knowledge of their antiretroviral medications – 99.6% knew the correct dosages, 99.6% knew the correct frequencies and 95.0% knew the correct schedules of administration (Table 4.3). The study centre places high premium on counseling and education and this may account for the knowledge of drugs by the participants. First, patients must complete a counseling course and be issued a certificate before commencing treatment. Second, patients compulsorily attend a health talk each time they visit the clinic to refill their prescriptions. The pharmacists and clinicians also provide some form of counseling to the patients as they attend to them. A high level of adherence is therefore expected at the treatment centre considering the fact that knowledge of drugs and patient counseling are associated with optimum adherence (Simoni *et al.,* 2006). However, the current study found a suboptimal adherence level, which does not support the knowledge of drugs by the participants. There is need to explore the factors that may be responsible for the suboptimal adherence to ART among

the participants despite having correct knowledge of dosing, frequency and schedule of drug administration.

5.6 Adherence to the ART in the FCT

Adherence by patient self-report

Adherence was measured using five different criteria: not missing dose, taking the correct dose, complying with the correct frequency, complying with the correct schedule and effective adherence. On the basis of not missing a dose in the past 3 days, adherence was 95.0%. However, on the basis of taking the correct dose, and complying with the correct frequencies and schedules of administration, adherence rates were 99.6%, 99.6% and 95.0% respectively. But when adherence was measured comprehensively (total adherence) by looking at correct dosing, frequency and schedule at the same time, the level dropped to only 53.6%, and significantly more men than women were adherent. Eighty point three percent (80.3%) of the participants who adhered to their drugs at a level of ≥95.0% had undetectable viral load level (Table 4.5). Prescription refill adherence was only 62.5%.

The above findings on the rates of adherence to ART make a strong case on seven important issues worth considering. These are: the reported suboptimal adherence rate by the current study; the reported high level of adherence in sub-Saharan Africa; suboptimal adherence with high viral suppression; different rates of adherence between men and women; validation of self-reported adherence information; and the measurement of adherence using the self-reported measure.

The reported suboptimal adherence rate by the current study

The 53.6% adherence rate for the FCT is suboptimal. Yet, disclosure of HIV status, constant availability of drugs and user friendly ARV regimens which have been shown to promote adherence to ART (Nachega*et al.*, 2010; da Salviera *et al.*, 2003) were reported at the study center by the current study. For instance, 95% participants disclosed their HIV status (Table 4.3), 99.6% had all the prescribed ARVs and most participants were using ARV regimen that had no dietary restriction and could be taken once or twice daily (Table 4.2). Why does suboptimal adherence persist in the midst of factors that ordinarily should have improved adherence to ART?

The current study did not explore the causes of suboptimal adherence; this is an area for future research. However, the failure to follow specific instruction around timing of taking medication may explain the suboptimal adherence level. As indicated above, adherence level was very high (95.0%) when measured by doses taken but when timing (frequency and scheduling) was considered together with the doses taken, the level went down to barely 53.6%. Essentially, patients thought they were adherent by simply taking the medication, but in truth it was only partial adherence because taking drugs off schedule does not allow adequate concentration of the drug in the blood and effective viral suppression cannot be guaranteed (Castleman, Seumo-Fosso and Cogill, 2003).

The suboptimal adherence level suggests that the adherence strategies that have been employed to improve adherence at the treatment center, which include treatment preparation and

counseling are not working as they should. There is need to develop an adherence model that would address taking medication on schedule among other factors. Future research must focus on this area so as to improve adherence to ART in the FCT.

The reported high adherence level in sub-Saharan Africa

Several studies in sub-Saharan Africa have reported very high adherence rates. For instance, a study in greater Cape Town reported a 93.5% adherence with 70.9% viral suppression (Orrell, Bangsberg, Badri and Wood, 2003b). The review of adherence studies from sub-Saharan Africa and North America by Mills *et al*. (2006b) also reported a higher pooled estimate of adherence in sub-Saharan Africa than in North America (77% vs 55%). Also, Nachega *et al* reported a median adherence level of more than 95% during a 2-year follow-up of patients from Cape Town, South Africa (Nachega *et al*., 2009b). However, the current study reported only 53.6% adherence rate which is a significant difference compared with the rates reported in other adherence studies.

Gill *et al* had argued that the high level of adherence to ART reported in sub-Saharan Africa is as a result of researchers using the self-reporting adherence measure (which overestimate adherence); taking smaller sample sizes; including participants that have been on therapy for shorter periods and using only one measure of adherence (e.g., number of pills taken) to evaluate adherence to ART (Gill *et al*., 2005). This argument is corroborated by Fong and his team; they reported a high adherence rate (80.7%) among Chinese patients on HAART but admitted that they did not measure adherence comprehensively, which according to them; led to the high adherence rate (Fong *et al.*, 2003). Similarly, Jean-Baptiste found that, adherence was very high

(99.9%) when measured by proportion of pills taken but dropped to only 73.0% when it was measured comprehensively (Jean-Baptiste, 2008). The current study is reporting a suboptimal adherence rate because adherence was measured comprehensively. If adherence had been measured by doses taken or not taken as done in other studies, the adherence level would have been 95.0% as stated above. The finding of the current study strongly questions the reported high adherence rates in Africa.Gill *et al.* (2005).

Suboptimal adherence with high viral suppression

The correlation between adherence and virologic suppression cannot be overstated. Studies have shown that with increase in the level of adherence, there is a corresponding increase in virologic suppression. For instance, a 95% adherence rate results in a virologic suppression success of more than 80%, while the success rate drops to 60% in patients with 80-94.9% adherences (Kleeber, Phair, Strathdee, Detels, Kingsley and Jacobson, 2001). In another study, it was found that as the level of adherence dropped to 90%, only 78% of patients could achieve UDVL (Arnsten*et al*., 2001). In the current study, the 53.6% adherence level is disproportionately lower than the 80.3% virologic suppression. In other word, suboptimal adherence persists in the midst of high viral suppression. One possible explanation for this is that adherence alone is not the only factor that contributes to virologic suppression eventhough; it is the principlal factor according to studies. Studies have shown that nutritional and immunal status of patients, the viral genome, socio-economic status, length of time on medication and the type of regimen can also affect virologic suppression (Weiser *et al.*, 2004; Maggiolo *et al.*, 2005; Bangsberg *et al.*, 2007; Wainberg *et al.*, 2007; Bangsberg *et al.*, 2004; Harrigan *et al.*, 2005; King *et al.*, 2005). It is

likely that these factors were responsible for the high viral suppression rather than adherence itself in the current study. If this is the case, achieving high level of adherence should not be the only focus of ART rather; all adherence determinants must be identified and addressed.

Different rates of adherence between men and women

The association between gender and adherence to ART has been a contentious problem. While several studies have failed to show a significant association between gender and antiretroviral adherence (Eldred *et al*., 1998; Moatti *et al*., 2000; Wagner *et al*., 2002; Carrieri *et al*., 2003; Holzemer *et al*., 1999; Bouhnik *et al*., 2002; Golin *et al*., 2002; Gordilo *et al*., 1999; Chesney *et al*., 2000; Paterson *et al*., 2000), a large body of studies have shown that women are less adherent than men (Arnsten *et al*., 2002; Turner *et al*., 2003; Altice *et al*., 2001; Delgado *et al*., 2003; Wenger *et al*., 1999; Montessori *et al*., 2000; Abriola *et al*., 2000; Arabe *et al*., 1998; Montaner *et al*., 2000). It is argued that most studies that found no association between gender and adherence were limited either by small numbers of women or by the use of self-report, which has been shown to overestimate adherence (Wagner, 2002). The current study included an equal proportion of men and women in the studied population and significantly more men than women were adherent (56.9% vs 43.1%; p=<0.001). This finding lent support to the conclusion that when it comes to adherence, it is the men that are getting it. But this is very strange because adherence to ART requires very stringent discipline with time keeping; the chaotic lifestyle associated with the behavior of most men cannot accomondate it. On the other hand, women are culturally more patient and would under normal circumstance want to live longer to take care of their children which is a strong motivation for adherence to ART. It is likely that the women in

the current study were more honest in providing adherence information with their experiences with the drugs than the men and that may explain why a fewer proportion were adherent compared to the men. Whatever is the reason, there is need to explore the factors that account for the significant difference in adherence to ART across gender.

Validation of self-reported adherence information

Evidence abound that the self-reported adherence measure is sensitive to desirability bias and adherence information could be exaggerated. Thus, validation of self-reported adherence information with viral load test has been recommended (Gill *et al.*, 2005). In the current study, the non-viral validated adherence rate was in the range of 95.0% to 99.6%, while the viral load validated adherence was 80.3% (Table 4.5). This finding validates the adherence information provided by the participants. It also questioned the generally accepted claim that patients who struggle with adherence would be unwilling or unable to admit to non-adherence to health care professionals. However, it has been recommended that researchers evaluating adherence through the self-reported measure should endeavour to validate self-reported adherence information with viral load test (Gill *et al*., 2005).

Measurement of adherence using the self-report measure

The self-report measure of adherence has been shown to generate different levels of adherence to ART (Jean-Baptiste, 2008). When this method was used in the current study, different levels of adherence were found with different adherence masures as stated above. This has confirmed that adherence level measured through self-reporting will vary depending on the criteria that are used.

Thus, to measure adherence comprehensively, critical criteria, like dose taking, frequency and schedule of drug administration must be considered. However, in most adherence studies in sub-saharan Africa that used self-reporting, "pills missed" or "pills taken", were the criteria frequently used to assess adherence level without considering whether the drugs were taken at the correct times or not (Jean-Baptiste, 2008). Frequently, if a patient says he/she did not miss a dose, it was assumed that the patient had taken the correct dose and maintained the correct frequency and schedule of administration. But the finding of the current study does not support this assumption; patients who may not be missing their doses of medication may not be taking them appropriately and this has serious consequences. A study conducted to evaluate the effect of taking medication at the correct frequency and correct schedule showed that patients who took their medicines off schedule or without the required food restrictions were not getting the full benefits of the medicine and were experiencing treatment failure (Castleman, Seumo-Fosso and Cogill, 2003). The current study therefore affirms that, assessing adherence by the self-reported measure is much more complex; future researchers should not limit themselves to using only the "doses taken" or "missed" as the basis of assessing adherence to the ART. We must change the way adherence to ART is evaluated using the self-reporting measure.

Barriers to the ART

No study has systematically investigated the barriers and facilitators of long-term adherence to ART in the Federal Capital Territory (FCT), Abuja, Nigeria. Elucidating the barriers and facilitators is critical if policy makers in the FCT and Nigeria are to identify pitfalls in current strategies that should be addressed while devising effective AIDS treatment programs. In the current study, "forgetfulness" (43%), "travelled away from homes" (21%), "ran out of

medication" (16%), "busy at work" (13%), "lack of food" (5%) and "medication snatched by armed robbers" (2%) were found to be barriers to adherence to the ART (Figure 4.7)

Forgetfulness

Forgetfulness (43%) was the major cause of poor adherence among the participants who reported missing at least a dose of their medication. Other studies have also found forgetfulness as a barrier to ART adherence (Roberts, 2000; Reynolds *et al*., 2004; Marais, 2006; Mills *et al*., 2006a; WHO, 2006b; Dieckhaus and Odesina, 2007; Wang and Wu, 2007; Amberir *et al*., 2008; Thobias, 2008; Malangu, 2008).

Interventions that have been designed to address forgetfulness have involved patient education, counseling and the use of external devices that prompt patient to take medications. A meta-analysis of randomized controlled trials of clinic-based patient education and counseling found that participants who received education and counseling were significantly more likely (OR=1.5) to reach the optimal level of 95% adherence; and to have an undetectable viral load (OR-1.25) than those who were not offered such counseling (Simoni *et al.,* 2006). The importance of counseling, over and above external reminders (as highlighted in the meta- analysis) was confirmed by a recent multi-center trial in the United States. This trial compared the effects of an electronic medication alarm system with those of "medication managers" —clinic staff who were given two days of training on how to conduct adherence counseling and how to help patients identify and overcome barriers to adherence. Medication managers were found to have significantly helped to increase the levels of optimal adherence, which was not the case for the

electronic medication alarms (Mannheimer *et al.*, 2006). Thus, counseling can be deployed to address forgetfulness. However, the quality of counseling can be strengthened further by:

• Fully evaluating patients' motivation for treatment before starting the ART

• Performing proper opportunistic infection (OI) screening, adverse drug reaction (ADR) and adherence monitoring

• Training staff, including other support staff, in communication skills and adherence counselling.

Emerging technologies, particularly the use of cellular telephone technology has also been advocated for addressing the problem of forgetfulness. The cellular phone approach is culturally relevant for telephone owners; in Nigeria, practically every adult has a cellular telephone. The telephone is largely confidential, (particularly if text messages are used), is not affected by distance, and can be uniquely modified to meet patients' individual education or lifestyle needs. The telephone strategy was particularly useful during stock shortages during the political violence in Kenya in 2008 (Nachega *et al.*, 2010). To minimize the suboptimal adherence reported in the current study, the use of medication managers, counseling and the telephone strategy are all recommended.

Travelling away from home and busy with work

Travelling away from home (21%) and busy at work (13%) were identified as barriers to ART adherence in the current study. Stout *et al.* (2004) also found travelling and being busy with work

as a barrier to the ART. Over busy patients are likely to forget their medication behind or they may carry them along but forget to take them. Thus, patients' counseling as recommended above under forgetfulness can be used to address these factors.

Running out of medication

Sixteen per cent (16%) of participants gave running out of medication as their barriers to adherence. Running out of medication has been reported as an adherence barrier to the ART in sub-Saharan Africa. For instance, a cohort analysis from Uganda found that initially excellent adherence declined over one year as patients experienced pharmacy stock-outs (Oyugi *et al*., 2007). In South East Nigeria, another adherence study found running out of drugs as an adherence barrier (Uzochukwu *et al*., 2008). Similarly, Mills *et al*. (2006b) indicated that the most important and frequent factors reported to negatively impact adherence in developing countries are cost of drugs (Weiser *et al*., 2003; Laniece *et al*., 2003) and structural barriers, such as pharmacy stock-outs, among others (Oyugi *et al*., 2007).

It is not clear why the participants at the study center should experience "running out of medication" considering the constant availability of drugs reported in the current study. It is likely that economic factors constrained them from travelling to the study center to access drugs because; participants paid a median of ₦500.00 to travel to the clinic according to the current study. There might also be problems with the logistics of drug distribution and this can create temporary drug stock-outs, leading to participants running out of their medications. To address all these, home delivery of drugs or giving sufficient quantities of drugs e.g., three months'

supply may address the problem if poverty was the problem. If drug distribution was the problem, facility staff responsible for requesting drugs from the central store may need to improve on inventory management generally. For instance, the pull system of drug distribution should be used instead of the push system. The pull system is a system of drug distribution that depends on using consumption data to generate drug requisition for re-stocking. The system delivers only what is needed and as such, it addresses under-stocking which often leads to drug stock-out. Practical steps that may be deployed to address the problem of running out of medication may include:

• Assigning responsibility for drug supply to one person who is supported by the management

• Supporting stable donorship and efforts to reduce costs for OI medicines or make arrangements for completely free medicines

• Stabilizing delivery of drugs, clarify the question of responsibility when problems arise with drug delivery and service

Lack of food

Only a small proportion of participants (2%) complained of lack of food as a barrier to adherence to the ART in the current study. However, lack of food was found to be a very serious barrier to the ART in Uganda where food shortage was a serious concern for the majority of patients (INRUD-IAA *et al.*, 2008). The experience of an increased appetite when on the ART presented yet an even greater barrier to adherence and was reported as a reason for patients to stop the treatment (INRUD-IAA *et al.*, 2008).

Food distributions programs have been used to address lack of food, but sustaining such programs are quite challenging. A study in Uganda found that the food distribution program that was deployed to address the persistent food shortage later collapsed as a result of lack of funds (INRUD-IAA *et al.,* 2008).

As policy makers devise strategies to address the identified barriers in the current study, much emphasis should be focused on the psycho-social factors (forgetfulness, travelling away from home and being busy with work), because these factors are largely responsible for poor adherence among the non-adherent participants. However, the socio-economic and structural factors (running out of medications) should be addressed if only to minimize the poor adherence level reported in the current study.

Facilitators of adherence to the ART

Improvement in health condition

Improvement in health condition does not support the suboptimal adherence reported in the current study, because suboptimal adherence predicts poor virologic suppression and poor improvement in health condition (Paterson *et al*., 2000). Nevertheless, the efficacy of medication or the type of medication may have led to the improvement in health condition. For instance, the combination of non-nucleoside reverse transcriptase inhibitors (NNRTIs) and boosted protease inhibitor-based cART can achieve virologic suppression at a moderate adherence of 70 – 90%

(Nachega *et al*., 2007; Shutter *et al*., 2007; Martin *et al*., 2008). If this was the case, then the procurement of efficacious and quality drugs would be an important step towards sustaining adherence to ART at the study center. Storage of drugs at the recommended temperatures would also improve the efficacy of drugs, which the study center must pursue. However, patients' confidence on the efficacy of medication is very important. A practical strategy that may enhance patients' confidence on medication is to have the ART programs take more active part in community life through support groups and enhance sensitization through people living with HIV/AIDS (PLWHA) who can attest to benefit of life-saving drugs.

Desire to live

The desire to live can be promoted by counseling and education. Anxiety and depression are common among persons living with HIV/AIDS, with a prevalence of nearly 50% in a U.S. screening sample of 2,864 HIV infected persons (Ammassari *et al*., 2004a). When people are presented with the HIV infection, they may suffer psychological depression leading to low morale, loss of interest in life and the desire to live (Ammassari *et al*., 2004a). But these can be reversed with effective counseling particularly when the benefits of adherence to the ART are expounded and patients realize that they can do what others are doing and may even live longer by simply adhering to their medications. The study center, as found out in the current study, provides integrated counseling and routine patient education on each clinic visit. Patients were not started on the ARV medications until they have completed the compulsory counseling education and a certificate of completion issued. This practice is most likely contributing to the participants' desire to live and therefor, should be sustained and strengthened.

Support group

Providing support from the immediate family of the participants as well as from social organizations like the support group network, were promoters of adherence to the ART according to the current study. In other studies, consistent support from the family was found to facilitate adherence to the ART (Chesney *et al*., 2000; Bearman and La Greca, 2002; Simoni, Frick, Lochkart and Liebovitz, 2002; Attawell and Mundy, 2003; Hofer, Schechter and Harrison, 2004; Kagee, Le Roux and Dick, 2007). According to Attawell and Mundy (2003), a spouse support and support groups play a crucial role in HIV medication adherence.

The role that family support and the support group system have played in promoting adherence to the ARVs have been reported in some studies (Chesney *et al*., 2000; Bearman and La Greca, 2002; Simoni, Frick, Lochkart and Liebovitz, 2002; Attawell and Mundy, 2003; Hofer, Schechter and Harrison, 2004; Kagee, Le Roux and Dick, 2007). Therefore, there is need to strengthen community linkages as this will strengthen the support group system. The following practical strategies are recommended:

• Use relevant number of peripheral trained community-based health workers, preferably those with experience of living with HIV/AIDS

• Collect information on patients' health status and adherence, thus detecting defaulters, which are communicated by cell-phones back to the clinics

• Use community-based health workers for support in a home-based model on HIV/AIDS care.

5.7 Limitations of the study

The *cross sectional design*

As stated above, the cross sectional design was adopted for the current study because it is the best design for describing the scope of problems in operational/health system research (Grimes and Schuz, 2002). However, a cross sectional design does not allow causal relationships to be established, unlike cohort or case control studies (Grimes and Schuz, 2002). For instance, the cause of psycho-social factors as barriers to adherence to the ART in the current study cannot be clearly stated because of this limitation. As a result, program implementers may have to identify the causes through further studies before addressing them (Grimes and Schuz, 2002).

The *quantitative data collection technique*

A structured questionnaire was used for the data collection. Thus, participants had no chance of expressing their opinions on very critical matters, which would have shed more light, for instance, on the factors associated with adherence. It means that ART program implementers who are interested in addressing the adherence determinants constraining and facilitating adherence to the ART may do a qualitative study to have a comprehensive and in-depth understanding of the adherence determinants reported in this study. Addressing problems without a comprehensive understanding of the problem is superficial, which strongly supports the need for a qualitative study.

The adherence measures: self-report and prescription refill

The self-reported and prescription refill adherence measures were adopted for evaluating the scope of adherence to the ART. Both measures have been shown to correlate with viral suppression and optimal clinical outcome (Nieukerk and Oort, 2005) and have been used in several studies to measure adherence to the ART (Mills *et al*., 2006b). However, the two measures are not totally free from weaknesses that may affect the validity and overall result findings of a study.

The self-report measure is sensitive to desirability bias since participants are more likely to provide information that they consider socially desirable rather than being totally honest. Over estimation of adherence information leading to inflated adherence rates has therefore been linked to the self-report measure (Chesney, 2006; Gill *et al*., 2005). The prescription refill measure is not sensitive to desirability bias; however, recorded data may be incomplete and may provide incomplete information that is out-dated. The quality of information may be compromised, because the information was recorded by different people for different purposes other than research (Araoye, 2003). Similarly, transcription errors where data clerks enter data incorrectly, e.g., recording 0 instead of 10 are common with retrospective data. It has also been suggested that retrospective data usually need to be updated before they are used because certain information recorded in the past may have changed at the time of the study (WHO, 2004). The tear and wear of the papers where the data were entered initially may lead to incompleteness of the original information, which may also require updating.

In the current study, much effort was invested in updating the pharmacy records. For instance, participants who were considered lost to follow up (LTFUP) in which case, they did not visit the clinic to refill their prescriptions for the past 4 months but suddenly showed up during the data collection period, were excluded for having incomplete prescription data. Despite this effort, it is impossible to have ruled out all the errors associated with using retrospective data and therefore, the prescription refill adherence rate reported in this study must be viewed within the confine of these errors.

The use of a single site

Conducting the study at one site rather than at multiple sites within the territory, suggests that the finding of the study may only be generalized to the treatment centers that are similar to the University of Abuja Teaching Hospital, e.g., the PEPFAR supported public health facilities, which constituted over 90% of health facilities. However, caution is required in generalizing findings to treatment centers that are totally different from the University of Abuja Teaching Hospital, e.g., the private hospitals without the PEPFAR support and treatment centers located in the remote rural areas.

The exclusion criteria

Younger persons less than 18 years were excluded as they are not adults legally. Patients considered as "lost-to-follow-up patients" and those newly initiating therapy at the time of the study were also excluded from the study. Lost-to-follow-up patients were excluded because they

had incomplete prescription refill data and constituted a subset of the target population. Patients newly initiating therapy were less than 12 months on therapy and could not possibly have viral suppression, which is known to occur after six to ten months on therapy (Nachega *et al*., 2004; Pradier *et al*., 2001; Clay, 2005). The exclusion of these groups from the study means that findings of the current study are not generalizable to them. With adherence patterns likely to be different among these groups, other studies are recommended.

The limitations highlighted above should not discourage the implementation of the recommendations of the current study by policy makers and the ART program implementers. However, it is very important that the implementation is done within the context of these limitations.

5.8 Strengths of the study (contributions of the study to existing knowledge and practice)

The current study has contributed to both knowledge and practice.

a) Contribution to practice in combination anti-retroviral therapy in the FCT, Nigeria and sub-Saharan Africa

Practice is defined as a way of doing something that is the usual or expected way in a particular organization or situation. Some findings of the current study may contribute to current practice in the area of combination anti-retroviral therapy (cART), particularly in the FCT and Nigeria. The most important contributions are listed below:

The identification of adherence barriers and facilitators

This is the first study that described in a comprehensive way, the adherence level and its determinants in the FCT. Policy makers and the ART program implementers for the first time know the factors that constrain and promote adherence and can devise interventions to address them to promote adherence in the FCT and Nigeria. The recommendations and limitations of the study, which have been fully discussed, would help streamline the interventions and safe cost in the process.

Switching of patients with suspected treatment failures

The current study found that among the participants who claimed adherent to their regimens, 12.2% women and 8.1% men, had viral load >3000 copies/μl^3 despite being on therapy for at least 12 months (Table 4.2). According to the Nigerian treatment guideline, treatment failure is expected with these patients (FMOH, 2009). The World Health Organization (2009) and the Nigerian treatment guideline (FMOH, 2009) recommend the switching of patients with treatment failure to second line regimen. Thus, the finding of the current study might likely alert and drive the study centre to embark on the switching of these patients to the appropriate regimen. Other treatment centres might be encouraged by this and promote the same practice at their centres.

Antiretroviral drugs can be tolerated

The current study found that most participants did not suffer side effects from their drugs. Considering the fact that ARVs are seen as toxic drugs with serious fatalities, this is an

encouraging report that may boost confidence on the use of ARVs and consequently increase their usage.

b) Contribution to existing knowledge in cART in the FCT, Nigeria and sub-Saharan Africa

The WHO defines knowledge as the information, understanding and skills that are gained through education or experience (WHO, 2006a). Some findings in this study were consistent with findings in other adherence studies and as such, contribution to existing knowledge is made.

Supobtimal adherence in sub-Saharan Africa

Emerging studies are reporting high levels of adherence in sub-Saharan Africa (Nachega *et al*., 2010). The finding of suboptimal adherence in the current study lent support to the concern raised by Gill *et al* that adherence rates in sub-Saharan Africa have been exergerated and true adherence rates remain unknown (Gill *et al.*, 2005). The current study contributes to knowledge by questioning the way adherence has been measured by previous researchers in Africa. The reported high adherence levels are also questioned and it is insisted that adherence must be measured comprehensively in sub-Saharan Africa.

Measuring adherence by self-report should be comprehensive

One major finding of the current study that reflects independent thinking and originality and may contribute to existing knowledge in cART, is the finding that assessing adherence by self-report using only one criterion, e.g., doses missed or taken, is not comprehensive enough. The review

of literature showed that only one adherence study in sub-Saharan Africa has evaluated self-reported adherence using different criteria (Jean-Baptiste, 2008). This is a significant contribution to existing knowledge considering the limited studies evaluating self-reported adherence using different criteria.

Self-report and prescription refill measures of adherence correlate with virologic suppression

The current study found a positively statistically significant association between adherence and virologic suppression, consistent with findings in many studies (Bangsberg *et al.*, 2000; Gifford, Bormann, Shively, Wright, Richman and Bozzette, 2000; Haubrich *et al.*, 1999; Chesney *et al.*, 2000; Paterson *et al.*, 2000; Arnsten *et al.*, 2001). This clearly contributes to knowledge in this area.

5.9 Summary

The current study found a suboptimal adherence rate in the FCT. Significant findings that were positively statistically and significantly associated with adherence were: virologic suppression and age. Psycho-social factors were the major barriers and motivators of adherence to the ART, which added to the reflection that drug adherence is a human behavior dependent on psycho-social attributes.

CHAPTER SIX
CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

The current study described adherence to anti-retroviral therapy as well as analyzed the factors that might constrain (barriers) and motivate (facilitators) adherence among adults who were on highly active anti-retroviral therapy in the Federal Capital Territory, Abuja, Nigeria, from 2005 to 2010.

Data were collected from exit-interviews, prescription refill records and viral load tests from consented patients systematically sampled from the ART clinic of the University of Abuja Teaching and analysed.

Suboptimal adherence (53.6%) with high virologic suppression (80.3%) was reported; age and viral load were positively, statistically and significantly associated with adherence to ART. Similarly, forgetfulness, being busy with work and traveling was common barriers to adherence to the ART, while the perception that health condition improved as well as the desire to live had the greatest potentials of influencing adherence to ART according to current study.

The current study questioned the way adherence to ART has been measured using the self-reporting measure in sub-Saharan Africa. It insists that adherence must be measured comprehensively. The failure to follow specific instruction on timing of taking medication was

the critical reason for suboptimal adherence to ART, which health providers and the participants must address.

6.2 Recommendations for improving adherence to highly active anti-retroviral therapy

The current study found several adherence determinants that have the potentials of influencing adherence to the ART. The major determinants were divided into psychosocial, health system and community factors and were ranked in order of priority for the ease of intervention. By this ranking, the psycho-social factors have the highest priority and the community factors, the least. It is suggested that as interventions are deployed, this order of ranking should be followed particularly, if limited resources will not allow a comprehensive intervention on all the factors. Future areas of research are also recommended as the current study could not address all the critical issues identified in this study.

Psychosocial factors

The suggestions for addressing the psychosocial factors are listed below:

a) *Strengthen quality in counselling*:

- Fully evaluate patients' motivation for treatment before starting the ART
- Perform proper opportunistic infection (OI) screening, adverse drug reaction (ADR) and adherence monitoring
- Train staff, including other support staff, in communication skills and adherence counselling.

- Use modern technology, for instance cellular telephones
- Use external prompts to help remind patients to take their medications as scheduled.

Health system factors

b) Reduce transport costs to the clinics:

- Provide patients with drugs for a longer period and arrange for better laboratory services so patients will not have to return so frequently
- Bring services closer to the patients, and use peripheral community-based health workers for drug distribution
- Give direct economic support and/or initiate income-generating programs

c) *Reduce waiting times in clinics*:

- Arrange more efficient flow of patients between different providers and stations appointment schedule,
- Split appointments into two half days,
- Keep clinics open on additional days,
- Increase number of staff
- Decentralize services to the communities

d) Strengthen conditions for constant supply of the ARVs, OI drugs and laboratory services:

- Assign responsibility for drug supply to one person who is supported by the management

- Support stable donor-ship and efforts to reduce costs for opportunistic infection medicines or make arrangements for completely free medicines
- Stabilize delivery of laboratory material; clarify the question of responsibility when problems arise with equipment maintenance and service
- Support the use of the pull system for drug distribution
- Train health staff who are involved in drug requisition on inventory management with focus on how to maintain constant availability of drugs
- Modern drug forecasting tools should be provided to enable health staff involve in drug management to accurately forecast the needed quantities of drugs

e) Strengthen the stocking of high quality and efficacious ARVs and opportunity infection drugs (OIs):

- Procure drugs from reputable drug manufacturers that have met both the World Health Organization and the local regulatory agency such as, the National Agency for Food and Drug Administration and Control (NAFDAC) pre-qualification standards on manufacturing.
- ARVs should be stored at the manufacturers' recommended temperatures to maintain their integrity. As temperatures in the FCT are higher than the recommended 25 degree Celsius, Air Conditioners, Fans and other cooling systems should be provided and room temperatures in the drug stores should constantly be monitored using wall thermometers.

f) Strengthen the stocking of user friendly ARVs

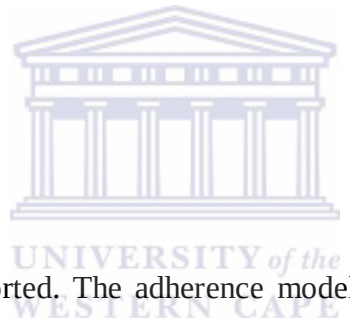
- Focus on stocking the fixed dose combinations ARVs which are user friendly

Community factors

g) *Strengthen community linkages*:

- Use relevant number of peripheral trained community-based health workers, preferably those with experience on living with HIV/AIDS
- Collect information on patients' health status and adherence, thus detecting defaulters, which is communicated by cell-phones back to the clinics
- Use community-based health workers for support in a home-based model on nutritional matters and HIV/AIDS care.

Future areas of research



Suboptimal adherence

A suboptimal adherence was reported. The adherence model presently in use at the treatment centre does not seem to be effective. There is need to design an adherence model to address the poor adherence among the patients with confirmed treatment failure.

Causation

Analytical studies should be designed to evaluate the causes of poor adherence in the FCT. The cross sectional nature of this study did not allow this.

Months on therapy and side effects of drugs

Majority of the participants in this study were on therapy for a longer duration and only a few of them experienced side effects from their medications. Does the length of time on the HAART medications completely eradicate the risks of side effects? Or is there a time frame when the side effects of the ARVs completely disappear? These questions need further investigations.

Potential adherence determinants

The study did not look into some of the potential socio-economic and psycho-social factors influencing adherence, such as income level (Kleeberger, Phair, Strathdee, Detels, Kingsley and Jacobson, 2001), housing (Duran *et al*., 2001), life event (Moatti, Carrieri, Spire, Gastaut, Cassuto and Moreau, 2000) and depression (Moatti, Carrieri, Spire, Gastaut, Cassuto and Moreau, 2000). Overall, various findings of the current and other studies on the impact of demographic and psycho-social variables call for the need to seriously attend to these potential factors in adherence to anti-retroviral therapy.

In conclusion, ARV adherence rate in the FCT is low with high virologic suppression. To help patients manage a life long adherence to the ART, emphasis on the correct use of medication is necessary. Psychosocial factors contrain and motivate adherence to ART; they must be addressed in order to improve adherence to ART in the Federal Capital Territory, Abuja, Nigeria.

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APPENDIX 1 University of Abuja Teaching Hospital Health Research Ethics Approval

UNIVERSITY OF ABUJA TEACHING HOSPITAL

P. M. B. 228, ABUJA - F.C.T. NIGERIA
☎ 09-2905535, DL.09-8821128. Fax: 09-8821382
www.uath_ng.org.

Our Ref: _____

Your Ref:_____

1st April, 2010

Date:_____

FCT/UATH/HREC/115

Mr Avong Yohanna Kambai
Institute of Human Virology, Nigeria
Pent House , Maina Courts, Plot 252, Herbert Macaulay Way
Central Business District,
P.O. Box 9396, Garki. Abuja

Approval to Carry Out Research Work on: Adherence *to Antiretroviral Therapy in the Federal Capital Territory, FCT Abuja.*

I am pleased to inform you that your protocol , consent forms and materials specified for the conduct of the study have been approved for the above mentioned study to be conducted in the University of Abuja Teaching Hospital.

The approval date is 1 April, 2010 to 31 March, 2011.

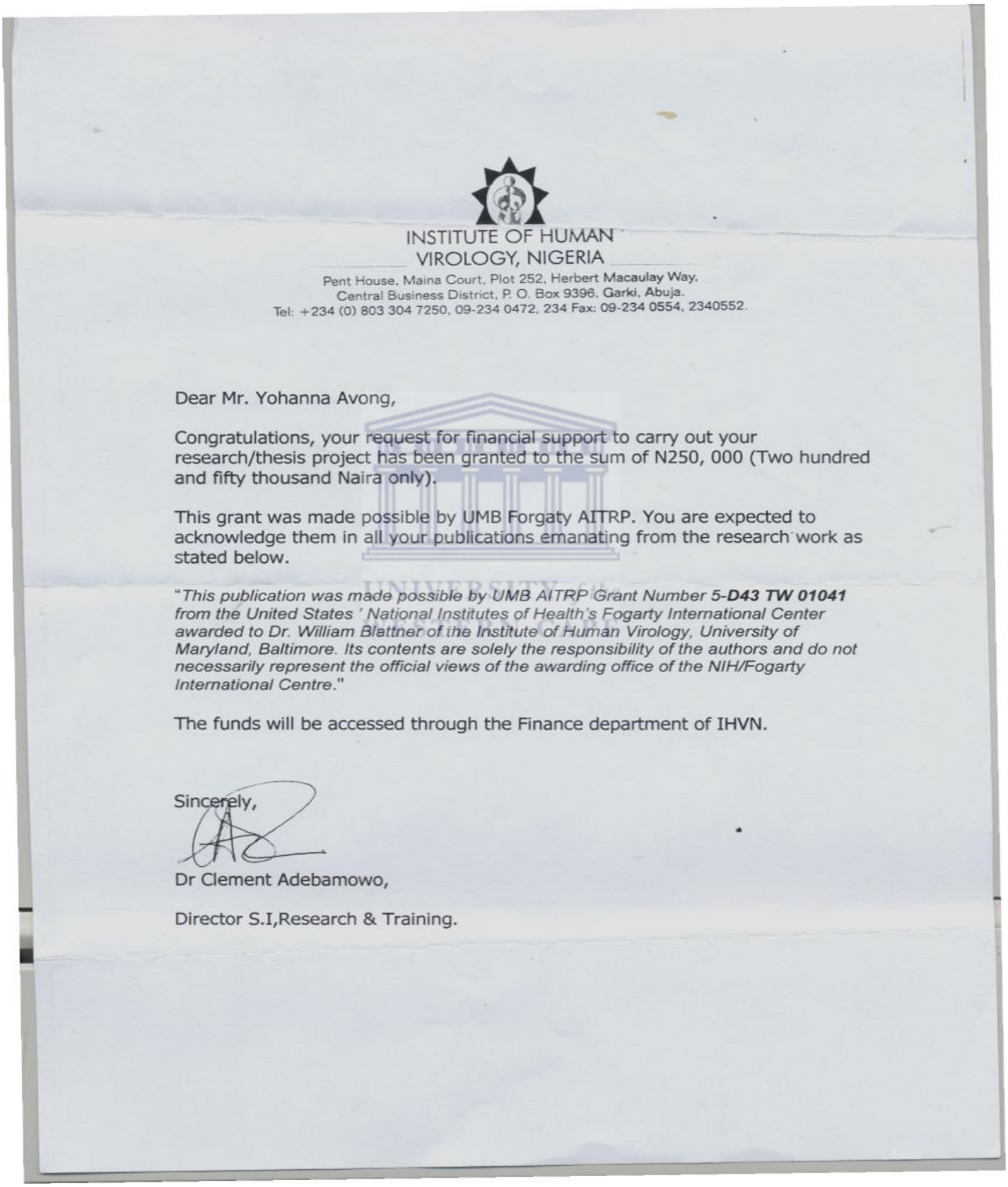
You are requested to confine yourself to the research design as submitted and approved by the Medical Research Ethics Committee.

In the event that the need arises for you to modify any aspect of the research, you will be required to resubmit same for consideration and approval.

Congratulations

Andrew Zamani, PhD
For: Chairman, Medical Research Ethics Committee

APPENDIX 2 UMB Forgaty Financial Support



INSTITUTE OF HUMAN VIROLOGY, NIGERIA

Pent House, Maina Court, Plot 252, Herbert Macaulay Way,
Central Business District, P. O. Box 9396, Garki, Abuja.
Tel: +234 (0) 803 304 7250, 09-234 0472, 234 Fax: 09-234 0554, 2340552.

Dear Mr. Yohanna Avong,

Congratulations, your request for financial support to carry out your research/thesis project has been granted to the sum of N250, 000 (Two hundred and fifty thousand Naira only).

This grant was made possible by UMB Forgaty AITRP. You are expected to acknowledge them in all your publications emanating from the research work as stated below.

"*This publication was made possible by UMB AITRP Grant Number 5-**D43 TW 01041** from the United States ' National Institutes of Health's Fogarty International Center awarded to Dr. William Blattner of the Institute of Human Virology, University of Maryland, Baltimore. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the awarding office of the NIH/Fogarty International Centre.*"

The funds will be accessed through the Finance department of IHVN.

Sincerely,

Dr Clement Adebamowo,

Director S.I,Research & Training.

APPENDIX 3 Institute of Human Virology Health Research Ethics Approval

INSTITUTE OF HUMAN
VIROLOGY, NIGERIA
Pent House, Maina Court, Plot 252, Herbert Macaulay Way,
Central Business District, P. O. Box 9396, Garki, Abuja.
Tel: +234 (0) 803 304 7250, 09-234 0472, 234 0474, 234 6780 Fax: 09-234 0554, 2340552.

IHVN HREC Protocol number: NHREC/05/01/2010a-0004

Re: Adherence to Antiretroviral Therapy in the Federal Capital Territory, F.C.T Abuja.

Name of Principal Investigator: Mr. Avong Kambai Yohanna

Address of Principal Investigator: Institute of Human Virology, Nigeria, Pent House, Maina Court, Plot 252, Herbert Macaulay Way, CBD, Abuja.

Date of receipt of valid application: 9th February, 2010

Date of meeting when final determination of research was made: 18th February 2010

Notice of Full Approval after full Committee Review

This is to inform you that the research described in the submitted protocol, the consent forms, advertisements and other participant information materials have been reviewed and *given full approval by the Health Research Ethics Committee.*

This approval dates from **18th /02/2010 to 17th /02/2011.** If there is delay in starting the research, please inform the IHVN HREC so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside of these dates. *All informed consent forms used in this study must carry the IHVN HREC assigned number and duration of approval of the study.* Endeavor to provide ***IHVN HREC*** with progress reports at the end of the study in order to obtain renewal of your approval and avoid disruption of your research.

In line with the National Code for Health Research Ethics you are required to comply with all institutional guidelines, rules and regulations and with the tenets of the Code.
*Institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly. No changes are permitted in the research without prior approval by the **IHVN HREC** except in circumstances outlined in the Code. The IHVN HREC reserves the right to conduct compliance visit your research site without previous notification.*

24th /02/10

Prof. Ayuba Zoakah
Chairman, IHVN HREC

APPENDIX 4: Participant Information Sheet (English)

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa

Tel: 021- 959 2809, Fax: 021- 959 2872

November 2009

Dear Participant

Thank you for your willingness to be informed about this study. What follows is an explanation of the study and your potential involvement. This study is being conducted for a mini-thesis as part of the requirements for a Masters in Public Health degree which I am completing at the University of the Western Cape. You are free to ask me anything that may be unclear or that you

do not understand. My contact details and those of my supervisor can be found at the end of this memo.

TITLE OF RESEARCH

Adherence to Antiretroviral Therapy in the Federal Capital Territory, Abuja, Nigeria

PURPOSE OF THE STUDY

This study is set out to estimate the level of adherence to antiretroviral medicines and other medicines use in the management of HIV/AIDS. The factors that may hinder adult people living with HIV/AIDS from taking their HIV medicines as recommended for them by the health worker will also be looked into. The result of the study will provide information on how to improve adherence and reduce the barriers to adherence so that people living with HIV/AIDS can take their medicines properly and reduce the problems cause by HIV/AIDS.

DESCRIPTION OF THE STUDY AND YOUR INVOLVEMENT

The study will include interviews with adult people living with HIV/AIDS. Questions about your experiences/views with HIV medicines will be asked. In particular, you will be asked to say how you have been taking your HIV/AIDS medicines and the challenges you have been having with taking these drugs and other drugs you have been given. Participants will also be requested to go to the laboratory to do a viral load test so as to know the level of the viruses in their body.

CONFIDENTIALITY

Your name will be kept confidential at all times and I shall keep all records of your participation, including a signed consent form which I will need from you should you agree to participate in the study, locked away at all times and will be destroyed after the study is completed.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is entirely up to you as you may not participate if you so decide. However, if you choose to participate, you may withdraw at anytime or may choose not to answer particular questions that may be asked. Please feel free to inform me if there is anything that you would prefer not to discuss. If you decide not to participate or withdraw from the research at any point, please be assured that you will not be adversely affected in any way.

BENEFITS AND COSTS

You may not get any immediate benefit from this study. However, you will know the level of viruses in your body which the doctors may need to treat your health problems better. It is also hoped that the information and the suggestions gathered from this study will act as a guide to inform policy-making by the relevant authorities and the overall benefit of all concerned. The only costs that accrue to you for participating in this study is the time you spend in the interviews and the small amount of blood you will provide for the viral load test.

INFORMED CONSENT

Your signed consent to participate in this study is required before I proceed to interview you. I have included the consent form with this information sheet so that you will be able to review the consent form and then decide whether you would like to participate in this study or not.

QUESTIONS

Should you have further questions or wish to know more, I can be contacted as follows:

Avong Yohanna Kambai

Student Number: 2831679

Mobile phone: 234 8033159205

E-mail: yavong@gmail.com

Office telephone: 234 8033159205

I am accountable to my supervisor, Dr. Brian van Wyk at The University of the Western Cape, South Africa.

Dr van Wyk's contact details are:

E-mail: bvanwyk@uwc.ac.za; Tel No. +27828049055 while

Dr. Brian could also be contacted at:

The School of Public Health

Fax: +27 21 959 2872

APPENDIX 5: Participant Information Sheet (Hausa)

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa

Tel: 021- 959 2809, Fax: 021- 959 2872

November 2009

Ya me shiga wannan aikin

Ina maka/miki godiya domin ka/kin yarda na yi maka/miki bayani game da wannan aikin bincike. Zan yi maka/miki bayani akan yadda aikin zai kasance da abubuwan da zaka/zaki yi. Ina yin wannan aikin bincike ne domin yana cikin aiyukan da ya kamata nayi a karatuna na ilimin kiwon lafiyar jama'a a Jami'an Western Cape. Kana/kina iya yi mani tambaya akan abun da baka/baki gane ba. Akwai lambar waya na da na malamina me duba aikin a *k*arshen wannan takardan.

SUNAN BINCIKEN

Yadda mutane ke mannewa wa shan magungunar *k*wayar cutar HIV, wato magungunar ARV a birnin Abuja a Najeriya

DALILIN YIN WANNAN BINCIKEN

Wannan aikin bincike zai duba yanayin da mutane ke mannewa wa shan magungunar ARV tare da sauran magunguna domin kula da lafiyarsu ko da suna *d*auke da *k*wayar cutar HIV. Zamu kuma duba dalilan da kan iya hana manyan mutane masu *d*auke da *k*wayar cutar HIV daga shan magungunar yadda masu aikin asibiti suka tsara musu. Sakamakon wannan aikin zai taimaka wa mutane masu *d*auke da *k*wayar cutar HIV su samu shan magungunarsu yadda ya kamata, ya kuma rage matsalolin da sukan fuskanta.

BAYANI AKAN YADDA AIKIN ZAI KASANCE DA ABUWAN DA ZAKA/ZAKI YI

Za'a tattauna tare da manyan mutane masu *d*auke da *k*wayar cutar HIV. Za'a yi maka/miki tambayoyi akan yadda kake/kike shan magungunarka/ki da ra'ayoyinka/ki game da magungunar ARV. Za'a yi maka/miki tambaya musamma akan yadda kake/kike shan magunguna da matsalolin da kake/kike fuskanta wajen shan magungunar ARV da sauran magunguna. Za'a nema wanda suka shiga wannan aikin bincike su je *d*akin gwaji a auna jininsu domin a gane yawan *k*wayoyin cutar da suke *d*auke da shi.

SIRRI

Zan addana sunanka/ki a sirrance a ko wanne lokaci tare da takarda bada yardanka/ki wanda zaka/zaki sa hannu akai idan ka/kin yarda ka/ki shiga wannan bincike, zamu addana wa*d*annan tarkardu a kulle a kowane lokaci kuma za'a *k*ona su bayan an gama wannan aikin.

SHIGA KO FITA DAGA WANNAN BINCIKE

Shiganka/ki cikin wannan bincike ba tilas bane ba, zaka/zaki shiga ne domin ka/kin ga damar shiga ne. Idan kuma ka/kin shiga cikin wannan binciken zaka/zaki iya fita a kowanne lokaci da ka/kika ga dama, kuma zaka/zaki iya *k*in amsa tambaya wanda baka/baki ga damar amsawa ba. Zaka/zaki iya mun bayani akan irin abubuwan da baza ka/ki so ka amsawa ba. Idan baka/baki so ka/ki shiga wannan binciken ba, ko kuma ka/kin fita bayan ka/kin shiga babu wata hukunci da za'a yi maka/miki.

AMFANI DA KU*D*IN WANNAN BINCIKEN

Zai iya yuwa baza ka/ki samu amfanin shiga wannan bincike ba kai tsaye. Amma dai zaka/zaki samu sani akan yawan *k*wayoyin cuta dake cikin jikinka/ki wanda zai taimakawa likitoci su gane yadda zasu kula da kai/ke a wata hanya mafi kyau. Kuma ana fatan cewa bayanen da zamu samu a wannan aikin bincike zai taimaka wajen gyara manufan shugabanne domin sauran mutane. Abun da zamu tambaya daga gare ka/ki shine lokacin da zaka/zaki bamu da *d*an *k*ankanin jini wanda zamu *d*iba domin gwajin *k*wayoyin cuta.

SAMUN CIKAKKEN BAYANI DA BADA YARDA

Sai na samu izinika/ki da sa hannunka/ki a takardan bada yarda kafin na fara tattaunawa tare da kai/ke game da wannan binciken. Takardan bada yarda na ha*d*e da wannan takardan, zaka/zaki samu ka/ki karanta shi ka/ki san ko kana/kina son ka/ki shiga cikin wannan binciken.

TAMBAYOYI

Idan kana/kina da wasu tambayoyi ko kuma kana/kina son ka/ki *k*ara sani na, zaka/zaki iya samu na a:

Avong Yohanna Kambai

Lambar makaranta: 2831679

Lambar wayar hannu: 234 8033159205

Adireshi yanar gizo: yavong@gmail.com

Lambar ofis: 234 8033159205

Zaka/zaki kuma iya samun malami mai duba aiki na, Dr. Brian van Wyk, a kasar South Africa.

Adireshin Dr van Wyk's shine:

Adireshi yanar gizo: bvanwyk@uwc.ac.za; Tel No. +27828049055

Za'a kuma iya samun Dr. Brian a:

The School of Public Health

Fax: +27 21 959 2872

APPENDIX 6 Informed Consent Form

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa

Tel: 021- 959 2809, Fax: 021- 959 2872

RECORD OF INFORMED CONSENT TO CONDUCT INTERVIEW

Thank you for agreeing to participate in this study.

As part of my Masters in Public Health, I am required to carry out an interview to obtain the necessary information needed for my thesis. I will be focusing on the adherence to antiretroviral therapy in the Federal Capital Territory, Abuja.

This research is intended to look at the level people living with HIV/AIDS (PLWHA) are using HIV medicines and other drugs as well as look at the factors that hinder people from using their medicines as recommended by the health worker. The level to which these factors hinder proper usage of HIV medicines and other medicines and the relationship between the factors and adherence will also be looked at.

As has been mentioned in the Participant Information Sheet, acceptance to participate in this study is your choice and is completely voluntary. You may choose to withdraw from the study or refuse to participate in the study at any time. Such refusal to participate will not result to your loss of any benefit or to any penalty. You may also choose not to answer particular questions that may be asked. If there is anything that you do not feel comfortable to discuss, feel free to say so.

At all times, I will keep the source of the information confidential and refer to you or your words by a pseudonym or invented name which I would like you to choose. I shall keep any other records of your participation locked away and destroy them after the data has been collected.

In order for us to start, you are required to sign a consent form below as a sign of your approval.

I have read the information about this research study on the Participant Information Sheet, or it has been read to me. I have had the opportunity to ask questions and any questions that I have asked has been answered to my satisfaction.

I hereby consent to participate in this study.

My signature attests to my acceptance to participate in the study.

Name of Participant…….

Participant signature ……Consent Date……

Researcher's Name…….

Researcher Signature……Date

APPENDIX 7 Informed Consent Form (Hausa)

UNIVERSITY OF THE WESTERN CAPE

School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa

Tel: 021- 959 2809, Fax: 021- 959 2872

TAKARDAN BADA YARDA A SHIGA AIKIN BINCIKE

Ina maka/miki godiya da ka/kika yarda ka shiga wannan aikin bincike.

Ina yin wannan aikin bincike ne domin yana cikin aiyukan da zan yi a karatuna na ilimin kiwon lafiyar jama'a a babbar jami'a. Zan yi bincike ne akan yadda mutane ke manne wa shan magungunar *k*wayar cuta me karya garkuwar jiki (HIV), wato magungunar ARV a birnin Abuja.

Wannan binciken zai duba yanayin da mutane masu *d*auke da *k*wayar cuta me karya garkuwar jiki ke amfani da magungunar ARV da sauran magunguna, kuma zai duba ire-iren abubuwan da zasu iya hana su amfani da magungunar kamar yadda masu aikin asibiti suka tsara musu. Ana son a kuma gane tsananin wannan rashin amfani da magungunan da kuma dangantakansa da mannewa wa shan magunguna.

Kamar yadda aka bayyana a takardan bada bayani shiga wannan bincike ba tilas bane ba kuma kana/kina iya fita daga cikin binciken a kowanne lokacin da ka/kika ga dama. Ba za'a yi maka/maki wata hukunci ba domin ka *k*i ka shiga wannan binciken ba ko kuma domin ka/kin fita daga cikinsa ba. Kana kuma da dammar kin amsa tambayoyin da basu yi maka ba, zaka/zaki iya gaya mana irin wa*d*annan tambayoyin.

Zan addana takardun aikin nan da kyau a sirrance kuma zan yi amfani da wata suna daban wanda zaka/zaki za*b*a yanzu. Zan addana takardun aikin nan a kulle kuma zan *k*ona su bayan an gama wannan aikin binciken.

Kafin mu fara wannan aikin zan nemi ka/ki saka hannu a *k*arshen wannan takardan domin nuna bada yardanka/ki.

Na karanta bayanen game da wannan aikin binciken akan Tarkardan Bayani, ko kuma an karanta mun wannan bayani. An kuma bani dammar yin tambayoyi kuma an amsa mani tambayoyin a kamar yadda nake so.

Yanzu na yarda na bada izini na shiga wannan aikin binciken.

Sa hannuna a wannan takardan ya shaida yarda na na shiga wannan aikin binciken.

Sunan me shiga binciken ……..…….

Sa hannun me shiga binciken …….…… Bada yarda

Ranar wata ……

Sunan me aikin bincike …….

Sa hannun me aikin bincike ……. Ranar wata …….

APPENDIX 8 Viral Load Order and Results Form

Viral Load Order and Results Form

Facility Name: _____ **1. Collection Date** (dd/mm/yyyy) **/ /20**

2. Name Surname | Other Names

3. ID State | Facility No. | Serial Enrollment No. **4. Hospital No.**

5. Sex ○ **F** ○ **M** **6. Age** years If < 5 years months **7. Lab Reg. No.**

ORDERS **RESULTS** **INDICATION FOR THE VIRAL LOAD TEST:**

○ Viral Load copies/ml

○ Take Repository Sample

○ Drug resistance testing (Genotyping)

Approved by _____

○ Prior ART treatment, now on ART ≥ 4 months (child or adult)

○ Poor adherence history, now adherent ≥ 4 months (child or adult)

○ Immunological failure (child or adult)

○ Clinical failure (child or adult)

○ Child infected in spite of PMTCT

○ Child breast fed with Mom on HAART

○ Other _____

○ Research _____ (Indicate Study)

Ordered by:

Clinician Name	*Signature*	*Date (dd/mm/yyyy)*

Reported by:

Print Name	*Signature*	*Date (dd/mm/yyyy)*

Checked by:

Print Name	*Signature*	*Date (dd/mm/yyyy)*

In folder by:

Print Name	*Signature*	*Date (dd/mm/yyyy)*

PMM-LOV.3.02.02062009

APPENDIX 9 Standard Operating Procedure forViral Load Sample Collection, Processing, Storage and Shipment

BENCH TOP SOP

FOR

VIRAL LOAD SAMPLE COLLECTION, PROCESSING STORAGE AND SHIPMENT

***Warnings and Precautions**: All the procedures performed here must be done with standard, universal biosafety precautions. All required materials and equipment should be available prior to collection!*

Specimen

The test is for use with human plasma (EDTA) specimens only.

Specimen Collection;

1. Confirm patients' identification prior to collection,
2. Label the EDTA vacutainer (tubes) with ***Clients identifiers, date and time of blood draw,***
3. Wear powder free gloves for the blood draw,

4. Draw 10mls of blood into (10 ml volume) EDTA tube **OR** use two 5ml volume EDTA,
5. Allow blood flow to stop by itself,
6. Mix the blood by inverting the tube 15times,
7. Pack samples into tube rack and place in Specimen transport box for transfer to the Lab
8. Change gloves before **and after** blood draw from each Patient,
9. Blood tubes must not be opened until samples are ready to be processed in the laboratory.
10. Whole blood must be transported to the Lab at 2-25oc and processed within 6 hours of collection .

Specimen Handling/Processing;

1. Each Specimen and batch should be accompanied by appropriate documentation
2. Separate plasma from whole blood within 6 hours of collection.
3. Centrifuge sample at 800-1600x g for 20minutes at room temperature.
4. Transfer plasma to a sterile 2 ml polypropylene screw capped tube
5. Aliquot 1ml of sample each into **three,** sterile 2ml cryovials.

Specimen storage;

1. Plasma may be stored at 2 - 8 ^{0}C for up to 5 days in cryovials or frozen at –70 ^{0}C in 1000 ul (1ml) amounts in sterile screw cap tubes.
2. Pack vials into labeled freezer storage boxes and store. Note the position of each sample and document on a storage spreadsheet.
3. Create a freezer storage box map indicating position of each sample.

Specimen Transport/Shipment to PCR reference Labs

1. Plasma may be transported at 2 - 8 ^{0}C or frozen.
2. Ensure that samples are properly sealed and there is no leakage.
3. Pack samples into freezer storage boxes in an orderly fashion (serially or numerically)
4. Generate a list of the samples to match their positions in the freezer storage box

5. Prepare the transport box; line the bottom and sides with ice packs
6. Pack samples (i.e. those in the freezer boxes) into the transport box for shipment.
7. Each specimen and batch must be accompanied by appropriate documentation.
8. Ship specimen to PCR testing centre

Specimen Reception/rejection;

1. Check sample labels, integrity and suitability.
2. Match samples with the accompanying document and request form
3. Document contents, check contents against accompanying manifesto.
4. Note date and time of receipt.
5. Reject any sample with questionable integrity, samples with missing or mis-matched identifiers.
6. A feedback communication should be sent to where the samples came from.

APPENDIX 10 Standard Operating Procedure for Blood Collection

BLOOD COLLECTION MATERIALS

PPE

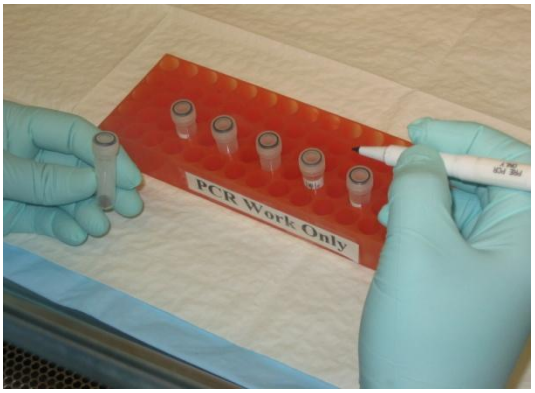
•Disposable powder free latex gloves

•Lab coats

•Goggles

COLLECTION DEVICE

- Alcohol Wipes
- Vacutainer Needles
- Vacutainer/ Blood Collection Tubes-EDTA
- Vacutainer holder
- Tourniquet (Elastic Band)
- Plasters (optional)
- Biohazard Waste Container
- Markers
- Gauze or cotton wool
- Test Tube Racks
- Transport boxes



STORAGE DEVICES

- 2ml polypropylene screw-cap tubes
- Freezer storage boxes

DOCUMENTS

- Patient Forms
- Transfer Documents

APPENDIX 11 Standard Operating Procedure for Viral Load Estimation Using Amplicor HIV-1 Monitor Test, Version 1.5

Bench Top Reference

FOR

VIRAL LOAD ESTIMATION USING AMPLICOR HIV-1 MONITOR TEST, VERSION 1.5

PCR REAGENT PREPARATION AREA 1

***Warnings and Precautions**: Always wear new gloves and lab coat when proceeding to the next area. All Amplification reagents must be at room temperature (RT)!*

<u>REAGENT PREPARATION-</u> (MASTER MIX-AMPLIFICATION REAGENT)

1. Determine the number of samples and controls to be tested.

2. Place the tray on the MicroAmp base,
3. Assemble the appropriate number of MicroAmp tubes in the tray and place retainer on the tray and tubes.
4. Prepare working Master Mix by adding 100ul of Mn^{2+} solution to 1 vial of Master Mix.
5. Mix well by inverting 10-15 times. Pink color denotes presence of Mn^{2+} in the Master mix.

No. Of Test	**12**
MMX	1Vial (700ul)
Mn^{2+}	100ul

6. Pipette 50ul of Working Master Mix into each Micro Amp tube. Visually inspect tubes to ensure that Master Mix has been added. (Place MicroAmp tray in resealable plastic bag and place sealed bag in the refrigerator at 2-8oC in AREA 2 until ready to add samples).

NOTE: ***AMPLIFICATION MUST BEGIN WITHIN 4 HOURS OF PREPARATION OF WORKING MASTER MIX***

NOTE: ***ALL VORTEXING SHOULD BE DONE FOR AT LEAST 3 SECONDS UNLESS OTHERWISE NOTED.***

PCR SPECIMEN PREPARATION AREA 2

REAGENT PREPARATION-(EXTRACTION)

- Prepare 70% ethanol. For 12 tests, mix 11.0ml of 95% ethanol with 4.0ml deionized water (Make fresh daily).

- Visually inspect Lysis Reagent to make sure that it is homogenous and there is no precipitate present. (The lysis reagent should be placed in an incubator at 37^{0c} for at east 30 minutes prior to reconstitution)
- Vortex QS well. Prepare working lysis Reagent by adding 100ulof QS to one vial of lysis Reagent. ***Vortex thoroughly***; Note: working Lysis Reagent must be used within 4 hours of preparation.

SAMPLE PREPARATION- *(Bring out samples to thaw about 30mins before assay)*

1. Complete "Tray Map" for sample and control identifications.
2. Determine the correct number of 2.0ml Sarstedt tubes needed for samples and controls. Label and place an orientation mark on each tube.
3. Add 600ul of thoroughly mixed working Lysis Reagent to each Sample and control tube.
4. For the controls (negative, low and High positive controls), add 200ul of Normal Human Plasma (NHP) to the appropriately labelled tubes containing the Working Lysis Reagent and vortex immediately.
5. Vortex controls and add 50ul of the appropriate controls to the tubes containing NHP and working Lysis Solution. Vortex immediately.
6. Vortex thawed patients' samples. Add 200ul of patients' samples to the appropriately labelled tubes containing Working Lysis Reagent and vortex immediately.
7. Incubate all tubes at room temperature for 10mins(could exceed 10mins, start timer after last tube)
8. Add 800ul of 100% Isopropanol to each tube and **vortex immediately.**
9. Position the tubes in the centrifuge so that the orientation marks are facing outward. Centrifuge tubes for 15minutes at ≥12, 500x g at room temperature.
10. Using a fresh fine tip transfer pipette for each sample, carefully aspirate and discard the supernatant without disturbing the pellet. (sometimes the pellet will not be seen).
11. Add 1 ml of 70% ethanol to each tube and vortex. Centrifuge for 5 minutes at ≥12, 500x g at room temperature.

12. Using a fresh fine tip transfer pipette for each sample, carefully aspirate and discard the supernatant without disturbing the pellet.
13. Centrifuge for 5 minutes at ≥12, 500x g at room temperature (to spin down excess ethanol), use a fresh fine tip transfer pipette for each sample, aspirate and discard the supernatant.
14. Resuspend the pellet in 400ul of Specimen diluent. Vortex each sample for 10 seconds. (Scratch each tube vigorously to mix). If the resuspended sample will not be amplified within 2 hours of preparation, store at -20^{oC} or colder for up to 1 week.
15. Remove MicroAmp Tray from the refrigerator, Pipette 50ul of each extracted sample or control into the appropriate Micro Amp tube containing the Working master Mix.
16. Cap tubes tightly using Capping tool.
17. Move capped tray to AREA 3 for amplification and detection.

PCR AMPLIFICATION AND DETECTION AREA 3

Warnings and Precautions*: Always wear new gloves and lab coat when proceeding to the next area. All Amplification reagents must be at room temperature (RT)!*

Amplification and Detection Area- (Put on the Thermocycler for about 2 minutes to warm up before loading the tray into it)

1. Place sample tray into the thermocycler sample block.
2. PROGRAM The Gene Amp™ PCR System as follows (This is already programmed as method 5 in the Thermocycler):

- HOLD Program: 2 min @ $50^{o}C$
- HOLD Program: 30 min @ $60^{o}C$

- Cycle Program (8 cycles): 10 sec @ 95 ^{o}C, 10 sec @ 52 ^{o}C, 10 sec @ 72 ^{o}C
- Cycle Program (23 cycles): 10 sec @ 90 ^{o}C, 10 sec @ 55 ^{o}C, 10 sec @ 72 ^{o}C
- HOLD Program: 15 min @72 ^{o}C

POST AMPLIFICATION;

- Remove the MicroAmp tray from the Thermal Cycler and place into the tray base. Carefully remove all caps from the tubes avoiding creating aerosols of the amplification reaction mixtures.
- Immediately add 100 ul of Denaturation Solution (1) each reaction tube using a multichannel pipettor with plugged tips.
- Mix by pipetting up and down 5 times.

Note: Do not hold denatured Amplicons at RT for more than 2 hours. If detection will not be performed within 2 hours recap the tubes and store the denatured amplification reaction mixtures at 2 – 8^{oC} for up to one week.

DETECTION

1. Remove Microwell plate (MWP) from the foil pouch.
2. Pipette 100ul of Hybridization solution into each well of the MWP (Impact pipettor program2)
3. Using plugged tips and a multichannel pipettor; add 25ul of the denatured amplicons from the first row (Row A) of the MicroAmp tray to the first row (Row A) of the MWP. Mix well by pipetting up and down 5 times, and then transfer 25ul to the next row of wells (Impact Pipettor Program 3).
4. Repeat this procedure 4 more times through Row F so as to generate 5; five fold dilutions (1:5, 1:25,1:625, 1:3125). Remember to remove and discard 25ul from the last row of wells after mixing.

5. Add 25ul of dentured amplicons from the first row (Row A) of the Micro Amp tray to the first green trimmed row (Row G) on the MWP. Mix well by pipetting up and down 5 times, and then transfer 25ul to the next row of wells on the MWP (Impact Pipettor Program 3). After mixing in Row H, remove and discard 25ul of this mixture.
6. Cover the MWP with the plastic notched lid and incubate for 1 hour at 37oC.
7. Prepare the working Wash Solution by adding 1 part of 10X Wash Concentrate to 9 parts of distilled or deionised water. Mix well.
8. Wash the MWP 5 times with Working Wash Solution.
9. Add 100ul of AV-HRP Conjugate Solution to each well (Impact Pipettor Program 2). Cover plate and incubate for 15 minutes at 37 oC.
10. After the 15 minutes incubation, wash the MWP 5 times with working Wash Solution.
11. Prepare Working Substrate by measuring and mixing 12.0ml of substrate A and 3.0ml of Substrate B. Protect from exposure to light.
12. Add 100ul of Working Substrate to each well of the MWP (Impact Pipettor Program 2). Allow color to develop in the dark for 10 minutes at room temperature.
13. Add 100ul of Stop Solution to each well of the MWP (Impact Pipettor Program 2)
14. Measure the optical density at 450nm within 10 minutes of adding Stop Solution. Using these absorbance values, do the appropriate calculation.

APPENDIX 12: Exit Interview Questionnaire

ADHERENCE TO ANTIRETROVIRAL THERAPY IN THE FEDERAL CAPITAL TERRITORY, NIGERIA

EXIT INTERVIEW QUESTIONNAIRE
STUDY SITE : UNIVERSITY OF ABUJA TEACHING HOSPITAL, GWAGWALADA

INTERVIEWER CODE _____ DATE OF INTERVIEW ___/___/20___ (dd/mm/yyyy)

RESPONDENT PEPFAR ID [ ][ ][ ] – [ ][ ][ ] – [ ][ ][ ][ ][ ] Hospital No.
State Facility Serial Enrollment Number

SOCIO-DEMOGRAPHIC (Tick where appropriate)

1. **Sex:** ○ Male ○ Female
2. **Age in years:** ----------
3. **Religion:** ○ Christianity ○ Traditional ○ Islam ○ No religion
4. **Marital status:** ○ Never married, single ○ Cohabiting ○ Steady partner, not cohabiting
   ○ Married, monogamous ○ Married, polygamous
   ○ Separated ○ Divorced ○ Widow/Widower
5. **Highest educational level attained:** ○ None ○ Primary ○ Completed Primary
   ○ Completed Secondary ○ Secondary ○ Post Secondary ○ University Graduate ○ Qu'ranic Education
6. **Occupation:**
   ○ Household/Domestic work ○ Unemployed ○ Student
   ○ Farmer ○ Artisans (Automobile mechanic, furniture) ○ Civil servant
   ○ Business/trading ○ Professional/Executive ○ Clergy

DISCLOSURE

7 Have you disclosed your HIV Status? ○ Yes ○ No

8 If yes, to question 7, to who? (Tick all that apply) ○ Relatives ○ Spouse ○ Close Friend ○ Family
○ Children ○ Support group ○ Religious leader ○ Community member

DISEASE STATE

9 With your condition, are you now able to actively continue with your normal work?

○ Yes ○ No

TREATMENT PREPARATION

10 Did you go through treatment preparation before you started taking ARV medicine? ○ Yes ○ No

11 If yes to question 10, was a certificate given to you? (Show a sample of certificate to the patient) ○ Yes ○ No

MONTHS ON ARVS

12 When did you start taking the medicines for HIV/AIDS? (write time in months) _____

12b ARV start date in the record----------

COST HOME TO CLINIC

13 On average, how much did it cost you to travel to the clinic from your house/place of work? (write cost in Naira) #_____

TIME HOME TO CLINIC

14 On average, how long did it take you to travel to the clinic from your house/place of work?(write time in minutes) _____

TIME IN CLINIC

15 On average, how long have you been in the clinic from the time you arrived to this time? (Write time in minutes_____

LABELLING OF ARV

Note: If the ARV drug container or plastic wallet is labeled with: the name of the drug, dose per day and number of times to be taken, please tick "Yes" otherwise tick, "No".

16	**Check if ARV medicine container or envelope contains:**	**Yes**	**No**
	Drug name		
	Dose per time		
	Number of times per day		
	Remark: Was the ARV Medicine properly labeled? (Tick Yes or No)		

LABELLING OF NON-ARV

Note: If the Non-ARV drug container or plastic wallet is labeled with: the name of the drug, dose per day and number of times to be taken, please tick "Yes" otherwise tick, "No".

17	**Check if Non ARV medicine container or envelope contains:**	**Yes**	**No**
	Drug name		
	Dose per time		
	Number of times per day		
	Remark: Was the Non-ARV Medicine properly labeled? (Tick Yes or No)		

QUANTITY OF ARVs DISPENSED :

18 Were you given all the HIV medicine prescribed to you today? ○ Yes ○ No

QUANTITY OF NON-ARV DISPENSED

19 Were you given all the Non-ARV medicine prescribed to you today? (e.g. Cotrimoxazole, multivitamins)

○ Yes ○ No

ADHERENCE TO ARV MEDICINES (PILL TAKEN AND CORRECT USE ADHERENCE)

Note: Ask patients to show you the ARV medicines dispensed to him/her by the pharmacist

20 **Name of first ARV in patient regimen (Check the drug dispensed and write the name using standard symbols)**_____

21 Indicate the type of regimen and formulation ○ 1st line ○ 2nd line ○ FDC ○ Stand alone

22 In the past 3 days, how many tablets of this medicine did you take in one dose? _____

Was the correct dose taken in the past 3 days? (Tick appropriately) ○ Yes ○ No

23 In the past 3 days, how many times a day did you take this medicine? _____

Was the correct frequency of administration maintained? (Tick appropriately) ○ Yes ○ No

24 At what times were you taking this medicine in a day for the past 3 days (specify the hours e.g. 8am and 8pm) _____

Was medicine taken at the correct schedule? (Tick appropriately) ○ Yes ○ No

25 How were you taking this medicine in relation with eating food for the past 3 days?

○ Taken before Food ○ Taken after Food ○ Taken with or without Food

Was food restriction complied with? (Tick appropriately) ○ Yes ○ No

26 Since you have been taking this medicine, have you experienced any problem you did not like? ○ Yes ○ No

27 If you have experienced any problem, what is the nature of the problem? ○ Tiredness ○ Fever ○ Nausea ○ Vomiting ○ Dizziness or lightheadedness ○ Skin problems ○ Diarrhea ○ Nervousness/anxiety ○ Others (Specify)

28 Did you report this problem to any of the hospital staff (e.g. the doctor, pharmacist or nurse)? ○ Yes ○ No

29 If you reported the problem, what action was taken? ○ Medicine was changed ○ Problem was treated ○ Medicine was changed and problem treated ○ No action was taken

30 **Many patients have troubles in taking their ARV medicine doses as prescribed. How many of the doses did you missed in the last 3 days?(circle the appropriate option)** 0 1 2 3 4 5 6

30 **Name of second ARV in patient regimen (check the drug dispensed and write the name using standard symbols)**_____

31 Indicate the type of regimen and formulation ○ 1st line ○ 2nd line ○ FDC ○ Stand alone

32 In the past 3 days, how many tablets of this medicine did you take in one dose? _____

Was the correct dose taken in the past 3 days? (Tick appropriately) ○ Yes ○ No

33 In the past 3 days, how many times a day did you take this medicine? _____

Was the correct frequency of administration maintained? (Tick appropriately) O Yes O No

34 At what times were you taking this medicine in a day for the past 3 days (specify the hours e.g. 8am and 8pm)

_____

Was medicine taken at the correct schedule? (Tick appropriately) O Yes O No

35 How were you taking this medicine in relation with eating food for the past 3 days?

O Taken before food O Taken after Food O Taken with or without Food

Was food restriction complied with? (Tick appropriately) O Yes O No

36 Since you have been taking this medicine, have you experienced any problem you do not like? O Yes O No

37 If you have experienced any problem, what is the nature of the problem? O Tiredness O Fever

O Nausea O Vomiting O Dizziness or lightheadedness O Skin problems O Diarrhea

O Nervousness/anxiety O Others (specify)

38 Did you report this problem to any of the hospital staff (e.g. the doctor, pharmacist or nurse)? O Yes O No

39 If you reported the problem, what action was taken? O Medicine was changed O Problem was treated O Medicine was changed and problem treated O No action was taken

40 How many of the doses did you missed in the last 3 days?(circle the appropriate option) 0 1 2 3 4 5 6

41 **Name of third ARV in patient regimen (check the drug dispensed and write the name using standard symbols)**_____

42 Indicate the type of regimen and formulation O 1st line O 2nd line O FDC O Stand alone

43 In the past 3 days, how many tablets of this medicine did you take in one dose? _____

Was the correct dose taken in the past 3 days? (Tick appropriately) O Yes O No

44 In the past 3 days, how many times a day did you take this medicine? _____

Was the correct frequency of administration maintained? (Tick appropriately) O Yes O No

45 At what times were you taking this medicine in a day for the past 3 days (specify the hours e.g. 8am and 8pm)

_____

Was medicine taken at the correct schedule? O Yes O No

46 How were you taking this medicine in relation with eating food for the past 3 days?

O Taken before food O Taken after Food O Taken with or without Food

Was food restriction complied with? (Tick appropriately) O YesO No

47 Since you have been taking this medicine, have you experienced any problem you do not like? O Yes O No

48 If you have experienced any problem, what is the nature of the problem? O Tiredness O Fever

O Nausea O Vomiting O Dizziness or lightheadedness O Skin problems O Diarrhea

O Nervousness/anxiety O Others (specify)

49 Did you report this problem to any of the hospital staff (e.g. the doctor, pharmacist or nurse)? O Yes O No

If you reported the problem, what action was taken? O Medicine was changed O Problem was treated O Medicine was changed and problem treated O No action was taken

50 How many of the doses did you missed in the last 3 days?(circle the appropriate option) 0 1 2 3 4 5 6

BARRIERS TO ADHERENCE

Note: If the patient said he/she missed a dose for the past 3 days, ask for reasons for missing dose. But if the patient did not miss a dose for the past 3 days, please jump to question 52 and ask for the facilitators.

51 What are the reasons for missing doses in the past 3 days? O Forgot O Felt well O Ran out of medication

O Got pregnant O Pharmacy did not have any medicines O Fell asleep/slept through dose

O Not able to pay O Felt sick O Patient moved/transferred

O Travelled/away from home O Felt overwhelmed O Busy with work/study

O Did not understand how to take medications O Affected by drug side effects (fatigue, fever, nausea, vomiting, dizziness or lightheadedness, skin problems, diarrhea, and nervousness/anxiety)

O Stigmatization(did not want others to know) O Took holy water O Change of regimen O Fasting

O Alcohol usage O Family problems O Shared drug with others

O Others O Depression Lack of Food

FACILITATORS OF ADHERENCE

Note: For patients who did not missed a dose for the past 3 days

52 You did not miss a dose in the past 3 days. Which factors encouraged or helped you to take your medicines without missing any dose?

O Depended on treatment O Availability of food OHospital staff treating me kindly and with compassion support group

OFamily support (Husband/Wife/children) ONot wasting my time in the clinic O Having a business/employment

OTelephone calls by hospital staffs OVisitation by home base care people OHaving a means of transportation to the clinic

Other (specify) O Using adherence reminders (e.g. alarm clock, taking pill with OThe desire to live

SOCIAL SUPPORT

53 Do you belong to a support group? O Yes O No

54 Do you have treatment support partner? O Yes O No

PATIENT SATISFACTION

55 Since you have been attending this Clinic, how will you rate your level of satisfaction with? (Tick the appropriate options)

Level of Satisfaction	Very poor	Poor	Fair	Good	Very good
Attitude of Hospital Staff (Kindness/compassion)					
The Clinic environment (cleanliness and orderliness)					
Drug availability					
Effectiveness of treatment (Improvement in health condition)					
Laboratory services (Willingness to conduct tests)					

STANDARD OF LIVING

Note: The following questions focus on your standard of living. Whatever answer you give will not be disclosed to other people. You are also free not to answer any of the questions.

56 Type of house: O Stand alone O Family unit O Duplex O 2-3bedroom apartments

O Thatched house O Self contained/Studio O Yard/compound

57 Source of drinking water: O Stream/spring O Deep well in residence O Borehole in residence

O Pipe borne water supply Buy water from water sellers Fetching water from neighbors

58 What is your main source of cooking fuel? O Firewood/charcoal O Kerosene stove

O Gas cooker O Electricity cooker

59 Do you have a separate room for cooking where you live (like a kitchen)? O Yes O No

60 What type of toilet facility do you use? O Water cistern O Aqua privy O Pit toilet O Bush O None

61 **Which of these items do you own?**	**Yes**	**No**
Car		
Motorcycle		
Refrigerator		
TV		

Bicycle		
Fan		
Internet		
Cable TV		
Computer		
Washing Machine		
Pressing Iron		
Air conditioner		
Others specify:		

PATIENT CLINICAL CHARACTERISTICS:
Note: Do not complete this section during the interview session

VIRAL LOAD LEVEL AT THE TIME OF INTERVIEW----------

LATTEST CD4+ COUNT----------

WHO STAGE----------