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Adherence to Antiretroviral Medicines Among Adolescents and Young Adults in Benue State, Nigeria

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Walden University
2018

Abstract

Adherence to Antiretroviral Medicines Among Adolescents and Young Adults in Benue

State, Nigeria

by

Amom Jonah Tor-Anyiin

MPA, Benue State University, Nigeria, 2013

MSc, University of Debrecen, Hungary, 2007

B Pharm, University of Jos, Nigeria, 2003

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

January 2018

Abstract

Adherence to antiretroviral medicines is essential to halt human immunodeficiency virus

progression, increase CD4 counts, decrease virologic impact, and improve quality of life

for the infected people. However, sustaining good adherence among adolescents and

young adults (AYA) has been a challenge caused by various problems such as distance to

clinic, improved CD4 count which lead to complacency in adherence, and the nature of

the environment. This was a quantitative, retrospective, correlational, cross-sectional

study anchored by the transtheoretical model, which was used to understand how

adherence rate among the study population was impacted by the predictive factors.

Secondary data was collected from patient's medical records at the Federal Medical

Center, Makurdi in Benue State, Nigeria. Univariate analysis was conducted using

descriptive statistics. The study sample size of 656 patients was drawn from AYA ages

15–24 years. Independent t tests showed a statistically significant difference in adherence

rates between rural (94%) and urban (89%) AYA, $t(424) = -3.280$, $p = 001$. There was

also a statistically significant difference in adherence rates of ART for patients who lived

within 50 kilometers of the hospital and those who lived more than 50 kilometers away

from the hospital, $t(509) = -2.37$, $p = .018$. Also, there was a statistically significant

correlation between adherence rate to ART and CD4 of less than 500 cells/mm^3, $R =$

$.214$, $p = .003$. This study provides findings for HIV implementing partners (IPs) and

relevant health professionals in Nigeria useful for designing strategies that would

improve adherence rate to antiretroviral therapy among AYA in Nigeria.

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Dedication

The dissertation is dedicated to the Almighty God whose grace saw me through the research work in the midst of daunting challenges.

Acknowledgments

The Almighty God deserves a foremost acknowledgement for the successful completion of the dissertation. His grace over my life kept me above daunting challenges. Even when it looks like I will drop out of the PhD program, the mercy of the Lord saw me through. In the course of the program, I experienced an unprecedented favor from my Creator, God. To Him, I return the glory and honor for bringing me to the end of the study. It is a dream come true.

My wife, Mrs. Keryn Tor-Anyiin who is my sinoatrial node that I fondly called 'Myluv" remained the ideal 'helpmate' personified that I have known to be throughout the study period. From the very day of my enrolment into Walden University to the end of the study, she has remained unflinchingly supportive. During the course work phase, it became so overwhelming that I contemplated a quit but for her encouragement I continued. As I navigated through the dissertation process, she was always there with encouragement. She is simply the greatest gift I have ever gotten in life. I appreciate my four lovely children namely Mimidoo, Lianater, Tertsua and Nguavese. Their young ages notwithstanding, they demonstrated an uncommon understanding of co-operating with me at home to create an enabling atmosphere for my studies – God bless them all.

Worthy of mentioning is my dissertation Chair, Dr. Frazier Beatty. From the very day Dr. Beatty agreed to chair my dissertation, our interactions remained fruitful at every occasion. Dr. Beatty's comments and contributions were not only invaluable and accurate but timely while. He remained accessible via email, phone and text messages throughout the study period. Dr. Frazier Beatty is simply the ideal Chair every student longs to have.

The guidance the Dissertation Committee Chair provided in no small measure has contributed to the timely completion of the dissertation phase of my study. I wish could appreciate my chair with better words. I simply say 'thank you Dr. Frazier Beatty'. My second committee member and the University Research Reviewer (URR), Dr. Simone Salandy and Dr. Cheryl Cullen respectively, I appreciate each of you for adding value to my dissertation work through your various feedback.

Lastly, I appreciate my mother, Mrs. Becky Usua Amom Tor-Anyiin for her doggedness in ensuring that being a widow from a polygamous family was not enough to stop her from single-handedly ensuring I went to primary school through secondary school to my bachelor's degree level. It is the foundation she labored to overcome all odds and laid that has brought me to this academic height. May you live long to enjoy the fruits of your labor. God bless you richly.

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Chapter 1: Introduction to the Study

Introduction

Human Immunodeficiency Virus (|HIV) remains a pandemic that has claimed many lives and has impacted the healthcare systems of many countries, especially those in developing nations (Volberding, 2011). The advent of effective Antiretroviral (ARV) medicines has changed the landscape of medical intervention in HIV, which is now considered a chronic illness (Groh et al., 2011; Tougas, Hayden, McGrath, Huguet, & Rozario, 2015). One useful strategy in the management of the HIV virus is ensuring patients' good adherence to ARVARVs. The ARVs work better when there is adherence to the treatment, which goes beyond the act of taking the ARV to include the individual's attitude towards treatment (Jimmy, Jose Beena Jimmy, & Jose, 2011; Viswanathan et al., 2015).

In this study, I focused on adherence to ARV medicines among AYA in Benue State, Nigeria. My emphasis was on how adherence to ARV relates to (a) distance from patient's place of residence to the HIV treatment center, (b) environment where patient lives (urban versus rural) (c) low CD4 (less than 500 cells/mm^3) and high CD4 (more than 500 cells/mm^3). Adherence to ARV medicines is essential in the management of HIV infection (World Health Organization, 2015). There is a plethora of ARVs used in the cocktail to manage HIV, but these drug combinations give the desired therapeutic result only when patients are adherent to the medicines. Understanding covariates of adherence to ARVs would help the various HIV implementing partners (IPs) working in conjunction with the Federal Ministry of Health (FMoH) in Nigeria to make a shift in

how patients are enrolled into care, and in how measures are transformed to enhance adherence among HIV patients in care. Findings from this study could provide a basis for the HIV IPs in Nigeria to encourage HIV clients to enroll for treatment in treatment centers proximal to their place of residence. A positive correlation between adherence and high CD4 counts would help adherence counselors reinforce adherence counselling continually for clients instead of the common practice of focusing on new enrollees.

In Chapter 1, I offer a brief overview of HIV infection in Nigeria and offer the problem statement. Next, I present the researcher questions and discuss the theoretical framework. I then highlight the assumptions I made in the research, and discuss the scope, delimitation, and limitations of the research. The chapter ends with a discussion of the significance of the study and summary of the chapter.

Background of the Study

According to the World Development Indicator, in 2013, per capital GDP in Nigeria was only $2,980, ranking it 131st in the world (Ajakaiye, Jerome, Nabena, & Alabi A. Olufunke, 2015). The country is categorized as among the low- and medium-income countries. The first diagnosis of HIV in Nigeria was in Lagos in 1986. The following years saw numbers jump dramatically with two reported cases in 1987, 33 in 1988, and 9715 in the year 2000. At the onset of HIV in the country, there was a lot of skepticism about whether the disease was real or a mere ploy by the Western world to discourage sex and limit the perceived growth of African populations (Zeleza & Kakoma, 2003). Such skeptics even dubbed the acronym as "American idea of discouraging sex" (AIDS). Before the first sentinel survey in Nigeria, the prevalence of HIV was on a

steady rise. It was 1.8% in 1991, 3.8% in 1993, 5.4% in 1999, and 5.8% in 2001

(National Agency for the Control of AIDS (NACA), 2015). In 2011, with an estimated

population of 180 million people, Nigeria had HIV prevalence rate of 3.3% (Bashorun et

al., 2014). In 2015, the country had a projected population of 185 million (49% female

and 51% male) with a recorded HIV prevalence rate of 3.1% (PEPFAR, 2016). The 2012

National HIV/AIDS and Reproductive Health Survey (NARHS), which was a more

comprehensive survey compare to the ante-natal clinic (ANC) sentinel survey, reported

the prevalence of HIV at 3.4% (National Agency for the Control of AIDS (NACA),

2015).

There are six geo-political zones in Nigeria: South South, South East, South West,

North East, North West, and North Central (The Federal Republic of Nigeria, 1999). The

distribution of HIV prevalence in Nigeria is not homogenous among the six geo-political

zones. Initially, the southern axes had a comparatively higher rate; but over the years, the

Middle Belt region of the country, made up of parts of North East, and North Central, has

taken over (Bashorun et al., 2014). In 2012, South South, had the highest prevalence of

5.5%, while South East had the lowest prevalence of 1.8%.

HIV prevalence by Zones and National
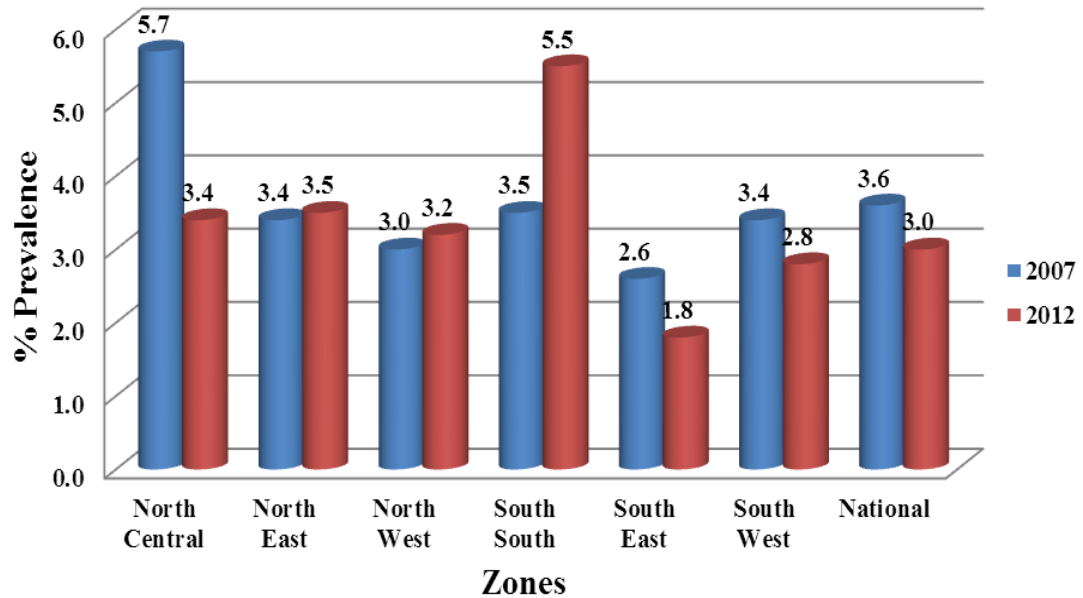
Figure 1. HIV prevalence by geopolitical axes including national rates.

Compared to the national prevalence of 3.0% in 2012, only South West and South East (with prevalence of 2.8% and 1.8%, respectively) had less than the national prevalence as displayed in Figure 1 (National Agency for the Control of AIDS (NACA), 2015). In 2012, four states shown in Figure 2 had a prevalence greater than 8%, including Rivers (15.2%), Taraba (10.5%), Kaduna (9.2%), and Nasarawa (8.1%) respectively (National Agency for the Control of AIDS (NACA), 2015).
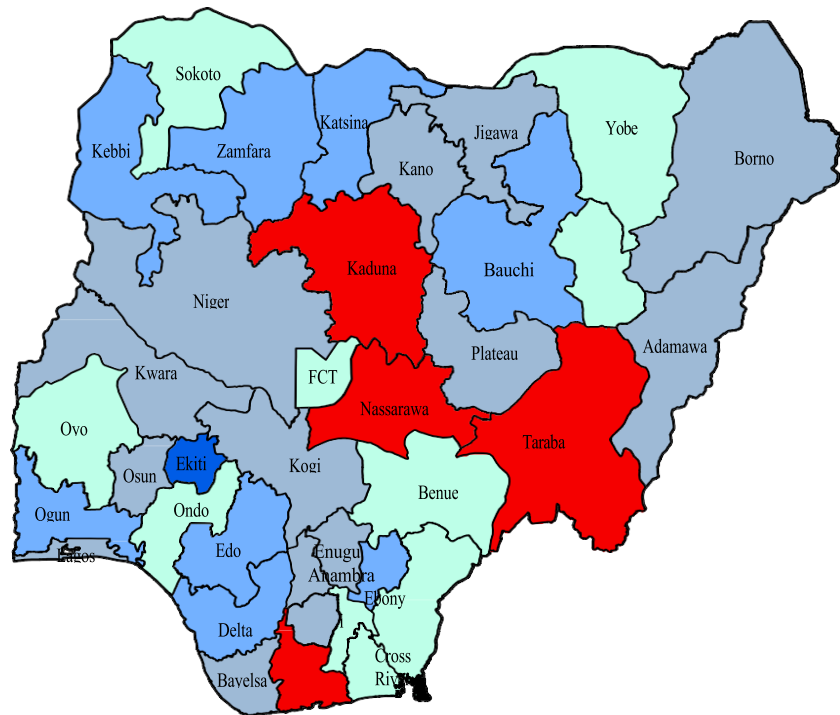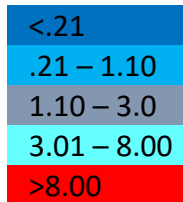
Figure 2. Spread of HIV prevalence by states (National Agency for the Control of AIDS (NACA), 2015)

There is a disparity in prevalence between urban and rural settlement with the former having a higher prevalence of HIV (Mahy et al., 2014). Also, the prevalence was higher among female than male with 4.0% and 3.2% respectively in 2007. Five years later (2012), the female rate declined to 3.5% but was still higher than the male rate of 3.3% (National Agency for the Control of AIDS (NACA), 2015). The age group 35 – 39 years had the highest prevalence in 2012 with 4.4% compared to age 15 – 24 which accounts for 42% of new infections globally (Kharsany & Karim, 2016; Wang et al., 2016).

The incidence of HIV peaked in 2009 with 278,061 new infections, and the rate of new infections has continued to decline with 262,238 in 2011, 239,155 in 2013 and 227, 518 in 2014 (National Agency for the Control of AIDS (NACA), 2015). Table 1 shows the trend of HIV incidence in Nigeria between 2009 and 2014. In 2015, Nigeria was responsible for over 30% of new infection among children globally (President's Emergency Plan for AIDS Relief [PEPFAR], 2016).

Table 1

Showing Trend of New Infection

Year	Female	Male	Total
2009	151,495	126,566	278,061
2010	145,245	123,422	268,667
2011	142,542	119,696	262,238
2012	137,671	115,835	253,506
2013	129,976	109,179	239,155
2014	123,601	103,917	227,518

Source: National Agency for the Control of AIDS, 2015.

Mortality

The total number of deaths from HIV in Nigeria is unknown because there was no proper data documentation at the initial stage of HIV outbreak in the country. However, available data showed that mortality rate dropped from over 210,0000 in 2013 to slightly above 174, 000 in 2014 (President's Emergency Plan for AIDS Relief [PEPFAR], 2016). The figure from the agency officially mandated by the federal government of Nigeria to

control HIV in the country, the NACA, estimated that 180,000 deaths in 2015 resulted

from HIV-related causes (National Agency for the Control of AIDS (NACA), 2015).

However, on the African continent to which Nigeria belongs, an estimated 790,000

people died of HIV-related causes in 2014, and this was less than the 1.2 million in 2009

and 1.5 million in 2004 (Granich et al., 2015). Maternal death related to HIV is fast

emerging as the leading cause of pregnancy-related mortality (Onakewhor et al., 2011).

HIV is one of the five preventable diseases that account for more than 70% of the leading

causes of 1 million annual deaths of children under 5 in the world, annually. The other

diseases are malaria, diarrhea, measles, and pneumonia (NACA, 2015). The number of

children orphaned by HIV was estimated to be 1.7 million in 2013 (PEPFAR, 2016).

HIV Mode of Transmission

HIV transmission routes vary widely in different regions of the world. In Eastern

Europe, South America, and Central Asia, the predominant routes are sex, drug, and men

having sex with men (Shaw & Hunter, 2012). In Nigeria, researchers have conducted

many studies on the transmission of HIV in Nigeria over the last two decades. The

converging point for researchers on this seems that the primary means of HIV

transmission in Nigeria remains men who have sex with men (MSM), use of intravenous

drug, sexual contact with commercial sex workers (The Joint United Nations Programme

on HIV and AIDS UNAIDS, 2010). Others means include through, blood transfusion,

blood products, and maternal-infant infection (Shubber, Mishra, Vesga, & Boily, 2014;

UNAIDS, 2010). Among the most at-risk populations, there has been a shift in

prevalence. The group includes female sex workers, men who have sex with men (MSM),

long journey travelers, and IDUs (NACA, 2015). There is a prevalence of 27.4% among

brothel-based female sex workers, 21.7% among non-brothel-based female sex workers,

and 17.2% for MSM (National Agency for the Control of AIDS (NACA), 2015). Two

decades ago, sex workers were thought to have the highest prevalence of HIV, but that is

fast changing as the prevalence for MSM was 13.5% in 2007, but rose to 23% in 2015

(Entonu & Agwale, 2007).

Intervention and Adherence Challenges

International health initiatives have focused on expanding access to ART in

countries with high levels of HIV endemicity, including Nigeria ART (Monjok, Smesny,

Okokon, Mgbere, & Essien, 2010). The incidence of HIV in Nigeria peaked in 2009 with

278,061 new infections, and the rate of new infections has continued to decline with

262,238 in 2011, 239,155 in 2013, and 227, 518 in 2014 (National Agency for the

Control of AIDS (NACA), 2015). The estimated total number of deaths due to HIV in

Nigeria is unknown because there was no proper data documentation at the initial stage of

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dropped from over 210,0000 in 2013, to slightly above 174, 000 in 2014 (PEPFAR,

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Nigeria to control HIV in the country, NACA estimated that 180,000 deaths in 2015

were due to HIV-related causes (NACA, 2015).

About two decades ago, the available ARV medicines were beyond the reach of

most who were in need in Nigeria because the cost for a year treatment was between

$5,000 - $15,000 (Bendavid, Leroux, Bhattacharya, Smith, & Miller, 2010). The Doha

Declaration on the Agreement on Trade-Related Aspects of Intellectual Property Rights by the World Trade Organization in 2001 (Hoen, Berger, Calmy, & Moon, 2011) was a milestone that improved access to the ARVs. Before this time, ARVs were patented, thereby making it difficult for low - and medium-income countries to have access to it (Hoen et al., 2011). Unlike the ugly situation where only one in 1000 had access to ARVs in Africa in the late 1990s, there are several treatment centers now in sub-Saharan Africa (Kharsany & Karim, 2016). The increased access to ART has led to the decline in the number of new infections (Pustil, 2016). Sub-Saharan Africa, which constitutes only 12% of the world population, is still home to between 66% and 71% of HIV prevalence globally (Kharsany & Karim, 2016). While HIV incidence in Nigeria, when compared to other African nations, has been steadily low, its global share is huge because of its size with an estimated population of 180 million people (National Population Commission, n. d.).

With the intervention of the United States government through the PEPFAR in 2001, ARVs became free for those enrolled in care in treatment centers in Nigeria (Collins & Beyrer, 2013). However, that also came with adherence challenges because ARVs are drugs to be taken for life. No matter the potency of the ARVs, without adherence to prescribed regimen ARV, there will be no effective management of HIV. In Nigeria, as in advanced nations, adherence to antiretroviral therapy (ART) has its challenges. According to Monjok et al. (2010) who did a systematic review of 13 published studies on adherence in Nigeria, the success of the ART expansion programs by global health initiatives is depended on individuals' adherence to HIV medicines.

Adherence is associated with most of the parameters that defined a good ART outcome such as low viral load, high CD4 counts, and low morbidity and mortality.

Adherence has virologic, immunological, and clinical implications for HIV management outcomes. For example, poor adherence in pregnancy is known to increase disease progression and increase the risk of virus transmission to the child (Bailey et al., 2014; Ekama et al., 2012; Kanters et al., 2016; Nachega et al., 2016; Vitalis, 2013). Studies among geriatric patients also have shown that adherence is a challenge that cut across all ages (Jin, Kim, & Rhie, 2016). In a comprehensive systematic review and meta-analysis study of adherence in adolescents and young adult aged 15–24 years from 53 countries, 62.3% was found to be adherent. The highest adherence rates were from Africa (84%) and Asia (84%). This was followed by South America (63%), Europe (62%), and North America (53%) had the poorest rates of adherence (S.-H. Kim, Gerver, Fidler, & Ward, 2014). A meta-analysis of adherence in sub-Saharan Africa indicated adherence rates of less than 80% among 23% of Africans (Croome, Ahluwalia, Hughes, & Abas, 2017). While there is no particular cut-off mark for adherence to be described as good adherence, most studies framed an adherence rate of 85% and above as good adherence (Falang, Akubaka, & Jimam, 2012; Suleiman & Momo, 2016a). Adherence rates among people living with HIV (PLHIV) in Nigeria vary considerably depending on the instrument used in the measurement. There are several ways to measure adherence which include direct measures, secondary database analysis, electronic medication packing, pill count, clinician assessment and self-report (Lam & Fresco, 2015). Patient

self-report, pharmacy refill records and pill counts are the commonest instruments of measure (McMahon et al., 2011).

In a descriptive cross-sectional study of participants accessing ART care in a tertiary institution in a southern Nigeria urban setting, 411 people living with HIV were interviewed about their adherence to ARVs in the week before the study. Researchers found the total adherence rate to be 59.9%. (Oku, Owoaje, Ige, & Oyo-ita, 2013; Oku, Owoaje, Oku, & Monjok, 2014). A related study in a rural setting in the same sub-region in Nigeria showed a 50.4% adherence rate (Oku et al., 2014). Onyeonoro et al. (2013) found a good adherence rate in the southern sub-region of Nigeria in the study of adherence among 282 children ages 4 months to 15 years in Nnamdi Azikiwe University Teaching Hospital, Nigeria. Adherence rates were 92% for females, and 90% for males. In a study in Ilorin, South-West Nigeria sub-region, Bello (2011) found that adherence rates meased through pill count and self-report for a 20-month period in May 2009– December 2010 was 73.3%. A study in the Middle - Belt region of Nigeria reported a better adherence. In a cross-sectional study of 250 participants who had been enrolled in care at the Federal Medical Center Keffi for more than 6 months, researchers found that 62.8% had more than 95% adherence rate, while 31.2% reported 100% adherence rate (Pennap, Abdullahi, & Bako, 2013). Adherence inhibitors have been found to include stigma associated with taking ARVs, the cost of ARVs (suffice to say the drugs are heavily subsidized), side effects associated with ARVs, and education level (Ankrah et al., 2016; Gare et al., 2015). According to Ankrah et al. (2016), other factors include distance from the clinic as reported by patients, transportation costs, and forgetfulness. In

addition, marital status, occupation, health-related illness polypharmacy, and unavailability of ARVs are said to impact adherence (Ankrah et al., 2016; Gare et al., 2015; Jin et al., 2016; Shigdel, Klouman, Bhandari, & Ahmed, 2014).

Problem Statement

Adherence is a term used to describe the extent to which a patient's behavior relating to medical treatment aligns with what was collectively agreed to between the patient and prescriber (Bello, 2011). Poor adherence to ART has been associated with failure of therapy, whereas good adherence is essential for the desired treatment outcomes such as improved quality of life and survival (Akahara, Nwolisa, Odinaka, & Okolo, 2017). For most of the countries where HIV is endemic like Nigeria, refill of ARVARVs at treatment centers is based on appointment (Mori & Owenya, 2014). Patients are thus expected to also adhere to their clinic dates soas to have their prescriptions refilled. The ARV medicines are free of charge in Nigeria and other sub-Saharan Africa with support from the U.S. government and other foreign agencies (OGAC, 2014). The problem, however, is that HIV patients rarely attained a 100% rate in their pharmacy ARV refill. Pharmacy ARV refill is a proxy measure of adherence to ART (Sangeda et al., 2014a, 2014b). There have been reported challenges that inhibit adherence as enumerated earlier on such as transportation cost, forgetfulness, side effects associated with the ARVs and stigma (Arnet, Walter, & Hersberger, 2013; Groh et al., 2011; Hatah, Lim, Ali, Mohamed Shah, & Islahudin, 2015). The life-saving significance of the ARV medicines notwithstanding, adherence has been a challenge among AYA (Ankrah et al., 2016).

Globally, while 83% of adolescents living with HIV are in sub-Saharan Africa, their ART outcomes are poor when compared to adults (Ankrah et al., 2016; Maskew et al., 2016). Also, once on ARV, one is expected to be adherent to obtain and maintain good health outcomes (Heestermans, Browne, Aitken, Vervoort, & Klipstein-Grobusch, 2016). However, poor adherence has been reported among people with prior good adherence (Ngarina, Popenoe, Kilewo, Biberfeld, & Ekstrom, 2013). Some of the inhibitors to adherence among this population include financial barriers, adverse side effects of the ARV, forgetfulness, and stigma (Gare et al., 2015; Shigdel et al., 2014). Thus far, there have been no studies in developing nations comparing rural and urban settings' impact on adherence. A study in Uganda indicated that rural health facilities were associated with poor adherence measured by hospital prescription refill for patients who reside and access care in such rural areas (Nabukeera-Barungi et al., 2015). There is therefore a need to explore such association for patients who live in the rural area but access their care in faraway urban settings. Also, distance to the treatment center as reported by patients has been cited as an inhibitor of adherence (Conley et al., 2012). However, no known study has explored this further using patient hospital records to correlate such claims.

Purpose of the Study

The purpose of the research was to explore the difference in adherence rate to ART in patients who resided in a rural setting and those who resided in urban settings. Because patients have reported distance as a barrier, I also stratified the population by distance to the treatment center and explored for correlation with adherence. In addition, I

explored relationship between a high CD4 count and adherence. Therefore, the specific goals of the quantitative study were (a) to explore the difference in adherence among adolescents and young adults (AYA) accessing care in the same treatment center but resident in rural and urban settings, (b) to explore the association between adherence in AYA stratified by distance from treatment center, (c) to determine the nature of the relationship between adherence and CD4 counts after an adolescent or young adult attained a good CD4 cell count greater than 500 cell/ mm^3.

Research Questions

I developed the following three research questions (RQs) for this study:

RQ1: What is the difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings?

Ho1: There is no statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

Ha1: There is statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

RQ2: What is the association between distance from treatment center and adherence to ART among AYA?

Ho2: There is no statistically significant association between distance from treatment center and adherence to ART among AYA

Ha2: There is statistically significant association between distance from treatment center and adherence to ART among AYA.

RQ3: What is the relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA?

Ho3: There is no statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA.

Ha3: There is statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA.

Theoretical Framework

The theoretical base for the study was the transtheoretical model (TTM) of behavior change. The theory holds that health behavior change involves six stages, which include pre-contemplation, contemplation, preparation, action, maintenance, and termination (Prochaska & Velicer, 1997). The theory was developed by Prochaska and Di Clemente (2005) in 1977 and has been used widely in the study of patient health behavior change programs like physical exercise, adherence, diet, and smoking cessation (van Leer, Hapner, & Connor, 2008a). Recently, the theory has gained popularity in understanding patients' adherence to medicines (Johnson et al., 2006). TTM served as my framework for understanding changes in adherence as AYA living with HIV continue to take ARV medicines. In Chapter 2, I offer a detailed explanation of the theory.

Nature of the Study

This was a quantitative study with a cross-sectional design (see Creswell, 2009; Gordis, 2009). When making a choice of research design, it is important to ensure that the

design is appropriate for the study and would lead to a valid conclusion (Creswell, 2009).

Researchers use cross-sectional studies to describe a pattern of relationship between

variables (Mann, 2003). Also, cross-sectional studes are efficient, effective, easy and

quick to conduct, and can easily be reproduced (Campbell & Stanley, 1963; C Frankfort-

Nachmias & Nachmias, 2015). Therefore, the design was appropriate for my study in

which I sought to explore the relationship among the various variables that impact ART

adherence. Independent variables in the study included CD4 cell counts, the distance

between patient's home and treatment center, and the type of the home environment

(urban or rural). The dependent variable was adherence. I will thoroughly discuss the

study methodology in Chapter 3.

Definitions of Study Variables and other Terms

Acquired immune deficiency syndrome (AIDS): A collection of symptoms that is

best described as a syndrome caused by HIV (Sharp & Hahn, 2011).

Adherence: A term used in describing the extent to which a patient's behavior

relating to medical treatment agrees with what was collectively agreed with the prescriber

(Bello S.I, 2011).

Adolescent: A person between 10 and 18 years old. Defining adolescent strictly

from the perspective of age has been criticized by many. A complete definition of an

adolescent should consider the biopsychosocial stage of a young person entering an adult

stage of life (Curtis, 2015).

CD4 count: A test that measures the number of CD4 cells in the body. These CD4

cells, also called T cells, are the type of white cells that defend the body against infection.

It does not measure HIV but is a surrogate HIV marker that indicates not just presence of HIV but how much damage it has caused to the body. CD4 count serves as an indicator of body immunity (Nwokedi, Ochicha, Mohammed, & Saddiq, 2007).

Distance to treatment center: This refers to the distance between the ART center and where the participant resides.

Geopolitical zone: Refers to the zones in Nigeria based on geographical location and political consideration. Economic, political, and educational resources often are shared across the zones (Ibrahim & Ibrahim, 2014).

HIV treatment center: This is a designated health facility for management of HIV/AIDS.

Human immunodeficiency virus (HIV): The virus that spreads through bodily fluids and causes AIDS, a life-threatening disease, by attacking CD4 cells.

Mortality: Incidence of death with a particular group in a specified period.

Pharmacy refill: Prescription refill in pharmacy.

Rural: This refers to a hamlet or village settlement.

Self-disclosure: The act of revealing information about oneself to another person (Nöstlinger, Bakeera-Kitaka, Buyze, Loos, & Buvé, 2015).

Self-report: Report about a patient as presented by the patient.

Serodiscordance: A term use in reference to a couple that has "mixed serostatus." That is one partner is HIV-positive while the other is HIV-negative (Irungu et al., 2016).

Urban: This refers to a town or city settlement.

Young adult: According to WHO, a young adult is a person aged 12–24 (Geiger & Castellino, 2011).

Justification for Set Values

CD4 counts. The research question four (RQ4) set CD4 counts at 500 cells/mm3 to assess adherence because the standard CD4 counts for a healthy person is between 500 cells/mm^3–1500 cells/mm^3 (Ying, Granich, Gupta, & Williams, 2016). Normally, those with CD4 below 500 cells/mm^3 are unlikely to feel well compare to those with CD4 above 500 cells/mm^3 (Crampin, Mwaungulu, Ambrose, Longwe, & French, 2011).

Distance to treatment center: The distance between client's resident and the ART center.

Assumptions

I made the following assumption when conducting this study:

- I would have unrestricted access to the medical records of clients accessing HIV care at FMC Makurdi located in Benue State, Nigeria to extract the requisite data for the analysis.

- There would be maximum cooperation from the staff of the medical record department in the FMC Makurdi in the process of data abstraction from patients' medical records.

- Physicians, nurses, pharmacists and all the health care workers in the FMC Makurdi collected and documented accurate primary data of clients such that conclusions based on the data will reflect the truth.

- My analysis based on data obtained from AYAs from FMC Makurdi that has

  over 10,000 patients would be a true representation of AYA in Benue State,

  Nigeria.

- My research assistants would be very honest in data extraction and as such

  information extracted from the clients' medical records would be accurate and

  valid.

Scope and Delimitations

I explored the adherence rates of AYAs in Nigeria accessing ART between 2011

and 2014 to see how the group differs with respect to distance, CD4 counts and type of

environemnt. Adherence is crucial for the successful management of HIV globally. AYA

are the links between pediatric and adult, and as such, poor adherence to ARVs from this

group could mean a serious public health issue given that one has to remain on these

drugs for life. HIV is prone to becoming resistant to ARVs if the adherence component of

HIV management is not handled carefully. Once there is resistance to any ARV, HIV

infection becomes a public health challenge.

The study was restricted to data from AYA who are living with HIV/AIDS and

are currently enrolled in ART in the FMC Makurdi, Benue State, Nigeria. I used a

retrospective, correlational, cross-sectional design for quantitative analysis (Gordis,

2009). This methodology is employed when a researcher wants to explore relationships

between variables without establishing causation (Campbell & Stanley, 1963; C

Frankfort-Nachmias & Nachmias, 2015; Mann, 2003). This study does not establish

causality but shows association, so the methodology is appropriate because the focus of

my research was not to establish causality but to explore the nature of relationship

between adherence rate and predictor variables—namely CD4 counts, distance from ART

center and nature of settlement among adolescents and AYA. Also, the secondary data I

used was collected at one particular point in time, which fulfills the requirements of a

cross-sectional study. Another merit of the cross-sectional methodology is that it could be

used for description of the odds ratio, absolute risks, and relative risk from prevalence

(Thompson, Myers, & Kriebel, 1998).

Limitations

- Adherence has relationship with other variables that have been studied, but

  my research was limited to the relationship between adherence and CD4

  counts, distance from a treatment center, and residential setting (urban/rural).

- There could have been other factors that confound the correlation between

  adherence and the variables in the study that influenced the outcome variable.

- Findings from the study might not apply to all environments in the world as

  several factors influence adherence including economy, culture, and political

  environment. Also, one of the disadvantages of a cross-sectional study is

  limited generalizability of the study because it is a snapshot study that is not

  always a representative (Sedgwick, 2014).

- Part of the data on adherence was based on patient self-report. Self-report has

  a validity problem resultant from respondents' desire to appear "acceptable"

  (Jimmy & Jose, 2011; Lam & Fresco, 2015). For example, a young HIV

positive unmarried woman could lie that she is married in order not to be seen as social deviant in some communities.

Significance

ART adherence improves quality of life, reduces hospitalization with attendant cost implications, and reduces the incidence of HIV-related morbidity and mortality (Falang et al., 2012). Adherence at rates below 85% a serious public health issue because it potentially causes resistance to the currently limited available ARVregimens (Kadhiravan, 2013). For example, resistance to first-line ARVs means a patient would have only a second-line regimen and salvage regimen as the remaining options (Masikini & Mpondo, 2015). There is an attendant increased total health cost associated with poor adherence as well because health outcome is impacted negatively, thereby increasing the frequency of clinic visits, transportation costs, and pill burden with an additional cost implication. Non-adherence has been linked to treatment failure as well (Inzaule, Hamers, Kityo, Rinke De Wit, & Roura, 2016).

Two-thirds of new infections of HIV in 2012 were among AYA aged 15-24 years (Bekker, & Hosek, 2015). Between 2002 and 2012, AIDS-related mortality dropped by 30% for all age categories except AYA, whose rate *increased* by 50% for the same period (Bekker et al., 2015). The research is unique because despite many studies on factors that negatively influence adherence among AYA, researchers have not explored the effect of an environment such as urban or rural setting. Also, if the distance to a treatment center is stratified and there is no correlation with adherence, then findings from the research would shed knowledge on a need for a shift in the current adherence strategies.

Furthermore, identifying an adherence inhibitor would call for a counter strategy that would be in line with the ambitious treatment target of the UNAIDS to have viral suppression in 90% of people living with HIV globally (UNAIDS, 2014). For a HIV-free generation, viral suppression in 90% of the infected population is essential.

Implication for Social Change

The positive social change implications of the study cannot be overemphasized. Given the high prevalence of AYA under care in ART in Nigeria (John, Okolo, & Isichei, 2014), my findings may help in several ways. The findings may identify potential factors that influence adherence to ARV medicines among AYA. Adolescence is an important stage in life because it is the transitionary stage from childhood to adulthood. This comes with attendant challenges including psychological problems, sexual health issues, aggression and violence, health problems, and physical and emotional changes (Shlafer et al., 2014). Thus, findings could provide a scientific basis for a shift in the current adherence strategies in the management of HIV patients. Further, they could form the basis for health policy makers to develop measures that will place emphasis on adherence among AYA. Poorly managed adherence to ARV is a potential for development of drug-resistance, which could become a public health issue that will impact treatment and management of HIV in the country because there are limited ARV options available (Cihlar & Fordyce, 2016)

Findings could also help to provide insight for health care providers into correlates of adherence to ARV medicines by AYA. A strong correlation between distance to treatment center and residential address of clients could be a call for a robust

adherence counselling during enrolment in HIV care, with emphasis on encouraging

clients to choose treatment centers that are proximal to their locations. This may, for

example, lead to increasing the number of health facilities providing ART so as to

encourage those living with HIV and ready to enroll in care to do so in health facilities

closer to their localities. The research findings could also have potential for patients

themselves by encouraging them to appreciate the role of adherence even when CD4

counts are high. Overall, a good adherence has potentials for decreased disease

progression, improved quality of life, decrease rate of hospital visitation, reduced cost,

and reduced burden on health systems. As a result, there may be more money available

for other development projects benefitting all Nigerians.

Summary

Medication adherence is important in the management of HIV/AIDS. Poor

adherence has the potential to become a public health issue because adherence is

associated with virologic, immunologic, and clinical outcomes. While 80% of HIV-

infected persons in sub-Saharan Africa are adolescents, their rate of ART adherence is

poor compared to other populations.

In Chapter 1, I provided background on HIV in Nigeria and globally. The virus

disproportionally affects AYA in sub-Saharan Africa. I also discussed the prevalence of

HIV by zones in Nigeria. The problem statement was introduced, which highlighted the

existing gap in the literature on adherence to ART among AYA. I then introduced the

three research questions, with adherence as the outcome variable while the distance to the

treatment center, CD4 counts, and type of residential setting (urban/rural) were the the

predictor outcomes. I also introduced the theoretical framework upon which I built the study, and discussed the study's purpose and significance. In the next chapter, I review the current literature on ART adherence among AYA.

Chapter 2: Literature Review

Introduction

I conducted a literature review to develop a comprehensive understanding of the current scientific knowledge on adherence in ART among AYA adults with a focus on Nigeria. Adherence is an essential component of HIV/AIDS management that, when compromised, affects the desired therapeutic effect of ART (Castro, Gonzalez, & Perez, 2015).This review will encompass all the variables in my research work, which included CD4 cell counts in relation to location of ART treatment centers and rate of adherence. Also, the influence of environment (urban or rural dwelling) on adherence by people living with HIV will be reviewed. Further, I review factors that influence adherence together with measurement of adherence. ART adherence and public health are reviewed as well.

The theoretical base for the study was the TTM of health behavior change. It is also called the stages of change model, and it holds that health behavior change involves six stages which include pre-contemplation, contemplation, preparation, action, maintenance, and termination (Prochaska & Velicer, 1997). The theory has been used widely in the study of patient health behavior change programs involving physical exercise, adherence, diet, and smoking cessation (van Leer et al., 2008a). In recent time, the theory has gained popularity in understanding adherence to medicines (Johnson et al., 2006). TTM served as the framework I used to understand changes in adherence as AYA living with HIV continue to take ART. The chapter will end with a highlight of findings from the literature review and the summary of the chapter.

Literature Search Strategy

I used a variety of electronic bibliographic databases to carry out the literature search, including PschINFO, MEDLINE through PubMed, ProQuest, Science Direct, Google Scholar, and Cumulative Index to Nursing and Allied Health Literature (CINAHL). The search was focused mainly on articles written in English and published from 2011 to present. Key search terms included *Nigeria, HIV, antiretroviral, CD4 count, urban, rural, adolescents, young adults, distance, adherence, adherence inhibitors, adherence facilitators, youth, children, ART, pharmacy, pharmacy refill,* and *resistance.* I used Boolean operators terms such as *AND, OR,* and *NOT* to combine the various key search terms. I considered only articles and books with specific relevance to the dissertation focus.

Theoretical Framework

People in care receiving ART are expected to adhere to their treatment to achieve a good health outcome. Remaining adherent is important because patients may need to protect an unborn child or uninfected partner, and typically desire to get better and remain healthy (WHO, 2015). While adherence is desirable, for some people, attaining and maintaining adherence of greater than 85% is hard. In this section, I will discuss three theories that I used or considered using for my research.

The health belief model (HBM) was first developed by Hochbaum, Rosenstock and Kegels in the 1950s. The model explains health behavior and researchers use it to predict individuals' health behaviors (H.-S. Kim, Ahn, & No, 2012). The model has six constructs that predict health behavior, including risk susceptibility, risk severity, benefits

to action, barriers to action, self-efficacy, and cues to action (Jones et al., 2016). In the

HMB, if an individual perceives the benefit of an action to be greater than the perceived

threat or risk of not acting, then the individual will act (Kim et al., 2012). While the HBM

is important, I did not use it because of the inherent weakness of the HBM which include

non-inclusion of positive effects of negative behaviours and social influence (Jones et al.,

2016; Munro, Lewin, Swart, & Volmink, 2007). Another theory widely used in health

behavior is social cognitive theory (SCT), which began as social learning theory (SLT)

by Albert Bandura in the 1960s. The theory posits that learning occurs in a context that

result from interaction of environment, the person, and behavior (Stacey, James,

Chapman, Courneya, & Lubans, 2015; Tougas et al., 2015). The model could also be

used as a framework to explore adherence to ART among AYA. However, I did not use it

because its wide-ranging focus makes it difficult to operationalize the theory (Munro et

al., 2007). I therefore, used the TTM discussed below for my study.

The TTM of health behavior change, also called the SCM, is a model developed

by Prochaska and Di Clemente in 1977 (Prochaska & DiClemente, 2005). They named

the model "transtheoretical" because it incorporated elements from different

psychotherapy theories. Researchers use it widely in the study of health behavior. The

theory holds that health behavior change involves six stages, which include pre-

contemplation, contemplation, preparation, action, maintenance, and termination

(Prochaska & Velicer, 1997). These stages serve as lenses for understanding adherence to

ARV among AYA. Among SCT, TTM and HBM, the TTM fit best into my study, as I

show in the following detailed explanation of the theoretical framework.

The Transtheoretical Model

The popularity of the TTM in research involving health behavior is understandable because the theory is useful for categorizing health behavior into constructs that explain why individuals tend to take some action regarding their health (Prochaska & Velicer, 1997). The focus is the patient's readiness to change. The theory has been used widely in the study of patient health behavior change programs such as those for physical exercise, diet, and smoking cessation (van Leer et al., 2008a). Recently, the theory has gained popularity in understanding adherence to medicines (Johnson et al., 2006). It may be of help for health care providers in predicting adherence of their clients to ART (Genberg, Lee, Rogers, Willey, & Wilson, 2013).

Precontemplation. Precontemplation is the stage where behavioral change is not taken seriously by individuals (van Leer et al., 2008a). It is the stage of diagnosis of illness or commencement of medication where the individual concerned needs to take ownership of the issue at hand by understanding consequences of action and inaction—for example, the negative or positive consequence of not taking or taking prescribed medicines (Konkle-Parker, 2001). In this stage, individuals can be grouped into two categories: those who are ignorant that it is possible to change their behavior. and those who deliberately decide there is no need to change behavior (van Leer et al., 2008a). The individual in this stage typically is not contemplating making any decision in the next 6 months (Genberg et al., 2013). The advent of ARV on a public health scale in sub-Saharan Africa initially was a concern amongst health officials because poor adherence holds potential for viral resistance. However, years after, adherence to ART in

developing nations has been found to be equal, or in some circumstances better, than that in the Western world (Chung et al., 2011). For the ART-naïve patient at the stage of precontemplation, researchers have found that adherence counselling is effective in improving adherence. In a randomized controlled trial study at the Coptic Hope Center for Infectious Diseases in Nairobi, Kenya conducted between May 2006 and September 2008, adherence of 310 participants was compared between those who had intense adherence counselling at the ART initiation stage and those who did not (Chung et al., 2011). According to Chung et al. (2011), participants who got adherence counselling at the initial stage were comparatively better in remaining adherent. That is, they were 29% less likely to have monthly adherence of less than 80% There were also 59% comparatively less likely to experience viral failure (HIV-1 RNA $\geq$ 5,000 copies/ml) compared to those who received no counseling (Chung et al., 2011).

Contemplation. Contemplation is the stage where an individual considers changing behavior, taking into consideration benefits and risks involved in the change. The contemplative individual could be likened to someone on the fence considering jumping to either side of the divide. At this stage, there is acknowledgement of existence of problem, but no certainty on whether to act or not. Therefore, individual is considering making a decision in the next 6 months, and as such, could be said to be in a state of ambivalence (Genberg et al., 2013). In a randomized controlled trial in New England for 137 participants accessing ART, adherence to ARV at an early stage (contemplation and pre-contemplation stages) was compare with that at a later stage (maintenance state). The mean age for the 22% female, 48% white, and 28% African American population was 42

years (Genberg et al., 2013). According to the study, those in the early stage had adherence that was significantly lower (-9.8%, $p = 0.04$) compare to those in maintenance stage.

   Preparation. At this stage the individual becomes more serious regarding the need for action towards change and is comparatively less ambivalent (van Leer, Hapner, & Connor, 2008b). This is the stage where you hear statements like "there is every need for me to do this now," "I think I can do it," and "what do I do?" People in this stage try to get information and resources that would help them change their behavior, and at this stage, self-efficacy plays an important role in transiting to the action stage (Jeon, Kim, & Heo, 2014). Too often, some skip this stage to the next phase called "action" (Jeon et al., 2014).

   Action. Action is the stage where individuals are actively engaged in modifying their behavior (Prochaska & Velicer, 1997). There is the confidence to make a change and the amount of time spent here differs, as it could literally be within an hour and could also take months (generally found to be within 6 months). Individuals in this stage are open to receiving help and may also seek help from others. To the changer, it is the time when new skills, both cognitive and behavior are learned and applied for a change (Konkle-Parker, 2001).

The Stages of Change Model

Enter → Precontemplation → Contemplation → Determination → Action → Relapse → Maintenance

Exit & re-enter at any stage
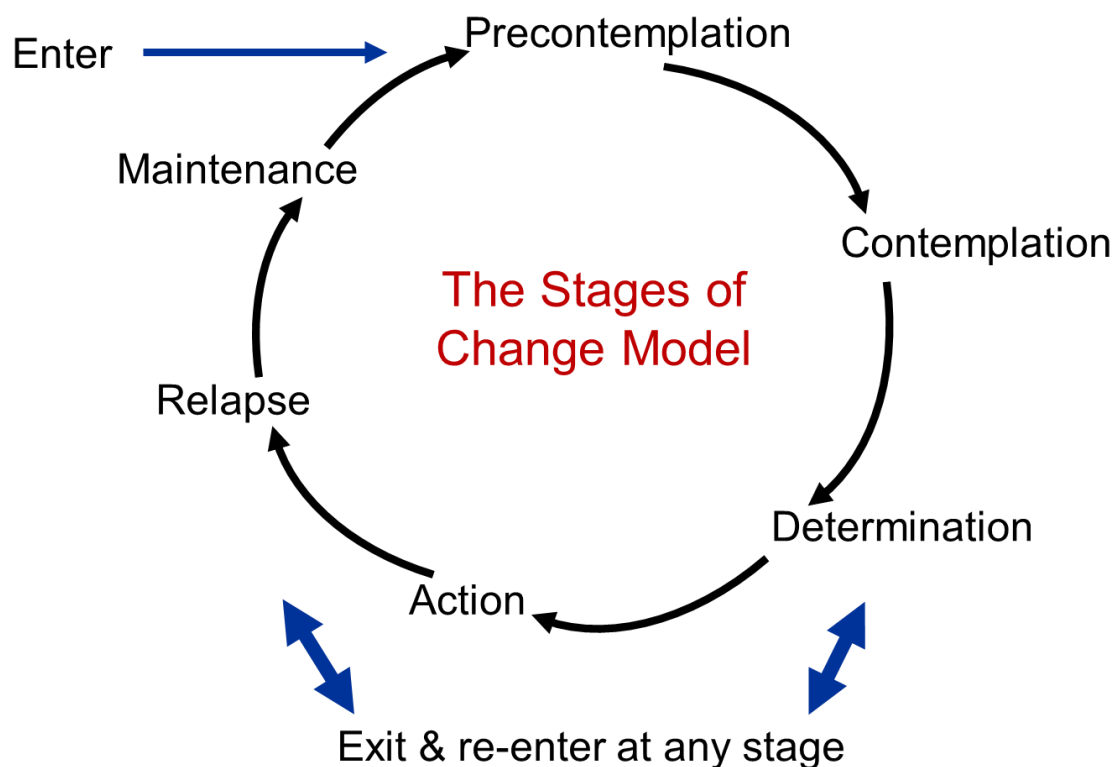
Stage	Precontemplation	Contemplation	Preparation	Action	Maintenance	Termination
Standard time	More than six months	In the next six months	In the next month	Now	At least six months	Anytime

Figure 3. Modified diagrammatical representation of TTM and time.

Maintenance. This is a stage where the new health behavior is incorporated into an individual's way of life. Individual here make efforts to sustain the new behavior by constantly reminding themselves of the change they have made. In ARV adherence, this is a very important stage. The goal of this maintenance stage is to sustain the newly learned behavior and resist every temptation to return to the old behavior by devolving strategies that overcome lapses becoming complete of reversal (Chung et al., 2011; Genberg et al., 2013; Konkle-Parker, 2001).

Termination. Termination is where there no desire to return to the old way of doing things (Johnson et al., 2006). According to Prochaska and DiClemente, (2005) and Prochaska and Velicer, (1997) at this stage former behavior are no more desirable. From the model in figure 1, these stages are cyclical implying one could exit and re-enter at any stage.

<center>**Global Overview of HIV**</center>

Since the discovery of the first case of HIV in 1981, the number of people infected with the virus has continued to rise (Sharp & Hahn, 2011). In some countries, while the incidence has declined, prevalence has continued to increase partly due to increase in lifespan of those on ART (Wang et al., 2016). According to Wang et al., (2016), the peak of HIV incidence globally was in 1997 with a size of 3.3 million people, and this continued to decrease at the rate of 4.8% per year until the year 2005. Between 2005 and 2015, the incidence remained steady at about 2.5 million infections per year (Wang et al., 2016). Among adult females living with HIV in 2015, 17.8 million representing 51% was those that were 15 years and older whereas adolescent girls constituted 60% of young people living with HIV and this represents 2.3 million human beings (UNAIDS, 2016). In 2015, among the 1.8 million adults with new infections, 47% were female, and 58% of the new infections were in the age category of 15 -24 years. At a global level, there were differences in new infections and proportion of prevalence among young adult male and female between age 15 and 24 years (WHO, 2015). In 2015 for instance, in eastern Europe and central Asia, 31% of the new infection among females, 46% was between age bracket of 15 and 24. For the same period, in North

Africa and the Middle East, of the 38% of new infections among adult female, 48% was between aged 15 and 24 years (Wang et al., 2016). In Latin America, there was 29% new infection that was an adult female and the age bracket 15 – 24 years constituted 41%. As for Asia-Pacific, new infection among adult female was 32% while age bracket 15 – 24 years was 41% (Wang et al., 2016). There was a difference in new infection in western and central Europe and North America where 22% new infection was recorded among adult female with 29% aged between 15 and 24 years (Nations, 2015).

The prevalence of HIV, on the other hand, rose from 2.4 million in 1985 to 28 million in the year 2000 while between 2000 and 2015, the number of people living with HIV increased by 0.8% per year (Wang et al., 2016). In 2015, the world prevalence of HIV/AIDS was 38.8 million (Fettig, Swaminathan, Murrill, & Kaplan, 2014; Wang et al., 2016). Mortality of HIV had its peak in 2005 with 1.8 million deaths, and this dropped by 5.5% per year to 1.2 million in 2015 with the highest mortality rate in sub-Saharan Africa (Wang et al., 2016). In 2015, 1.8 million children under the age of 15 years were infected while 100,000 was associated with AIDS-related deaths (Wang et al., 2016). The new infection was 150, 000 but incidence has dropped by more than 70% since 2001 (Kaiser Family Foundation, 2016). In 2015, there were 1.8 million new infections of which sub-Saharan Africa had a disproportionate burden of 75.4%, South Asia 8.5%, Southeast Asia 4.7%, and East Asia 2.3%. HIV rates across countries also vary significantly with the highest rate in Southern Africa with more than 1% in Lesotho, Botswana, and Swaziland (Wang et al., 2016). In Europe, Russia has the highest incidence rate while in Asia Cambodia is the country with the highest incidence (Fettig et al., 2014; Wang et al.,

2016). Haiti, Guyana, and Belize are the only countries in Americas with a rate greater

than 50 per 100,000 people. Globally, incidence has decreased between 2005 and 2015

while rate has continued in some countries (Wang et al., 2016). The number of people

living with HIV/AIDS who are on ART rose from 6.4% to 38.6% for male while those of

female increased from 3.3% to 42.4% between 2005 and 2015 (Wang et al., 2016).

Overview of Adherence in ART

The term adherence is often used interchangeably with compliance. While both

measure extent to which prescribed medicine is taken by a patient, the latter refers to the

traditional expectation to stick to what a prescriber says while the former has to do with

the extent to which drug is taken as it was agreed by both prescriber and patient (Brown

& Bussell, 2011; Hugtenburg, Timmers, Elders, Vervloet, & van Dijk, 2013). The WHO

defines adherence as a the extent to which person's drug taking behavior agrees with a

collective understanding the person has with a health care provider (Jimmy et al., 2011).

When medicines are prescribed, it for such to be taken so adherence to medicines is

essential if desired therapeutic response is to be achieved. There is a plethora of studies

on adherence to ARV medicines with different findings on level of adherence and how it

relates to achieving a good therapeutic effect. Adherence has virologic, immunological

and clinical implication on HIV management outcome. For example, poor adherence in

pregnancy is known to increase disease progression and increase risk of virus

transmission to child (Bailey et al., 2014; Ekama et al., 2012; Kanters et al., 2016;

Nachega et al., 2016; Vitalis, 2013).

Global Overview of Adherence

According to the WHO revised protocol, it is hard to accurately tell who will have suboptimal adherence using demographics and that individual adherence also varies (WHO, 2012). In a world-wide systematic review and meta-analysis study of adherence in adolescents and young adult aged 15 – 24 years from 53 countries, 62.3% was found to be adherent. The highest adherence was from Africa [84% (95% CI 79–89; I^2:93%)] and Asia [84% (95% CI 77–91; I^2:0%] follow by South America [63% (95% CI 47–77; I^2:85%] while Europe [62% (95% CI 51–73; I^2:97%)] and North America [53% (95% CI 46–59; I^2:91%)] were the poorest (Kim, Gerver, Fidler, & Ward, 2014). The Kim et al. (2014) study showed Africa and Asia had the highest adherence suffice to say the adherence rate was below the generally acceptable level of minimum of 85% (Falang et al., 2012; Suleiman & Momo, 2016b). Mountain et al. (2014) did a similar world-wide systematic and meta-analysis study on adherence among female sex workers. Data bases from Embase and MEDLINE through PubMed, were used where 39 studies relevant to the review were included. These studies were from Africa, North America, South America, Central America, Asia and Caribbean. According to the (Mountain et al., 2014), after enrolment, those lost to follow up was 6% (95% CI: 3%–11%, $I^2 = 0\%$, 3 studies) and those who died after enrollment into ART in was also 6% (95% CI: 3%–11%, $I^2 = 0\%$, 3 studies). Those with greater than 95% adherence rate of prescribed pills was 76% (95% CI: 68%–83%, $I^2 = 36\%$, 4 studies), while 57% (95% CI: 46%–68%, $I^2 = 82\%$, 4 studies) of FSWs on ART had a viral suppression (Mountain et al., 2014) . From the study population, 24% were below the desired 95% adherence rate. Factors associated

with adherence in the studies varied greatly as it was a systematic review that cut across five continents.

In a related study, Hudelson and Cluver, (2015) carried out a systematic review and meta-analysis of adherence in low and medium income countries for 4,363 adolescents ages 10 -19 who were on ART. Only quantitative observational studies were included in the review. Journal and trial databases and conferences databases were used to search for the published articles that met inclusion criteria. Databases that were used included MEDLINE (through PUBMED), CINAHL, SIGLE, LILACS, World Health Organization (WHO), Web of science, Health Library, U.S Institute of Health's Clinical Trials Registry. The researchers found adherence varies greatly among nations with different factors impacting adherence. In the review, adherence was as low as 16% from Zimbabwean population to as high as 99% among Thai population (Hudelson & Cluver, 2015). In Cuba, a cross-sectional study of 876 patients on ART was carried out for patients aged greater than 15 years and who have been in care for at least six months prior to the study. Through administration of questionnaire, adherence rate of participants was assessed (Aragonés, Sánchez, Campos, & Pérez, 2011). The researchers categorized adherence into five groups namely perfect adherence (100%), good adherence (95% - 99.9%), moderate adherence (80% - 94.9%), poor adherence (1% - 79.9%) and drop out (<1%). The result showed 62.6% had perfect adherence, 8% had good adherence, 14.1% had moderate adherence, 13.3% had poor adherence while 2.0% dropped out from care (Aragonés et al., 2011). From the study, 70.6% (62.6% perfect adherence + 8% good adherence) of Cuban patients receiving ART had high adherence rate. The relatively

higher level of adherence recorded in Cuba is consistent with the findings of adherence in

Africa and other developing nations (Hudelson & Cluver, 2015; Kim et al., 2014).

In South Africa, Morojele et al. (2014) studied adherence and correlates such as

alcohol and psychosocial factors. It was a across sectional study where structured

questions were administered on HIV clients accessing care in two district hospitals in

South Africa after obtaining their informed consent. Cohen was used to determine that

304 patients was enough sample size for the study. The study had 205 (68 %) women and

98 (32 %) men in the sample with one participant having a missing gender. About 50% of

the study sample was aged between 30 and 39 years. Because of the likelihood of

differences in some of the determinants under study, both township and a health facility

in city were included. The study looked at the prevalence of HIV in South Africa where

over 1.7 million people are estimated to be living with the virus and carried out an

analysis to see if there was a correlation between the use of alcohol, psychosocial factors

and ART to adherence among ART recipients in South Africa (Morojele et al., 2014).

The aim of the study was to determine association of alcohol with ART non-adherence

over and beyond structural and psychosocial factors. The authors named structural factors

such as food insecurity, transport costs to health facility, travel times to health facilities

and waiting times at clinics. Whereas, HIV stigma and HIV non-disclosure were

considered as psychosocial factors. Multiple regression was used in the analysis because

the study had several predictors with a single dependent variable which is adherence.

Where we have more than two variables, multiple regression becomes a good statistical

test to predict the relationship between those variables (Alexopoulos, 2010). The result

showed only 54.7% had a good adherence as measured by Center for Adherence Support

Evaluation adherence index with female (59.9%) significantly more likely than males

(43.9%) to report good adherence (v2 = 6.84; df = 1; p\0.01). Also, alcohol plays a role

independent of psychosocial factors in affecting adherence (r = -0.36, p\0.001). Findings

from the study agreed with Achappa et al. (2013) who found a negative correlation

between adherence and alcohol intake. The study by Morojele et al., (2014) is related to

my research because like in my research, adherence is the single dependent variable and

the statistical test used, multiple regression is the same test I intend to use.

Overview of Adherence to ART in Nigeria

Adherence to ART is well a well-studied concept in Nigeria based on the

quantum of publications available compare to other thematic areas of HIV. Adherence to

ART among people living with HIV AIDS (PLWHA) varies across different categories

of patients and location of patients and it is understandable considering the diversity of

Nigeria socio-culturally and economically. Adherence among people living with

HIV/AIDS attending PEPFAR-funded clinic in University of Calabar Teaching Hospital,

Cross – River State in Nigeria was explored using a cross-sectional design (Oku et al.,

2013). Data was collected from 411 eligible participants using semi-structured

questionnaire. The mean age of the participants was 35.7 ± 9.32 years with a higher

number of females (68.6%). Using a logistic regression, the authors found perceived

improved health status [OR 3.11; CI:1.58-6.11], reduced pill load [OR 1.25; 95% CI:

0.46-2.72] and non-use of herbal remedies [OR 1.83; 95% CI: 1.22-2.72] were key

predictors for adherence to ART. Resident outside of Cross River State 42 (72.4%) were

significantly more likely to be adherent to HAART when compared with 204 (57.8%)

being resident within the state (p < 0.05). This contradict other similar studies that found

distance from treatment center as adherence inhibitor (Arage, Tessema, & Kassa, 2014;

Wasti, Simkhada, Randall, Freeman, & Van Teijlingen, 2012). The study is relevant to

my research from several angles. The demographics of the participants is similar to my

study population. The study design and methodology are similar to my research. While

the study found those within Calabar metropolis had lower adherence compare to those

from a far distance, my research hope to stratify patients distance from treatment center

and explore the association to adherence. Also, my research will objective by using

patient's medical records to determine distance from treatment center as opposed to self-

report.

In a related study of adherence among pediatrics between less than a year and 15

years, some researchers explored the relationship between duration of treatment, patient

education, and drug administrator and adherence. In a study in Federal Medical Center

Owerri, Imo State Nigeria, 210 participants were enrolled in the study between

September and December 2013 (Akahara et al., 2017). From the 108 males and 102

females, 64 (30.5%) were single orphans, 22 (10.5%) were dual orphans while 146 (9%)

had the drugs administered by their biological parents. The result from the research

showed 191 (91%) with good adherence defined as adherence equal or greater 95%. The

study showed adherence had a significant relationship with patient educational level (p =

0.004), duration of treatment (p = 0.001), drug administrator (p = 0.005), and orphan

status (p = 0.001). From the study, reason for adherence was patient not feeling as sick as

before. The study is related to my research work since part of my study is to explore adherence after a patient on ART start feeling well with increased CD4. My study seeks to explore association between adherence rate before CD4 count reaches 500 cells/mm^3 and after attaining 500 cells/mm^3.

The objective of vision '90-90-90' by UNAID is to have an HIV-free generation (UNAIDS, 2016; UNAIDS, 2014) and one way to achieve this is to ensure there is prevention of mother to child transmission of HIV by pregnant women who are living with the virus. In a research to explore level of adherence and factors that influence pregnant women who are on ART, 170 eligible pregnant women accessing care in HIV Clinic in Nigeria Institute of Medical Research, Lagos were studied (Ekama et al., 2012). Through a cross-sectional design study, a semi-structured questionnaire was administered to the participants who were aged 30 – 34 years between September and November 2009. Using a bivariate and multiple logistic regression, the result showed 137 (80.6%) had minimum of 95% ($\geq$ 95%) adherence rate. Non-adherent rate was 19.4%. Fear of stigma (63.6%) was the main reason for non-adherence while the desire to protect the unborn was the greatest motivation (51.8%). Through a bivariate analysis, factors associated with good adherence included marital status, disclosure, good knowledge of ART, and having a treatment support partner (Ekama et al., 2012). The study population comes from a population that shares similar demographics with my studied population. Also, I intend to use a cross-sectional design like the study by Ekama et al. (2012). Among adolescent and young adult in my study population, pregnancy will not be excluded. So, the research by Ekama et al., (2012) is relevant to my study.

In a study of patient - factors influencing ART adherence in the Middle-Belt region of Nigeria, Falang et al. (2012) studied 461 eligible patients accessing care at the Jos University Teaching Hospital, Nigeria. Interviewer administered structured questionnaire was used to collect the desired data from eligible participants between November 2009 and January 2010. In the cross-sectional design study, Falang et al. (2012) found that adherence was 87.9%. Factors that were found to be strongly associated with adherence in a univariate analysis included age (OR 1.04), sex (OR 1.14), employment (OR 1.29), knowledge of ARVs (OR 1.23), pill burden (OR 1.20), HIV status disclosure (OR 1.08), knowledge of HIV (OR 1.11), thrice daily frequency of drug intake (OR 1.68), twice daily frequency (OR 2.18), and alcohol non-intake (OR 0.29). Whereas, in the multivariate analysis, age, frequency of drug intake and alcohol non-intake and twice daily affected adherence ($P < 0.05$). Findings from the Falang et al. (2012) study on the strong association between good knowledge of ART and adherence agrees with the study by Ekama et al. (2012). In a related study, 250 participants accessing care for ART in Federal Medical Center Keffi, in Nasarawa State Middle-Belt region of Nigeria were assessed for adherence (Pennap et al., 2013). In the cross sectional study, Pennap et al. (2013) found adherence rate was 62.8%. Only 78 (31.2%) had adherence of 100%. Living with family members was strongly associated with adherence (85.8%) ($p \leq 0.05$) and likewise disclosure to a family member 77.6% ($p \leq 0.05$). Level of education and marital status in the study were strongly correlated with adherence in the study ($p \leq 0.05$). The strong association between adherence and disclosure to family member agreed with Ekama et al. (2012).

In south west Nigeria, the geo-political zone in Nigeria deemed to be the relatively most educated, 237 participants who were enrolled into ART care at Sobi Specialist Hospital were studied (Bello, 2011). The cross-sectional study was between May 2009 and December 2010 with participants aged 16 – 60 years. Both self-report and pharmacy re-fill records were used to assess adherence rate among participants. Pharmacy refills (70.8%) and participant self-report (73.3%) had adherence rate greater than 95% ($\geq$ 95%). Factors that were associated with adherence included adverse side effects (6.6%), low education (4.7%), pill burden (3.7%), stigma (3.3%), forgetfulness (1.4%) (Bello S.I, 2011).

Adherence rates from study by Falang et al. (2012) in Middle-Belt region of Nigeria who used data of participants in 2009 -2010 was 87.9%. The study by Bello (2011) who used participants records between 2009 and 2010 from the western region was 73.3%. In south east Nigeria, researchers found adherence rate of 86% in 2008 (Ukwe, Ekwunife, Udeogaranya, & Iwuamadi, 2010). Ekama et al. (2012)'s study within the same period, 2009 -2010 showed 80.6% of participants had adherence rate greater than 95%. This stands different from other studies but it is understandable as the study was among pregnant women who are comparatively better adherence because of their concern about their unborn baby (Ekama et al., 2012). More recent studies on adherence to ARV in Nigeria show a comparatively better adherence (Akahara et al., 2017; Olowookere, Fatiregun, Ladipo, Abioye-Kuteyi, & Adewole, 2015).

Adherence Rates Among Adolescents

Adolescents have a disproportionate rate of HIV in sub-Saharan Africa as 80% of the estimated two million adolescent aged 10-19 years living with HIV are from sub-Saharan Africa (Maskew et al., 2016). In HIV management, adherence at all stages of life is important in ensuring good health outcome and also preserving the current HIV drug treatment options because resistance is correlated to poor adherence (Coker et al., 2015). Studies that involved this group have identified unique challenges associated with the group in maintaining a good level of adherence. Challenges of adolescent and young adult include puberty with attendant implications, sexual debut where escapades of unhealthy sex become pronounced. HIV and STI acquisition also increase in the group (Maskew et al., 2016). According to Maskew et al. (2016), among the adolescents (aged 12 - 20 years) that were enrolled into the prospective cohort study in South Africa, 38% (n= 47) missed a clinic appointment within 24 months. Missing clinic appointment could be a potential signal for a compromised adherence. The study revealed younger adolescents below 15 years are more likely not to miss a clinic visit when compared with the older ones who are 15 years and above.

Existing studies have shown a comparatively lower adherence rate among adolescents and different reasons have been advanced for this (Xu, Munir, Kanabkaew, & Le Coeur, 2017). Adolescent stage determines the trajectory of HIV management globally as the stage serves as the transition from pediatric to adulthood as such the adolescent is often without some defined health services as they are not considered to be pediatric nor adult (Maskew et al., 2016). In a systematic review of adherence among

adolescents of ages 10 – 19 years of age in Africa, four important themes emerged as been common barriers to adherence to ART. These include impact from family structure, nature of ARV regimen, urban versus rural location, and knowledge of HIV status and gender (Hudelson & Cluver, 2015).

In Thailand, a study of adherence among perinatally infected adolescents was carried out. The study used a cross-sectional survey data of 20 ART facilities including urban, peri urban and rural and also did an in-depth-interview with adolescents and caregivers (Xu et al., 2017). Multiple factors were enumerated as adherence inhibitors for the adolescents. These included non-disclosure of sero-status which made it difficult for the adolescents to adhere to their ARVs. Strained relationship with caregivers was another reason for missing doses or not taking the ARVs at scheduled times. In addition, forgetfulness because one was busy was another factor (Xu et al., 2017a). According to Xu et al. (2017), younger age was related to sub-optimal adherence. This contradict the study by Maskew et al. (2016) on younger adolescent (below 15 years) been relatively more adherent than older ones. The Thailand study also had having a boy/girlfriend, self-reported unhappiness and frequent online chatting as adherence inhibitors. Other factors influencing adherence negatively among adolescents in the study included not been comfortable asking doctor questions and when a family member was the caregiver. Xu et al. (2017) found 48% (n = 275) adolescents in the study was sub-optimally adherent evidenced from rating of drug taking habit of participants by caregivers, missing doses as self-reported and having the most current available HIV-RNA of greater than 1000 copies/ml.

The studies by Maskew et al. (2016) in South Africa and Xu et al. (2017) in Thailand among adolescent are quite relevant to my research focus. The stratification of adolescents by age to assess their adherence by the two studies will also provide a basis for me to stratify my study population to see if there is any variation in their respective adherence before and after attaining a high CD4 count. The study population by the two studies is focused on the same population of my interest, the adolescents.

Determinants of ART Adherence

A systematic review of 13 peer-reviewed articles on adherence to ART that were published since the ART program began in Nigeria between 2002 and 2009 was carried out. The reviewers searched for all published literature electronically using three key search terms namely 'adherence,' 'ART,' and 'Nigeria' (Monjok et al., 2010). Database that were searched included PLoS Medicines, PubMed®, and ISI Web of Science®, Science Citation Index® including all indexed journals on HIV/AIDS which involved adherence to ART in Nigeria for the reviewed period. Several other sources were explored for articles and these included HIV/AIDS foundations, international conferences that focused on HIV/AIDS and websites of international organizations. Monjok et al., (2010) found that availability of ARVs was one of the commonest barriers to adherence. Other obstacles included cost, stigma, alcohol abuse and transportation to the clinic. The systematic review showed availability of ARV at HIV treatment center is a problem that affects the hallmark of ART. Drug availability, therefore, improves the quality of care as patients receive their prescribed medicines leading ultimately to improve health. Poor adherence caused by unavailability of drugs has far reaching consequences which include

impacting the virologic, immunological and clinical outcome of treatment (Monjok et al.,

2010). This is because a good adherence which is only achievable with available ARVs

decreases viral load, increase CD4 counts and in overall improves quality of life. The

mortality rate among HIV clients is also dependent on ARV availability. Research from

both Mkoka et al., (2014) and Kranzer and Ford, (2011) suggest ARV is, of course, the

center stage in the management of HIV/AIDS. The studies relate to my studies as the

dissertation work seek to explore adherence in AYA in Nigeria.

Adherence to ARV medicines is only realizable if they are available ARV when

needed by patients. The importance of the availability of ARVs in adherence in drug

management of HIV has been variously studied. In a research work in two ART clinics

one located in the rural area and the other in urban in southern Malawi, the perception of

eight healthcare providers on adherence to ART was explored (Mckinney, Modeste, Lee,

Gleason, & Maynard-tucker, 2014). Most of the patients in the two clinics were from

low-income and low-education backgrounds according to the studies. Mckinney et al.,

(2014) through the qualitative study found several barriers to adherence including

unavailability of ARVs, disclosure, and discrimination, side effects of medicines, belief,

and knowledge of ART outcomes, lack of access to food and shortage of staff. Another

study in Kinondoni Districts in Dar es Salaam in Tanzania, 20 health facilities were

investigated by Mori and Owenya, (2014). The 20 health facilities included 12 public

facilities, seven privates and a parastatal institution. Among these health facilities, 50%

of them were hospitals while the remaining 50% were primary health facilities. Mori and

Owenya, (2014) interviewed one person in charge of the facility and a member of

pharmacy staff in each of the health facilities. The researchers found that of the 32,147

clients enrolled into care in the facilities, 20,831 (64.8%) were on ART, and there was

unavailability of ARVs in 16 out of the 20 facilities (80%). Out of the number, 10

facilities (62.5%) changed the regimens of 201 clients. Change of regimen is

recommended when there is a combination or any of the following; clinical failure,

immunological failure and/or virologic failure (WHO, 2010; WHO, 2015). The research

relates to my study as adherence to ARV is dependent on product availability at treatment

centers. Persistent unavailability of ARV could turn around to discourage patients from

keeping up prescription -refill appointments.

ART Adherence Inhibitors

Non-adherence has a lot of consequences which include impaired quality of life,

disease progression, medication waste, increased hospital visits, admissions and medical

resources (Jimmy et al., 2011). Researchers have revealed multiple factors that inhibit

adherence. In a cross-sectional study, assessment of factors influencing adherence to

ART in 261 patients in ART in Sulianti Saroso Infectious Disease Hospital in urban

Jakarta, Indonesia was carried out between August 2012 and November 2012 using

questionnaires to collect data (Weaver et al., 2014). In the study, 75% of the participants

were male with mean age of 33. 4 years, 54% were unmarried, 75% were Muslim among

whom 51% observed the religious fasting very year (Weaver et al., 2014). According to

Weaver et al. (2014), 77% reported been adherent to ART in the 90 days prior to the date

of interview. In the study, there was a correlation between adherence and level of social

support ($p = 0.018$) compare to poor social support. Reasons that were frequently

provided for failing to take medicines included been asleep during medication time (60%), forgetfulness (67%), and busy with something else (63%) (Weaver et al., 2014). In a related research, 19 adolescents who have been minimum of six (6) months on ART with age range of 12 – 19 years participated in a qualitative cross-sectional study to assess adherence barriers and facilitators in Fever Unit of the Department of Medicines and Therapeutics of the Korle-Bu Teaching Hospital, Ghana (Ankrah et al., 2016). Among the participants, seven (7) were boys while 12 were girls. The identified inhibitors of adherence among this age category included forgetfulness to take medicines at the appropriate times, financial constraint, perceived stigma, and side effects of ART. Frequently mentioned facilitators included support from health care worker (Ankrah et al., 2016). Both (Weaver et al., 2014) and (Ankrah et al., 2016) studies share demographics characteristics with my target population with respect to age and socio-cultural environment. Also, the study design in both research is similar to my study.

Nyogea et al. (2015) carried out a research on determinants of adherence among children and adolescents in Tanzania. The 116 participants aged 2 -19 years were assessing ART care at Kilombero and Ulanga ARV Cohort, at the Chronic Diseases Clinic Ifakara in St Francis Referral Hospital. Among participants who have been in care in at least the previous 150 days before interview, 67 (58%) were males while the median age for the participants was 9.8% (interquartile range: 5.7 – 13.3, range 2–19). The study found average adherence of 84% among 70% of participants. The average adherence rate from the research agrees with the findings of a research by Kim et al., (2014). The quantitative analysis component of the mixed methods study did not show any

association between adherence rates and CD4 + T cells counts, pill burden, WHO clinical

staging, socio-economic status, sex, duration on ART, disclosure status and education.

This study relates to my study as one of my research questions is to compare adherence

prior to attaining CD4 counts of 500 cells /mm^3 and after the 500 cells /mm^3. Also, the

study population, adolescent is my population of interest.

The perception of community members (irrespective of sero-status) and that of

health care workers as to what constitute adherence barriers for patients was explored

through focused group discussions in Zambezia Province in Mozambique. Groh et al.

(2011) employed phenomenology to understand the view of these categories as to what

they think constitute barriers to adherence for those taking ARV. They were 124

community participants (51.6% men) and 40 health care workers (16 female while 14

were male). In separate focused group discussions, several themes emerged. The common

ones that were identified as adherence barriers for those taking ART included economic

barriers which has to do with financial constraint in buying food and transportation to the

clinic. Patient-provider challenge was also listed. Community participants emphasized

there was absence of trust in the ability of health care workers to maintain confidentiality.

Poor treatment by hospital staff was also identified as an adherence barrier. Social barrier

mentioned included fear of stigma, fear of divorce and use of traditional healers (Groh et

al., 2011). The study is significant as I explored adherence among AYA in Benue State,

Nigeria.

Other barriers to ART adherence include religion and rituals, perception about

ART, substance misuse, industrial action, dissatisfaction with health services, and long

patient wait time (Castro et al., 2015; Haberer et al., 2012; Kreitchmann et al., 2012; Mayanja et al., 2013; Mckinney et al., 2014; Mepham, Zondi, Mbuyazi, Mkhwanazi, & Newell, 2011; Nyamathi et al., 2012; Paschoal et al., 2014; Senkomago, Guwatudde, Breda, & Khoshnood, 2011).

ART Adherence Facilitators

Among adherence facilitators, multiple factors have been identified. In Nepal, a qualitative study used semi-structured questionnaire in a face-to-face interview to obtain views of participants as to what constitute adherence facilitators. Through purposive sampling, the researchers sampled 34 participants out of which 17 were health care providers (doctors, nurses and pharmacists), three policy makers and 17 ART-prescribed patients (Wasti et al., 2012). The identified themes included trusting health worker, positive beliefs about ART and family and mechanical support. The findings corroborated the study by Ekama et al. (2012) in Lagos Nigeria where HIV positive women in a study of adherence assessment listed facilitators to adherence to include desire to remain healthy, to have HIV-free children and the belief in the potency of ARVs (Ekama et al., 2012).

Among people in Ethiopia, facilitators to adherence were identified as use of reminders, desire to remain alive and raise children, improved health on ART, social support, disclosure of HIV status, receiving adherence counselling (Bezabhe et al., 2014). This was in a study in Felege-Hiwot Hospital and Gondar University Hospital in Ethiopia where a total of 58 participants were part of the focused group discussion and semi-structured interview between February 2013 and July 2013 (Bezabhe et al., 2014). In a

meta-analysis study of adherence in sub-Saharan Africa, adherence rate was found to be less than 80% among 23% of Africans (Croome et al., 2017). In a systematic review of 154 studies, 30 facilitators to adherence to ART were reported across sub-Saharan Africa. These included social support (n= 60), good relationship with a health provider (n= 22), disclosing HIV status (n = 26), reminders (n = 55), and healthier or feeling better after taking ART (n = 22) (Croome et al., 2017).

Ankrah et al.(2016) studied 19 adolescents who have been on a minimum of six months on ART with age range of 12 – 19 years through a qualitative cross-sectional study to assess adherence barriers and facilitators in Fever Unit of the Department of Medicines and Therapeutics of the Korle-Bu Teaching Hospital, Ghana. Among the participants, 7 were boys while 12 were girls. Main facilitators of adherence included support from health care providers and parental support. Just like Ekama et al.(2012) found out in their research, patient's knowledge of disease, self-motivation, patient's perceived positive outcomes, and dispensed formulation were other promoters of adherence.

<div align="center">**Measurement of Adherence**</div>

The importance of adherence has been elucidated in the preceding review however, so much variations in adherence rates were observed even where adherence measure was carried out in settings with similar characteristics (Akahara et al., 2017; Oku et al., 2013, 2014). This can also be explained with the absence of a perfect adherence measure as there is no gold measure of adherence (Lam, & Fresco, 2015). Some of the tools that are used in measuring drug adherence can be categorized into objective and

subjective measures. The former includes pill count, pharmacy refill, biological makers, attendance log, electronic monitoring of medication administration such as medication electronic monitoring system, secondary database analysis, and clinical outcome (Lyimo et al., 2011; McMahon et al., 2011). Examples of subjective measures include family or clinician report, patient interview and self-report (Chalker et al., 2010).

Other studies classified adherence measuring tools into direct and indirect measures. Direct measures refer to measurement of drug metabolite in urine, blood or body fluid to identify markers that were given with the drug. Measurement of drug adherence using biological markers is considered the gold standard by some but this measure also has its disadvantages (Modi, Ingerski, Rausch, Glauser, & Drotar, 2012). Metabolic product is influenced by physiological state and metabolic rate. In addition, drug plasma level differs for different individuals that took same drug at the same time. Apart from been comparatively expensive, there is the white coat phenomenon where patient takes the drug around clinic visit time (Modi et al., 2012). Another objective tool is the electronic monitoring of medication administration. This adherence monitoring devices is incorporated into drug prescription and it measures medication event such as times bottle is opened. This tool comes in different forms and some of the features of this tool include (i) recorded dosing events and stored records of adherence; (ii) audiovisual reminders to signal time for the next dose; (iii) digital displays; (iv) real-time monitoring; and (v) feedback on adherence performance (Lam et al., 2015). One of the assumptions with medication electronic monitoring system is that each time a prescription bottle is

opened, drug is administered but this is not always the case (Lyimo et al., 2011). The tool

is also comparatively very expensive hence its unpopularity in sub-Saharan Africa.

Pill count is an objective method that physically counts the number of pills during

clinic visit. Common way of calculating pill count which gives adherence ratio is using

the formula: Pill count = (Number of dosage units dispensed − number of dosage units

remained)/ (prescribed number of dosage unit per day × number of days between 2

visits). While this direct and objective measure is reliable, it is based on the same

assumption as medication electronic monitoring system (Lam & Fresco, 2015). An

unannounced phone pill count to assess adherence to pharmacotherapy in smoke

cessation found the pill count method to be very reliable to assess adherence to

medication (Thompson et al., 2011). A setback for the measure is absence of means to

verify time. Also, patient can decide to open and discard the pill before clinic visit to

appear to be following prescribed regimen (Jimmy & Jose, 2011). Patient self-report is

believed to the least reliable of all the methods yet the most used of all adherence

assessment tools because it is simple and cheap. It is done in several ways but the most

common is use of questionnaire where patient provide response to some questions. There

is clear absence of standard as questions are framed in different ways. The method has

high reliability but low specificity (Stirratt et al., 2015). Validity is a problem because

due to its prone to desire of respondents to appear adherent and memory bias could lead

to overestimation of adherence(Jimmy & Jose, 2011; Lam & Fresco, 2015). In a study in

Tanzania among ART patients in 2010, pharmacy refill, pill count, self-report and

adherence rates were all compared and pharmacy refill adherence less than 95% (<95%)

emerged as the best method for predicting virologic failure (Sangeda et al., 2014b). The study is related to my research work because I am going to use pharmacy refill as means of assessing adherence. Also, in one of my research questions, I hope to look at changing CD4 counts to see they could be predicted by adherence among adolescent and young adult in Nigeria.

Health Facility Location and Adherence

Demographic characteristics of a people reflect in their adherence to medicines from a plethora of studies on the concept of adherence (H. Kim, Kim, Bowman, & Cho, 2016; Magnabosco et al., 2015). Understanding factors behind adherence would help in developing intervention that would remove or minimize such obfuscation. In HIV management, adherence to ART among rural dwellers has been studied and likewise urban dwellers. In Uganda, 1824 adolescents on ART in 30 different health facilities were studied between December 2013 and February 2014. The cross-sectional study made use of ART card to assess adherence to ART among participants (Nabukeera-Barungi et al., 2015). The result showed adherence of greater than 95% among 90.4% (N = 1588). Poor adherence to ART was independently associated with location of health facility in rural area. According to Nabukeera-Barungi et al. (2015), outstanding factors for poor adherence were stigma, discrimination and disclosure. This is quite understandable as people in rural areas know each other better and the communal lifestyle reduces confidentiality. However, a descriptive cross-sectional study of adherence to ART among rural people in Nigeria found different reasons for non-

adherence. Outstanding factors for non-adherence included being busy, forgetfulness, and religious constraint (Oku et al., 2014).

Adherence among people in rural and urban dwellers has also been compared. Distance to treatment center is said to be associated with adherence as those in rural areas farther from treatment centers have been found to be comparatively less adherent (Yaya et al., 2014). In South Africa (Eyassu, Mothiba, & Mbambo-Kekana, 2016); Nepal (Wasti et al., 2012); Kenya (Wakibi, Ng'ang'a, & Mbugua, 2011); and Nigeria (Chineke, 2015; Falang et al., 2012) researchers association between adherence and distance to treatment centers. Reda and Biadgilign, (2012) and Heestermans et al.,(2016) corroborated this in their systematic review of publications of articles on adherence to ART in Africa. Those coming from father distance are said to be less adherent. What however is lacking in literature is objective assessment of distance to treatment centers and adherence to ART. All the studies are based on self-report questionnaires. Self-report was earlier mentioned as a subjective form of adherence measurement (Chalker et al., 2010). These studies used prospective cross-sectional methods, have adherence as their common outcome variables like my studies. In addition, my study intends to further explore the issue of distance by employing an objective study instead of the most common studies that have been based on patient-report. Rather than a questionnaire, patient medical records will be used to estimate distance to treatment center.

Adherence and Drug Resistance

Suffice to say the current availability of ARV is the hallmark of HIV/AIDS management. In low and medium-income countries, there has been a surge in the number

of people enrolled into ART care. In 2003, there were about 400,000 people enrolled into

care in sub-Saharan Africa and the number rose to 8 million in 2011 (Bosten et al., 2015).

Scale-up of ART in Africa correlates with a decrease in morbidity and mortality of cases

and likewise a decline in mother to child transmission. However, it is important to know

that the future of the current ARVs depend largely on adherence to ART. Unfortunately,

there is an emerging challenge with adherence as resistance to ARV has been linked to

poor adherence in some studies (Bosten et al., 2015). Acquired HIV drug resistance in

Africa relates with poor adherence and likewise viral load suppression is known to be

directly related to adherence (Castelnuovo, Sempa, Agnes, Kamya, & Manabe, 2011;

Kalichman et al., 2014). The UNAIDS has a vision to ensure 90% of those in care have

their viral load suppressed but this will remain a mirage in poor adherence.

In related research, Teklu and Yirdaw (2017) carried out a study on consequences

of ARV poor adherence and interruption in Ethiopia. Randomly selected ARV health

facilities in the country with a total of 22, 647 ARV patients were followed. The

longitudinal and retrospective cohort design covered the period between September 2005

and November 2013. There was treatment interruption of at least a month at some point

in 39% (8,759/22,647). Using Cox proportional hazards model, regression analysis was

carried out. Death for those who re-started treatment at the 6th, 12th, 18th and 24th months

was higher by 1.9, 2.4, 2.6 and 2.4 respectively compare to those who never had

interruption at those points. Finding from the research was that interruption was common

in Ethiopia. My study which is also going to be retrospective would equally use

regression analysis to explore the relationship between pharmacy refill among AYA.

Findings from the Literature Review

A fair research work has been carried out on adherence to ARV medicines both in developed and developing nations based on my findings. Adherence rates among several studies differ and it is understandable as there is absence of a gold standard for adherence measurement (Jimmy et al., 2011; Lam et al., 2015; Williams, Amico, Bova, & Womack, 2013). Most of the studies researched on the variables of my focus namely adherence, CD4 counts, and factors that facilitate and inhibit adherence. Another striking thing is majority of the studies are either prospective or retrospective cross-sectional studies with most using patient self-report as measure of adherence. There is absence of study that objectively examines adherence factor like distance from patient resident to treatment center. All the studies as reviewed earlier used patient self-report. There is also absence of studies that look at how adherence relates to CD4 when patient has high and low CD4 counts respectively. In addition, there is no literature available on association between adherence when is detectable and when it turns undetectable. Lastly, studies that have been identified only explored the influence of rural setting on adherence for patient residing and accessing care in the same rural environment. My study intends to explore the relationship between adherence and environment for those residing in rural setting but accessing care in urban ART center.

Summary

In Chapter 2, TTM was used to understand stages of adherence as people initiate and continue ART. Factors facilitating and inhibiting adherence have been revealed while measures of adherence have been identified to include objective and subjective

assessment tools. Distance to health facility that is well referenced as adherence inhibitor is based on subjective assessment. What is however lacking, is the absence of using an objective measure of adherence to draw a conclusion between adherence and distance to the clinic. Also, there is no known study that attempts to compare adherence of patients before and after CD4 counts dramatically improved. For example, from below 200 cells/mm^3 to greater than 500 cells/mm^3. These gaps are the areas of the focus of my study. The next chapter will provide detail on methodology as it relates to data collection and analysis to answer the research questions.

Chapter 3: Research Method

Introduction

I developed this quantitative study to determine the following: (a) the difference in adherence among AYAs accessing care in the same treatment center but resident in different rural and urban settings, (b) the association between distance from treatment center and adherence among AYAs, (c) the relationship between CD4 counts and adherence among AYAs.

In this chapter, I describe how I secured approval from ethics committee of the FMC Makurdi, the Walden University Institutional Review Board (IRB), and how the secondary data from the FMC Makurdi in Benue State, Nigeria was collected. Further, I offer a description of the sample population, and discuss sample size determination and sampling procedure. I also discuss the statistical tests that I carried out in the course of data analysis. Other areas of the study that I discuss in the chapter include threats to the validity of the study, ethical procedures, and data operationalization.

Research Method and Rationale

This was a retrospective, cross-sectional, descriptive, quantitative study (see Creswell, 2009; Gordis, 2009). I used secondary data from the Federal Medical Center located in Makurdi, Benue State, Nigeria. I chose the cross-sectional method for the study because I sought to establish a relationship between the variables involved without establishing causality (Campbell & Stanley, 1963; Frankfort-Nachmias & Nachmias, 2015; Mann, 2003). The design was appropriate for my study because my goal was to explore the relationship between adherence rates, CD4 counts, environment, and distance

to treatment center among AYA in Nigeria. Also, the method was comparatively cheap, and since I had no sponsorship, I could not afford an expensive research project given my personal resources.

The data for the research was collected at a particular point in time, which made the cross-sectional study ideal. Merits of cross-sectional study are numerous, and include a provision of data for odds ratio, absolute risks, and relative risk from prevalence (Thompson et al., 1998). Multiple outcomes, along with exposures, could also be concurrently explored using a cross-sectional study, and one does not need to follow up with participants, making it ideal for a descriptive study (Thompson et al., 1998). Also, the influence of a researcher in a quantitative study is minimal, and result from the method are generalizable when they are based on the larger population (Polit & Beck, 2010). Disadvantages of the study approach include a potential for misclassification because of bias, and inability to distinguish which comes first between exposure and outcome. I used both independent t test and ANOVA in the data analysis to explore differences between variables, and carried out bivariate analysis to assess association. These statistical tests are ideal for a study that has a continuous dependent variable and categorical or continuous predictor variables (Hellevik, 2009; Schneider, Hommel, & Blettner, 2010).

I used the TTM to explain differences in adherence relating to the independent variables such as CD4 counts, environment, and distance to the treatment center. The theory has been used widely in the study of patient health behavior change programs like those for physical exercise, diet adherence, and smoking cessation (van Leer et al.,

2008a). Recently, the theory has gained popularity for understanding adherence to medicines (Johnson et al., 2006).

Methodology

Study Area and Population

This study began with a definition of my study area and population alongside determination of sample size. Data for the study was collected from the FMC located in Makurdi, Benue State, Nigeria. Makurdi is the capital of Benue State, which is located in the Middle-Belt region of Nigeria. The state had a population of 4.2 million in the last census conducted in 2006 (National Population Commission, n.d.). The land mass is 33, 955 square kilometers and lies between Latitudes 6.5° and 8.5° N and Longitudes 7.47° E and 10^0 E, and is accessible by road (Goon et al., 2011). There are 21 local government areas in the state, which is surrounded by Cross River, Ebonyi and Enugu States to the south; Kogi State to the west; Nasarawa State to the north; and Taraba State to the east. The state also shares an international boundary with the Federal Republic of Cameroon on the southeast flank. It is an agrarian state made up of two major tribes namely Tiv and Idoma, with Igede. And Etulo as minority tribes. Most of the inhabitants are farmers and are mainly Christians with a few idol worshippers (Akaakohol & Aye, 2014). Because the health facility is a referral center, it serves populations from the surrounding states as well.

Population

The population of interest in the study was composed of AYAs enrolled in HIV treatment in the FMC Makurdi, Benue State in Nigeria. I selected this tertiary hospital for

the study because it has a large population of ART clients. The large population could be

due to the quality of care, and size and accessibility of Makurdi, which is accessible by

road, rail, and water (Goon et al., 2011).

Sample Size

In research, it is not always feasible to study the entire population, hence the use

of sample size. Appropriate sample size determination is significant because it helps to

identify relevant differences in studies. For sample size determination, there are many

methods and formulae available, including the web-based G*power which requires

imputation of the desired parameters depending on the statistical test. Factors to consider

while deciding on which method to use in sample size calculation include the nature of

the variables and whether they are categorical or continuous (Altman & Royston, 2006;

Turner, Dobson, & Pocock, 2010). Beside the desired power, marginal error and the level

of significance are other factors to consider (Suresh, Thomas, & Suresh, 2011; Suresh &

Chandrashekara, 2012). The relationship among variables also influences the method of

sample size calculation and the statistical test a researcher intends to employ in the

analysis.

For my study, which was descriptive, the Leslie and Kish formula was applied

(Eng, 2003). The formula for sample size calculation was:

$$n = \frac{Z^2 \, p \, q}{\delta^2}$$

In this equation, *n* equals the sample size required. *Z* is the critical value that

corresponds to the selected significance criteria (significance level or level of alpha) and

confidence interval (CI) obtained from the statistical table. At 95% CI, the value obtained

is 1.96. The abbreviation *p* marks the proportions of the attribute in the population under investigation. Several studies in Nigeria have a different prevalence for the proportion of ART clients that is 100% adherent. The range is between 31.2% and 91% (Akahara et al., 2017; Bello S.I, 2011; Ekama et al., 2012; Lawan, Amole, Gambojahun, & Eneabute, 2015; Pennap et al., 2013). I used the proportion from a descriptive cross-sectional study of adherence to ART among HIV-infected adolescents in Kano, Nigeria. The proportion of adherent adolescents was 90.5% (Lawan et al., 2015). So, in this study, $p = 0.905$ (90.5%). Delta (δ) equals the total width of the expected CI (marginal error), and I made an assumption of 0.025 (2.5%). That is the level of precision taken: $Q = 1 - p$.

Substituting these in the formula above, it becomes:

$n = 1.96^2 * 0.95 (95\%) (1 - 0.905) / 0.025^2 = 528$

Adding a 10% gives required sample size of 581. The 10% was added in case of incomplete data from some patients' files. However, the sample size that I collected and included in the analysis was 656.

Sampling and Sampling Procedure

I sampled the available secondary data to get a subset (sample) of a population of interest (Chava Frankfort-Nachmias & Leon-Guerrero, 2015). I used purposive sampling, which is a non-probability type of sampling (Palinkas et al., 2015), so as to get samples that have variables of interest which included CD4 counts result, pharmacy refills, and physical contact address (distance and location). From the medical records, files (hard copy) of clients were pulled out and reviewed, and only patients with variables of interest were selected. The process continued until the sample size of 656 was reached.

Inclusion and Exclusion Criteria

To be included in the study, participants must have met the following criteria:

- Must be HIV seropositive because the outcome of interest is about adherence among participants who are HIV seropositive.

- Must be between ages 15 and 24 years because the study group is for AYA between these ages.

- Must have started ART within the study period of 2010-2016. This is to observe how CD4 relates to adherence as patients continue in care.

- Must be enrolled in care at the FMC Makurdi

Exclusion criteria included:

- Any patient below 15 years of age or above 24 years of age because the study population included only those within ages 15–24 years.

- Any patient not enrolled in ART in the FMC Makurdi. This was because this was where I obtained ethical clearance for the study.

- Any patient who enrolled in ART care within the study period but had been on ART elsewhere. This was because of potential for such patients to have high CD4 count.

- Any client that is not HIV seropositive because the outcome of interest was for clients who are on ARV.

<center>**Gaining Access to the Data Set**</center>

From my previous personal work experience (former employee of the FMC Makurdi), I knew my variables of interest were captured in patient's medical records in

the FMC Makurdi. However, to be sure nothing had changed, I wrote an email to a staff

member at the FMC Makurdi who confirmed that the variables of interest were still

captured in patients' files. With the background knowledge, I wrote an application letter

to the ethics committees of the FMC Makurdi and requested ethical approval to access

patient data (see appendix A). Once my proposal was approved, I submitted the study

proposal to the Walden University Institutional Review Board (IRB) to ensure the study

complied with the university's ethical standards. With approval from Walden's IRB

(approval number 10-19-17-0434421) data was collected in line with my study protocol

(see Figure 4). Collected data was saved on my laptop, was pass-word protected, and will

be destroyed after 5 years.
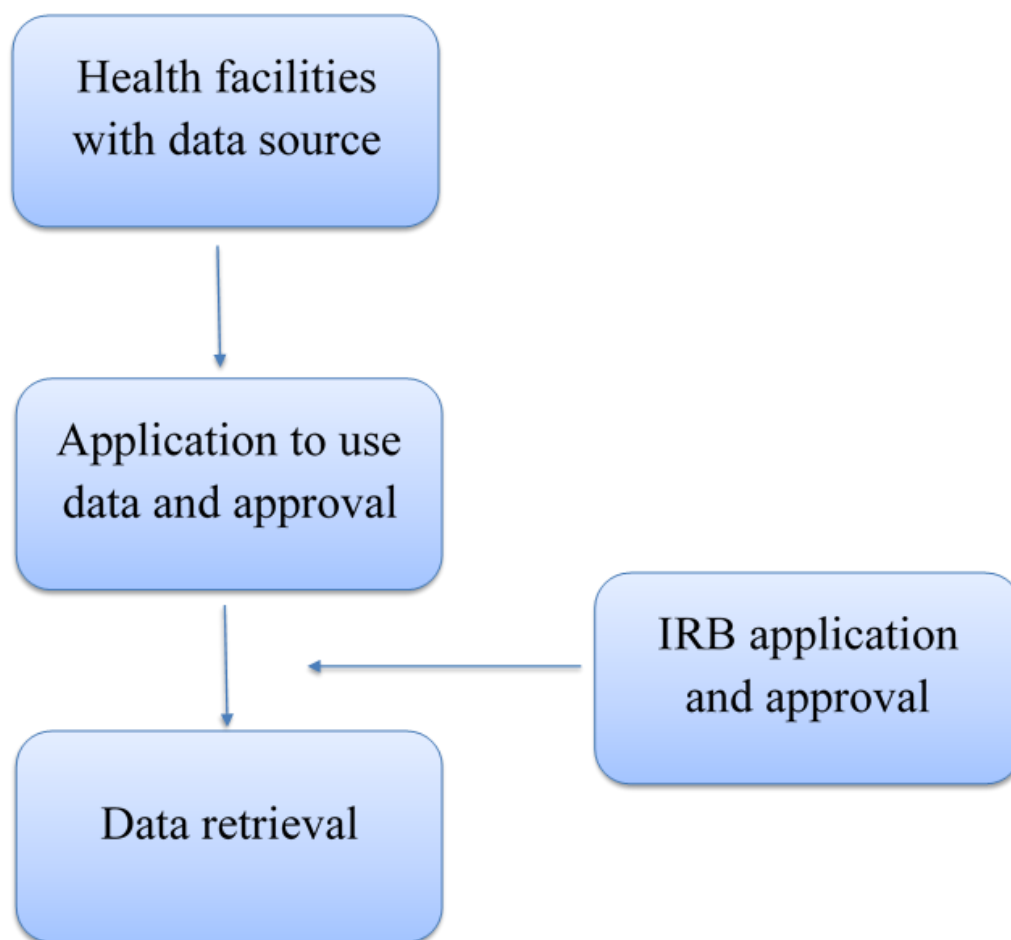
Figure 4. Data extraction process.

Operationalizing Variables

The independent variables in the study included: CD4 cell counts (cell/mm^3); the

location of patient's residence (urban/rural); and distance from the treatment center. The

dependent variable in the study was be adherence rate. For the study, adherence rate of

≥85% was considered good adherence while adherence rate of <85% was deemed

suboptimal or poor adherence. Adherence rate which refers to the extent patient drug

taking behavior corresponds with what was collectively agreed with the health care

provider was based on pharmacy refill. It was calculated using the formula (Olowookere, Fatiregun, Akinyemi, Bamgboye, & Osagbemi, 2008):

Adherence rate is equal to difference between number of expected pharmacy refills and number of missed pharmacy refills divide by expected number of pharmacy refills and multiply by 100%.

Covariates in the study were sociodemographic data which will included; age; gender; marital status (married, widowed separated, and single); employment (employed, unemployed, farming and business persons); the number of years in treatment (expressed in years); and educational level (no education, primary school, secondary school and post-secondary school). These covariates were identified based on previous studies where they have been found to influence adherence individually (Jobanputra et al., 2015; Mayanja et al., 2013; Shigdel et al., 2014; Yaya et al., 2014).

Independent *t-test* and ANOVA were used in the analysis since the outcome of interest, adherence rate was continuous variable. Variables were coded as Adherence (ADH); CD4 counts (CD4T); distance to the ART center (DART); while environment (SETN) was either rural or urban. For the demographic data: age (AGE); gender (GEND) was be male, female; employment (EMPL) was be grouped as employed, unemployed, farming and business person. Unemployed' (including those working but not salaried). The number of years (YERS) since enrollment was categorized into less than five years (< 5 years) and greater than five years (≥ 5 years). Marital status (STAT) was grouped into married, widowed, single and separated (Separated would include divorced).

Education (EDUC) was coded into no education, primary education, secondary education
and post-secondary education.

Data Collection

With approval from the ethical committee of the FMC Makurdi and Institutional
Review Board in Walden University, I recruited two clinical staff from the FMC
Makurdi, provided them with the orientation to support in extracting the needed data
from patients' medical records in line with the sampling method for the study.

The secondary data from and the FMC Makurdi were originally collected from
clients who were enrolled into ART. Treatment and care from the hospital for HIV is free
as a result of the fund from President's Emergency Plan for AIDS Relief (PEPAR) by the
United States Agency for International Development (USAID) (Oku et al., 2013). There
were various points where these biodatas were collected from clients during enrolment
into ART, and these included at the patient registration point, laboratory unit,
adherence/counseling unit, and pharmacy unit. All the information captured went to a
single file and saved in the medical records department of the hospital. Therefore, gaining
access to patient medical records we were able to easily extract variables that were of
interest to me. The variables of interest were extracted and saved in an excel format pass-
worded. After it was cleaned, the data was imported into SPSS v24.0 for data analysis.

Codebook

I created a codebook. The book contains names of all the variables, variable
labels, value labels, and it also shows changes that were made such as fixing raw
variables or creating new variables (Moreno, Egan, & Brockman, 2011). It helped me

throughout the analysis in getting confused in the course of data analysis and also provided a guide in interpreting data analysis result.

Data Cleaning

After the data was collected with the support of the research assistants, I manually cleaned the data. With the support of the two supporting clinical staff, we were able to trace patients with missing contact address in the main hospital registration records. Also, variables that were missing and could unnecessarily skewed the analysis were not included in the analysis.

<div align="center">

Data Analysis Plan

</div>

I performed a univariate analysis on the study sample to provide descriptive statistics for all the variables. For categorical variables, appropriate descriptive statistics included pie and bar charts, frequencies, and percentages. For the continuous variables the appropriate descriptive statistics included histogram, measure of dispersion or variation (range, variance, and standard deviation), measures of central tendency (mean, median, and mode) and normality statistics such as Kurtosis and Skewness (Larson, 2006) depending on the data. Then Pearson correlation was carried out to test for correlation between adherence and each of the predictors. Where the p value less .05, the null hypothesis was rejected. Where the null hypothesis was rejected, a bivariate regression was performed ANOVA to test for the overall significance of the correlation. Descriptive statistics was also be carried for the demographic data including age, gender, marital status, employment, the number of years in treatment, and education and figures and tables will be presented (Hidalgo & Goodman, 2013).

Independent *t-test* was used to assess the difference in adherence to ART

medicines between patients in urban and those who resided in rural areas. Several other

comparisons using *t-test* were carried out to test for statistical significant difference in

adherence rate to ART and these included adherence rate by gender; between ages 15 and

19 years and 20 and 24 years; between those who have been on ART for less than 5 years

and those who have been on ART for at least five years; between those with CD4 counts

of $\geq$ 500 cell/mm^3 and those with <500 cells/mm^3; between those who lived $\leq$ 50

kilometers away from the hospital and those that lived > 50 kilometers away from the

hospital. In order to test for any statistical significant difference in adherence rate based

on level of education, marital status, distance to the hospital and employment, ANOVA

was performed. This was because these variables have more than two categories and the

dependent variable is an interval-ratio level of measurement. See Figure 5.
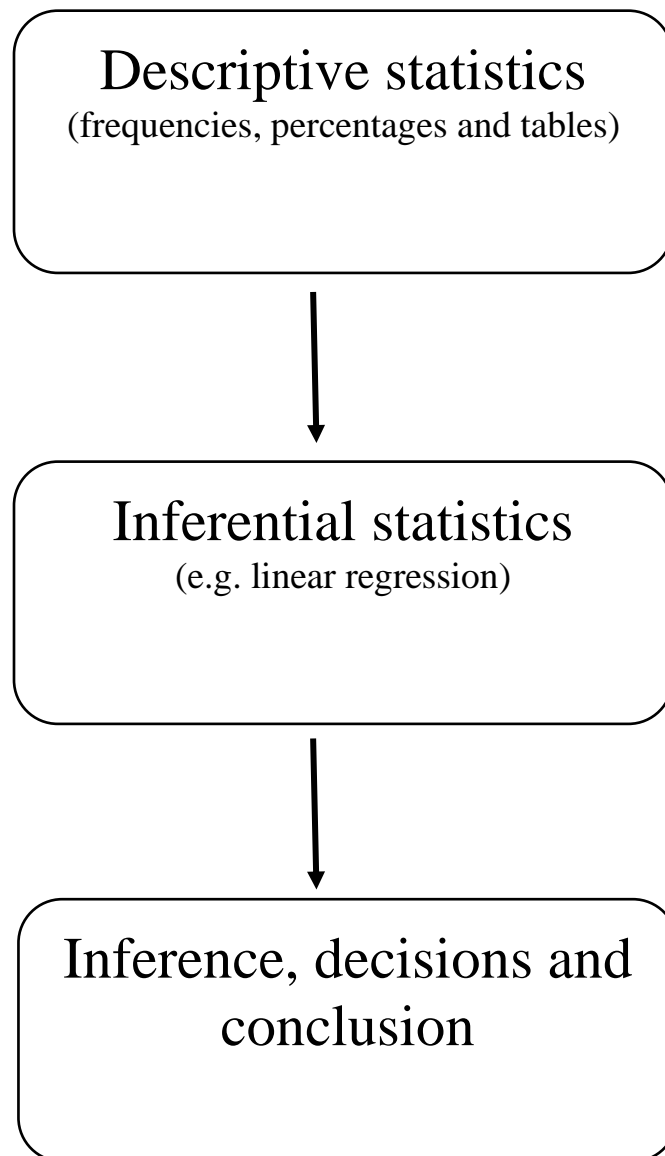
Figure 5. Summary of data analysis.

Analysis of Research Questions and Hypotheses

I conducted data analysis to answer the following three research questions:

RQ1: What is the difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings?

Ho1: There is no statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

Ha1: There is statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

RQ2: What is the association between distance from treatment center and adherence to ART among AYA?

Ho2: There is no statistically significant association between distance from treatment center and adherence to ART among AYA

Ha2: There is statistically significant association between distance from treatment center and adherence to ART among AYA.

RQ3: What is the relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA?

Ho3: There is no statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA.

Ha3: There is statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA

For RQ1, because the question seeks to evaluate the difference in adherence rate, *t-test* was employed. It was used to test for the difference in adherence between participants resident in rural and urban settings but accessing care in ART clinic in the FMC Makurdi. The effect size of the difference was calculated using Cohen's *d*. When the *t-test* is large the bigger is the difference in adherence between the two groups and the more significant the result which makes it easier for the null hypothesis to be rejected. From the SPSS result, effect size was estimated by calculating Cohen's *d* value from the formula:

Cohen's d $= (M_2 - M_1)/SD_{pooled}$

$SD_{pooled} = \sqrt{(SD_1{}^2 + SD_2{}^2)/2}$

M_1 = Mean difference of adherence for participants resident in urban setting

M_2 = Mean difference of adherence for participants resident in rural setting

SD_1 = Standard deviation for adherence among urban participants residents

SD_2 = Standard deviation for adherence among rural participants residents

For RQs 2 and 3, the questions seek to explore the association between the predictors and the outcome. As a result, a correlation and bivariate tests were performed between adherence rate to ART and distance to the hospital while linear regression was the statistical model that was used to predict the relationship between adherence rate and distance to the hospital. Correlation test was also performed between high CD4 (≥ 500 cell/mm^3) and adherence rate to ART and a low CD4 counts (< 500 cell/mm^3) adherence rate. In order to test for a difference in adherence rate between the two sub groups of CD4

(≥ 500 cell/mm^3 and < 500 cell/mm^3), the independent *t-test* (two-tailed) was employed. The acceptable significance level (α) will be set at .05. If the p-value is $< .05$, the null hypothesis (Ho) will be rejected while the alternative hypothesis will be accepted.

Threat to Validity

The validity of a research determines if the research truly measures what it was set to measure from the beginning (Nahid Golafshani, 2003). However, in a practical sense, there could be a threat to accomplishing the goal of validity. In my research, secondary data was used, and it comes with limitations such as the challenge in constructing validity, missing data, an absence of some variables. Missing data could make the generalization of such research inaccurate. Also, because the data sample was purposively sampled, external validity, that is generalizing findings from the study will be impacted. The study period was about five years ago; it is possible some structural and functional changes have occurred in the treatment and management of HIV clients in Benue State. The cross sectional nature of my research also makes generalization limited to sampled population (Chava Frankfort-Nachmias & Leon-Guerrero, 2015).

Ethical Procedures

In carrying out research, there is a basic ethical principle as outlined in principles of Belmont Report that has to be followed because research involves human subjects and these principles include respect for persons, beneficence, and justice (*The Belmont Report*, n.d.). Respect for persons implies participant in research should be accorded respect and individuals with diminished autonomy are entitled to protection while in addition to respecting decisions of participants and protecting them efforts have to be

made to secure their well-being (*The Belmont Report*, n.d.). It is the hallmark of the

principle of beneficence. Because I made use of secondary data, the issue of obtaining

informed consent from participants would not arise, but approval was still obtained from

the IRB and the ethics committee the FMC Makurdi. After receiving letter of cooperation

from ethics committees of the FMC Makurdi, and IRB, I proceeded to obtain the

secondary data. With the two approvals (FMC Makurdi and IRB Walden), a copy of the

dissertation will be shared with the FMC Makurdi before embarking on the publication of

my research findings. Any variable capable of identifying a participant such as patient

identification numbers were excluded from analysis. Also, data was saved and pass-

worded.

Post Data Analysis

Once data analysis has been completed, and study officially ended, data on my

laptop will be permanently deleted after 5 years.

Summary

The study was a retrospective cross-sectional study design where adherence rate

for AYA in Benue State in Nigeria was analyzed. Secondary data from the FMC Makurdi

was used. *T-test* was performed to explore the difference in adherence between city and

urban dwellers accessing care in the same ART treatment center. Other statistical tests

used included bivariate analysis, ANOVA and linear regression (Greenland et al., 2016).

The chapter provided an overall in depth on the methodology of the study. In Chapter 4,

the result of the study was analyzed and discussed.

Chapter 4: Results

Introduction

I conducted this study to explore (a) any difference in ART adherence rates among AYA who resided in rural or urban setting and access care in an urban treatment center, (b) the association between distance to a treatment center and adherence rate to ART, and (c) the relationship between a high CD4 ($\geq$ 500 cell/mm^3) and adherence. According to the literature, factors that influence adherence include distance to ART treatment center, environment (urban/rural), age of patient, and duration of treatment, as I discussed in Chapter 3. As of November 2017, no researchers have studied adherence to ARV medicines in relation to these mentioned variables among AYA in Benue State, Nigeria. In the study, I was therefore, guided by the following RQs and hypotheses:

RQ1: What is the difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings?

Ho1: There is no statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

Ha1: There is statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

RQ2: What is the association between distance from treatment center and adherence to ART among AYA?

Ho2: There is no statistically significant association between distance from treatment center and adherence to ART among AYA

Ha2: There is statistically significant association between distance from treatment center and adherence to ART among AYA.

RQ3: What is the relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA?

Ho3: There is no statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA.

Ha3: There is statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA.

In Chapter 4, I discuss data collection and present the result of the study. Results, analysis, and findings on adherence to ART among AYA in Benue State, Nigeria was based on the use of different statistical tools. I used descriptive and inferential tests, which I present in the chapter. The data collected, though constrained by the nature of the cross-sectional study design, is a representation of the general population in Benue State, Nigeria that accesses ART at the FMC Makurdi. The total sample size ($n = 581$) was needed for my study. However, a sample size ($n = 656$) that surpassed what was originally planned was used.

Data Collection

After ethical clearance from the Ethics Committee of the FMC Makurdi, I

collected data on patients who attended the ARV clinic of the hospital for between 2010

and 2016. This was done with the support of two clinical support staff members at the

hospital. There was no need to obtain informed consent because I used secondary data. I

sequentially followed the serial numbers in the enrolment register to obtain the first 656

patients who met the inclusion criteria as outlined in Chapter 3. The data was de-

identified at the point of collection where all identifiable information was deleted.

Results of the Study

In the following subsection, I present the results of the analyses.

Descriptive Statistics for the Study Population

Categorical variables. The study had a population of ($n = 656$) and most were

females ($n = 590$, 89.9%). Males comprised only 10.1% of the population ($n = 66$; see see

Table 2).

Table 2

Descriptive Statistics by Gender

		Frequency	Percent	Valid percent	Cumulative percent
Valid	Female	590	89.9	89.9	89.9
	Male	66	10.1	10.1	100.0
	Total	656	100.0	100.0	

The unemployed constituted a largest population the group ($n = 251$, 38.3%), while about one-third were farmers ($n = 204$, 31.1%). Others were either employed ($n = 14$, 2.1%) or business owners ($n = 82$, 12.5%). Types of businesses included selling oranges, operating hair dressing salons, roadside electrical work, fuel dealing, upholstery work, food vending, clothes tailoring (seamstress), clothes sales, and the like. For the employment status variable, the data was missing for 105 participants (16%; see Table 3).

Table 3

Descriptive Statistics by Employment Status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Unemployed	251	38.3	45.6	45.6
	Employed	14	2.1	2.5	48.1
	Business person	82	12.5	14.9	63.0
	Farming	204	31.1	37.0	100.0
	Total	551	84.0	100.0	
Missing	-99	105	16.0		
Total		656	100.0		

The level of education among the study population also varied, with the largest having only secondary education ($n = 238$, 36.3%) while the least was those with tertiary (post-secondary) education ($n = 48$, 8.6%). Others included those with primary education

(n = 185, 28.2%) and those who have never been to school or did not complete primary

school (n = 87, 13.3%). Missing data for the category was (n = 98, 14.9%) (see Table 4).

Table 4

Descriptive Statistics by Education

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	None	87	13.3	15.6	15.6
	Primary	185	28.2	33.2	48.7
	Secondary	238	36.3	42.7	91.4
	Tertiary	48	7.3	8.6	100.0
	Total	558	85.1	100.0	
Missing	-99	98	14.9		
Total		656	100.0		

A majority were married (n =245, 37.3%), single (n = 228, 34.8%), divorcees (n

= 7, 1.1%) and those that separated from their spouses (n = 43, 6.6%) had the least

population. Missing data accounted for (n = 98, 4.9%) (see Table 5).

Table 5

Descriptive Statistics by Marital Status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Single	228	34.8	40.9	40.9
	Married	245	37.3	43.9	84.8
	Divorced	7	1.1	1.3	86.0
	Widowed	35	5.3	6.3	92.3
	Separated	43	6.6	7.7	100.0
	Total	558	85.1	100.0	
Missing	-99	98	14.9		
Total		656	100.0		

A higher proportion of the study population resided in urban areas (n = 275, 41.95%), while those in the rural areas constituted 23.3% (n = 153). Missing data was (n = 228; 34.8%). See Table 6.

Table 6

Descriptive Statistics by Environment

		Cumulative
Percent	Valid Percent	Percent
41.9	64.3	64.3
23.3	35.7	100.0
65.2	100.0	
34.8		
100.0		

Summary of the descriptive statistics for the categorical variables is displayed in Table 7

Table 7

Summary Descriptive Statistics for the Categorical Variables

		Gender	Employment status	Education	Marital status	Environment
N	Valid	656	551	558	558	428
	Missing	0	105	98	98	228

Continuous variables. Adherence rate: The mean, median and mode were 92.05, 100 and 100 respectively. The standard deviation (SD = 14); kurtosis was -2.68 and Skewness was 8.77 while the maximum and minimum values were 100 and 9 respectively with a range of 91. Final CD4 count: The highest CD4 was 1356 cells/mm^3 while the lowest was 10 cells/mm^3. The mean and standard deviations were respectively $M = 568.48$, $SD = 274.39$. Those with a CD4 less than 500 cell/mm^3 were 188 (28.7%) while 250 (38.1%) had a CD4 count at least 500 cell/mm^3. A third of the data, 218 (33.2%) was missing. The six CD4 count values are displayed in Table 8. With respect to age, $M = 21.37$, $SD = 2.42$. Those between the age bracket 15 and 19 were 109 (16.6%) while about two – third, 413 (63%) was between ages 20 and 24 years. Missing data accounted for one -fifth, 134 (20.4%). Distance to the hospital: The maximum distance from the hospital was 306 kilometers while the minimum was 2 kilometers. $M = 51.58$, $SD = 55.29$. Half of the study population, 329 (50.2%) lived at most 50 kilometers away from the hospital where they received ART. Those between 51 and 100 kilometers away

from the hospital were 88 (3.4%) while those between 101 and 150 kilometers were 56

(8.5%). A total of 36 (5.5%) participants lived between 151 and 200 kilometers whereas

2 (.3%) participants lived between 201 and 250 kilometers. Participants that lived

between 251 and 300 kilometers were 2 (.3%) while 1 participant lived between 301 and

350 kilometers away from the hospital. Missing data accounted for about a fifth, 142

(21.6%). Duration on ART: $M = 2.99$, $SD = 3.92$. The duration on ART among the study

population shows those less than 2 years were 244 (37.2%); those between 2.01 and 4.00

years were 163 (24.8%). Ages 4 – 6 years were 229 (34.9%) while those who have been

on ART between 6.01 and 8.00 years were 15 (2.3%). Missing data was 5 (0.8%). See

Tables 8 - 13 for details.

Table 8

Mean CD4 Values

		First CD4 value	Second CD4 value	Third CD4 value	Fourth CD4 value	Fifth CD4 value	Sixth CD4 count
N	Valid	645	509	591	550	475	438
	Missing	11	147	65	106	181	218
Mean		320.41	400.35	418.39	454.83	504.75	568.48

Table 9

Adherence rate Statistics

N	Valid	652
	Missing	4
Mean		92.05
Median		100.00
Mode		100
Std. Deviation		14.030
Variance		196.828
Skewness		-2.678
Std. Error of Skewness		.096
Kurtosis		8.770
Std. Error of Kurtosis		.191
Range		91
Minimum		9
Maximum		100
Sum		60017

Table 10

Descriptive Statistics for CD4 Count (Categorized)

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0-499	188	28.7	42.9	42.9
	500 – 1500	250	38.1	57.1	100.0
	Total	438	66.8	100.0	
Missing	-99	218	33.2		
Total		656	100.0		

Table 11

Descriptive Statistics for Age

	Frequency	Percent	Valid Percent	Cumulative Percent
15 -19	109	16.6	20.9	20.9
20 – 24	413	63.0	79.1	100.0
Total	522	79.6	100.0	
-99	134	20.4		
Total	656	100.0		

Table 12

Descriptive Statistics for Distance

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0-50	329	50.2	64.0	64.0
	51-100	88	13.4	17.1	81.1
	101-150	56	8.5	10.9	92.0
	151-200	36	5.5	7.0	99.0
	201-250	2	.3	.4	99.4
	251-300	2	.3	.4	99.8
	301-350	1	.2	.2	100.0
	Total	514	78.4	100.0	
Missing	-99	142	21.6		
Total		656	100.0		

Table 13

Descriptive Statistics for Years on ART

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0-2.00	244	37.2	37.5	37.5
	2.01-4.00	163	24.8	25.0	62.5
	4.01-6.00	229	34.9	35.2	97.7
	6.01-8.00	15	2.3	2.3	100.0
	Total	651	99.2	100.0	
Missing	-99.00	5	.8		
Total		656	100.0		

Table 14

Descriptive Statistics for the Continuous Variables

	N	Range	Minimum	Maximum	Sum	Mean	Std. Deviation	Variance
Years on ART	656	6.41	.00	6.41	1962.92	2.9923	1.98037	3.922
Age	656	9.39	15.01	24.40	14019.74	21.3716	2.42174	5.865
Adherence rate	652	91	9	100	60017	92.05	14.030	196.828
CD4 count	438	1346	10	1356	248996	568.48	274.387	75288.131
Distance to hospital	514	304	2	306	26511	51.58	55.287	3056.650
Valid N (listwise)	356							

Statistical Analyses

Research Question 1

RQ1: What is the difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings?

Ho1: There is no statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

Ha1: There is statistically significant difference in adherence to ART among AYA accessing ARV medicines in the same treatment center but residing in rural and urban settings

T-test analysis. For assessment of the difference in adherence to ART medicines between patients in urban and those who resided in rural areas, *t-test* analysis was carried out. Assumptions that must be taken into consideration while using t-statistics include the variable having a discernible distribution that approximate normal and the grouping variable is categorical and dichotomous (Field, 2013). The assumption of discernible distribution was violated (Skewness = - 2.678; kurtosis = 8.770) as a result the data was transformed for the purpose of conducting a t-test (i.e. skew < |2| and kurtosis < |9| (Schmider, Ziegler, Danay, Beyer, & Bühner, 2010). However, a *t-test* analysis with the transformed data gives a result that was similar when the data was untransformed. As a result, I present the results with the untransformed data which also makes the interpretation of the result less complicated. The independent *t-test* (two-tailed) was used and the SPSS output is shown in Table 15.

Table 15

Independent Samples Test for Adherence rate and Environment

| | | Levene's Test for Equality of Variances | | *t-test* for Equality of Means | | | | | 95% Confidence Interval of the Difference | |
		F	Sig.	T	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Adherenc e rate	Equal variances assumed	14.568	.000	-3.280	424	.001	-4.661	1.421	-7.455	-1.868
	Equal variances not assumed			-3.731	419.033	.000	-4.661	1.249	-7.117	-2.206

Adherence rate to ART for those who lived in urban settlements ($N = 274$) was $M_1 = 89.42$ ($SD_1 = 15.909$). Comparatively, those in rural settlements ($N = 152$) had adherence rate $M_2 = 94.08$ ($SD_2 = 9.843$). In order to test for the hypothesis that there is statistically significantly difference in adherence rate to ART between the population in urban and rural settlements, I performed an independent *t-test*. Levene's test for equality of variance was examined. The key assumption in this test is that the variances for both

categories of patients are equal (Anderson, Burnham, & Thompson, 2000). Therefore, we test for equal variance assumed. The *t-test* result showed statistically significant difference in adherence rate to ART between those who lived in urban and rural settlements, t (424) = -3.280, .001, p < .05. Therefore, we failed to accept the null hypothesis that there is no significant difference in adherence rate to ART between urban and rural population.

In order to understand and appreciate the effect size of the difference, Cohen's *d* was estimated as follows:

Cohen's $d = (M_2 - M_1)/SD_{pooled}$

$SD_{pooled} = \sqrt{(SD_1^2 + SD_2^2)/2}$

M_1 = Mean difference of adherence for participants resident in rural setting = 89.42

M_2 = Mean difference of adherence for participants resident in urban setting = 94.08

SD_1 = Standard deviation for adherence among rural participants residents = 15.909

SD_2 = Standard deviation for adherence among urban participants residents = 9.843

d = .4923. This is approximately .5. The scale for Cohen's *d* is *small* (d=0.2), *medium* (d=0.5), and *large* ($d \geq 0.8$). This implies the mean variance between the adherence rates of patients in rural and urban setting is of moderate effect (Sullivan & Feinn, 2012).

Several other comparisons using *t-test* were carried out to test for statistical significant difference in adherence rate to ART and these included adherence rate by gender where there was no statistically significant difference between male and female, *t* (650) = .066, .947, *p* >.05. Between ages 15and 19 years and 20 and 24 years, there was no statistically significant difference, *t* (518) = .304, .761, *p* > .05. With respect to

duration on therapy, between those who have been on ART for less than five and those who have been on ART for at least five, t (650) = 1.830, .068, $p > .05$. There was however, a statistically significant difference between those with CD4 counts of at least 500 cell/mm^3 and those with less than 500 cells/mm^3, t (436) = -2.819, .005, $p < .05$ with a Cohen's d value of .38. i.e. approximately .4. A statistically significant difference was also observed between those who lived at most 50 kilometers away from the hospital and those that lived more than 50 kilometers away from the hospital, t (509) = -2.37, .018, $p < .05$ with Cohen's d value of 0.044 (Approximately .04).

In order to test for any statistically significant difference in adherence rate based on level of education, marital status, distance to the hospital and employment, ANOVA was performed. This was because these variables have more than two categories and the dependent variable is an interval-ratio level of measurement (Frankfort-Nachmias, C., & Leon-Guerrero, 2015).

Education: For education, the result of the ANOVA analysis is displayed in Table 16. The mean difference to adherence rate between groups was statistically significant (F = 7.2, $p <$.000). Therefore, the null hypothesis that there was no statistically significant mean difference between the groups was rejected.

Table 16

ANOVA by Adherence Rate Based on Education Level

	Sum of Squares	Df	Mean Square	F	Sig.
Between groups	3851.552	3	1283.851	7.231	.000
Within groups	97826.055	551	177.543		
Total	101677.607	554			

Since there was a statistically significant mean difference between the two groups, post-hoc was used to explore if there was any variance within the group. The Levene's test for homogeneity of variance shows $p < .05$ (.001) which rejected the null hypothesis that variances are equal. The post-hoc from the SPSS output is displayed in Table 17

Table 17

Test of Homogeneity of Variances of

Adherence Rate Based on Education

Levene Statistic	df1	df2	Sig.
7.879	3	551	.000

Bonferroni approach was employed to control for Type I error and a *p* value of less than.05 was required for significance. From the SPSS output (Table 18), there were statistically significant difference in adherence rate between those with tertiary education and no education *p* < *.05* (.002); tertiary education and primary education *p* < *.05* (.001); and tertiary education and secondary education *p* < .05 (.032). The partial ETA square was less than 5% (.038). A 95% confidence interval was maintained throughout the levels.

Table 18

Multiple Comparisons for Dependent Variable: Adherence rate

Bonferroni

(I) Education	(J) Education	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
None	Primary	-.406	1.747	1.000	-5.03	4.22
	Secondary	2.944	1.684	.486	-1.51	7.40
	Tertiary	8.833[*]	2.406	.002	2.46	15.20
Primary	None	.406	1.747	1.000	-4.22	5.03
	Secondary	3.349	1.308	.064	-.11	6.81
	Tertiary	9.239[*]	2.160	.000	3.52	14.96
Secondary	None	-2.944	1.684	.486	-7.40	1.51
	Primary	-3.349	1.308	.064	-6.81	.11
	Tertiary	5.890[*]	2.108	.032	.31	11.47
Tertiary	None	-8.833[*]	2.406	.002	-15.20	-2.46
	Primary	-9.239[*]	2.160	.000	-14.96	-3.52
	Secondary	-5.890[*]	2.108	.032	-11.47	-.31

*. The mean difference is significant at the 0.05 level.

Employment. For employment, the result of the ANOVA analysis is displayed in

Table 19.

Tables 19

Test of Homogeneity of Variances of
Adherence Rate Based on Employment

Levene Statistic	df1	df2	Sig.
8.408	3	544	.000

The mean difference to adherence rate between groups was statistically significant ($F =$

6.2, $p <.001$). Therefore, the null hypothesis that there was no statistically significant

mean difference between the groups was rejected (Tables 20).

Table 20

ANOVA by Adherence Rate Based on Employment

	Sum of Squares	Df	Mean Square	F	Sig.
Between groups	3331.662	3	1110.554	6.253	.000
Within groups	96619.212	544	177.609		
Total	99950.874	547			

There was a statistically significant mean difference between the two groups, so, a post-hoc was used to explore if there was any variance within the group. The Levene's test for homogeneity of variance shows *p* less than *.05* (.001) therefore, the null hypothesis that variances are equal was rejected. Again, Bonferroni approach was employed to control for Type I error and a *p* value of less than .05 was required for significance. There were statistically significant differences in adherence rate between farmers and unemployed with p value of less than .05 (.003) and between farmers and employed, p of less than .05 (.022). The partial ETA square was less than 5% (.033). A 95% confidence interval was maintained throughout the levels.

Marital status. For marital status, the resulting p value of Levene's test is .120 (*p* >.05). The mean difference to adherence rate between groups was statistically non-significant (*F* = .657, *NS* .622, *p* >.05). Therefore, we failed to reject the null hypothesis that there was no statistically significant mean difference between the groups.

Distance. For a stratified distance to the hospital, the resulting p value of Levene's test is .084 ($p > .05$). The mean difference to adherence rate between groups was statistically non-significant ($F = 7.66$, *NS* .622, $p > .05$). Therefore, we failed to reject the null hypothesis that there was no statistically significant mean difference between the groups.

Research Question 2

RQ2: What is the association between distance from treatment center and adherence to ARV medicines among AYA?

Ho2: There is no statistically significant association between distance from treatment center and adherence to ARV medicines among AYA

Ha2: There is statistically significant association between distance from treatment center and adherence to ARV medicines among AYA

Correlation and bivariate analysis. Correlation test was performed between adherence rate to ART and distance to the hospital and Spearman's *rho* = -.088 with a significant value of .048 ($< .05$), we therefore, reject the null hypothesis that said there was no correlation between distance to the hospital and adherence rate to ART. Correlation was also performed for all the metric-interval variables which include CD4 count, age of study population and years on ART. There was correlation between adherence rate to ART and years on ART (*rho* = -.405, *NS* = .001, $p < .05$) and between adherence rate and CD4 counts (*rho* = .122, *NS* = .011, $p < .05$). Correlation with the other categorical predictors was carried out and there was statistically significant correlation between adherence rate to ART and education (*rho* = -.166, *NS* = .001, $p <$

.05); employment (*rho* = .257, *NS* = .001, *p* < .05); environment (*rho* =.165, *NS* = ,001, *p* < .05); and marital status (*rho* =.104, *NS* = .015, *p* < .05). There was no statistically significant correlation between adherence rate and gender (*rho* = -.012, *NS* = .765, *p* < .05) and age (*rho* = .29, *NS* = .464, *p* > .05.

     Linear regression. Linear regression was the statistical model that was used to predict the relationship between adherence rate and distance to the hospital. The statistical output from the linear regression shows R = .045, R^2 = .002, B (unstandardized coefficient) = -.011, *NS* = .312, *p* > .05. The result shows absence of statistically significant linearity between adherence rate and distance to the hospital with 95% confidence interval (-.033, .011) crossing the zero value. With the absence of linear relationship with the outcome variable, there was no need to proceed with further statistical tests.

Research Question 3

     RQ3: What is the relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA?

     Ho3: There is no statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA.

     Ha3: There is statistically significant relationship between a high CD4 counts (> 500 cell/mm^3) and adherence to ART among AYA.

     Correlation and bivariate analysis. Correlation test was performed between high CD4 ($\geq$ 500 cell/mm^3) and adherence rate to ART and Pearson R = -.053, *NS* = .389, *p* >.05. This shows there was no statistically significant correlation between the two

variables. We therefore, failed to reject the null hypothesis that said there was no statistically significant association between a high CD count (≥ 500 cell/mm^3) and adherence rate. In the absence of a correlation, there was no need for a regression between a high CD4 counts (≥ 500 cell/mm^3) and adherence rate.

A correlation test was also performed between a low CD4 counts (< 500 cell/mm^3) adherence rate and there was correlation of Pearson $R = .214$, NS $= .003$, $p < .05$. This showed a statistically significant correlation between the two variables. With the correlation between adherence rate to ART and low CD4 (< 500 cell/mm^3) established, linear regression was used to predict the relationship between the two variables. The statistical output shows $R = .215$, $R^2 = .046$, $B = 1.956$, $NS = .003$, $p < .05$. The result shows presence of statistically significant linearity between adherence rate and CD4 (< 500 cell/mm^3) with 95% confidence interval (.663, 3.249) not crossing the zero value.

In order to test for a covariance between the outcome variable, high CD4 count (≥ 500 cell/mm^3), and other variables in the study, Pearson correlation was performed between high CD4 count and employment status ($R = .036$, $NS = .590$, $p > .5$); years on ART ($R = .031$, $NS = .619$, $p > .05$); environment ($R = .029$, $NS = .714$, $p > .05$); marital status ($R = .010$, $NS = .885$, $p > .05$); distance ($R = -.076$, $NS = .219$, $p > .05$); education ($R = -.076$, $NS = .255$, $p > .05$); gender ($R = -.065$, $NS = .297$, $p > .05$); and age ($R = .007$, $NS = .907$, $p > .05$). The result shows no correlation with any of the variables.

In order to test for a difference in adherence rate between the two sub groups of CD4 (≥ 500 cell/mm^3 and < 500 cell/mm^3), the independent t-test (two-tailed) was

employed. Assumptions that must be taken into consideration while using t-statistics include the variable having a discernible distribution that approximate normal (Field, 2013). The assumption of discernible distribution was met (i.e skew < |2| and kurtosis < |9| (Schmider, E., Ziegler, M., Danay, E., Beyer, L., & Bühner, 2010). The mean adherence rate to ART for those with low CD4 (< 500 cell/mm^3) ($N = 188$) was $M_1 = 90.86$ ($SD_1 = 14.763$). Whereas, those with high CD4 (≥ 500 cell/mm^3) (N = 250), $M_2 = 94.38$ ($SD_2 = 11.373$). Independent *t-test* was performed. Levene's test for equality of variance was examined. The key assumption in this test is that the variances for both categories of patients are equal (Anderson et al., 2000). Therefore, we test for equal variance assumed. The *t-test* result showed statistically significant difference in adherence rate to ART between those with low CD4 (< 500 cell/mm^3) and those with high CD4 (≥ 500 cell/mm^3), $t(436) = -2.819, .005, p < .05$. Therefore, we failed to accept the null hypothesis that there is no significant difference in adherence rate to ART between low and high CD4 counts among the study population.

The effect size of the difference in adherence between those with low and high CD4 was estimated using Cohen's *d* as follows:

Cohen's d $= (M_2 - M_1)/SD_{pooled}$

$SD_{pooled} = \sqrt{(SD_1^2 + SD_2^2)/2}$

M_1 = Mean difference of adherence for those with CD4 < 500 cells/mm^3 = 90.86

M_2 = Mean difference of adherence for those with CD4 (≥ 500 cell/mm^3) = 94.38

SD_1 = Standard deviation for adherence for those with CD4 (< 500 cells/mm^3) = 14.763

SD_2 = Standard deviation for adherence for those with CD4 (≥ 500 cell/mm^3) = 11.373

$d = .378$. This is approximately .38.

Summary

In Chapter 4, I examined the difference in adherence rate to ART based on location (urban and rural) among AYA including the effect size of the difference that was found. The statistical difference in adherence rate among several variables was also tested and these variables included age of patients; gender; number of years on ART, CD4 counts, distance from patient's home to the ART center; level of education, marital status; and employment status. Where differences existed, the effect size of the difference was estimated using Cohen's d. The association between adherence rate to ART and distance was explored in the chapter. In addition, the relationship between a high CD4 count described as CD4 $\geq$ 500 cells/mm^3 and adherence rate to ART was explored.

The results show differences in adherence rate to ART between urban and rural dwellers. There was difference in adherence rate between farmers and unemployed; farmers and employed. Those with tertiary level of education also had difference in adherence with those with no education or primary education or secondary education. Difference in adherence was also observed between those living at most 50 kilometers away from the ART center and those living farther than 50 kilometers away from the ART center. While correlation exists between distance to the ART center and adherence rate, there was absence of linearity between the two variables. There was no association between CD4 that was at least 500 cells/mm^3 and adherence rate. However, CD4 that was less than 500 cells/mm^3 was linearly related to adherence rate. The result also shows that there was no correlation between CD4 that was at least 500 cells/mm^3 and age of patients;

gender; number of years on ART, distance from patient's home to the ART center; level of education, marital status; and employment status.

In Chapter 5, the results in Chapter 4 was reviewed and related to what is obtained in current literature. I discussed findings from the result alongside social implication for change. I also looked at the appropriateness of applying the result in the larger population. I equally provided insight into the limitations of the study and offered recommendations for future research.

Chapter 5: Discussion, Conclusions and Implications

Introduction

Adherence to ART among AYAs is very important in the management of HIV as the AYA stage is the transition to full adulthood. However, suboptimal adherence to ARV has been reported among AYAs (Xu, Munir, Kanabkaew, & Le Coeur, 2017b). Involvement in risky sexual behavior with little interest in engaging appropriate health services is not uncommon for individuals in this age bracket. World-wide, only 62% of AYAs on ART adhere to ARV medicines (S.-H. Kim et al., 2014). My specific goals in this quantitative cross-sectional study were (a) to explore the difference in adherence to ART among AYAs accessing care in the same treatment center but resident in different rural and urban settings, (b) to explore the association between adherence of AYAs stratified by distance from the treatment center, and (c) to determine the nature of the relationship between adherence and CD4 counts after an AYA attained a CD4 cell count greater than 500 cell/ mm^3.

Secondary data was obtained on patients who accessed HIV care and treatment from FMC Makurdi, Nigeria for the period between 2010 and 2016. Data obtained included pharmacy refill records, distance from patient's home to the ART center, CD4 counts, and environment (urban or rural). Demographic variables that were also collected included age of patients, number of years on ART, employment status, level of education, and marital status. Various statistical tests were carried out using SPSS version 24. I carried out independent *t* tests to assess the difference in adherence rate to ART patients in urban and rural areas accessing health care at the FMC Makurdi. I found a statistically

significant difference in adherence rate to ART between the two groups at t (424) = -3.280, .001, $p < .05$. Cohen's d of the effect size was .5. A statistically significant difference in adherence rate was also observed between those who lived at most 50 kilometers away from the hospital and those that lived more than 50 kilometers away from the hospital, t (509) = -2.37, .018, $p < .05$ with Cohen's d value of 0.04. In addition, there was a statistically significant difference in adherence rate between those with CD4 counts of at least 500 cell/mm^3 and those with less than 500 cells/mm^3, t (436) = -2.819, .005, $p < .05$ with a Cohen's d value of .4. A simple linear regression between CD4 count of less than 500 cells/mm^3 and adherence rate to ART shows a significant regression (F (1,184) = 8.907, $p = .003$) with an R and R^2 of .215 and .046 respectively.

Interpretation of Findings

The dearth of studies on the differences in ART adherence rates among AYAs in Nigeria based on environment (urban or rural) made my research necessary to extend the body of knowledge in this area of HIV management with ART. I assessed the difference in ART adherence rates among AYAs from the FMC Makurdi, Benue Sate, Nigeria and found a mean adherence rate of 94% and 89% for patients who resided in rural and urban environment, respectively. The difference was statistically significant: t (424) = -3.280, .001, p < .05. This agrees with Oku et al .(2013) in their study of adherence to ART by people living in Calabar (a major city in Nigeria) and accessing care in University of Calabar Teaching Hospital and those coming from rural areas where there was a difference between the two groups with the latter having a better adherence to ART. Suffice to say the Oku et al .(2013) study was a study based on patient self-report while

my study was based on pharmacy refill records. My findings also align with those in a study conducted in another part of Africa, the Republic of Togo (Hudelson & Cluver, 2015). This cross-sectional study of 291 people living with HIV AIDS ages 10 – 19 years, at the regional hospital of Sokode showed that those residing in rural areas had a comparatively better adherence rate than those in the urban areas (81%; p value less than .05). According to Hudelson and Cluver (2015) who carried out the systematic study, environment (urban versus rural) could have impact on adherence to ART. The effect size of the difference in my study has a Cohen's *d* value of .5 (Sullivan & Feinn, 2012). This implies the mean variance between the adherence rates of patients in rural and urban setting is of moderate effect. My study finding indicated that the AYAs in Benue State who reside in the rural area are better in adherence to ART than their counterpart in the urban areas.

For the RQ 2, I attempted to explore the association between distance to the ART treatment center and adherence to ART. My findings disconfirm those in studies by Eyassu et al. (2016) in South Africa and Chineke (2015) and Falang et al. (2012) in Nigeria. These earlier studies indicated that distance to treatment center was associated with adherence, and that those father from treatment center were less adherent. There was no association between distance and ART adherence rate except when distance was categorized into "near" and "far." It is imperative to mention that previous studies never mentioned the specific distances that were considered far or near. The mean adherence rate for AYA who lived within a 50-kilometer radius (90.66%) was different from those who lived beyond a 50-kilometer radius (93.53%). Though the difference was observed

to be statistically significant (t (509) = -2.37, .018, $p < .05$), the Cohen's d value of 0.044

shows the effect size of the difference is trivial (Sullivan & Feinn, 2012).

I categorized distance into at most 50 kilometers and greater than 50 kilometers as

"near" and "far" respectively to see if there was difference between those groups. It is

instructive to note that because Makurdi metropolis is only about 20-kilometers in radius,

those considered "near" are not exclusively residents in the Makurdi metropolis. The

finding was not expected under normal circumstances because people living near a health

facility are naturally expected to be more adherent in keeping to their pharmacy refills

appointments. My research finding showed that factors that influence adherence could be

multifaceted and not just limited to proximity to the ART center. However, when the

distance was stratified into 0-50, 51- 100, 101-150, 151 – 200, 201 – 250, 251 -300, and

301 -350 kilometers, there was no correlation with adherence rate. Also, there was

absence of statistically significant linearity between adherence rate and distance to the

hospital (R = .045, R^2 = .002, B (unstandardized coefficient) = -.011, NS = .312, $p > .05$)

with 95% confidence interval (-.033, .011) crossing the zero value. This confirms

Carlucci et al. (2008) who carried out a study in South Africa and concluded distance

could not predict adherence to ART.

In my RQ 4, I assessed the difference in ART adherence rates between individuals

with a CD4 count of 500 cells/mm^3 and greater, and individuals with a CD4 count under

500 cells/mm^3. The mean adherence rate for the groups was 94.38% and 90.86%

respectively. This was found to be a statistically significant difference: t (436) = -2.819,

.005, $p < .05$ with a Cohen's d value of .38. (i.e., approximately .4). This shows the effect

size of the difference was moderate (Sullivan & Feinn, 2012). My study did not show any correlation between a high CD4 ($\geq$ 500 cell/mm^3) and ART adherence rate (R = -.053, NS = .389, p >.05). This finding confirms those of Nyogea et al. (2015) who carried out a study on determinants of adherence among children and adolescents in Tanzania but found no association between adherence and CD4 counts. On the other hand, low CD4 of less than 500 cells/mm^3 correlated with adherence rate R = .215, R^2 = .046, B = 1.956, NS = .003, p < .05. This means that as adherence increases, the CD4 count would continue to increase until it reaches 500 cell/mm^3, at which point there will be no more correlation between the two variables. This aspect of the result disconfirms Nyogea et al. (2015). My finding is not surprising because a plethora of other studies have linked adherence rate to CD4 counts (Achappa et al., 2013; Alleemudder, Tai, Goyal, & Pati, 2014; Boussari et al., 2015; Lamiraud et al, 2012; Rai et al., 2013; Reda & Biadgilign, 2012). However, what is new is that my research shows the correlation stops at a CD4 of 500 cells/mm^3. Further research is needed to understand the absence of correlation at a CD4 count of 500 cells/mm^3 and over.

Also, at both CD4 levels ($\geq$ 500 cells/mm^3 and < 500 cells/mm^3), the mean adherence rate was deemed good adherence ($\geq$ 85%). Since both levels of CD4 counts have a good adherence, it suggests adherence might not be the only factor in an improved CD4 counts by patients on ART. For the patients (N = 656) in the analysis, 38.1% (n = 250) had counts greater than or equal to 500 cells/mm^3, while 28.7% had a count below 500 cells/mm^3. A higher CD4 counts is associated with low risk of opportunistic

infections (Young, 2012). This implies that many of the AYA on ART in Benue State, Nigeria are doing well.

Other findings from the study involve the relationship between adherence and other variables. Difference in adherence rate was statistically significant between different levels of education ($F = 7.2$; p < .05). Those with no education had a mean adherence rate of 94.15%, compared with 85.32% for those with tertiary education ($p = .002$). The mean adherence rate for those with primary level of education was 94.56%, which was found to be statistically significantly higher than those with tertiary level of education ($p = .001$). This shows that adherence to ART is not dependent on level of education, but the reason for this seeming aberration is not clear. Pennap et al. (2013) concluded that educational level was a positive predictor of adherence. The results from other studies are equally contradictory. For example, in a study of medication adherence to antihypertensive medicines in the United States, the result varies by gender. Among males, those with below high school education had a higher adherence compare to those with higher school and above, while the reverse was the case with females (Braverman & Dedier, 2009). My study shows no statistically significant difference in adherence between those with primary school (94.56%) and no education (94.15%), with both having the highest adherence rate comparatively. This does not confirm the expectation that the higher the level of education, the better the adherence to medication.

There was a slight difference in adherence rate between females (92.06%) and males (91.94%), but the difference was not statistically significant t (650) = .066, .947, p >.05. The findings confirm those of Akahara et al.(2017) and Pennap et al. (2013) who

both studied adherence among patients in Nigeria and also found no significant difference

in adherence by gender. However, my findings are at variance with those of Falang et al.

(2012) who found that adherence was strongly associated with gender among ART

patients in Nigeria.

With respect to age of patient, there was a mean difference in adherence rate

between ages 15 -19 years (93%) and ages 20 -24 years (92%). However, the mean

difference in adherence rate was not statistically significant t (518) = .304, NS = .761, p >

.05). The finding is not surprising as adherence rate in the age bracket have been found to

be fairly the same (Kim et al., 2014; Maskew et al., 2016; Shaw & Amico, 2016). It

shows the AYAs from Benue State, Nigeria are not different from their peers in other

parts of the world when it comes to impact of age on adherence to ART.

There was a statistically significant difference in the mean adherence rates based

on employment status (F = 6.2, p <.001). The mean adherence rate for farmers (95.35%)

was statistically significantly different from that of the unemployed (90.95%) with p =

.003. The mean adherence rate was also higher among famers compare to the employed

(84.58%) with p =.022. The adherence rate for business persons was roughly the same

with the unemployed, 90.88%. The study result shows that farmers have the highest

adherence rate. This is striking as it was observed earlier that those with no education had

higher adherence rate compare to those with secondary and tertiary education. So, the

findings confirm what is expected since most of the farmers in Nigeria are illiterates

(Dudafa, 2013). However, the partial ETA square of .033 with a 95% confidence interval

was maintained throughout the levels. The partial ETA square was .033 which implies the effect size is less than 5%, very small.

Falang et al. (2012) in their study found an association between adherence rate and employment but the association was not found to be statistically significant. The employed category had a smaller mean adherence rate. It could be that seeking permission from employer to keep up with routine pharmacy refill appointment was a challenge. This is possible especially in an environment where there is a high level of stigma to the HIV virus. The unemployed have an adherence rate comparable to those in business and this is surprising because typical unemployed AYA is an economically a dependent so one would expect cost of transportation to ART to pose a hinderance according to Groh et al. (2011). The finding suggests that when it comes to keeping up with pharmacy re-fill appointments for ART, the unemployed have adherence rate higher than the employed and almost comparable with business people. The result of the study shows there was no difference in adherence rate based on marital status ($F = .657$, NS .622, $p > .05$). However, in a related study of adherence to ART among pregnant women in Nigeria, marital status was found to be strongly related to adherence (Ekama et al., 2012).

The first mean CD4 counts for the study population irrespective of their distance; environment; level of education; employment status; marital status; age; and gender was 320 cells/mm^3. The mean CD4 value became 400 cells/mm^3 in the second year; 418 cells/mm^3 in the third year; 454 cells/mm^3 in the fourth year; 504 cells/mm^3 in the fifth year; and 568 cells/mm^3 in the sixth year respectively. This shows a continuous

improvement in the health of the patients. The overall findings support the concept of the

TTM, the theoretical framework which the study was premised. The protocol for HIV

treatment in Nigeria is to test and treat as many as are eligible. For the ART naïve

patients, ARV adherence counseling (pre-contemplation and contemplation stages)

precedes enrolment on the ARV medicines and patients are assumed to be in the

preparation or *action stage* of the TTM (Prochaska & Velicer, 1997) at the time of

commencing ART. The expectation at the stage is for a steady rise in CD4 count level

that reflect a high adherence; an acceptance of the new health style. The consecutive

increase in the CD4 counts for the AYA in the study is in line with the theoretical

framework.

Limitations of the Study

The scope of the study was about exploring adherence to ART among AYA with

respect to where patient resided, proximity to ART center among others. The adequate

sample size and power of the study sample notwithstanding, findings cannot be

generalized to the entire Nigeria because it is a cross sectional study. Also, because of the

nature of the study, I could not explore the role of other factors in influencing the study

outcome (adherence to ART) such as stigma; presence or absence of social support; and

ARV counseling prior to commencement of ART. Data composition was also a limitation

as sample was only from the FMC Makurdi ART center and attitude of health care

providers is known to influence adherence rate (Ankrah et al., 2016). Finally, the

purposeful sample selection means not all patients accessing care in the FMC Makurdi

stood equal chance of been selected for the study.

Recommendations

Though the difference in adherence rate between 'far' (> 50 kilometers) and 'near' ≥ 50 kilometers) clients was observed to be statistically significant, the effect size of the difference was trivial. A further study using a qualitative approach is recommended. The primary data for the study was not collected by the researcher as a result many variables that could have shed light such as peer-pressure, social support, religion, culture and stigma were not captured. These would have provided a better understanding of how the independent variables in the study influence the study outcome, adherence rate to ART. In the light of that, I recommend a more in-depth study among AYA using a qualitative approach like a focused group discussion where other factors such as the role of peer pressure, religion and social support in adherence rate to ART would be explored. Suffice to say that it will be expensive, however, my study would serve as the baseline for such proposed study.

In addition, an interview of AYA on ART who reside in both rural and urban areas would elucidate more knowledge on other factors that influence their adherence rate. Knowing what AYA in the FMC Makurdi think about the isolation of the HIV clinic building called the 'Riverside Clinic' from the main FMC Makurdi will be important – whether it impacts adherence rate. This is because stigmatization is still a serious issue in the Nigerian society. Future research should also incorporate data from more than a single health facility in order to explore the role attitude of health care providers play in adherence to ART among AYA. There was correlation of CD4 cell counts to adherence rate only at a CD4 of <500 cells/mm^3. Further research is needed to understand why

beyond 500 cells/mm^3, there is no more a correlation. This will provide basis for review

of the current continuous adherence counselling sessions for all patients irrespective of

their CD4 levels.

Implication for Positive Social Change

My findings have various implications for positive social change. The findings

have suggested a correlation between adherence to ART and a low CD4 counts of less

than 500 cells/mm^3; a difference in adherence rates between 'near' and 'far' kilometers;

and difference in adherence rates based on environment (urban and rural) among the

AYAs in Benue State, Nigeria. To the best of my knowledge, no similar study has been

carried out on these variables among AYAs in Nigeria.

Among the business owners, the employed, the unemployed and the farmers, the

employed clients had the lowest adherence rate from the research findings.

Stigmatization, humiliation and discrimination are still a challenge in Nigeria that makes

HIV positive people not willing to disclose their status in their working environment.

This might constitute a challenge in getting official approvals to keep a date with the

routine and regular clinical appointments for those on ART. In the light of the findings

from my research, the governments (Federal, State and Local) should ensure the *Anti-*

Discrimination Act 2014 which makes it illegal to discriminate *against* people based on

their HIV status (Guardian, 2015) is not only on pages of papers but fully implemented.

The impression that educated people because of their education are better

adherent was disconfirmed by my study. Based on the findings, adherence counselors

would need to evolve adherence counselling strategies that focus equally on both

educated and less or no educated clients. Also, the call for government to initiate a policy

that makes every health center an HIV treatment center for the purpose of improved

adherence is not confirmed by my research. Since I found finds a lower adherence rate

for clients within a radius of ≤ 50-kilometer to the ART center, making ART center

within 50-kilometer radius would reduce other attendant costs such as transportation for

patients but unlikely to improved adherence.

Findings from my study could have applicability on other health care services that

are carried out in designated places and based on clinical appointments like HIV. These

would include nephrology, oncology and diabetes. Clients living within 50-kilometer

radius to a health facility are not necessary going to be more adherent to their clinical

appointments than those farther away. Rather, those residents more than 50 kilometers

away are likely to be better adherent. As a result, during adherence counselling sessions,

additional strategies should be employed to encourage adherence amongst those living

'near'.

Because high adherence rate below 500 cells /mm^3 is positively relate with

adherence, during counselling sessions, adherence counselors could focus mostly on

those with poor or suboptimal levels of adherence (< 85 %) to adopt strategies to improve

their adherence rate in order to see a possible increase in CD4 counts. A higher

proportion of those in the higher level of socio-economic stratification in Nigeria is found

in urban areas compare to rural areas. As such, emphasis during adherence counselling

sessions is usually more on people from the rural areas. This might have contributed in

making them have a better adherence rate than those in urban areas. But the implication

of the findings in practice is that all clients should be equally counselled. In overall, the

IPs of HIV programs would make use of these findings to review their HIV adherence

counseling curriculum as some of the presumptions as listed above were not confirmed

by my research.

Conclusion

The findings from the study showed: (a) the AYAs on ART in the FMC Makurdi

who resided in rural areas had a better adherence compared to those who resided in urban

areas (b) the AYAs on ART in the FMC Makurdi who lived greater than 50 kilometers

away from the ART center had a better adherence to ART than those within a radius of

50 kilometers (c) CD4 counts was positively related to the adherence rate until when the

counts reached 500 cells/mm^3. These findings have contributed to the existing knowledge

on factors that influence adherence rate to ART among AYA in Benue State, Nigeria. In

the light of the research findings, IPs that are responsible in working in partnership with

governments in Nigeria to implement HIV management programs in various health

facilities need to devise new strategies that focus on those who are proximal to ART

center to improve their adherence to ART since they comparatively have a lower

adherence rate. The comparatively lowest adherence rate by clients who were employed

calls for an approach that would help improve their adherence rate (meeting up with

pharmacy refill appointments). A suggested approach would be an advocacy to executive

arms of the government to start enforcing the *Anti-Discrimination Act* 2014 which makes

it illegal to discriminate *against* people based on their *HIV* status. This would make

people living with HIV AIDS to freely to talk to their employers about their HIV status

and also apply for official approvals to attend to their clinical appointments including pharmacy refills.

AYA in Benue State have a very good adherence as the mean adherence for the study was 92%. This should be sustained since high adherence rate relates positively with CD4 count when the CD4 has not reached 500 cells/mm^3 knowing very well that high CD4 counts reduces risk of infection. Adherence to ART is one of the key indicators for a successful management of HIV as it reduces morbidity, mortality and also helps minimize transmission of the virus. While there is a plethora of ARV cocktail in the management of HIV, these drug combinations give the desired therapeutic result only when patients are adherent to the regimes. In order to achieve the vision '90-90-90' by UNAIDS which aims to end AIDS epidemic generation (UNAIDS, 2016; UNAIDS 2014*),* those who are on ART must be adherent.

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Appendix A: Approval Letter from Federal Medical Center, Makurdi, Benue
State, Nigeria