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From Fighting Wasting to Shedding Excess: An Explanatory Sequential Mixed-Method Study of Obesity Among People Living With HIV in Nigeria

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FROM FIGHTING WASTING TO SHEDDING EXCESS: AN EXPLANATORY SEQUENTIAL MIXED-METHOD STUDY OF OBESITY AMONG PEOPLE LIVING WITH HIV IN NIGERIA

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Abstract

The human immunodeficiency virus (HIV) infection is a global epidemic, with initial high mortality rates since the first diagnosis over three and a half decades ago. However, the use of antiretroviral therapy (ART) has led to longer, healthier lives for many people living with HIV (PLHIV). Accordingly, aging comes with associated co-morbidities like obesity, diabetes, and cardiovascular diseases. The purpose of this mixed-methods study was to further understand the emergent phenomenon of obesity and overweight among PLHIV who are on treatment with ART, using Nigeria as a case study.

An explanatory sequential mixed-method design was used that involved the analysis of de-identified, quantitative, secondary data from two states in southeastern Nigeria in the first phase, followed by 16 key informant interviews (KIIs) of healthcare providers (HCPs) in the second phase. The quantitative and qualitative strands were integrated at three critical points – in the design, methods, and results presentation phases.

The quantitative study included 3530 participants. The median age at ART commencement was 34 years (IQR: 28.0, 41.0), about 68% were female, and the median BMI at baseline was 21.8 kg/m^2 (IQR: 19.4, 24.5). After 24 months on ART, the number of participants who were obese increased by 186%, while those underweight decreased by 59%. The median BMI was 23.6 kg/m^2 (IQR: 21.1, 26.6) after 24 months. Overall, the BMI increased in 74.7% of the participants. Further analysis showed that age at ART commencement ($p<.001$; partial eta squared=.011), baseline BMI ($p<.001$; partial eta squared=.465), and CD4 category at baseline ($p=.02$; partial eta squared=.008) were all significantly associated with increased BMI after 24 months of ART. The qualitative results suggested that while several HCPs saw obesity among PLHIV on treatment as an important clinical problem, some were unconcerned as long as the PLHIV did not have any physical or

cardio-metabolic complications related to obesity. Interestingly, the HCPs all felt that obesity among PLHIV was not a significant public health problem because they perceived that very few PLHIV were obese.

In conclusion, HCPs should keep in mind the likelihood of excess weight gain among PLHIV and the associated cardio-metabolic effects and have a plan to address it, especially with the universal roll-out of ART for PLHIV. The findings from this study will help HCPs develop services that will aid PLHIV to achieve the highest possible quality of life.

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Dedication

To

Abiola, Oluwaferanmi, and Oyinloluwa.

I love you all, deeply.

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Chapter 1: Introduction

The human immunodeficiency virus (HIV) infection is a global epidemic that has defied a cure since it was identified over three and a half decades ago. Over this period, about 74.9 million people have been infected with HIV, globally, and about 43% of them have died from acquired immunodeficiency syndrome (AIDS)-related illnesses (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2019a). However, with the discovery and global availability of antiretroviral therapy (ART), many HIV-infected clients now live longer healthier lives, with mortality rates from HIV significantly reduced. In 2019, about 24.5 million people were accessing ART, globally (UNAIDS, 2019a). As more HIV-positive persons live longer, HIV is now been viewed as a chronic disease, with associated co-morbidities like obesity, diabetes, and cardiovascular diseases (Amorosa et al., 2005; Armah et al., 2013; Taramasso et al. 2017; Tate et al., 2012).

Obesity has been defined as having a body mass index (BMI) $\geq$30 kg/m^2 (kilogram per meter square). The BMI is usually measured by dividing a person's weight (in kilograms) by the square of the person's height (meters^2). This result is then classified as either underweight (BMI <18.5 kg/m^2); normal weight (BMI 18.5 - 24.9 kg/m^2); overweight (BMI 25.0 - 29.9 kg/m^2); and obese (BMI $\geq$30 kg/m^2). Obesity is further sub-classified as obesity class I (BMI 30.0 – 34.9 kg/m^2); obesity class II (BMI 35.0 – 39.9 kg/m^2); and obesity class III (BMI >40.0 kg/m^2) (National Heart, Lung, and Blood Institute [NHLBI], 1998). These sub-classes are also referred to as mild, moderate, and extreme obesity, respectively.

Furthermore, obesity is closely related with several other clinical conditions. The National Heart, Lung, and Blood Institute (NHLBI, 1998) describes obesity/overweight as a condition that can increase the risk of hypertension, dyslipidemia, Type-2 diabetes mellitus (T2DM), coronary

heart disease, stroke, sleep apnea, and certain cancers. Globally, the prevalence of obesity among adults continues to rise from about 3-6% in 1975 to 11-15% in 2017 (Jaacks et al., 2019). In the United States (US), the prevalence of obesity among adults (>20 years) increased from 22.9% (1988–1994) to 37.8% (2013-2014) (National Center for Health Statistics [NCHS], 2017). In Nigeria, Africa's most populated country, a systematic review reported a range of 20%–35% prevalence for overweight, and 8%–22% for obesity among adults (Chukwuonye et al., 2013). Additionally, the Nigeria Demographic and Health Survey (NDHS) reports the mean BMI of women 15-49 years old in the southeastern region as 23.9 kg/m^2, with a 20.8% prevalence of overweight and 9.5% prevalence of obesity (National Population Commission [NPC], 2014). Ahaneku, Ahaneku, Osuji, Oguejiofor, and Opara (2014) also reported a mean BMI of 25.08 kg/m^2 (SD ±5.18) for 191 participants in Enugu State, Nigeria.

HIV and Wasting

In the early days of HIV, severe weight loss was common among people living with HIV (PLHIV). In 1987, the Centers for Disease Control and Prevention (CDC) defined wasting as greater than 10% weight loss plus chronic diarrhea or chronic weakness (CDC, 1987). Wasting in PLHIV has been attributed to several causes like alterations in metabolism, malabsorption, chronic inflammatory processes, decreased food intake, and energy deficiency (Maas et al., 1998; Smit et al., 2002), and nutritional therapy alone does not address HIV wasting syndrome (Kotler, Wang, & Pierson, 1985; Nahlen et al., 1993). The diagnosis of HIV wasting is a very strong predictor of mortality and morbidity among PLHIV (Tang, Jacobson, Spiegelman, Knox, & Wanke, 2005; Wanke, Silva, Forrester, Speigelman, & Gorbach, 2000).

Several treatments have been proposed and used for HIV wasting including appetite stimulants (e.g. marijuana), anabolic agent (e.g. growth hormones), steroids (e.g. testosterone, oxandrolone), and cytokine modulators (e.g. thalidomide) (Pernerstorfer-Schoen et al., 1994; Hoy & Flanigan, 1994; Von Roenn et al., 1994; Waters et al., 1996). Some of these treatments, on their own, were effective to a small degree in increasing body weight among wasted clients, but the optimal treatment was to start the clients on ART (Silva et al., 1998).

Before the advent of potent antiretrovirals (ARVs), HIV was often referred to as the "slim disease" (Yuh et al., 2015), a stigma that remains difficult to shake even today. However, with the use of these ARVs, a new phenomenon, 'return to health', has been described (Jones et al., 2003). The 'return to health' concept postulates that the weight gain in PLHIV after they start ART may be due to the clients regaining their initial weight before the HIV infection.

Antiretroviral Drugs: History and Classes

Currently, there are many drugs to treat HIV, but this was not the case three decades ago. The first drug approved for HIV treatment was Zidovudine (also called ZDV or AZT) in March 1987 (United States Food and Drug Administration [FDA], 2018). However, potent ARVs were not available until the 1990s when stavudine (d4T), saquinavir (SQV), ritonavir (RTV), nevirapine (NVP), lamivudine (3TC), and a host of other drugs became available (FDA, 2018). In the late 1990s, triple drug therapy was found to be very effective for HIV viral suppression. This three-drug combination, from at least two different classes, was called highly active antiretroviral therapy, or HAART (National Institute of Allergy and Infectious Diseases [NIAID], 2018). As of 2018, there were about 30 different ARVs available (NIAID, 2018). The most common drugs have been classified based on their mechanisms of action in Table 1.1 below.

Table 1.1. Classes and mechanisms of action of common ARVs

ARV Class	Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Fusion Inhibitor	CCR5 Antagonists	Protease Inhibitors (PIs)	Integrase Strand Transfer Inhibitors (INSTIs)
Mechanism of Action	Blocks reverse transcriptase, an enzyme HIV-1 needs to make copies of itself.	Binds to and alters reverse transcriptase, an enzyme HIV-1 needs to make copies of itself.	Blocks HIV-1 from entering the CD4 cells of the immune system.	Blocks CCR5, a protein on the CD4 cells that a certain type of HIV-1 needs to enter the cell.	Blocks HIV-1 protease, an enzyme HIV-1 needs to make copies of itself.	Blocks HIV-1 integrase, an enzyme HIV-1 needs to make copies of itself.
Drugs (Abbreviated form)	Abacavir (ABC)	Delaviridine (DLV)	Enfuvirtide (T-20)	Maraviroc (MVC)	Atazanavir (ATV)	Dolutegravir (DTG)
	Didanosine (ddl)	Efavirenz (EFV)			Darunavir (DRV)	Elvitegravir (EVG)
	Emtricitabine (FTC)	Etravirine (ETR)			Fosamprenavir (FPV)	Raltegravir (RAL)
	Lamivudine (3TC)	Nevirapine (NVP)			Indinavir (IND)	
	Stavudine (d4T)	Rilpivirine (RPV)			Lopinavir (LPV)	
	Tenofovir (TDF/TAF)				Nelfinavir (NFV)	
	Zidovudine (ZDV)				Ritonavir (RTV)	
					Saquinavir (SQV)	
					Tipranavir (TPV)	

*Adapted from NIAID (2016) https://aidsinfo.nih.gov/contentfiles/hiv_pill_brochure.pdf

HIV and Obesity

Due to the stigma associated with HIV as a "slim disease" (Yuh et al., 2015), the general perception is that PLHIV are thin (Maia Leite & De Mattos, 2010; Shuter, Chang, & Klein, 2011). However, because weight gain after commencement of ART is a clinical indicator of treatment success, many physicians and healthcare providers (HCPs) actively encouraged weight gain among PLHIV. Hence, increase in BMI in adult HIV clients, secondary to weight gain while on treatment, was applauded. Consequently, several authors began to report increases in BMI among PLHIV on treatment that was equal to or surpassed that in the general population. One of the earliest studies was by Amorosa and colleagues who reported a 14% prevalence of obesity, and 31% prevalence of overweight among PLHIV in Philadelphia (Amorosa et al., 2005). Crum-Cianflone, Tejidor, Medina, Barahona, and Ganesan (2008) also reported a 63% prevalence for overweight and obesity in a cohort attending two large naval clinics in the US.

Outside of the US and other high income countries, a similar trend was also documented. In Brazil, researchers reported that the prevalence of overweight/obesity increased from 35.9% to 44.4% after 4 years among PLHIV on ART attending a university teaching hospital in Rio de Janeiro (Maia Leite & De Mattos, 2010). In South Africa, other researchers reported a similar picture where there was an increase in prevalence of overweight/obesity from 50% to 67% after 6 months of ART (Esposito, Coutsoudis, Visser, & Kindra, 2008). Among the PLHIV in this study, the mean BMI increased from 25.6 ± 5.7 kg/m^2 to 27.3 ± 5.6 kg/m^2 (p=0.007). In Nigeria, the country with the second highest burden for HIV after South Africa, this emergent phenomenon has also been reported. Mustapha, Ehianeta, Kirim, Osungwu, and Oladepo (2011) reported 8.9% prevalence of obesity and 19% prevalence of overweight in a cross-sectional study in one clinic in Abuja, Nigeria's capital city. Other studies from Nigeria are summarized in Table 1.2 below.

Table 1.2. A summary of some studies on obesity among PLHIV in Nigeria

Author (Year)	**Study Design (Duration of Follow-up)**	**Number of Participants**	**BMI results (in kg/m^2, unless stated otherwise)**	**Limitation**
Akinboro et al. (2013)	Prospective cohort (1 year)	35	Mean BMI increased from 20.65 ± 2.89 at baseline to 23 ± 3.03	One clinic, Small sample size
Alo et al. (2014)	Quasi-experimental (6 months)	42 (Female = 74%)	Mean BMI increased from 21.15 ± 3.3 at baseline to 22.5 ± 3.3	One clinic, Small sample size
Denue et al. (2013)	Prospective cohort (2.5 years)	120 (Female = 61%)	Obesity – From 2.5% to 6.4% Overweight - From 12.5% to 22%	One clinic, Small sample size
Ezechi et al. (2016)	Prospective cohort (5 years)	8819 (Female = 64%)	Obesity – From 7.4% to 26.5% Overweight - From 19.6% to 35.7%	One clinic, Included adolescents
Mustapha et al. (2011)	Cross-sectional	79	Obesity – 8.9% Overweight - 19%	One clinic, Small sample size
Olowookere et al. (2015)	Prospective cohort (3 months)	318 (Female = 54%)	Mean BMI dropped from 22.2± 5.2 at baseline to 20.8 ± 5.1	One clinic, Short follow-up, Included adolescents

Research Gaps

There are major limitations to the previous studies from Nigeria, including that: (a) they were conducted in a stand-alone clinic/site in a singular state; (b) they had small sample sizes; and (c) some included adolescents. There is need to further understand this emergent phenomenon of rising obesity among PLHIV on treatment in Nigeria. In addition, we could not find any qualitative study in Nigeria that has explored the HIV-obesity interface from the healthcare providers' prospective.

Research Purpose and Objectives

Mixed-Methods Statement of Purpose

The purpose of this study was to further understand the emergent phenomenon of obesity and overweight among PLHIV on treatment in Nigeria. An explanatory sequential mixed-methods design was used that involves collecting quantitative data first and then explaining the quantitative results with key informant interviews (KIIs). During phase one of the study, de-identified, quantitative, secondary data from two southeastern states in Nigeria was analyzed to assess the prevalence and trends of obesity/overweight among PLHIV who are on treatment, as well as the demographic and clinical factors associated with changes in BMI. In phase 2 of the study, KIIs of healthcare providers (HCPs) working in HIV clinics in these two states were done to help explain the results of the quantitative findings. HCPs were interviewed to understand their perceptions of the HIV-obesity phenomenon including its probable causes, the stigma associated with HIV and weight, and long-term health consequences of obesity among PLHIV.

Reasons to Support the Use of a Mixed-Methods Design

For this study, the investigator has chosen a mixed-method approach. There are several reasons for this. First, the reports of obesity and overweight among PLHIV on treatment is an emerging phenomenon, especially in Africa. Hence, it is less well understood. A mixed-method approach allows the investigator to explore the topic and get a deeper understanding of this phenomenon, the perceptions around the topic, and potential next steps from the findings. Second, the quantitative data to study this phenomenon already exist, while the sample of healthcare providers for the key informant interviews are accessible. Hence, the investigator had access to the required data sources for both steps of the mixed-method approach. Third, the alternatives (using either a quantitative method only or qualitative method only) would not provide sufficient information to further the understanding of this emergent phenomenon. While the investigator would have preferred to interview PLHIV who are obese or overweight, there were limitations due to the sensitive nature of the topic and the limited access to this population. Due to these reasons and because it is important to understand the healthcare providers' perspective of this phenomenon, the investigator interviewed healthcare providers from Nigeria who have a history of caring for PLHIV.

Research Questions

Research Question 1: Is there a difference in mean BMI between PLHIV starting treatment in the two states and the general population?

H_0: There is no difference in the mean BMI between the PLHIV starting treatment and the general population.

H_a: There is a difference in the mean BMI between the PLHIV starting treatment and the general population.

Research Question 2a: Is there a difference in mean BMI at baseline and at 24 months of treatment among PLHIV starting treatment in the two states?

H_o: There is no difference in the mean BMI at baseline and at 24 months.

H_a: There is a difference in the mean BMI at baseline and at 24 months.

Research Question 2b: Is there a difference in proportions in each BMI category at baseline and at 24 months?

H_o: There is no difference in proportions at baseline and at 24 months.

H_a: There is a difference in proportions at baseline and at 24 months.

Research Question 3: Is the BMI after 24 months of treatment associated with demographic factors (gender, marital status, education) and/or clinical factors (drug regimen, HIV stage, CD4 count, blood pressure, adherence to medication), after accounting for age and baseline BMI?

H_o: There is no significant effect of the demographic factors and/or clinical factors on the BMI at 24 months.

H_a: There is a significant effect of the demographic factors and/or clinical factors on the BMI at 24 months.

Research Question 4: What are the perceptions of healthcare providers about overweight/obesity among PLHIV on treatment in Nigeria?

Research Question 5: In what ways do the qualitative data from the interviews with healthcare providers further explain the quantitative findings from PLHIV on treatment in Nigeria?

Philosophical and Theoretical Foundations

In this study, we used both a post-positivist worldview in the first (quantitative) phase and a constructivist worldview in the second (qualitative) phase.

Theoretical Framework: Social Ecological Model

The phenomenon of obesity among PLHIV was viewed through the Social Ecological Model. This model facilitates the appreciation of the multi-layered challenge (Sallis, Owen, & Fisher, 2008) of obesity among PLHIV. The Social Ecological Model was first described by Urie Brofenbrenner (1977), and further developed by McLeroy and colleagues (1988), and Stokols (1992).

The Social Ecological Model approaches health behaviors from the perspective of "multiple influences" that "interact across different levels" (Sallis et al., 2008, p 466). These levels include the (a) intrapersonal or individual level, (b) the interpersonal level (family, friends, small group), and (c) the community level which is further explored either as institutional factors, community factors or public policy (Glanz & Rimer, 2005, p 11; Sallis et al., 2008, p 478)

For this study, the layers to be explored include: the individual (biological, ARVs, and psychological); the small group (family and friends); the clinic community (healthcare providers and other HIV clients); and the larger (policy) community (Sallis et al., 2008, p 477). The Social Ecological Model served as an explanatory framework for the phenomenon under study. This framework helped the investigator understand the healthcare providers (HCPs) perceptions about

obesity among PLHIV on treatment, its causes, and how serious they think this co-morbidity could be.

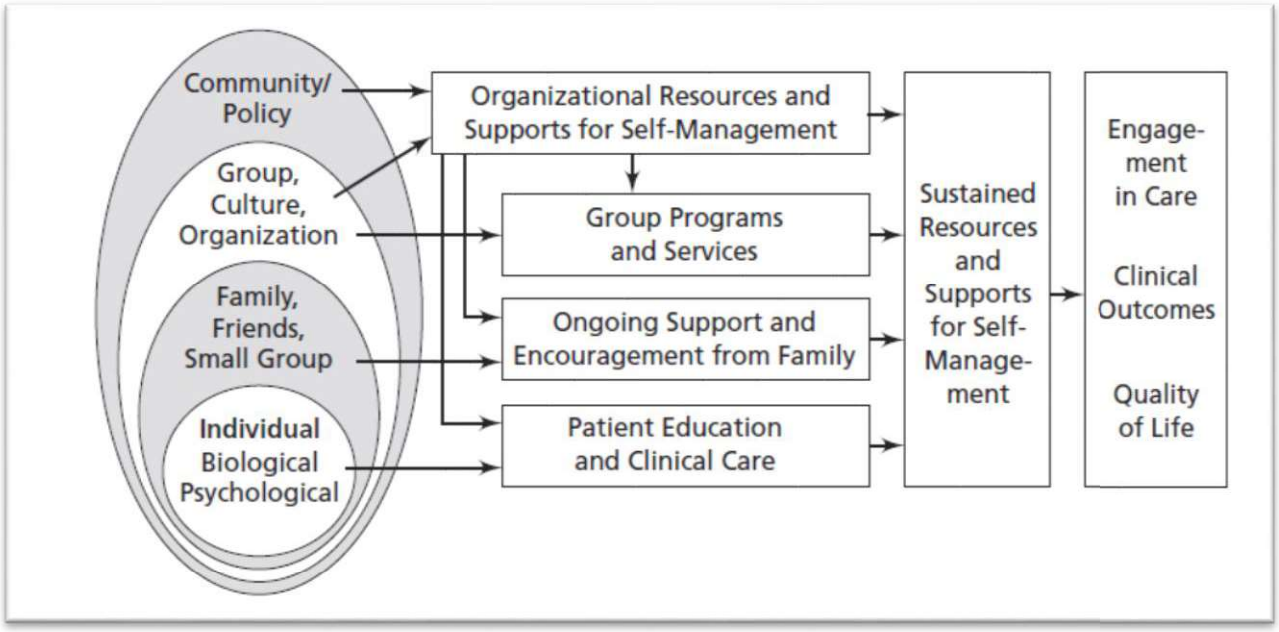


Figure 1.1. An illustration using the Social Ecological Model to explain obesity among PLHIV on treatment (from Sallis et al., 2008, p 477).

Summary

It has been over 35 years since the emergence of the HIV infection, and science has yet to find a cure. Several potent medications are available to manage HIV and have led to longer and healthier lives for PLHIV. The proportion of underweight PLHIV on treatment is on decline, and the proportion of overweight and obese clients continue to rise, leading to a 'double epidemic' of HIV and obesity. This study used a mixed-method design to study the emergent phenomenon of obesity among PLHIV on treatment in Nigeria. This chapter presents an overview of HIV, HIV

wasting, obesity, drugs used for HIV treatment, and the research purpose and questions, with the proposed theoretical framework. The next chapter covers a systematic review and meta-analysis on this topic.

Definition of Terms

Acquired immunodeficiency syndrome (AIDS): A more severe case of HIV. Usually due to non-treatment of HIV, non-adherence, or treatment failure.

Adherence: A HIV-positive client's level of compliance to taking medications and following agreed lifestyle and clinical guidance.

Antiretroviral (ARV): Drugs used to treat HIV.

Antiretroviral therapy (ART): The use of antiretroviral medicines to treat HIV infection.

Body mass index (BMI): A composite measure calculated from a person's height and weight (in kg/m^2).

CD4 T-lymphocyte cell: Special class of white blood cells that are attacked by the Human immunodeficiency virus.

Co-infection: The existence of another infection with the HIV in an individual. Usually due to a suppression of the body's immunity. Also called an opportunistic infection.

Co-morbidity: The existence of another illness/disorder with the HIV in an individual.

Healthcare providers: Healthcare professionals who render direct services to PLHIV on treatment. For example, physicians, nurses, pharmacists, and counsellors.

Highly active antiretroviral therapy (HAART): The use of at least 3 antiretroviral drugs from at least 2 different drug classes to treat HIV infection.

HIV viral load (VL): The amount of the HIV virus in the human body. Usually reported in copies/ml or $\log_{10}$ HIV RNA copies/ml.

Human immunodeficiency virus (HIV): A viral infection that attacks the body's immunity. Commonly classified as HIV-1 and HIV-2.

Joint United Nations Programme on HIV/AIDS (UNAIDS): The global body responsible for coordinating the HIV response and HIV reporting.

Key informant interviews: Qualitative interviews with experts or people who know a lot about a certain topic.

Lipodystrophy: An abnormal body fat re-distribution (George, Venter, van Deventer, & Crowther, 2009). Lipodystrophy is a known complication of certain drugs used in treating HIV.

Mixed-methods research: The combination of both quantitative and qualitative research design in an integrated manner.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI): A class of drugs used for treating HIV. Usually used as a third drug.

Nucleoside Reverse Transcriptase Inhibitors (NRTI): A class of drugs used for treating HIV. Usually used as the backbone (first and second drug).

Obesity: Having a body mass index $\geq$30 kg/m^2.

Overweight: Having a body mass index between 25.0 kg/m^2 and 29.9 kg/m^2.

People living with HIV (PLHIV): The general accepted term for referring to HIV-positive people.

Protease inhibitor (PI): A class of drugs used for treating HIV. Usually used as a third drug.

Return to health: A concept that tries to explain the weight gain among PLHIV after they start ART. It posits that the weight gain may be due to the clients regaining their initial weight before the HIV infection.

Social ecological Model: Describes how individuals and their multi-layered environment interact, and how it affects health outcomes (Golden & Earp, 2012).

Underweight: Having a body mass index <18.5 kg/m^2.

United States President Emergency Plan for AIDS Relief (PEPFAR): A program started by President George W. Bush to provide funding for free HIV services across the world.

Viral failure: Occurs when the HIV virus is detectable beyond a certain threshold in an individual on treatment with antiretroviral medicines.

Viral suppression: The decrease of HIV viral load below the level of test detection.

Wasting: Greater than 10% weight loss plus chronic diarrhea or chronic weakness (CDC, 1987).

Chapter 2: Literature Review

Background

Some researchers have documented a high prevalence of obesity among PLHIV who are on ART (Amorosa et al., 2005; Tate et al., 2012). These findings are surprising, especially with the clinical understanding of HIV as a wasting disease. In sub-Saharan Africa (SSA), there is a high burden of HIV, and obesity is also on the rise. Sub-Saharan Africa encompasses South Africa and Nigeria, the two nations with the highest and second highest burden of HIV in the world, respectively (Kharsany & Karim, 2016). In Nigeria, Ezechi, Musa, Otobo, Idigbe, and Ezechi (2016) reported a 35 percent point increase (from 27% to 62.2%) in overweight/obesity among HIV clients on ART from 2004 to 2009 in a large metropolitan treatment facility. In addition, Barth and colleagues (2008) reported a similar picture from South Africa where there was an increase in median BMI among clients on ART by 3.8 kg/m^2 (from 19.6 kg/m^2 to 23.4 kg/m^2) over a 52-week period. Though these findings further buttress the point that as PLHIV live longer, they are more susceptible to other co-morbidities associated with aging such as obesity, it also illustrates the progress that has been made in the field of HIV care and treatment.

Nduka, Uthman, Kimani, and Stranges (2016) carried out a previous systematic review and meta-analysis on body fat changes in PLHIV on ART. They reported on 60 studies with 53,199 participants and found an association between ART and increase in BMI (standardized mean difference [SMD]: 0.17 kg/m^2; 95% CI: 0.07-0.26). When the data was stratified further, they found that the association was stronger in PLHIV with baseline CD4 <350 cells/mm^3.

For this study, the investigator conducted a systematic review to: (a) build on the work by Nduka and colleagues (2016); (b) to further understand the prevalence of obesity among new PLHIV who are starting treatment; and (c) to understand the trend in BMI while on treatment. This

is imperative because this review differs from Nduka et al.'s in the following areas: (a) this review is restricted to clients on a 3-drug HAART combination, but theirs was not; (b) this review focused on the BMI trend of new clients starting treatment, while they did not distinguish between new clients and those previously on treatment; (c) this review did not have date restrictions, but theirs was within 1997 – 2015; (d) this review did not include cross-sectional studies, but theirs did; (e) this review focused on BMI only, while they looked at different body composition metrics; and (f) this review searched four databases, while they used only two databases.

Systematic Review and Meta-analysis on Obesity among PLHIV on Treatment

Objectives

The objectives of this review was to understand the prevalence of overweight/obesity among PLHIV who are starting treatment for the first time and the trend of BMI while they were on treatment (for at least 6 months).

Methods

This review was done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline by Moher and colleagues (2009). The databases used for the search were PubMed, EMBASE, CINAHL, and Scopus, while also scanning biographies for additional studies. The inclusion criteria were:

a) PLHIV newly started on treatment with HAART.
b) The same study population monitored for at least 6 months.
c) The same study population have both a baseline BMI and end BMI or a report of the change in BMI

The exclusion criteria included:

a) PLHIV on treatment for less than 6 months
b) Those less than 18 years old
c) Cross-sectional studies
d) Group BMI not reported
e) Non-pharmacological or non-orthodox treatment of HIV
f) Pregnant women or postpartum/breastfeeding women (within 6 months postpartum)
g) PLHIV receiving complementary nutritional interventions e.g. food or vitamin supplementation (if data is not disaggregated for those who are not receiving nutritional intervention).

After de-duplication, two reviewers screened the articles using the titles and abstracts. For the next step, the full texts were accessed and read independently by two reviewers to determine their eligibility for inclusion. Where the two reviewers disagreed, a third team member also reviewed and a consensus decision was reached.

Data abstraction, synthesis, and meta-analysis

Following this step, data extraction was completed by two people using a piloted data extraction form. General information (e.g. author[s], title, publication date, journal, country etc.), study details (design, population, year of data collection, duration of study etc.), and study results (e.g. mean age, gender breakdown, baseline and end mean/median BMI, CD4, viral load, and participant attrition) were extracted. The risk of bias was assessed using the Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies (EPHPP, 2010).

Table 2.1. Search strings used and the respective databases

Database	Search terms
Pubmed	((HIV[Title/Abstract]) AND (Antiretroviral therapy[Title/Abstract] OR ART[Title/Abstract] OR highly active antiretroviral therapy[Title/Abstract] OR HAART[Title/Abstract] OR HIV treatment[Title/Abstract])) AND (Body mass index[Title/Abstract] OR BMI[Title/Abstract] OR Obesity[Title/Abstract] OR wasting[Title/Abstract] OR overweight[Title/Abstract] OR underweight[Title/Abstract] OR weight gain[Title/Abstract] OR weight loss[Title/Abstract])
EMBASE	'hiv':ti,ab,kw AND ('antiretroviral therapy':ti,ab,kw OR 'art':ti,ab,kw OR 'highly active antiretroviral therapy':ti,ab,kw OR 'haart':ti,ab,kw OR 'hiv treatment':ti,ab,kw) AND ('body mass index':ti,ab,kw OR 'bmi':ti,ab,kw OR 'obesity':ti,ab,kw OR 'wasting':ti,ab,kw OR 'overweight':ti,ab,kw OR 'underweight':ti,ab,kw OR 'weight gain':ti,ab,kw OR 'weight loss':ti,ab,kw)
CINAHL	AB HIV AND AB (Antiretroviral therapy OR ART OR highly active antiretroviral therapy OR HAART OR HIV treatment)) AND AB ((Body mass index OR BMI) OR (Obesity OR wasting OR overweight OR underweight OR weight gain OR weight loss))
Scopus	(TITLE-ABS-KEY (hiv) AND TITLE-ABS-KEY (antiretroviral AND therapy OR art OR highly AND active AND antiretroviral AND therapy OR haart OR hiv AND treatment) AND TITLE-ABS-KEY (body AND mass AND index OR bmi OR obesity OR wasting OR overweight OR underweight OR weight AND gain OR weight AND loss))

The eligible articles were examined for summary statistical measures, primarily the mean or median BMI (at the beginning and at the end of the study) and the difference in the mean or median BMI at the two time points. For the studies that reported only the start and end mean BMI values, the mean differences and standard deviations were computed. Only the studies that had (reported or computed) mean BMI difference and standard deviation were included in the meta-analysis.

Data were analyzed using MetaXL version 5.3 (Epi-Gear; Sunrise Beach; Australia; https://www.epigear.com/index_files/metaxl.html), a freely available software. Due to the widely varying nature of the studies, the random-effects meta-analyses was used to combine all the studies that had mean BMI differences (reported or computed, in kg/m^2) between the start and the end of the study. The I^2 statistic was used to assess heterogeneity of the studies (Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0.). Sub-analyses was done by study designs, duration of study follow-up, and country income level as classified by The World Bank (The World Bank Group, 2019).

Results

The database search generated 4,946 articles. Two additional articles were identified from bibliographies. After de-duplication, 2967 articles remained. Following screening with titles and abstracts, 154 articles remained, and the full texts were read with another 124 excluded for varying reasons, leaving 30 eligible papers for qualitative synthesis (see Figure 2.1). The inter-rater agreement was 96.4%. Of the 30 papers, only 18 were included in the meta-analysis.

Description of Included Studies and Qualitative Synthesis

A summary of the 30 eligible papers can be found in Appendix A. Most studies were published between 2007 and 2016, with 20% (n=6) published before or in 2010. The studies had a global spread, with 4 multi-country studies that spanned all continents (Achhra et al., 2016; Erlandson et al., 2015; Huisin ’t Veld et al., 2015; Moyle, Hardy, Farajallah, Degrosky, & McGrath, 2014). Overall Africa had the most studies (47%, n=14), followed by North America (20%, n=6), Asia (13%, n=4), Europe (3%, n=1), and the Caribbean (3%, n=1).

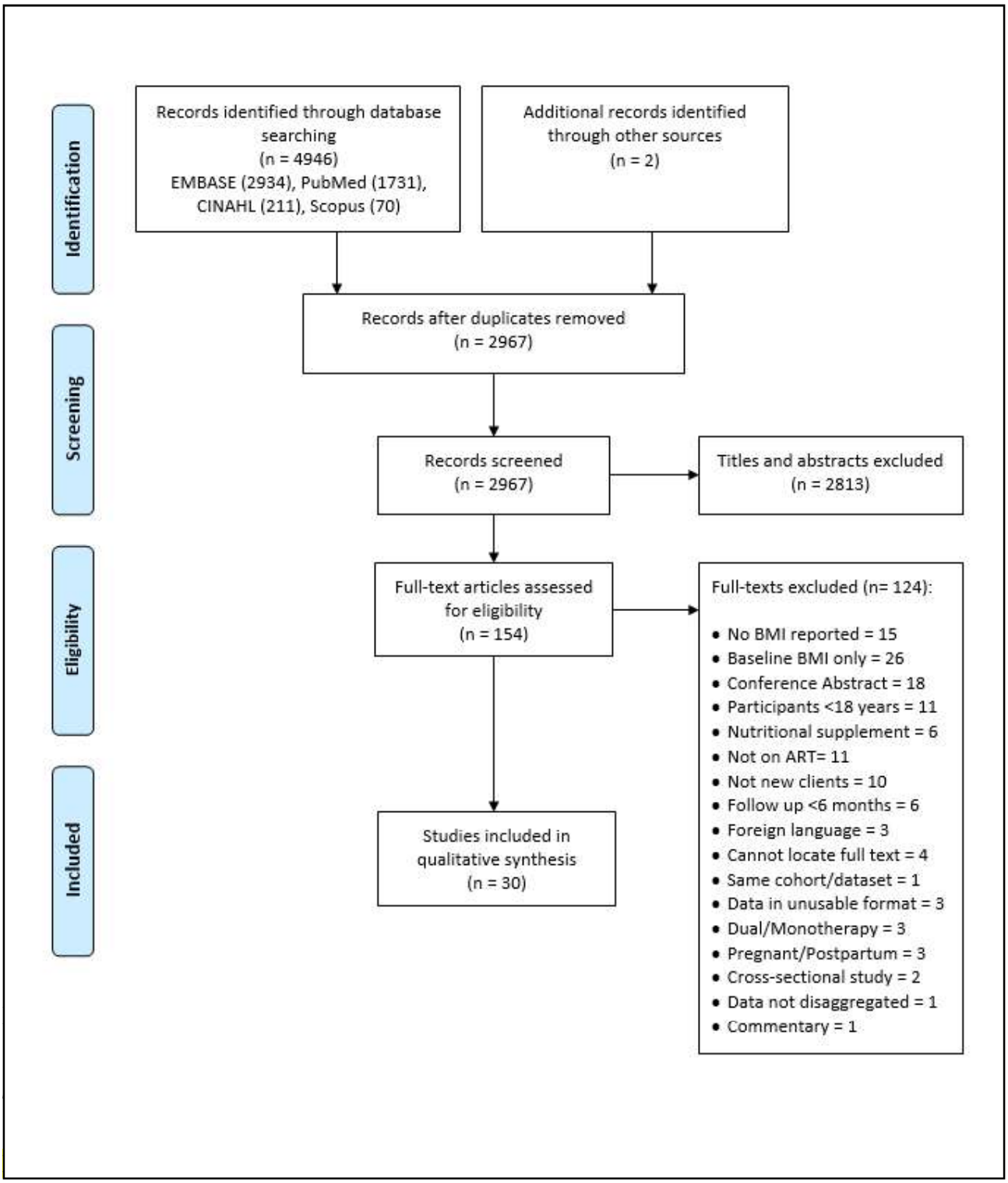


Figure 2.1. PRISMA flow diagram

About a third (33%) of the studies were in two countries - USA (n=6) and South Africa (n=4). Majority of the studies had a cohort design (n=23; 19 prospective, 4 retrospective), followed by randomized control trials [RCT] (n=6), and longitudinal data analysis (n=1).

The study population varied from outpatient clinics and rural community centers to larger university/teaching hospitals. About a fifth of the studies (20%, n=6) were from larger, well-established cohorts like the Veterans Aging Cohort study [VACS] (Herrin et al., 2016); Data Collection on Adverse Events of Anti-HIV Drugs [D:A:D] cohort (Achhra et al., 2016); International Epidemiologic Databases to Evaluate AIDS [IeDEA] (Huisin 't Veld et al., 2015); North America AIDS Cohort Collaboration on Research and Design [NA-ACCORD] (Koethe et al., 2016); UAB 1917 HIV/AIDS Clinic Cohort (Tate et al., 2012); and Rwanda Women's Inter-association Study and Assessment [RWISA] (Mutimura et al., 2015).

The total number of participants included in the 30 studies was 242,335 with females making up 55% (n=134,088). One of the studies (Huisin 't Veld et al., 2015) had a very large number of participants (n = 205,571) which made up 85% of all participants included in the systematic review. One study did not include any female participant because it was done among male injection drug users [IDUs] (Tang et al, 2011), while we could not extract the female numbers from 4 studies because the eligible participants were mainly subsets of the entire study participants (Akinboro, Onayemi, Ayodele, Mejiuni, & Atiba, 2013; Bala et al., 2016; Gil et al., 2011; Tieno et al., 2015). The study with the youngest participants had a mean age of 31.7 (±4.8) years (Tang et al., 2011), while the oldest group had a mean age of 42.3 (±14.5) years (Bonnet et al., 2013). For the studies that used median age, the youngest group was 32 years [IQR: 27, 38] (Bezabhe et al., 2015), while the oldest (VACS cohort) had a median age of 50 years [IQR: 43, 56] (Herrin et al., 2016).

The duration of follow-up for the studies ranged from 6 months (Evans et al., 2013; Gil et al., 2011; Gupta, Biswas, & Sharma, 2011; Messou et al., 2008; Ncube et al., 2008; Saghayam et al., 2007; van Oosterhout et al., 2010) to 7.5 years (Grant et al., 2016). Overall, 50% (n=15) of the papers had a follow-up period of 6 months to 1 year; 47% (n=14) had follow-up of >1 year to 5 years; and 3% (n=1) had follow-up >5 years. Over the period of follow-up, attrition (especially due to unavailable data on weight) ranged from zero percent (Bonnet et al., 2013; Gupta et al., 2011; Tieno et al., 2015) to 78.3% (Huisin 't Veld et al., 2015). Among the included RCTs, attrition ranged between 13.8% (Erlandson et al., 2015) and 21% (Evans et al., 2013; Guehi et al., 2016).

Antiretroviral Therapy and Body Mass Index

At baseline, the study with PLHIV in Malawi had the lowest group BMI with a mean of 16.6±1.5 kg/m^2 [n=104] (van Oosterhout et al., 2010), while PLHIV from a university medical center in the US had the highest group mean BMI of 26.4±6.8 kg/m^2 [n=92] (Lakey et al., 2013). The lowest reported end mean BMI was 18.50±3.05 kg/m^2 [n=101] among clients in a clinic in India (Bala et al., 2016), and the highest was 27.9 kg/m^2 in a clinic in the US (Lakey et al., 2013), although 8 studies (27%) did not report an end BMI for the participants, but rather the change in BMI**.** Overall, one of the multi-country studies had the least change in mean BMI with an increase of 0.67 kg/m^2 (Achhra et al., 2016), while the study from Cuba had the highest change in BMI with 3.4 kg/m^2 (Gil et al., 2011). Conversely, some of the studies reported a proportion of the study participants who also lost weight, varying between 5.9% and 45.8%, all from Sub-Saharan Africa and the Asia-Pacific region (Akinboro et al., 2013; Denue, Ikunaiye, & Denue, 2014; Huisin 't Veld et al., 2015; Hurley et al., 2011; Messou et al., 2008; Sagayam et al., 2007).

CD4 Count and Viral Load Suppression

At baseline, the lowest mean CD4 of all the studies was 80 cells/mm^3 [n=72] (Ncube et al., 2008), while the highest mean CD4 was 240 cells/mm^3 [n=35] (Bonnet et al., 2013). The lowest reported mean CD4 at the end of the studies was 194.6 cells/mm^3 [n=75] among male IDUs in Vietnam (Tang et al., 2011), with the highest being 495 cells/mm^3 among clients in France (Bonnet et al., 2013), though 67% (n = 20/30) of the studies did not report an end CD4 for the clients on treatment. Overall, the study with the least change in mean CD4 count while on treatment was among IDUs (Tang et al., 2011) with an increase of 98 cells/mm^3, while the highest change in mean CD4 was 144 cells/mm^3 (Akinboro et al., 2013).

At baseline, the lowest mean viral load (VL) of all the studies was 4.4 $\log_{10}$ HIV RNA copies/ml (Tate et al., 2012), while the highest mean VL was 5.8 $\log_{10}$ HIV RNA copies/ml (Lakey et al., 2013). Among the six studies that reported mean VL at end of the study, the lowest mean VL was 1.59 $\log_{10}$ HIV RNA copies/ml (Bonnet et al., 2013), while the highest was 3.7 $\log_{10}$ HIV RNA copies/ml (Gil et al., 2011). Overall, Abrahams, Levitt, Lesosky, Maartens, and Dave (2016) reported a viral suppression of 73%, while Tieno and colleagues (2015) reported a 96% VL suppression, the lowest and the highest, respectively, at the end of the studies.

Quality Ratings

Using the EPHPP tool, the quality assessment showed that 57% (n=17) had strong global ratings, 37% (n=11) had moderate global ratings, and 7% (n=2) had weak global ratings [see Appendix B]. The weak ratings in the 2 studies (Gil et al., 2011; Gupta et al., 2011) were mainly due to inadequate description of confounding and dropouts.

Summaries for the 30 eligible papers

Abrahams and colleagues (2016) studied the changes in distribution of body fat among 187 black South Africans using Dual-Energy X-Ray Absorptiometry (DEXA) scan. The clients were on ART for 24 months. Their findings showed that lipoatrophy was more common (greater than 2 times) in men than women, while there was no difference in the occurrence of lipohypertrophy. Data for the women showed that median BMI increased from 24.8 kg/m^2 (n=132 women) at baseline to 27.7 kg/m^2. There was no stated data for the 55 men in the study. A major limitation of this paper is the very high attrition of study participants (44% of total).

Achhra and colleagues (2015), using data from a multinational cohort (Data Collection on Adverse Events of Anti-HIV Drugs [D:A:D]), found that ART-naïve PLHIV who commenced treatment had a 12% increase in the risk of diabetes mellitus (DM) with every unit gain in BMI. There was also an 18-20% increased risk of cardiovascular disease among those in the normal (pre-ART) BMI category in this cohort. Among the 9321 clients in this sample, mean BMI increased by 0.67±2.0 kg/m^2 over a 12-month period on HAART. This study also had the added advantage of having participants from 21 countries and 3 continents [Europe, Australia, and North America] who were on contemporary HAART regimens.

Akinboro and colleagues (2013) conducted a cohort study over a 48-week period with 55 clients who commenced HAART in a clinic in southwestern Nigeria. All the clients were on AZT+3TC backbone, with either NVP (61.8%) or EFV (38.2%). At 48 weeks, the mean BMI had increased from a baseline of 20.65±2.89 kg/m^2 to 23±3.03 kg/m^2 ($p<0.001$). A major limitation of this study is the significant attrition (38%) of the study participants over the 48 week duration.

Bala and colleagues (2016) reported that the mean BMI of 101 clients newly commenced on ART increased from 17.33 kg/m^2 to 18.5 kg/m^2 over a 12-month period. This study was

conducted in 2010 and 2011 among clients with very low baseline BMI at the ART Centre of North Bengal Medical College, India. The clients' regimens included d4T/3TC/EFV (35.6%), d4T/3TC/NVP (30.7%), AZT/3TC/EFV (6.9%), and AZT/3TC/NVP (26.7%).

Bezabhe and colleagues (2015) carried out a prospective cohort study in Ethiopia to understand the adverse drug reactions (ADR), over a 12-month period, among 211 clients that initiated ART between 2012 and 2014. Their findings showed that 86% (n=181) had one ADR, and 31% (n=66) had a severe ADR within the period. The group that experienced at least one severe ADR had lower adherence to medications and lower BMI at the 12-month endpoint. The increase in mean BMI was 0.61±2.73 kg/m^2 and 1.50±2.22 kg/m^2 for the group with severe ADR and without severe ADR, respectively.

Bonnet and colleagues (2013) studied the effects of different ART regimens on bone mineral density (BMD) and fat mass among 70 PLHIV in France (75% of European descent, 25% of African origin). Over a 21-month period, the clients had reduced BMD, which was more pronounced in the PI group (vs NNRTI) and among Europeans (vs Africans). The authors further reported the mean BMI increased from 23.6±3.6 kg/m^2 to 25.7±5.5 kg/m^2 [p=0.02] for the PI group, while the NNRTI group increased from 23.9±3.6 kg/m^2 to 24.3±3.7 kg/m^2 [p=0.73]. A major limitation of this study was the very high attrition (50%), such that only 35 subjects completed the study at the 21-month endpoint.

Denue, Ikunaiye, and Denue (2012) reported findings from a prospective study among PLHIV on treatment in Maiduguri, Nigeria. Of the 120 participants followed over 30 months, 12% (n=13) lost weight, 83% (n=89) gained weight, while 4.7% (n=5) were weight stable. The majority (57%) of the participants were on ZDV/3TC/NVP. The prevalence of overweight/obesity increased from 16.9% at baseline to 28.4% at the end. Overall, BMI increased by 2.44 kg/m^2

among men, and 1.85 kg/m^2 among women. At the end of the study, increase in BMI among the study participants was associated with a higher baseline BMI and increasing CD4 while on treatment.

Dirajlal-Fargo and colleagues (2016) studied the changes in insulin resistance among 328 clients on integrase inhibitor (raltegravir) and PIs (ATV/r and DRV/r) over a 3-year period. Using the homeostatic model assessment of insulin resistance (HOMA-IR) method, they found that insulin resistance (IR) correlated with BMI changes at 48 weeks ($r = 0.12$, $p<=0.04$) and at 96 weeks ($r=0.22$, $P=0.005$). The median BMI changed by 1.025 (IQR: 0.976, 1.085) folds from baseline at the end of week 96.

Erlandson and colleagues (2015) conducted a randomized control trial (RCT) across nine countries with 1045 participants. This study showed that after 3 years on ART, PLHIV who were on FTC/TDF+EFV (526 patients) had a higher increase in mean BMI (1.8 kg/m^2) compared to 519 patients on 3TC/ZDV+EFV (1.1 kg/m^2). They also reported that about one fifth to one quarter of normal weight and underweight clients at baseline became overweight or obese after 3 years of therapy (25% in the FTC/TDF + EFV arm, and 18% in the 3TC/ZDV + EFV arm). Overall, the proportion of overweight and obese clients increased from about 25% to 40% in 3 years in this sample.

Evans and colleagues (2013) enrolled 38 ART-naïve clients in Johannesburg, South Africa, into a RCT to assess the effect of nutritional supplementation on immunological and nutritional parameters. Since the data for this study was disaggregated, we focused on the control arm which had only HAART. The authors reported that the median BMI increased from 19.3 (IQR: 18.4, 21.3) kg/m^2 to 20.0 (IQR: 18.5, 23.7) kg/m^2. This study had 11% attrition in the control arm on which we focused.

George, Venter, van Deventer, and Crowther (2009) described their findings from a longitudinal study of 42 clients who commenced ART (with stavudine) in South Africa. The authors reported that lipodystrophy (more lipoatrophy, than lipohypertrophy) was associated with clients who had a higher BMI before commencing ART. After 2 years of treatment with ART, clients who had lipodystrophy (43%, n=18) had a change in median BMI from 23.6 (IQR=3.5) kg/m^2 to 24.6 (IQR=3.4) kg/m^2, while those without lipodystrophy had a change in median BMI from 22.0 (IQR=2.2) kg/m^2 to 23.5 (IQR=3.7) kg/m^2. There was no statistically significant difference in the change in BMI seen in both groups.

Gil and colleagues (2011) studied oxidative stress among HIV-positive clients newly commenced on ART in Cuba and compared their findings to a control group of HIV-negative persons. Among the 56 clients on ART for 6 months, the mean BMI increased from 24.1 (SEM ±7.2) kg/m^2 to 27.5 (SEM ±6.8) kg/m^2 [p=0.091].

Grant and colleagues (2016) conducted a prospective cohort study on long term changes in body composition among HIV-positive clients newly commenced on ART and compared their findings to a control group of HIV-negative persons. Their findings showed that in the first 2 year of therapy ('early period'), HIV clients gained more fat and lean mass when compared to HIV-uninfected persons. Subsequently, however, clients on ART lost lean mass while gaining fat mass between 2 and 7 years after treatment initiation ('late period'). Over a period of 7.5 years, the median BMI for the 97 clients on ART increased from 24 (IQR: 22, 27) kg/m^2 to 27 (IQR: 23, 30) kg/m^2. This study's major strength is that it followed clients on ART over a long duration.

Guehi and colleagues (2016), in a sub-study of 755 clients in the ANRS 12136 Temprano Trial, documented the BMI changes among new ART clients in Abidjan over a 24 month period. They reported increasing CD4 count as the only factor significantly associated with change in BMI

over the study period. In this sample, prevalence of obesity remained stable among the men over the 24 months (from 20% to 22%, p=0.460), while the prevalence increased among the women (from 30% to 38%, p=0.0001), who made up 75% of the study participants. The median BMI remained stable: 22.3 (IQR: 20, 25.2) kg/m^2 at month zero [n=755] vs 22.5 (IQR 20.2–25.3) kg/m^2 at month 24 [n=597].

Gupta and colleagues (2011) conducted a prospective study with 68 clients commencing ART in New Delhi, India, to understand the changes in body composition. The authors found that all the body composition measures increased significantly after 6 months of ART, except for the waist hip ratio (WHR). The measures included weight, BMI, waist circumference, hip circumference, waist-to-hip ratio, mid upper arm circumference (MUAC), biceps skinfold thickness (BSF), subscapular skinfold thickness (SSF), supra-iliac skinfold thickness (SISF), and triceps skinfold thickness (TSFT). The mean BMI for the 68 clients increased from 18.3±2.8 kg/m^2 to 19.7±2.9 kg/m^2 [p<0.0001].

Herrin and colleagues (2016) reported on their findings from the Veterans Aging Cohort Study (VACS). The authors analyzed data from 7177 HIV-positive veterans who were on HAART between 2000 and 2001 (with a control group of 24621 HIV-negative persons) to understand the relationship between change in weight/BMI and incidence of diabetes. In this sample, there was a 14% increased risk of diabetes for every 5 pounds (2.3kg) gained in weight. The mean BMI of the HIV-positive clients increased from 25.1±4.6 kg/m^2 to 26.0±4.7 kg/m^2 over a 1-year duration on HAART.

Huisin ’t Veld and colleagues (2015) used data from 140 sites spread across sub-Saharan Africa and the Asia-Pacific region to analyze weight and BMI changes among PLHIV who newly commenced HAART. This huge study (with 205,571 patients) showed that clients gained weight

and BMI increased in the first year on treatment. However, in the second year, nearly half of these PLHIV lost weight compared to their weight at the end of the first year of treatment. Median BMI was 20.0 kg/m^2 (IQR: 17.9, 22.5), 21.4 kg/m^2 (IQR: 19.5, 23.9), 21.9 kg/m^2 (IQR: 19.9, 24.6), and 22.1 kg/m^2 (IQR: 19.9, 24.8) at baseline, 6, 12, and 24 months, respectively.

Hurley and colleagues (2011) reported on the weight change and perceptions of 230 PLHIV on treatment in an urban setting in South Africa over a 12-month period. In this population, males had a higher increase in BMI (2.4 kg/m^2 [95% CI, 1.7 - 3.1]) than the females (2.2 kg/m^2 [95% CI 1.5 - 2.9]). Additionally, those who gained weight (74%) and those who lost weight (26%) were spread across all the four baseline BMI categories. Interestingly, when the researchers compared the objectively measured baseline BMI with the clients' perception of their BMI, the researchers found that the participants tended to underestimate their weight. This may be a compensation for the need to gain weight so as to counter the stigma that associates HIV with wasting.

Koethe and colleagues (2016) studied a large cohort (North America AIDS Cohort Collaboration on Research and Design [NA-ACCORD]) in North America (USA and Canada) with data from 14,084 clients who commenced ART between 1998 and 2010. The authors reported that about a fifth of the normal weight and overweight clients at baseline (22% and 18%, respectively) moved to the next higher BMI category (i.e. overweight and obese, respectively) after 3 years of initiating HAART. They also reported that 16% of overweight persons and 13% of obese persons moved to a lower BMI class after 3 years of ART. Also interesting was the fact that within 3 years of commencing ART, this population of HIV infected persons caught up with the average general population BMI (using the United States National Health and Nutrition Examination Survey [NHANES] data), with a sub-set (HIV-infected white females) even

surpassing the average general population BMI. The major part (80%) of weight gained over 3 years in this population was gained in the first year after commencing treatment.

Lakey and colleagues (2013) carried out a prospective cohort study with 92 HIV-infected clients who commenced ART (and 94 age-matched HIV-uninfected controls) over a 12-month follow-up period between 1998 and 2008 at the Duke Medical Center in North Carolina, USA. Their finding show that HIV-infected women, those on PI-based regimen, and those with low baseline CD4 counts (<200 cell/mm3) had significant weight increase compared to other groups. Additionally, the mean BMI for the HIV-infected group increased from 26.4 kg/m^2 to 27.9 kg/m^2 ($p < 0.0001$), while the proportion of those overweight among the HIV-infected group also increased from 52% to 66% in the first year of treatment. The age-matched control group did not have any significant change in weight (92.7 to 93.0 kg, $p = 0.5$) or BMI (31.9 kg/m^2 to 32.0 kg/m^2, $p = 0.6$).

Messou and colleagues (2008) carried out a prospective cohort study (nested within a RCT) with 622 adult participants in Côte d'Ivoire to understand whether changes in BMI, and or CD4, predicted treatment success or failure after 6 months of ART. This study is important because it claims to be the first published study to report on the link between ART and BMI in sub-Saharan Africa. The authors reported an increase in median BMI and median CD4 count of 1.0 kg/m^2 (IQR: 0.0, 2.1) and 148 cells/µl (IQR: 54, 230), respectively. Interestingly, this study also showed that increase in BMI, following 6 months of ART, poorly predicted viral load suppression (or treatment success), as did decrease in BMI for viral load detectability (or treatment failure). A limitation of this study was that it was done among clients who started therapy with a BMI <25 kg/m^2 and CD4 count <500/µl, hence not very representative of a real life clinical situation.

Moyle and colleagues (2014) reported the BMI findings for 224 clients who were randomized to different regimens (TDF/3TC + ATV/r or TDF/3TC + LPV/r) in a RCT across multiple countries (Combination with tenofovir-emtricitabine to assess safety and efficacy [CASTLE] sub-study). They found that the ATV/r and LPV/r arms had increases in BMI of 2.0 kg/m^2 and 1.2 kg/m^2 ($p<0.05$), respectively, over a 96-week period on ART.

Mutimura and colleagues (2015), in a longitudinal study among women in Rwanda, reported that BMI at baseline, change in BMI over a two and a half year duration, and increasing fat mass were associated with increasing insulin resistance among both HIV-positive and HIV-negative women in the study population. Insulin resistance is usually a precursor to type 2 diabetes mellitus (T2DM). In this study, the authors also reported that the mean BMI of the 371 HIV-positive women on ART increased from 21.3±3.9 kg/m^2 at baseline to 22.3±3.9 kg/m^2, a mean BMI change of 0.95±3.01 kg/m^2. A key limitation is that this study was done with women only.

Ncube and colleagues (2008) used a pre-post design to study 72 ART clients newly commenced on treatment in Bulawayo, Zimbabwe. Though these clients had previous history of tuberculosis (TB) infection, and were highly impoverished (>33% reported having to go without meals), the mean BMI increased by 1.5 kg/m^2 over 6 months of treatment.

Saghayam and colleagues (2007) studied the impact of nevirapine-based HAART on body changes among 190 clients in southern India. Their findings showed that the mean BMI rose by 1.0 (±1.9) kg/m^2 at 6 months post-initiation of ART. When this population was stratified by regimen, they reported that clients on stavudine had a higher increase in BMI (1.5±2.0 kg/m^2) compared to those on ZDV (0.3±1.6 kg/m^2) ($p<0.001$). This study also showed that not all clients gained weight; while 59% (n=112) of the study participants had a mean BMI increase of 2.2 kg/m^2, 19% (n=37) had a stable BMI, and 22% (n=41) had a drop in BMI of 1.3 kg/m^2.

Sarna and colleagues (2008) reported on the BMI changes in a group of 234 participants on HAART in a RCT in Mombasa, Kenya. Their results showed an increase in BMI (from baseline) of 1.4 kg/m^2, 1.5 kg/m^2, and 1.6 kg/m^2 at 24, 48, and 72 weeks, respectively, in the control arm. The intervention arm (which received 24 weeks of twice weekly health center visits for nurse-observed pill ingestion, adherence support, and collection of medication) had an increase in BMI (from baseline) of 2.2 kg/m^2, 2.4 kg/m^2, and 2.4 kg/m^2 at 24, 48, and 72 weeks, respectively.

Tang and colleagues (2011) studied 99 male IDUs in Hanoi, Vietnam, over a period of 12 months post-initiation of ART. They reported that BMI increased by 1.1 kg/m^2 and 1.4 kg/m^2 after 6 and 12 months, respectively, when compared to baseline BMI. They also stressed the importance of adherence, especially in the early months as their results showed that those with higher adherence gained an average of 2.6 kg while those with poor adherence lost an average of 0.4 kg. This study population also had a very high rate of Hepatitis C co-infection (92%).

Tate and colleagues (2012) reported that 20% of those who were of normal weight before commencing HAART moved to being overweight or obese within a 24-month period on ART. This study was conducted among a majority black population using the data of 681 PLHIV on treatment (year 2000 – 2008) at the University of Alabama-Birmingham 1917 HIV/AIDS Clinic. They also reported that clients with low CD4 count (<50 cells/microliter) and those on PI (boosted or not) had higher increase in BMI compared to other group in the study.

Tieno and colleagues (2015) provided a description of 144 clients who commenced ART at a Teaching Hospital in Ouagadougou, Burkina Faso. Over a 9 month follow-up period, mean BMI increased from 19.6 kg/m^2 (144 clients) to 21.8 kg/m^2 (120 clients) [p = 0.004]. Majority of the clients were on a Zidovudine-based regimen (62.5%).

Van Oosterhout (2010) reported findings from a retrospective cohort study with three arms (2 with food supplementation, and one without) among clients who had wasting in Malawi. In this study, we focused on the control group of 102 clients who received only ART and standard care. These clients, who were newly commenced on treatment, had a baseline mean BMI of 16.6±1.5 kg/m^2 and recorded an increase in BMI of 2.1±2.1 kg/m^2 after 26 weeks (6 months) on therapy. We chose to ignore the other two arms since they received nutritional supplementation with ready-to-use fortified spread and corn/soyblended flour.

Meta-Analysis

Of the thirty eligible studies, eighteen were included in the meta-analysis, with a total of 11,112 study participants. Of the twelve that were excluded because they could not be combined, ten reported the group BMI using median and interquartile range, while the other two studies did not report measures of dispersion for the reported mean BMI (Ncube et al., 2008; Tieno et al., 2015).

HAART and BMI Changes

HAART was associated with increase in BMI among PLHIV who started treatment for the first time and were on treatment for at least six months (pooled effect size [ES] = 1.58 kg/m^2; 95% CI: 1.36, 1.81). The heterogeneity among the eighteen studies was high (I^2 = 85%; p <.01) (see Figure 2.2. below). The sensitivity analysis showed that none of the studies had undue influence on the result of the meta-analysis (Appendix C). After dropping the two weak studies, the pooled ES remained unchanged (pooled ES = 1.58 kg/m^2; 95% CI: 1.34, 1.81) (see Appendix D, Supplementary Figure 1).

Exploratory Subgroup Analysis

A. Study Design: Randomized Trials vs Observational Studies

A subgroup analysis using the study design was completed. There were only three randomized trials and the pooled ES was 1.66 kg/m^2 (95% CI: 1.27, 2.04), compared to a pooled ES of 1.55 kg/m^2 (95% CI: 1.29, 1.82) from the fifteen non-randomized studies (see Figures 2.3. and 2.4. below).

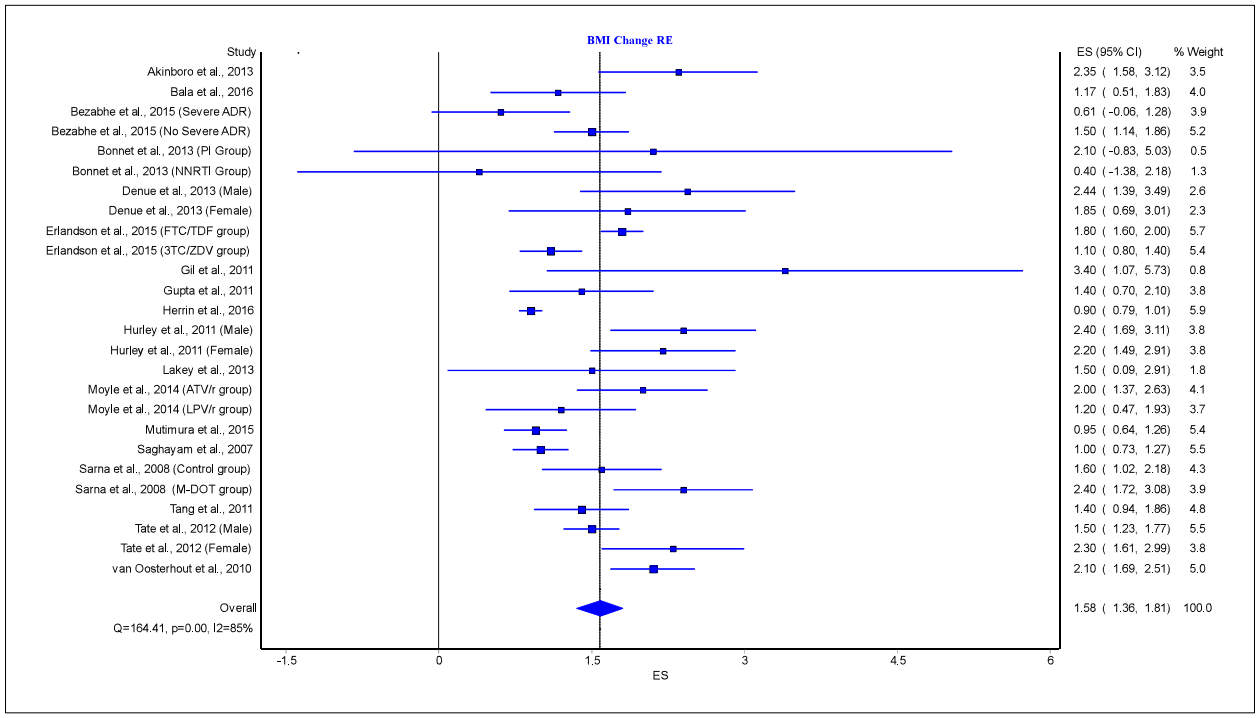


Figure 2.2. Pooled estimate from random effects meta-analysis of association between HAART and changes in BMI among PLHIV who are new on treatment.

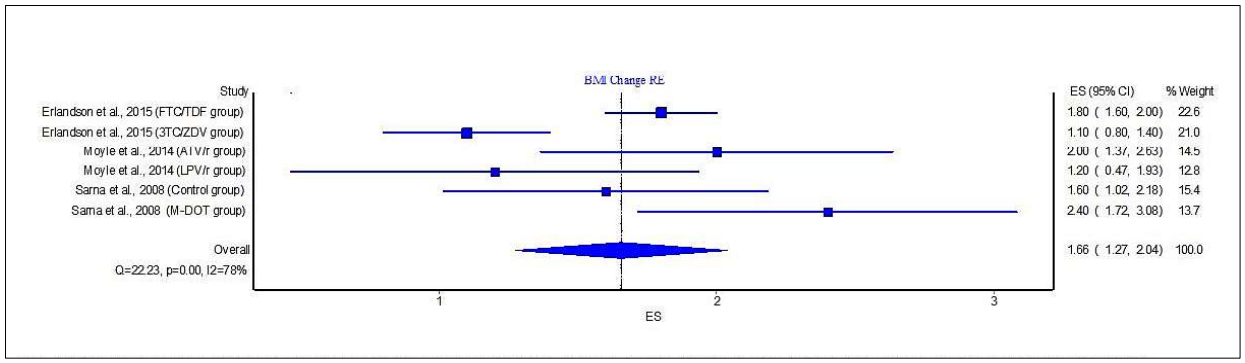


Figure 2.3. Pooled estimate from random effects meta-analysis of association between HAART and changes in BMI among PLHIV who are new on treatment (randomized controlled trials only).

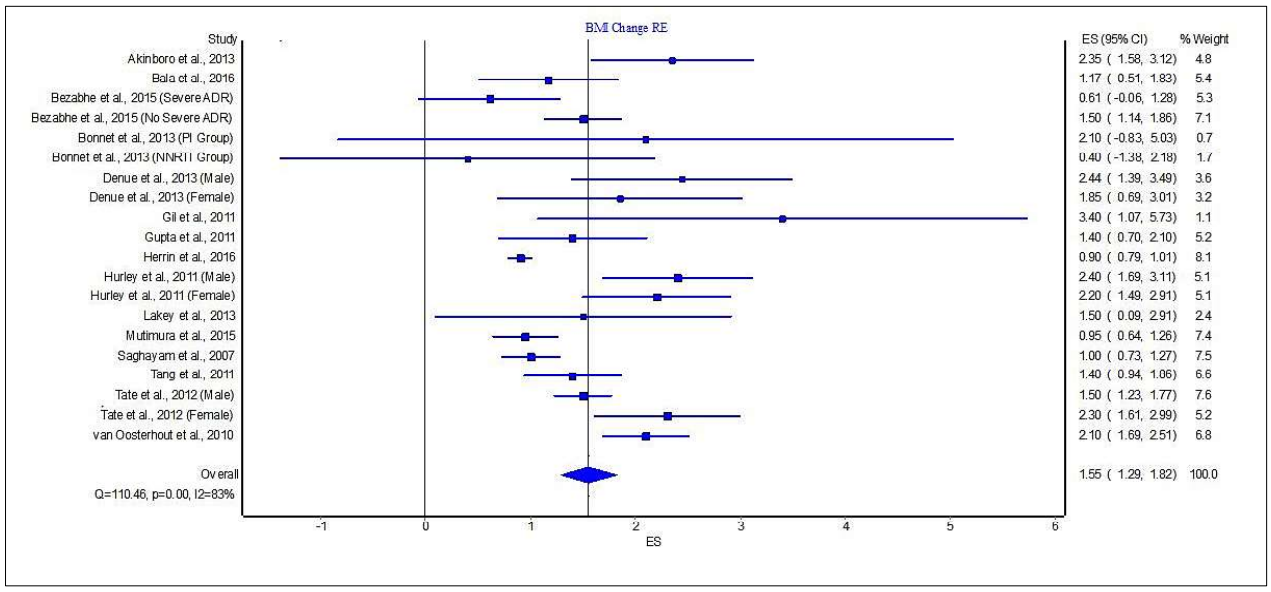


Figure 2.4. Pooled estimate from random effects meta-analysis of association between HAART and changes in BMI among PLHIV who are new on treatment (observational studies only).

B. Length of Study Participant Follow-Up: ≤1 year vs >1 year

The follow-up for the study participants ranged from six months to seven-and-a-half years. A subgroup analysis of eleven studies with follow-up ≤1 year and those (7 studies) with follow-up >1 year showed pooled ES of 1.54 kg/m^2 (95% CI: 1.21, 1.87) and 1.63 kg/m^2 (95% CI: 1.34, 1.91), respectively (see Appendix D, Supplementary Figures 2 and 3). Further exploratory subgroup analyses of the studies with >1 year follow-up showed an ES of 1.75 kg/m^2 (95% CI: 1.41, 2.10) for those with follow-up >1 year but ≤2 years; while those with follow-up >2 years has ES of 1.5 kg/m^2 (95% CI: 1.00, 1.99).

C. Country Income Level: LIC, LMIC, UMIC, and HIC

A final subgroup analysis was done using the economy of the country as classified by The World Bank (The World Bank group, 2019). Of the eighteen studies, three were in low-income countries (LICs), seven in low-middle income countries (LMICs), two in upper-middle income countries (UMICs), and four in high-income countries (HICs). Two studies were conducted in multiple countries and were left out of this subgroup analysis (Erlandson et al., 2015; Moyle et al., 2014). The pooled ES for the studies are shown in Table 2.2 below, while the forest plots are in Appendix D (Supplementary Figures 4-7). When the countries were collapsed into two groups (LICs/LMICs and UMICs/HICs), the pooled effect sizes were 1.53 kg/m^2 (95% CI: 1.23, 1.83) and 1.65 kg/m^2 (95% CI: 1.29, 2.01), respectively.

Table 2.2. Exploratory subgroup analysis using the economy of the countries

Country's Economy	Number of Studies	Effect Size (95% CI) [kg/m^2]	Heterogeneity (I^2)
LICs	3	1.32 (0.73, 1.90)	88%
LMICs	7	1.65 (1.27, 2.03)	71%
UMICs	2	2.35 (1.86, 2.84)	0%
HICs	4	1.42 (0.89, 1.95)	84%

Discussion

The most interesting finding from this review is that all the studies show an increase in mean or median BMI at the end of the study period. This is in concordance with findings from other studies on ART and BMI (Crum-Cianflone et al., 2008; Hasse et al., 2014; Nduka et al., 2016). Also important is the fact that though the mean BMI increases, some clients actually lose weight while on treatment. The proportion of participants who lost weight varied between 5.9% - 45.8% (Akinboro et al., 2013; Denue et al., 2013; Huisin 't Veld et al., 2015; Hurley et al., 2011; Messou et al., 2008; Saghayam et al., 2007). This weight loss can be due to undiagnosed treatment failure, opportunistic infections, or factors resulting from poverty and food insecurity (Huisin 't Veld et al., 2015; Kalafonos, 2010).

Second, the gain in weight/BMI appears to have a general trend with time on ART. This trend shows that in the first 6 months to one year, PLHIV starting ART gain most of the weight. With additional years on treatment, this weight gain begins to plateau off (Grant et al., 2016; Huisin 't Veld et al., 2015; Koethe et al., 2016; Tang et al., 2011; Tate et al., 2012). The increase in BMI generally follows the weight gain, though in a more moderate trend. After three years on treatment, the weight gain or increase in BMI is negligible. It is also important to point out that this 'rapid'

gain in weight and BMI has been associated with a risk of cardiovascular disease and Type 2 Diabetes Mellitus [T2DM] (Achhra et al., 2016; Herrin et al., 2016).

Third, the role of the economy and diet cannot be ruled out. From this review, the lowest BMI at baseline and at the end of follow-up were in LMICs in Africa and Asia (Bala et al., 2016; van Oosterhout et al., 2010). However, those with the highest baseline and end BMI were from HIC or UMIC (Gil et al., 2011; Lakey et al., 2013) where the prevalence of obesity is higher in the general population, compared to the LMICs. Though these studies did not track diet and exercise, it will be interesting to see the mediating role that these critical factors play in weight and BMI gain among PLHIV on treatment.

Finally, the role of different regimens in weight and BMI gain remains unclear. As a third drug in the HAART regimen, NNRTIs appear to be less obesogenic than PIs among clients in North America (Lakey et al., 2013; Tate et al., 2012), but more obesogenic than PIs among clients in Africa and the Asia-Pacific (Huisin ’t Veld et al., 2015). These findings are at best exploratory, and more rigorously designed studies are required to ascertain this association. A subgroup analysis of the studies using the different regimen could not be undertaken because the regimens were so diverse and very few studies properly described the proportion of the study participants that were on each HAART regimen. On the other hand, no association between the regimen and BMI gain was reported in a large European cohort (Hasse et al., 2014) and an African cohort (Guehi et al., 2016).

Limitations

The authors acknowledge some limitations to this study. First, the search was limited to peer-reviewed English Language articles. This could potentially affect the number of studies included in this review. However, the authors believe the strict inclusion was necessary to avoid an unwieldy review process with little pay-off in terms of the inclusion of additional articles. Second, about forty percent of the thirty eligible studies were excluded from the meta-analysis because they reported median values or mean values without standard deviations. This loss of data may have adversely impacted the power of the meta-analysis, and led to inflated heterogeneity among the studies; hence, we strongly encourage researchers to include comprehensive basic descriptive statistics in all manuscripts. Third, the authors could not do subgroup meta-analyses by HAART regimen because of the significant diversity of the HAART regimens and the poor description of the proportion of study participants that were on the different regimens. Many of the studies reported the proportion of participants on single drugs (which were not mutually exclusive), and it became nearly impossible to disentangle the numbers. Future studies should endeavor to report the proportion of study participants by their regimen and not only by the single drugs. Finally, the authors acknowledge the considerable heterogeneity in the meta-analyses. However, we believe that it is better to carry out a meta-analytic synthesis of the combinable studies, while understanding the caveats rather than stopping at a qualitative synthesis (Ioannidis, Patsopoulos, & Rothstein, 2008). The somewhat vast differences in variability among the studies underscores the importance of continuing investigation and highlights the hypothesis-generating nature of this meta-analysis.

Conclusions from Systematic Review

This systematic review has shown that in the era of potent ARVs, PLHIV who commence treatment have an increase in weight and BMI. We also conclude that the greatest gain in BMI is in the first 6 months to one year on treatment.

Qualitative studies on HIV and Obesity

An extensive search of the literature revealed that there were not many qualitative studies that have specifically explored obesity among PLHIV. This raises several challenges in our understanding of this interplay because quantitative data alone usually do not tell the full story However, several qualitative studies have explored HIV and quality of life (QoL), HIV and body image, and HIV and lived experiences. In this section, the author presents some of these studies.

The first paper describes the experiences of HIV caregivers in Lesotho before the advent of ART. Using a phenomenological approach, the researcher interviewed 21 lay caregivers using in-depth interviews. Several themes identified include: caregiving was both social, emotional, and physical work; difficulty in maintaining dignity when rendering bodily care; and perceptions of different bodily changes by seeing and touching the chronically ill (Makoae, 2009). These finding create a fine flip-sided template against which we can contrast HIV and obesity, because this was described when HIV and wasting was the common thing.

In another study, Palmer and colleagues (2011) explored how stigma and depression affect self-perceived body image in HIV positive people in Canada. Using the HIV/AIDS-targeted quality of life (HAT-QoL) tool, they found that positive body image was associated with perceived quality of life across all nine measures on the scale (Palmer et al., 2011). This is important because

it helps us understand that how one sees one's self, and the external appearance that people see, is critical to one's quality of life.

Two studies describe HIV patients' perceptions of lipodystrophy (body fat redistribution). Reynolds, Neidig, Wu, Gifford, and Holmes (2006), working in four states in the US, carried out six focus group discussions (58 total participants) and identified the following themes: significantly similar perceptions of body changes; physical, psychological, and social distress, with associated functional limitations; and frustration at self-management of ever-changing bodies (Reynolds at al., 2006). One of the patients said, ''I have a fear now of getting off the drugs. I'll stop my drugs and be dead in a year . . . Do I want to look like a cartoon character or be dead?'' (Reynolds et al., 2006). In the UK, Kelly, Langdon, and Serpell (2009) explored the perception of body image in HIV-positive gay men. While the superordinate themes were similar to that found by Reynolds and colleagues, the men in this study tried to exercise more in order to reduce lipodystrophy, since a slim muscular body was more acceptable in the gay community (Kelly at al., 2009).

Hurley and colleagues (2011) asked PLHIV who were commencing treatment if they were satisfied with their weight or wanted to gain/lose some weight. After 12 months on ART, those who wanted to gain weight (n=113) achieved a mean weight increase of 7.8 kg; those who wanted to maintain their weight (n=56) gained a mean weight of 2.7 kg; and those who wanted to lose weight (n=9) gained only 0.5 kg. At baseline, only 23 participants (10%) were underweight (BMI <18.5 kg/m^2), pointing to the potential mismatch between participants' actual weight, their perception of their weight, and their desire to gain/lose weight. It is important to note, however, that the role of diet and food intake was not fully explored in this study.

Croffut et al. (2017) used in-depth interviews to explore the perceptions of 64 HIV-positive women on how body size affects breastfeeding practices in Malawi. Among these women, those who preferred higher-order BMI silhouettes (overweight, obese, and morbidly obese) made up 80% of the participants. Additionally, only 57% of the women believed that women who were underweight could successfully do exclusive breastfeeding.

Munro, Dinatale, Hartley, St. Jacques, and Oursler (2017) used a mixed-method design to explore health behaviors of veterans and the barriers faced by those who have HIV and are overweight/obese. The participants placed value on their relationship with their peers and the ability to have a discussion with their healthcare providers. Based on their opinions, eating healthy was good, but exercise was more important for their weight management. The participants were all veterans (n=11), with a median age and BMI of 56 years and 30.9 kg/m^2, respectively.

Conclusion

There is an abundance of literature on obesity among PLHIV, although most of them are mainly quantitative and some have design issues such as a small sample size or include adolescents or pregnant women. Few qualitative or mixed-methods studies have explored this interface. The quantitative studies demonstrate an increasing BMI among PLHIV on treatment; however, we do not have sufficient qualitative studies to help us understand this trend. This study aims to address this research gap, using Nigeria as a case study. In this chapter, the author has presented a systematic review and meta-analysis of the literature, with a follow-up narrative review of some of the qualitative studies. The next chapter discusses the research methods.

Chapter 3: Methods

Explanatory Sequential Mixed-Method Study Design

For this study, the investigator used the explanatory sequential design (see Figure 3.1. below). The explanatory sequential mixed-methods design consists of two distinct phases: quantitative followed by qualitative (Creswell & Plano Clark, 2018). In this design, the investigator first collects and analyzes the quantitative data. The qualitative data are collected and analyzed second in sequence and help explain, or elaborate on, the quantitative results obtained in the first phase. The second qualitative phase builds on the first, quantitative, phase, and the two phases are connected in the intermediate stage in the study. The rationale for this approach is that the quantitative data and their subsequent analysis provide a general understanding of the research problem. The qualitative data and their analysis refine and explain those statistical results by exploring the findings in more depth (Rossman & Wilson, 1985; Tashakkori & Teddlie, 1998; Creswell, 2003).

This core design was chosen for its simplicity and because it is the most appropriate design for the intent of the study (Creswell & Plano Clark, 2018). The alternative to the explanatory sequential design would have been to use the convergent design or the more complex mixed-methods case study design. The convergent design was not chosen because it requires both qualitative and quantitative data to be collected from the same sample of people (Creswell & Plano Clark, 2018). This study did not allow for that. In addition, the complex mixed-methods case study design was not chosen because the HIV-obesity challenge is still seen as a singular and emergent phenomenon; hence, it is difficult to put it in blocks/cases that can be compared. The complex mixed-methods case study design can be used when the HIV-obesity phenomenon matures and different sub-populations can be compared.

Purpose

The purpose of this study was to further understand the trends and perception of obesity and overweight among PLHIV on treatment in Nigeria. An explanatory sequential mixed-methods design was used that involved collecting quantitative data first and then explaining the quantitative results with key informant interviews (KIIs). During phase one of the study, de-identified, quantitative, secondary data from two southeastern states in Nigeria (Enugu and Ebonyi) were analyzed to assess the prevalence and trends of obesity/overweight among PLHIV on treatment as well as to understand the demographic and clinical factors associated with changes in BMI. In phase 2 of the study, KIIs of health care providers (HCPs) working in HIV clinics in these two states were completed to provide potential explanations of the results of the quantitative findings. HCPs were interviewed to understand their perceptions of the HIV-obesity phenomenon including its probable causes, stigma association with HIV and weight, and long-term health consequences of obesity among HIV patients.

Research Questions

Research Question 1:

Is there a difference in mean BMI between PLHIV starting treatment in the two states and the general population?

H_o: There is no difference in the mean BMI between the PLHIV starting treatment and the general population.

H_a: There is a difference in the mean BMI between the PLHIV starting treatment and the general population.

Research Question 2a:

Is there a difference in mean BMI at baseline and at 24 months of treatment among PLHIV starting treatment in the two states?

H_o: There is no difference in the mean BMI at baseline and at 24 months.

H_a: There is a difference in the mean BMI at baseline and at 24 months.

Research Question 2b:

Is there a difference in proportions in each BMI category (i.e. underweight, normal weight, overweight, and obese) at baseline and at 24 months?

H_o: There is no difference in proportions at baseline and at 24 months.

H_a: There is a difference in proportions at baseline and at 24 months.

Research Question 3:

Is the BMI after 24 months of treatment associated with demographic factors (gender, marital status, education) and/or clinical factors (drug regimen, HIV stage, CD4 count, blood pressure, adherence to medication), after accounting for age and baseline BMI?

H_o: There is no significant effect of the demographic factors and/or clinical factors on the BMI at 24 months.

H_a: There is a significant effect of the demographic factors and/or clinical factors on the BMI at 24 months.

Research Question 4:

What are the perceptions of healthcare providers about overweight/obesity among PLHIV on treatment in Nigeria?

Research Question 5:

In what ways do the qualitative data from the interviews with healthcare providers further explain, or provide evidence for, the quantitative findings from PLHIV on treatment in Nigeria?

Study Period

The quantitative arm of this study used de-identified, secondary data from two states in the southeastern region of Nigeria. The data included 3530 PLHIV who were on antiretroviral therapy (ART) during the 5-year period between 2012 and 2016. The qualitative arm was carried out in the summer of 2019.

Study Design and Sample Size

The quantitative arm (phase 1) of this study used a retrospective cohort design. The secondary data (with 3530 adult PLHIV) was analyzed to derive the prevalence of obesity and overweight among adults commencing ART, and the trend of BMI over the 5-year period. The results of the quantitative arm of this study were used to design the interview questions and context of the second phase of the study.

In the qualitative arm (phase 2), the investigator carried out 16 key informant interviews (KIIs) of healthcare providers (HCPs) who work in HIV treatment clinics in the two aforementioned states. The interview explored the providers' knowledge of the HIV-obesity

phenomenon, and their perceptions on its probable causes and long-term health consequences. The interviews also explored the providers' views on how HIV affects weight/BMI changes, especially in terms of treatment success and stigma issues.

Recruitment and Study Procedures

For the quantitative study, the data were accessed from the Center for Clinical Care and Clinical Research – Nigeria (CCCRN). This organization ran a free HIV treatment program in the two southeastern states between 2012 and 2017. The data for this period were de-identified and stored in their archives. The secondary data for this study was accessed from the archives of CCCRN.

For the qualitative study, the investigator used snowball sampling. The recruitment started with a telephone call with three HCPs with whom the investigator had previously worked. The HCPs had a history of working in the HIV clinics in the states under consideration (Enugu and Ebonyi). These three HCPs served as the primary contacts, and they suggested other potential study participants. For each potential participant, the investigator explained the research and asked if he/she was willing to participate, while also confirming that the potential participant had worked in a HIV clinic in any of the two states for more than one year. If he/she agreed to participate and was eligible, then he/she was sent the electronic version of the consent form and an agreed date and time was scheduled for a one-hour phone interview.

At the beginning of each interview, the investigator (who is a male) informed the study participant that the interview would be recorded, and also briefly reviewed the consent form with the participant to confirm their voluntary participation. As part of the consent process, the participant was also given information about why the study was being conducted. After this, the

participant was asked to give a recorded verbal consent to the study. The investigator also collected basic demographic information like gender, professional qualifications, and years of experience. Each interview lasted less than one hour and the participant was given a 1500 naira (about $5) phone recharge card.

Inclusion and Exclusion criteria

Quantitative study - Inclusion criteria

- Male or female PLHIV who commenced treatment with ART in the two southeastern states between 2012 and 2015.
- PLHIV who remained on treatment for at least 12 months.

Quantitative study - Exclusion Criteria:

- Those <18 years old
- Those who did not get a 3-drug HAART regimen
- Those whose height and weight were not documented at baseline
- Those whose weight were not documented at 12 month and 24 month
- Pregnant women.

Qualitative study - Inclusion criteria

- Male or female healthcare provider in any of the two southeastern states (Enugu and Ebonyi).

Qualitative study - Exclusion Criteria:

- Healthcare provider with less than one year experience in a HIV clinic
- Those <18 years old.

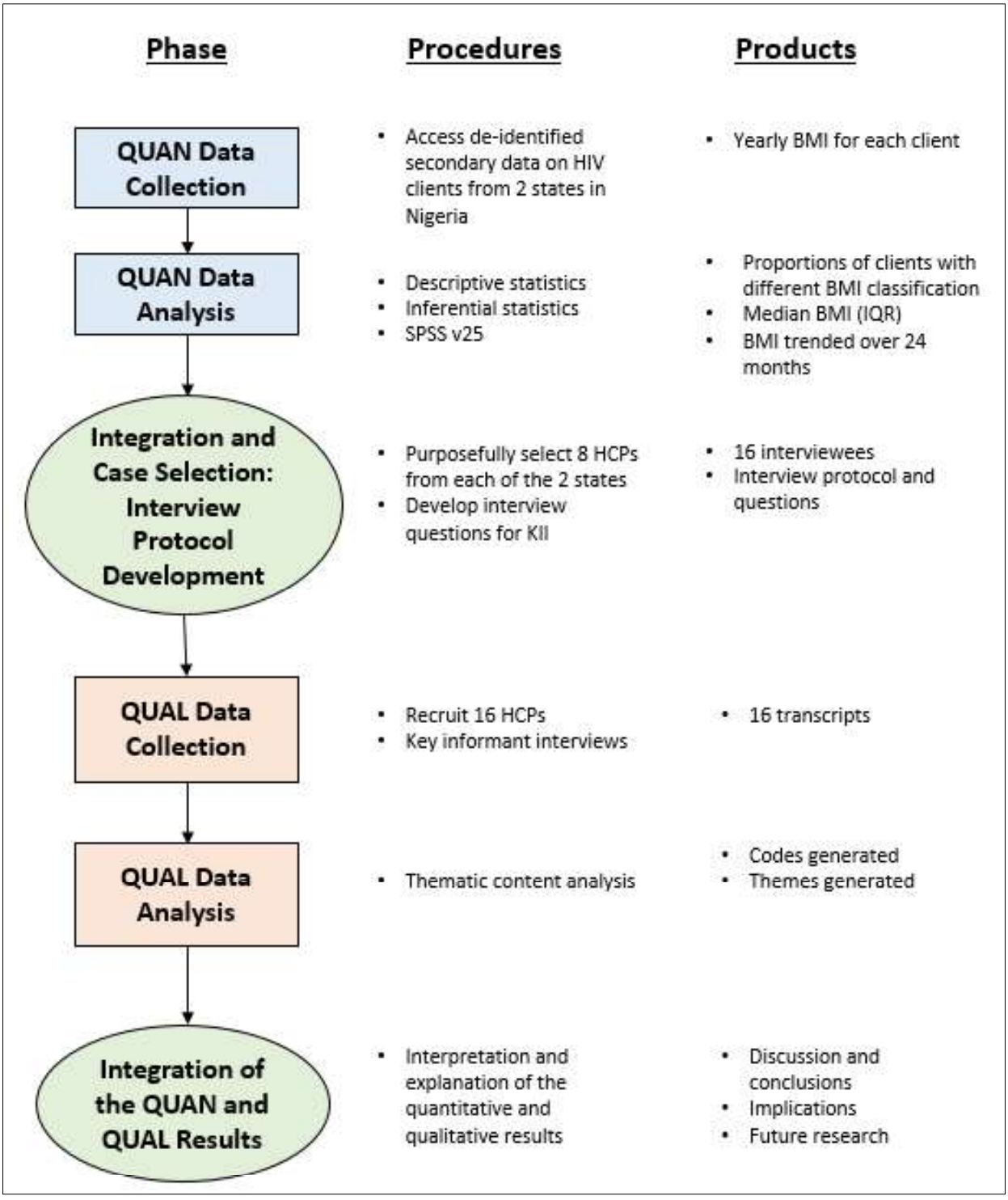


Figure 3.1. Explanatory Sequential Design for the study on HIV and Obesity in Nigeria.

*Figure 3.1 is adapted from Creswell & Plano-Clark (2018). **BMI=Body mass index, SD=Standard deviation, HCPs=Healthcare providers, KII=Key informant interview

Key Variables in Quantitative Data

Demographic Information

A. State – name of the state where the clinic is located

B. Year of Birth – used to calculate the clients age

C. Gender – male or female

D. Marital Status – describes the client's marital status at enrollment

E. Level of education - describes the client's highest educational attainment at enrollment

At Commencement of ART

A. Date HIV treatment started – the month and year the client commenced ART

B. Drug Regimen – the three drug regimen the client was commenced on

C. Weight – client's weight (in kilograms [kg]) at commencement of ART

D. Height - client's weight (in centimeters [cm]) at commencement of ART

E. Stage of HIV infection – classification of the progression of the client's disease using the World Health Organization (WHO) classification

F. CD4 count – client's immunity as measured by CD4 cells at commencement of treatment

G. Blood Pressure (Systolic) - client's systolic blood pressure at commencement of treatment

H. Blood Pressure (Diastolic) - client's diastolic blood pressure at commencement of treatment

At 12 and 24 months after commencement of ART

A. Change in drug regimen - any change in three-drug regimen during the year (Yes or No)

B. Current Drug Regimen - the three drug regimen client is currently taking

C. Weight - client's weight (in kilograms [kg]) at the last clinic visit

D. Drug Adherence Level – the client's level of adherence to medication use (Good, Fair, or

Poor) as at the last clinic visit

E. Stage of HIV infection - classification of the progression of the client's disease using the World Health Organization (WHO) classification
F. Current CD4 Count - client's immunity as measured by CD4 cells as at the last testing
G. Blood Pressure (Systolic) - client's systolic blood pressure at the last clinic visit
H. Blood Pressure (Diastolic) - client's diastolic blood pressure at the last clinic visit
I. Client's status - alive, dead, loss to follow-up, or transferred out.

Outcome measures

At Commencement of ART

A. Body mass index (BMI) at baseline – computed by dividing the client's weight (kg) at baseline by the square of the height (m^2).

At 12 and 24 months after commencement of ART

B. Body mass index (BMI) – computed by dividing the client's weight (kg) at each one year interval by the square of the height (m^2).

Data Analysis – Quantitative Study

The de-identified secondary data was imported into SPSS (version 25) for cleaning, recoding, and analysis. Frequency counts were obtained, and normality of the variables were explored. The variables were not normally distributed, and hence use of rank-based procedures was utilized in the analyses that follow. Height and weight data were re-coded into BMI for each year. Before commencing the data analysis, a codebook of all the variables was developed. BMI was also categorized into four - underweight (BMI <18.5 kg/m^2); normal weight (BMI 18.5 -

24.9 kg/m^2); overweight (BMI 25.0 - 29.9 kg/m^2); and obese (BMI ≥30 kg/m^2). The proportions in the different BMI categories were calculated at the start of ART and for each of the subsequent years (2012 – 2015).

Statistical Methodology

Research Question 1*:* Is there a difference in median BMI between PLHIV starting treatment in the two states and the general population?

Statistical Tests**:** The variables at baseline were reviewed using descriptive statistics to understand the data. A new variable (BMI categories) was computed. The median BMI was compared by gender using Mann-Whitney U test. In addition, the baseline median BMI of all the clients commencing ART was compared with published studies from Nigeria using a one-sample Wilcoxon signed rank test.

Research Question 2a: Is there a difference in median BMI at baseline and at 24 months of treatment among PLHIV starting treatment in the two states?

Statistical Test**:** The median BMI at baseline was compared with the median BMI at 24 months using a Wilcoxon signed-rank test.

Research Question 2b: Is there a difference in proportions in each BMI category at baseline and at 24 months?

Statistical Test: The difference in proportions in each BMI category at baseline versus at 24 months was tested with the McNemar-Bowker test.

Research Question 3*:* Is the BMI after 24 months of treatment associated with demographic factors (gender, marital status, education) and/or clinical factors (drug regimen, HIV stage, CD4 count, blood pressure, adherence to medication), after accounting for age and baseline BMI?

Statistical Test: This question was tested with Multiway-ANCOVA. The dependent variable was the BMI at 24 months. The covariates were the baseline BMI and the client's age. The independent variables included demographic variables (gender, marital status, education) and clinical variables (drug regimen, HIV stage, CD4 count, blood pressure, and adherence to medication).

Data Analysis – Qualitative Study

Research Question 4: What are the perceptions of healthcare providers about overweight/obesity among PLHIV on treatment in Nigeria?

Analysis: For the qualitative part, primary data was collected via KIIs with the HCPs telephonically using the interview guide (see Appendix E). The data (audio files and notes) from all 16 interviews were transcribed verbatim and subjected to a thematic analysis. The investigator and one other member of the team read the transcripts independently, to identify sentences/phrases/clauses meaningful to the research topic using both a deductive and inductive approach. The inductive approach was data driven, while the deductive approach was guided by the social-ecological framework of multiple layers of influence and the semi-structured interview guide. The coding was done manually and the initial codes were compared and differences were resolved by discussion. A codebook was created and used in the coding of all 16 transcripts. The investigator then used the generated codebook to independently complete the coding of all 16 transcripts.

The final codes were then aggregated to generate broad themes for further examination and discussion. A descriptive analysis was also done on the basic demographic data from the 16 interview participants. These data included profession, gender, and years of experience in the HIV clinic. The generated themes were used to understand the perceptions of HCPs about the HIV-obesity phenomenon including its probable causes, stigma association with HIV and weight, and long term health consequences of obesity among HIV patients. The qualitative analysis was done following the thematic analysis guide proposed by Braun and Clarke (2006), and the reporting was done following the consolidated criteria for reporting qualitative studies [COREQ] (Tong, Sainsbury, & Craig, 2007).

Integration of Quantitative and Qualitative Results: Connecting, Merging, and Joint Display

Research Question 5: In what ways do the qualitative data from the interviews with healthcare providers further explain and expand on the quantitative findings from PLHIV on treatment in Nigeria?

***Analysis*:** Using the explanatory sequential design, the quantitative and qualitative steps were both independent and interactive. The quantitative and qualitative strands were integrated at two critical points. First, when using the quantitative results to guide the generation of the qualitative interview questions, and second when doing the data analysis and results presentation of both arms. The joint display (Guetterman, Fetters, & Creswell, 2015) was used to present the results of the integration. The mixed-methods approach was done following the mixed methods integration guidelines proposed by Fetters, Curry, and Cresswell (2013) and the reporting was done following the GRAMMS (Good Reporting of a Mixed Methods) checklist (O'Cathain, Murphy, & Nicholl, 2008).

Data Management

The de-identified secondary data and the primary data from the qualitative study were treated as confidential according to the HIPAA principles (Health Insurance Portability and Accountability Act). This confidentiality spanned from collection through collation, analyses, and storage. For this study, all data collected from the interviews are stored in locked cabinet in the faculty advisor's office with access to only the PI and the other investigators. All the potential personal identifiers from the transcripts were removed (e.g. name, place of work etc.) with each participant assigned a serial number.

Ethical Concerns

The research proposal for this study was filed with the Institutional Review Board (IRB) of University of Nevada, Las Vegas (UNLV). The study commenced after approval by the IRB.

Chapter 4: Results

This chapter is divided into three sections. The first section covers the results from the quantitative study, the second section covers the qualitative study, and the third section summarizes the key results with a mixed-methods approach using a joint display.

Results of the Quantitative Study

Demographics & Descriptive Characteristic of the Sample

The total sample size for this analysis was 3530. Of this sample, 68.2% were female (n=2408) and the median age was 34 years (IQR: 29,42), though the females commenced ART earlier (median age = 32 years) than the males (median age = 39 years). A large proportion of the participants were married (48.5%, n=1711). At baseline, 61% of the PLHIV were of normal weight, while underweight and overweight were each about 17%. Only 3.7% were obese. The demographic description can be seen in Table 4.1 below.

Additionally, an exploration of the baseline clinical variables showed that most (61.3%) of the participants were enrolled into care in WHO HIV stage 1. About 35% of the participants also had baseline CD4 count of <200 cells/mm^3. Of the total sample, about two-fifths commenced treatment in 2012, another two-fifths in 2013, and one-fifth in 2014. Most of the PLHIV (60%) in this sample commenced Tenofovir-based regimen. As a third drug, Efavirenz was the most common (55.3%), while the protease inhibitors made up only 2.6%.

Table 4.1. Demographic characteristics of quantitative study participants

Gender	**Frequency**	**Percent (%)**
Female	2408	68.2
Male	1122	31.8
Age at ART Start	**Frequency**	**Percent (%)**
18-29	1020	28.9
30-39	1422	40.3
40-49	713	20.2
50-59	304	8.6
≥60	71	2.0
Educational Level	**Frequency**	**Percent (%)**
Primary	541	15.3
Secondary	808	22.9
Post-Secondary	512	14.5
None	131	3.7
Unknown	1538	43.6
Marital Status	**Frequency**	**Percent (%)**
Married	1711	48.5
Single	809	22.9
Widowed	377	10.7
Divorced	77	2.2
Unknown	556	15.7
BMI Category at Baseline	**Frequency**	**Percent (%)**
Underweight	621	17.6
Normal Weight	2152	61.0
Overweight	625	17.7
Obese	132	3.7

Table 4.2. Clinical characteristics of quantitative study participants

WHO Stage at Baseline	**Frequency**	**Percent (%)**
I	2164	61.3
II	297	8.4
III	208	5.9
IV	50	1.4
Unknown	811	23
CD4 category at Baseline	**Frequency**	**Percent (%)**
<200	1254	35.5
200 - <350	805	22.8
350 - <500	360	10.2
≥500	137	3.9
Unknown	974	27.6
Year ART Started	**Frequency**	**Percent**
2012	1435	40.7
2013	1371	38.8
2014	724	20.5
ART Regimen at Baseline (by backbone)	**Frequency**	**Percent (%)**
Tenofovir-based	2119	60
Zidovudine-based	1360	38.5
Abacavir-based	38	1.1
Tenofovir- and Zidovudine-based	9	0.2
Zidovudine- and Abacavir-based	3	<0.1
Stavudine-based	1	<0.1
ART Regimen at Baseline (by third drug)	**Frequency**	**Percent (%)**
Efavirenz	1951	55.3
Neviapine	1487	42.1
Lopinavir (boosted with ritonavir)	79	2.2
Atazanavir (boosted with ritonavir)	13	0.4

Research Question 1: Is there a difference in median BMI between PLHIV starting treatment in the two states and the general population?

The median BMI at baseline was 21.79 kg/m^2 (IQR: 19.4, 24.5). A Mann-Whitney U Test revealed a difference in the BMI for the females (median = 21.6, IQR: 19.1, 24.4, n = 2408) and the males (median = 22.0, IQR: 19.8, 24.6, n = 1122), [U = 1425595, z = 2.65, p = .008, r = 0.04].

Additionally, when the median BMI of this group was compared to the available BMI (mean = 23.9) from the Demographic and Health Survey (NDHS, 2013) using a One-Sample Wilcoxon Signed Rank Test, it showed that the observed median BMI in this sample was lower than the hypothetical BMI from the 2013 DHS (z = -25.27, p = <.001, r = -0.43).

Research Question 2a*:* Is there a difference in median BMI at baseline and at 24 months of treatment among PLHIV starting treatment in the two states?

The Wilcoxon Signed Rank Test revealed an increase in the median BMI following commencement of ART (z = -20.316, p<.001), with a moderate effect size (r =.397). The median BMI increased from baseline (21.8 [IQR: 19.4, 24.5]) to 24 months time period (23.6 [IQR: 21.1, 26.6]). Additionally, the group mean BMI for the participants trended up from baseline to month 12 and from there to month 24, with the most significant gain in the first 12 months (Figure 4.1).

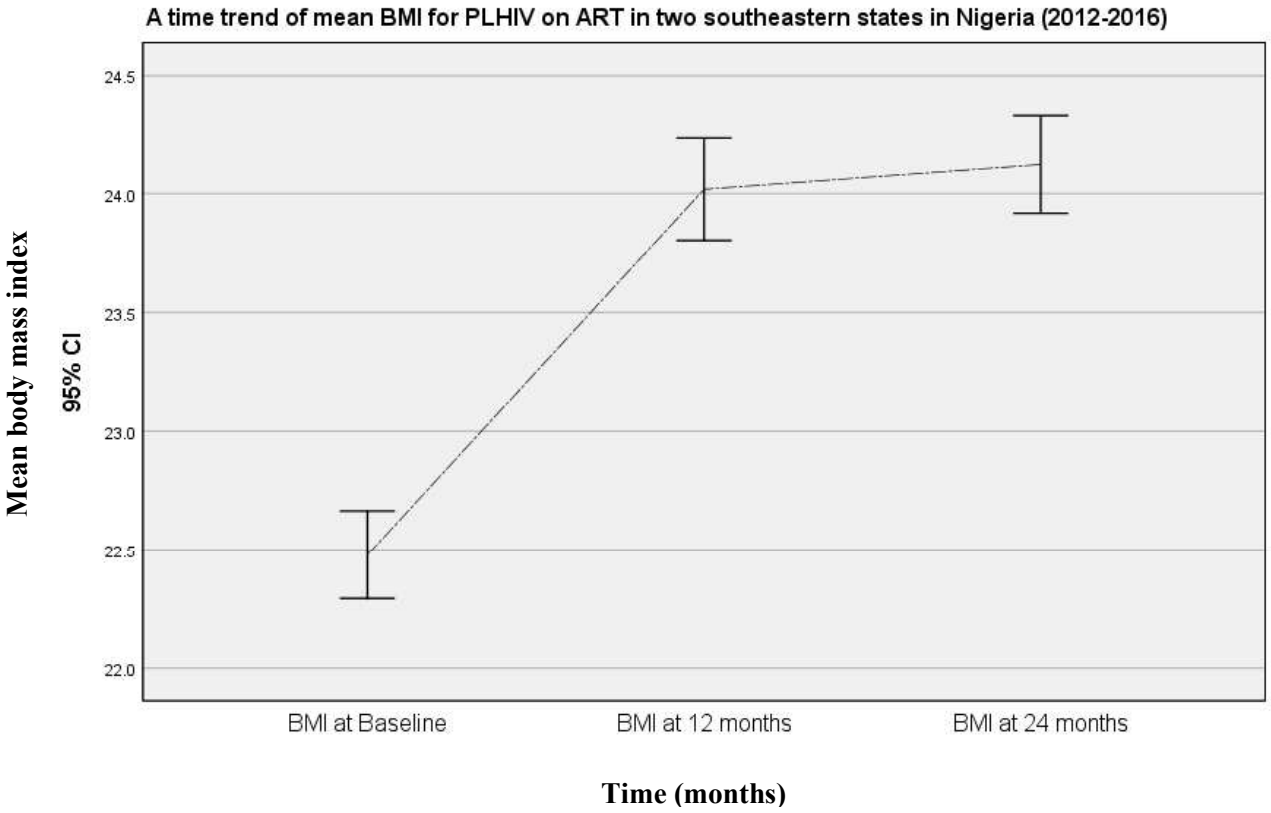


Figure 4.1. A time trend of mean BMI for PLHIV on ART in two southeastern states in Nigeria

***Research Question 2b*:** Is there a difference in proportions in each BMI category at baseline and at 24 months?

The McNemar-Bowker Test showed that after 24 months on ART, the number of participants who were obese and overweight increased by 186% and 42.3%, respectively. Additionally, the number of participants who were underweight or normal weight decreased by 59% and 9.4%, respectively (McNemar-Bowker Test statistic = 305.964, p<.001).

It is also worth noting that about a quarter of all participants who were obese at baseline became overweight at the end of this study. Interestingly, among all the participants who were

overweight at the beginning, about a fifth each moved one BMI category up (to obesity) and one BMI category down (to normal weight). In terms of absolute numbers, more particpants had an increase in BMI than those who had a decrease in their BMI.

Table 4.3. A crosstabulation of BMI categories at baseline versus at 24 months of ART

		BMI category at 24 months				
		Underweight	Normal Weight	Overweight	Obese	Total
BMI Category at Baseline	Underweight	68 (27.1%)	171 (68.1%)	10 (4%)	2 (0.8%)	251 (100%)
	Normal Weight	30 (2.7%)	753 (68.4%)	271 (24.6%)	47 (4.3%)	1101 (100%)
	Overweight	2 (0.6%)	70 (20.4%)	193 (56.3%)	78 (22.7%)	343 (100%)
	Obese	2 (3.4%)	3 (5.2%)	14 (24.1%)	39 (67.2%)	58 (100%)
	Total	102 (5.8%)	997 (56.9%)	488 (27.8%)	166 (9.5%)	1753 (100%)

***Research Question 3*:** Is the BMI after 24 months of treatment associated with demographic factors (gender, marital status, education) and/or clinical factors (drug regimen, HIV stage, CD4 count, blood pressure, adherence to medication), after accounting for age and baseline BMI?

A multiway analysis of covariance (ANCOVA) was used to test if the BMI at 24 months of treatment was associated with demographic and/or clinical factors. The independent variables consisted of gender, marital status, education, regimen at baseline, third drug in the regimen, HIV stage at baseline, blood pressure at baseline, and CD4 category at baseline. The dependent variable

was BMI at 24 months after commencing ART. Covariates were age at baseline and BMI at baseline.

The results of the preliminary checks for linearity, homogeneity of regression slopes, and reliability of covariates were all satisfactory. However, the assumptions of normality and homogeneity of variance were not met. Nevertheless, the ANCOVA test was still used because it is robust to departures from normality when there is adequate error degrees of freedom (Pallant, 2016). Additionally, the ranked data provided the same statistical result as the parametric procedure, further strengthening the argument for the use of ANCOVA. After adjusting for covariates, BMI at 24 months varied significantly with gender, HIV stage at baseline, and CD4 category at baseline, as summarized in Table 4.4.

Table 4.4. Analysis of Covariance for BMI at 24 months on ART (initial model)

Tests of Between-Subjects Effects						
Dependent Variable: BMI at 24 months						
Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	10467.727[a]	35	299.078	32.629	<.001	.486
Intercept	234.621	1	234.621	25.597	<.001	.021
Age	123.656	1	123.656	13.491	<.001	.011
BMI at baseline	9271.327	1	9271.327	1011.501	<.001	.456
Gender	103.152	1	103.152	11.254	.001	.009
Marital status	59.862	5	11.972	1.306	.259	.005
Education	43.558	5	8.712	.950	.447	.004
Baseline regimen	121.708	11	11.064	1.207	.277	.011
Regimen 3rd drug	.000	0	.	.	.	.000
Stage at baseline	96.009	4	24.002	2.619	.034	.009
CD4 category	263.441	3	87.814	9.580	.000	.023
SBP* category	27.584	2	13.792	1.505	.222	.002
DBP* category	.645	1	.645	.070	.791	.000
Error	11072.423	1208	9.166			
Total	752786.962	1244				
Corrected Total	21540.151	1243				
R Squared = .486, (Adjusted R Squared = .471)						

*SBP = Systolic blood pressure; DBP = Diastolic blood pressure

A parsimonious second model was then run with only the independeent variables that met a significance level of $p<0.05$ and the two covariates. The second model showed that after adjusting for covariates, BMI at 24 months varied significantly with CD4 category at baseline only, as summarized in Table 4.5, with $F(3, 1311) = 3.660$, $p=.012$. The strength of the relationship between adjusted BMI at 24 months and CD4 category at baseline was very weak, however, with partial eta square of 0.008.

Table 4.5. Analysis of Covariance for BMI at 24 months on ART (final model)

Tests of Between-Subjects Effects						
Dependent Variable: BMI at 24 months						
Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	11220.297[a]	37	303.251	32.687	<.001	.480
Intercept	663.992	1	663.992	71.571	<.001	.052
Age	108.086	1	108.086	11.650	.001	.009
BMI at baseline	10323.521	1	10323.521	1112.756	<.001	.459
Gender	3.399	1	3.399	.366	.545	.000
CD4 category	101.864	3	33.955	3.660	.012	.008
Stage at baseline	35.344	4	8.836	.952	.433	.003
Gender * CD4 category	38.383	3	12.794	1.379	.248	.003
Gender * Stage at baseline	16.801	4	4.200	.453	.770	.001
CD4 category * Stage at baseline	76.313	12	6.359	.685	.767	.006
Gender * CD4 category* Stage at baseline	92.225	8	11.528	1.243	.270	.008
Error	12162.712	1311	9.277			
Total	813094.828	1349				
Corrected Total	23383.009	1348				
R Squared = .480, (Adjusted R Squared = .465)						

Furthermore, there was no statistically significant main effect with gender or HIV stage at baseline, neither did the model reveal any significant interaction among the independent variables after adjusting for the covariates. For gender and HIV stage at baseline, partial eta squared was <0.001 and 0.003, respectively.

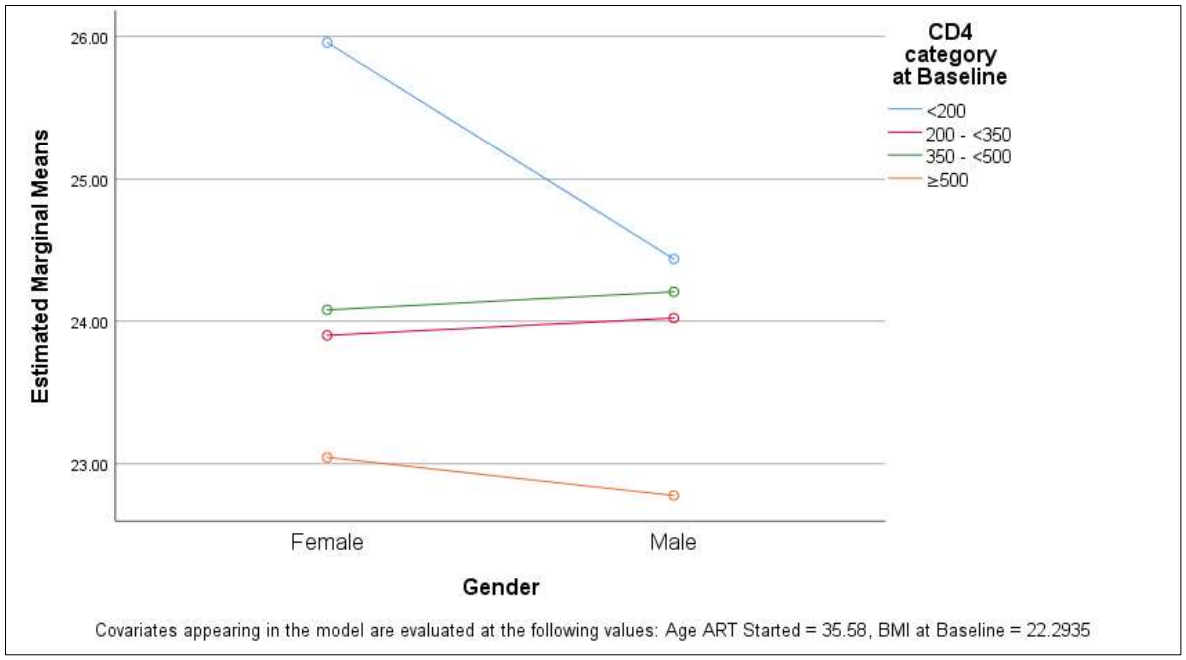


Figure 4.2. Estimated marginal means for BMI at 24 months on ART showing CD4 category and gender

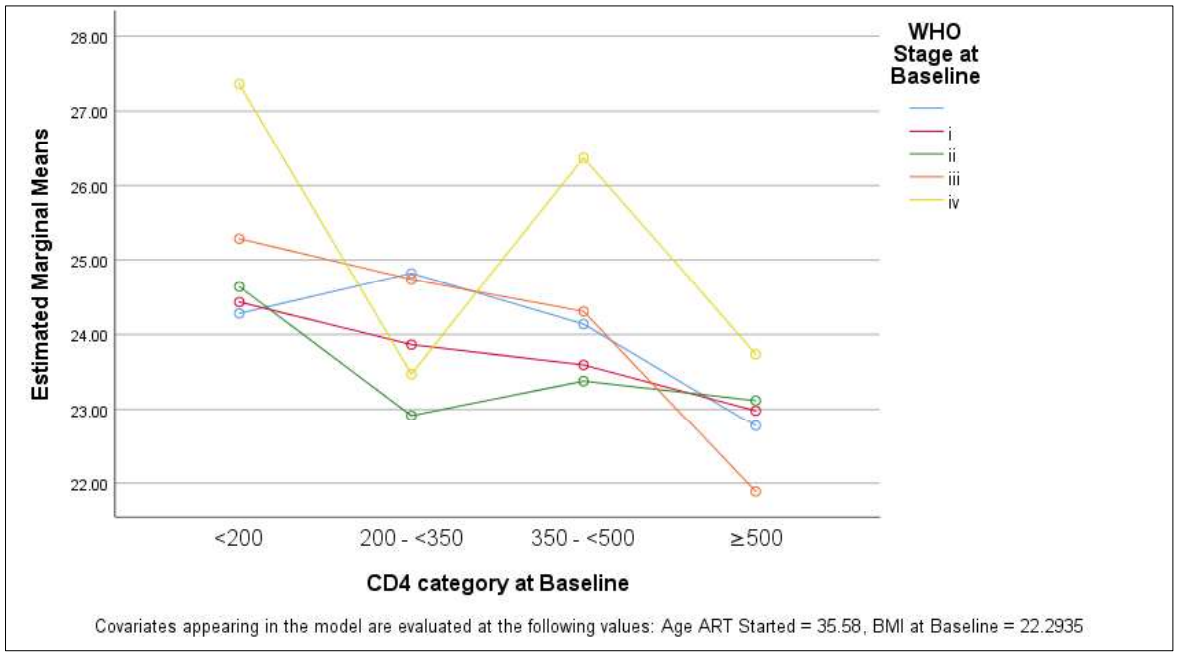


Figure 4.3. Estimated marginal means for BMI at 24 months on ART showing CD4 category and HIV stage

Finally, the model showed that the two covariates (BMI at baseline and age) were significantly associated with BMI at 24 months. However, only the BMI at baseline uniquely adjusted the BMI at 24 months [$F(1, 1311) = 1112.756$, $p < .001$, partial eta squared = 0.459] after covariates were adjusted for other covariates, main effects, and interaction. The effect size (partial eta squared = 0.459) shows that the strength of the relationship between adjusted BMI at 24 months and baseline BMI was very strong (Cohen, 1988; Tabachnick & Fidell, 2013).

Results of the Qualitative Study

Research Question 4: What are the perceptions of healthcare providers about overweight/obesity among PLHIV on treatment in Nigeria?

Sixteen healthcare providers (HCPs) from the two southeastern states in Nigeria (where the participants in the quantitative study received HIV care) were interviewed using a semi-structure guide. Of the 16 interview respondents, 62% (n=10) were female and 38% (n=6) were male. They included physicians (44%), nurses (25%), adherence counsellors (19%), and pharmacists (12%). They also had a combined work experience of 106 years in a HIV clinic, with a mean of 7 years (standard deviation [SD] ±4.03). Table 4.6. below shows these demographic details.

Table 4.6. Demographic data for the 16 key informant interviews of healthcare providers

Demographics		Number	%
Gender:	Female	10	62.5%
	Male	6	37.5%
State:	Enugu	9	56.2%
	Ebonyi	7	43.8%
Cadre of healthcare provider:	Medical Doctor	7	43.8%
	Nurse	4	25%
	Adherence counsellor*	3	19%
	Pharmacist/Pharmacy Assistant	2	12%
Experience in HIV Clinic:	1-3 years	4	25%
	4-6 years	4	25%
	7-9 years	3	19%
	≥10 years	5	31%

*Similar to a social worker

Thematic analyses

The thematic analyses revealed five major themes: (a) HCPs and PLHIV do not see excess weight gain as a problem, except when there are complications; (b) the society sees weight gain as a status symbol, but stigmatizes morbid obesity; (c) ARVs serve as a subconscious replacement for other drugs used to treat co-morbid diseases; (d) BMI is usually used at the initial assessment, while weight is routinely used for continuous monitoring; and (e) the use of dietetic services. The themes and sub-themes are shown in Table 4.7 below. A glossary of colloquial terms used in the interviews has also been attached (see Appendix F).

Table 4.7. Themes and sub-themes from qualitative study

Theme 1: HCPs and PLHIV do not see excess weight gain as a problem, except when there are complications
1.1 Strong association between HIV and weight loss
1.2. ARVs and weight gain
1.3. Weight gain from other causes
1.4. Weight gain or weight loss intention is contextual
1.5. Weight gain as a sign of a successful clinical treatment program
Theme 2: Society see weight gain as a status symbol but stigmatizes morbid obesity
2.1. Poor understanding of other chronic illnesses
2.2. Mental health issues
2.3. HIV Identity
2.4. PLHIV with co-morbidities encouraged to lose weight
2.5. Low index of suspicion of HIV until weight loss sets in
Theme 3: ARVs serve as a subconscious replacement for other drugs used to treat co-morbid diseases
3.1. PLHIV with co-morbidity practice selective adherence
3.2. Treatment fatigue
3.3 Drug adherence optimization
Theme 4: BMI usually used at initial assessment, while weight is routinely used for continuous monitoring
4.1. BMI mostly used at initial assessment
4.2. Weight routinely used for subsequent visits
4.3. Assumptions about BMI
Theme 5: Use of dietetic services
5.1. Referral to dietitian limited by several factors

Theme 1*: HCPs and PLHIV do not see excess weight gain as a problem, except when there are complications*

Unsurprisingly, the HCPs described a strong association between HIV and weight loss. The stigma of this association was so strong, such that:

> Irrespective of the other illnesses they (*underweight people*) may have, people will first think that they are HIV positive. (Interviewee #3)

> Anybody who has lost weight, the first thing people ask is, "does this person have HIV?" When it could be as well be type 1 diabetes, or malignancy, or even thyrotoxicosis. (Interviewee #5)

Additionally, this stigma is so entrenched in the local culture such that language groups that were hitherto unfamiliar with HIV easily ascribed a name that was associated with wasting:

> Even in some local dialect, when they want to refer to someone who has HIV, they refer to them as someone that is very skinny. (Interviewee #5)

According to the HCPs, the PLHIV who then comes into treatment are looking to escape this stigma. Hence, PLHIV strive to gain weight as quickly and as plentiful as biologically possible within the shortest time frame:

> Now, by the time the patient has lost so much weight, as a result of the continued disease progression and eventually there is a drug intervention. Now, the patient now is responding very well. The ideal thing is for the patient to do anything, eat anything he can, to make sure he regains his or her weight. (Interviewee #6)

> This person came to us, she was very thin. They started her on ARV. Later she started gaining weight, gaining weight. At a stage, we are even telling her, "you are gaining excess weight *ooo*." She was saying, "thank God, people will not think of what they are thinking before that I am HIV." (Interviewee #3)

Additionally, many of the HCPs see ARVs as leading to weight gain, either directly by boosting immunity or indirectly by stimulating the appetite of PLHIV with wasting.

> Yes, in my area, people believe that ARVs make one to gain weight. (Interviewee #9)

> They will be asking me if it is the drug that is making them to be gaining this kind of weight. I now tell them yes, because it makes you to add more weight due to the way you eat, and all that. (Interviewee #1)

This purported link between ARVs and weight gain also has an associated stigma, which one HCP described in these words:

> Another thing is that they will be saying that people say they are taking drugs that is making them fat. It is also a stigma to them. Some people that will come direct to you, they will say they do not know what to do, that people are mocking them that they are taking 'pig drug', drugs that will make them fat. (Interviewee #2)

However, the other HCPs pointed to some other factors that may be the potential causes of excess weight gain among PLHIV who are on treatmnet. These potential factors include proper dietary counseling, food and drug supplements, and hormonal treatments.

> Some will be on different types of multivitamins that will help them to gain so much weight. (Interviewee #6)

> You know some of this [*these*] things could be done consciously or unconsciously. Like somebody just discovered that by virtue of taking this thing, I am gaining so much weight. Now, it could be contraceptives. (Interviewee #6)

While the weight gain was obvious and acknowledged by both the PLHIV and the HCP, it rarely was a cause for concern. Only very few PLHIV on treatment wanted to lose the excess weight that was gained, though a few complained about this weight gain.

> Well, nobody living with HIV wants to lose weight *ooo*. That is what I will answer straight. (Interviewee #5)

> If he or she start to add weight, she will be complaining, saying that, "I have started adding weight, what can I do?" That they want to reduce their weight, they don't want to be like this. (Interviewee #2)

For the few HCPs that take it upon themselves to press the PLHIV to curb their weight gain and not become obese, the PLHIV may reject the idea of weight loss.

> Some of them will tell you, "Doc, I thought you people said we should gain weight?" And we are like, "yes we did, but this is not…I mean, you are going to the other end." (Interviewee #5)

And even if the PLHIV acknowledges the excess weight gain and agrees to work with the HCP to address it, they usually counsel the PLHIV on diet and physical activity, and do a review of their current medications.

> …and those of them that are on multivitamin, that is, supplement, if they complain about their weight gain, that they are gaining weight more, the doctor normally stops the multivitamin. Because they will tell you that it is because of the multivitamin, that it is making them to eat more. (Interviewee #8)

In fact, many a time, the HCPs encourage the weight gain by PLHIV and see it as a sign of the success of their clinical treatment program.

> First of all, being big or overweight shouldn't really be a very big problem, in my own opinion. So I don't make it look like it's a very big problem. Once your blood pressure is okay, your other health reports are okay, and the person is happy. (Interviewee #16)

> …rather, maybe some health workers are even seeing it as it's a sign that we are doing well, that at least our patients are gaining weight, they are doing well. (Interviewee #14)

And finally, the only time when the HCPs see excess weight gain as a problem is when the PLHIV develops other health challenges related to obesity. Even the PLHIV themselves are difficult to convince, and one of the HCPs mentioned that an early sign that pushes the PLHIV to accept their excess weight gain is truncal obesity:

> I think the only time they may start feeling it's a problem, especially for the men, when they start having truncal obesity. And it's like when they point it out to them like, "hmm chief, this your *belle* is becoming … you know." They will say, "it is true *ooo*, I have noticed." Then they start seeing it as this is the problem. (Interviewee #14)

Overall, while obesity is not a problem with the general population of Nigerians, this thinking also pervades HIV care and treatment. Paradoxically, for each individual PLHIV who was burdened by overweight or obesity, they were happy to have escaped the stigma of the wasted

HIV-positive client and moved on to 'normality', even if that 'normality' portends dangers to their health in the near future.

Theme 2: *The society sees weight gain as a status symbol, but stigmatizes morbid obesity.*

Interestingly, the data revealed a certain paradox about the HIV-obesity relationship. While the society saw a higher BMI as a sign of wealth, a status symbol, they were also dismissive or unaccommodating to those who were morbidly obese.

> …but then in this society or in this part of the world, they see someone that is overweight or obese as being healthy. You are actually eating well, you are actually being taken good care of. (Interviewee #4)

> However, for the general population, I have not seen that they are stigmatized because they are obese. Obesity in Africa is not a big problem … We see it is an evidence of living good. Except when the person is morbidly obese. For instance … you want to take a commercial bus, and somebody says, "I cannot carry two people." Meanwhile it is just you. Other than that, if it is BMI less than 30, between 25 to 30, or BMI less than 35, people don't really stigmatize. The people that are stigmatized are those who have lost weight. That is my own experience. (Interviewee #5)

Hence, for the PLHIV who gain excess weight while on treatment, they are further predisposed to other common chronic illnesses like type 2 diabetes, hypertension, and

osteoarthritis. And because the PLHIV do not understand these co-morbidites as well as they understand HIV, their treatment outcomes and their overall quality of life, are negatively impacted:

> I normally explain to them that why I said they should not gain too much weight is to avoid other ill health that may arise from that overweight, like hypertension or diabetes. (Interviewee #5)

> Again, the ART treatment is constant, it goes on. It should not be interfered with, for any reason. But first, the immediate problem, like hypertension, can kill a patient even before HIV. The patient could go into hemorrhagic stroke and go down. (Interviewee #10)

Additionally, the HCPs pointed out the critical mental health challenges faced by PLHIV who are obese or who have other co-morbidites, especially as regards depression:

> But being HIV positive and being obese has a psychological effect on the patient who knows that he or she has these two morbidities. And it puts more work on the healthcare giver to help educate this patient and also counsel the patient. And also work on the patient's psychology to help the patient not go into depression, which is another thing we battle with among these patients. (Interviewee #10)

> Hypertension is not curable, it is only manageable, and HIV is manageable. Putting those things into consideration will only make the person to feel more rejected, I am having this, I am having this, that the world is end. (Interviewee #11)

The overwhelming feeling of dealing with multiple morbidities, the mental health issues, and the associated stigma of HIV, alone, or together with obesity, all create a unique identity for PLHIV. This is also further compounded by the counseling that some HCPs give PLHIV.

> I tell them you are just healthy *ooo*. If you have a stroke now because your blood pressure is high, you are obese, some people will think you died of HIV. They won't know that it is not the HIV that killed you, that you developed other problems outside HIV. (Interviewee #5)

> So, they don't see it…'must we be taking medications every day', and therefore, 'can't we just leave it for some time?' So those are the things, but we try to counsel them and let them know that they must see those medications as their food and they must take it every day, in order to help themselves. (Interviewee #13)

Furthermore, because the HCPs are not very bothered about excess weight gain among PLHIV who are on treatment, they usually do not discuss weight loss strategies early on. However, a critical threshold is usually reached when the obese PLHIV develops other co-morbidities associated with excess weight. At this point, the HCPs begin to stress the importance of weight loss and maintaining optimal BMI.

Paradoxically, the data also showed that for PLHIV who were newly diagnosed, many of them, and their HCPs, had a low index of suspicion of having HIV before the diagnosis. It was usually the weight loss that pushed them to get HIV testing and it was also the self knowledge of this weight loss that moved them beyond the stage of denial of a positive test result to enrolling in HIV treatment:

> Initially, it wasn't the HIV that they were treating. They were treating malaria, treating typhoid, treating other things, and even gone to the extent of treating poison, and before somebody now say go to the hospital and do so so so test, because of the underweight in question. (Interviewee #13)

> …those who are just going to be tested for that [*HIV*], one of the reasons they accept they actually have HIV is when they notice that they've been losing weight. So they are very frantic about gaining weight, it's like covering up this stigma that is being seen. So most people are particular about gaining weight. (Interviewee #14)

Theme 3*: ARVs serve as a subconscious replacement for other drugs used to treat co-morbid diseases*

Another imporant theme from the data was the idea that PLHIV who had other co-morbidities felt they would be fine as long as they were taking their ARVs, regardless of whether they were taking the treatment for the other co-morbidities or not.

> …the person had hypertension and I noticed the BP was spiking like mad and the person was not on, the person has been placed on drugs, but he or she wasn't taking the drugs. So I tried to find out why, the person was just like, nothing, that he or she felt she's already on HIV drugs, so why, that she felt this one can cover for the other one. I was like hell no, that there are two different things that you are being treated for and they are not the same. (Interviewee #4)

The HCPs described this behavior as leading to a kind of selective adherence by PLHIV with co-morbidities, with a high preference for their ARVs instead of the other drugs:

> They say that the drug is too much for them. That instead of them to combine the medicine, it is better they take this one and if the other one starts to disturb them then they will start taking that one. (Interviewee #2)

> You know the one they normally focus on is the HIV drug. They will tell you that instead of them to miss this ARV, it is better they don't take the other drug that they are taking, that the HIV is more important to them. (Interviewee #2)

It is a well known fact that people with chronic diseases sufffer from treatment fatigue and pill burden issues (Benner, Glynn, Mogun, Neumann, Weinstein, & Avorn, 2002; Osterberg & Blaschke, 2005). This was further reiterated by the HCPs about PLHIV on treatment, especially when these patients have other co-morbidities. This negatively afffects optimal drug adherence:

> It is a big blow, they usually find it very difficult, because they are already complaining that there is a specific drug they will take for life and we are adding more to what they have. Like see, some of them come in with diabetes, some of them come in with hypertension, some of them come in with hypercholesterolemia, and some other symptoms…so we are finding it difficult. (Interviewee #12)

> You can understand that for patient who is on an antiretroviral therapy regimen, that has to be taken twice daily, and other persons who has *[have]* diabetes and hypertension complicating their problem, basically increases the pill burden for that patient. (Interviewee #15)

However, the HCPs also stressed the role of fixed dose combination (FDC) drugs in relieving some of this anxiety, either for HIV treatment or for other illnesses, especially by reducing the number of pills taken daily, thereby improving adherence to treatment:

> But I always advise them that thank God that they have fixed doses in their antiretroviral. For most of them, it is one once a day for 24 hours. But when we started, it was separate. They have made this drug to be easier for you people. (Interviewee #1)

> We also try to…like for the hypertensives, there are also drugs that come in combinations. Rather than give that three classes of drugs, there are formulations that contain these three in one. So we opt for those formulations so that we try to

reduce the pill burden of these patients and encourage compliance. (Interviewee #10)

Many current regimen for HIV come in one pill that contains three drugs, and they are usually taken once a day. Such combinations have also being created for the treatment of hypertension and diabetes.

Additionally, the HCPs also discussed some other factors that possibly increase adherence to treatment among PLHIV, especialy for those who have co-morbid conditions. Such factors include access to free ARVs, prescription of generic and cheaper brands for hypertension or diabetes, and the fact that the repreated counseling received in the HIV clinic may also contribute to increase adherence to other medications:

I have seen a couple of patients who by the time they oblige and go for such cheaper options, they are doing well, they will be doing well. They will be coping. (Interviewee #6)

If a client is found to have a disease like diabetes or hypertension, actually the client will be given a referral to go to the medical outpatient to see a physician. Then after their review, if the client is being placed on either anti-hypertensive or anti-diabetic, we also implement adherence counseling in regards to the HIV drugs and either the anti-diabetic or anti-hypertensive. (Interviewee #8)

Theme 4: *BMI usually used at initial assessment, while weight is routinely used for continuous monitoring.*

A fourth theme from the data was that BMI was used only sporadically in many clinics, usually only at enrollment into care and treatment. The HCPs unconsciously defaulted to using weight on a routine basis even though there is a BMI column, for every visit, in the PLHIV's chart. Although, two of the HCPs spoke about actively calculating and documenting the PLHIV's BMI at each visit.

> You see there is what we call the care card. The care card of each client, or the care card for ART, has a column that gives you the various…less than 18.5 is low weight, 18.5 to is it 24 point something is normal, 25 and above…you know, they have this there on the care card. It is just that people don't take time to calculate the BMI, like once it is calculated that first time it is done. Subsequently, even though there is a column for BMI, subsequently, people hardly calculate that, especially when they come for their routine refill. (Interviewee #14)

> But for somebody whose BMI…because I have actually calculated some of their BMI in the clinic, and I will give them the value of the BMI, and explain to them what it means. (Interviewee #13)

Some reasons that may be adduced for this oversight include the fact that some of the HCPs do not have a BMI chart in their office and that some HCPs may also not remember off-hand the

BMI categories and their cut off points to aid effective classification. However, two of the HCPs specifically mentioned their use of BMI register and BMI charts in the clinic.

> We are supposed to have, but I don't…we don't have. But I usually try to draw them [*illustrative BMI charts]* for them [*PLHIV*], I show them what normal one is and teach them how it is done. (Interviewee #12)

> Because of her weight, and everything, we automatically know that she was obese. With her height and her weight, we checked her BMI, it was 25. (Interviewee #7)

Perhaps, as a result of these identified gaps, the HCPs default to using weight alone for routine monitoring in the HIV clinic. Hence, the HCPs think in terms of weight alone, and not a more composite metric like BMI:

> Each of their visit we monitor the weight to see if it has started increasing. (Interviewee #1)

> The concern is that it is not good for them to gain more weight. It is better for them to be normal weight. Like somebody that is 100 or 90 (*kg*), I would advise the person that you have started gaining weight, it is better you maintain it, that you come to normal weight, so that it will not affect you. (Interviewee #2)

Interestingly, this gap translates to some HCPs making clinical decisions based on weight alone without thinking more holistically about the BMI. The HCPs usually do a visual assessment of BMI and make a lot of assumptions about the PLHIV's BMI:

> Once he comes into your clinic and you are getting a weight of maybe hundred and something, and you look at the height of this person is around may be 1.6 meters or thereabout or 1.5. So the first thing is to counsel the woman or the man on the aspect of the weight, to lose weight. (Interviewee #13)

> I have a patient whose weight is as much as 100kg. Of course even if the person's weight is 2 meters, the BMI will certainly be more than 30. (Interviewee #5)

Overall, a general trend was evident such that whenever the obese or overweight PLHIV had any health challenge, their BMI was computed and used for decision making. Otherwise, only the weight was used for decision making at each visit.

Theme 5: *Use of dietetic services*

The fifth major theme from the data was about access to dietitians and the use of dietetic services. Dietitians, locally referred to as nutritionists, were not very common in the hospitals and their availability was dependent on what level of services the hospital or clinic operated at generally. Most primary and secondary level clinics/hospitals did not have dietitians, but tertiary hospitals did.

Table 4.8. Access to a dietitian in HIV care and treatment facility

	Question asked: Do you have a dietitian or nutritionist in your clinic or hospital?	
Was question asked?	**Dietitian present**	**Interviewees answering**
Question was asked	Yes	6
	No	3
	Dietitian mentioned	
Question was not asked	Yes	3
	No	4

This theme was not somehing we had set out to explore but it arose after the fourth interview. Probe questions were therefore discussed on subsequent interviews. Overall only 9 of the HCPs were directly asked about access to a dietitian and only 9 HCPs answered in the affirrmative or specifically mentioned access to a dietitian (see Table 4.8 above).

In the clinics without a dietitian, the other HCPs did the dietary or nutritional counselling:

> So, the point is that she needs to understand what she needs to do so that she can do it, vis-a-vis talk to the dietician, and all that. Usually, I would want them to see a dietitian because the dietitian will be able to tell them what they can do [*about excess weightt gain*]. (Interviewee #5)

> In my own facility, I don't have dietitians working with me. Though the nurses and doctors have been trained to have the knowledge of the dietary aspect of the patient.

It is the duty of the nurses and the doctors to do that, to give them dietary education. (Interviewee #11)

Even in hospitals where a dietitian is present or a hospital that has a dietetics unit, the level of integration with a HIV clinic varies:

> …we presently have nutritionist as integral part of our health team in HIV clinic. And each of our patient goes through the nutritionist before he or she leaves the clinic. In fact, for every clinic visit, every patient goes through the nutritionist where they will check their weight, calculate the BMI, and of course counsel the patient, trying to identify any nutrition-related issues. (Interviewee #6)

> But healthcare providers in my clinic agreed that if there is any client who is obese that came to the hospital for his or her ARVs, that such client should go for nutritional counseling every visit. (Interviewee #9)

Apart from availability and level of integration of the dietitian, several others factors were described by the HCPs that may limit or promote the use of dietetic services by PLHIV who are on treatment. One of these factors was whether the PLHIV had other co-morbidities apart from HIV, for example PLHIV who were underweight or obese.

> First of all, we start by consulting a dietitian for them in order to direct them on the best food or meal to take. (Interviewee #7)

Another factor is the self-perception of the HCPs, especially the doctors and nurses, about their skills in providing adequate dietary counseling for PLHIV who need these services:

> But most healthcare providers will refer to a dietitian, but someone who has nutrition knowledge, you could talk about diet modification for the patient and write out proper diet plan for the person, to be able to lose weight or to be able to gain weight. Yeah. (Interviewee #4)

Finally, the ability or the likelihood of the PLHIV to consider using the dietetics unit, if referred, and the ability to pay out-of-pocket for this service are also limting factors described the HCPs:

> Most of the time when you refer them [*to a dietitian*] they say they don't want to see, they don't have money to see another person. But for those who accept, we refer them to see a dietitian. (Interviewee #13)

A mixed-method summary of results

To achieve a high degree of integration, the investigator aimed to connect the quantitative study finding with the qualitative study. While attempting to achieve this, the investigator also sought to expand on the understanding of the emergent HIV-obesity phenomenon. This was done by using the findings from the quantitative study, in conjunction with the social ecological model, to frame the semi-structured interview guide.

For example, at the individual level, the questions included in the KII sought to explore issues like why PLHIV wanted to gain weight, the long-term health issues that obese PLHIV may face, whether the HCPs and/or the PLHIV were concerned, and the specific future co-morbidities that the HCPs worried about the most in regards to the health of obese PLHIV. At the interpersonal level, a key question was the role that family members could play to support obese PLHIV. The third level of the social ecological model (organizational) explored the roles played by HCPs and the clinic setting as a whole. The probe questions explored the kind of counseling given for weight issues in the clinic and the available support structures. Finally, the fourth and fifth levels explored the role of the community, the culture, and the government policies. Issues like stigma, anti-stigma policies, and national guidelines for treatment were described by the HCPs.

In summary, we see that among the popualtion of PLHIV who commenced treatment, weight and BMI generally increases.The proportion of those who were underweight dropped from 17% to 5.8%, and overweight and obesity jointly increased from 20.7% to 37.3% over the 24 month period on ART. And, more importantly, this was generally corroborated by the HCPs who often encouraged and applauded this weight gain. The mixed approach also gave some deeper insights on the demographics of people who get screened at the different points of service in the hospital and the likely BMI category (see Appendix G).

In conclusion, the mixed-methods findings, characterized in the joint display table in Appendix G, summarize the changes for the different BMI categories and the qualitative findings (with exemplar quotes) that agree, diagree, or could possibly further explain the individual quantitative findings. This table was an adaptation of the ‘fit of data integration’ approach proposed by Fetters et al (2013), where ‘confirmation’ means agreement, ‘discordance’ means

disagreement, and ‘expansion’ describes a complementarity that provides additional insights about the topic.

Chapter 5: Discussion

This chapter summarizes a retrospective cohort data analysis of BMI trends among PLHIV who are on treatment and the key informant interviews on perception of healthcare providers about this trend. It also provides an explanation of the key findings in the light of contemporary knowledge of the topic and proposes solutions and a way forward.

Study Synthesis

In Nigeria, HIV screening can be carried out in the health facility or in the communities. A rapid expansion of HIV testing services (Avert, 2019) had led to increased access to care and treatment services after 2010. This service expansion was primarily funded by PEPFAR and the Global Fund for AIDS, TB, and Malaria [GFATM] (Avert, 2019). It is estimated that Nigeria has about 1.9 million PLHIV, with only about 1 million of them on treatment (UNAIDS, 2019b). After commencing treatment, PLHIV usually have a review for treatment success or failure (usually with CD4 count and or viral load, where available) at the 6-month mark, after which they are placed on a 2-3 monthly clinic visit for their ARV refills (Federal Ministry of Health [FMOH] Nigeria, 2016).

The first part of this study examined BMI data (height and weight) from 3530 PLHIV who participated in a free HIV care and treatment program in southeastern Nigeria between 2012 and 2017. The second part was a qualitative study using key informant interviews of HCPs who work in a HIV clinic in the same two states in southeastern Nigeria. The qualitative study was carried out between June and August 2019.

Discussion

First, the increase in weight among 74% of this population is similar to that of other studies previously conducted in Nigeria in which 83.1-85.3% gained weight (Akinboro et al., 2013; Denue et al., 2013). A study in South Africa also showed that 74% of the 230 PLHIV on treatment gained weight over a 12-month period (Hurley et al., 2011). Concerning BMI, a larger proportion of the participants in this study were in the normal weight category at treatment initiation (61%) and after 24 months on ART (56.9%). However, a significant drop in the proportion of those underweight from 17% to 5.8% shows that many of the PLHIV were having a "return to health" pattern (Jones et al., 2013; Kumar & Samaras, 2018). In another study in Nigeria, Denue and colleagues had documented a drop in the proportion of underweight participants from 27% to 11.4% after 30 months on ART (Denue et al., 2013). With earlier commencement of therapy in the current era of 'treat all', more normal weight people are coming into treatment with a concomitant drop in the number of people who come in underweight or wasted.

More interestingly, the increase in the proportion of overweight (17% to 27.8%) and obese (3.7% to 9.5%) participants is a cause for concern, especially in the light of the current understanding that the PLHIV themselves want to gain weight to dispel stigma, while the HCP applauds this weight gain. Other studies from Nigeria show similar trends. Ezechi and colleagues had documented that the prevalence of obesity among PLHIV on treatment in a large metropolitan clinic increased from 7.4% to 13.9% and then to 26.5%, after 2 and 5 years on ART, respectively (Ezechi at al., 2016). The same study also reported that the overweight participants increased from 19.6% to 35.7% at the end of the study (Ezechi at al., 2016).

Globally, this same trend has been recorded, albeit to higher or lesser degrees. Erlandson and colleagues studied PLHIV in nine countries and showed that after 3 years on ART, about one

fifth to one quarter of participants who were normal weight or underweight at baseline became overweight or obese. Overall, the proportion of overweight or obese clients increased from about 25% to 40% in 3 years in this sample (Erlandson at al., 2015). Other studies that have documented this increase in obesity across countries like the USA (Lakey et al., 2013; Tate et al., 2012), USA and Canada (Koethe et al., 2016), Cuba (Gil et al., 2011), and France (Bonnet et al., 2013). Some of the studies also show that the weight and BMI rise steeply in the first 12 months of treatment and begins to plateau after 24 months (Koethe et al., 2016; Lakey et al., 2013; Tate et al., 2012), similar to the findings from this study (Figure 4.1).

It is well documented that obesity has several deleterious effects on human health, even among the general HIV-negative population. These deleterious effects include increased risk of type 2 diabetes (T2DM), cardiovascular disease (CVD), hypertension, dyslipidemia, stroke, sleep apnea, and certain cancers (Flegal, Kit, Orpana, & Graubard, 2013; NHLBI, 1998; Ogden, Yanovski, Carroll, & Flegal, 2007; Reaven, 2011). But these concerns go beyond just the increase in weight and BMI. They become more alarming among PLHIV who are on treatment with ART. Several researchers have documented increased rates of T2DM and CVD among PLHIV on treatment. Compared to 5% of HIV-negative people who were diagnosed with T2DM, 14% and 7% of PLHIV who were on treatment and who were not on treatment, respectively, were diagnosed with T2DM (Brown et al., 2005; Willig & Overton, 2016). Additionally, for each unit gain in BMI (1 kg/m^2), there is a 12-14% increased risk of T2DM (Achhra et al., 2016; Herrin et al., 2016). Furthermore, compared to HIV-negative persons, PLHIV on treatment have about two times higher likelihood of being diagnosed with hypertension, myocardial infarction, and CVD (Grinspoon, 2014; Triant, Lee, Hadigan, & Grinspoon, 2007).

With this in mind, it is understandable that all the HCPs in this study mentioned either hypertension, diabetes, and/or arthritis as potential complications of obesity. While they understood these potential complications of obesity and overweight, many of the HCPs did not bring much urgency into their counselling, seeing obesity as a distant worry to be dealt with in the future. Perhaps, this is because the obese/overweight PLHIV themselves were not concerned or they (the PLHIV) were worried about losing weight and returning to their pre-treatment, HIV-stigma-inducing, weight (Duncan, Peters, Rivas, & Goff, 2019; Panza, Wing, & Wing, 2019).

It could also be that, perhaps, the HCPs saw weight gain as a sign of a successful treatment program or they perceived that the obese/overweight PLHIV were very few such that the problem did not rise to the priority level. According to one of the HCPs, "They are few and far between. They are not many. It is not that one person is not important, but it has not gotten to that alarming proportion, or significant proportion." (Interviewee #5).

In contrast, however, the quantitative data showed that about 1 in 10 PLHIV were obese and another 2-3 out of every 10 PLHIV on treatment were overweight after 2 years on ART. Additionally, while only less than 1% (n=2) of those underweight at baseline moved to obesity at the end, 4.3% (n=47) of normal weight participants and 22.7% (n=78) of overweight participants, respectively, became obese at 24 months.

This calls into question the perceptions of what obesity, overweight, and normal weight mean when HCPs do not actively compute the BMI for every client. While a few of the HCPs in this study acknowledged the clinical challenges that come with obesity, there was no active tracking of the BMI, except with the PLHIV who had comorbidities associated with obesity. In a study in sub-Saharan Africa, silhouettes of the BMI categories were shown to HIV-positive women to elicit their preferences for body shapes. Of the 61 women, none chose the underweight

silhouette, while the normal weight, overweight, obese, and morbidly obese silhouettes were preferred by 18%, 67%, 11%, and 3% of the women, respectively (Croffut et al., 2017). In fact, none of the women described the normal weight silhouette as healthy (Croffut et al., 2017).

This reality-perception divide of obesity may lead us to ponder certain aspects of HIV care delivery. One is that visual assessments do not work. Until the BMI is computed, one never knows what one would find. Two, perhaps, people from sub-Saharan Africa, have shifted their perception of what the BMI categories mean, or ought to mean, based on cultural needs. Perhaps, internally, BMI categories like normal weight, overweight, obese, and morbidly obese are translated as underweight, normal weight, overweight, and obese, respectively, in the cultural African mind. But what does this reality-perception divide mean for obesity research, especially HIV obesity research? The implications may be far reaching. Perhaps it is time to re-open the 2004 debate about appropriate body-mass index for non-white populations (World Health Organization [WHO] expert consultation, 2004).

Potential Solutions

While the challenges might seem daunting, there are potential ways of addressing them to ensure a higher quality of life (QoL) for PLHIV who are on treatment. Using the social ecological model (Brofenbrenner, 1977; Golden & Earp, 2012), and based on the findings from this study, the investigator proposes some solutions below. Though these solutions are proposed at different levels of the social ecological model, in reality they can function on multiple levels.

First, at the individual level, the PLHIV need to be educated about the potential future challenges of excess weight gain while on ART. This education should be designed, very early, to move the PLHIV beyond knowledge to self-efficacy (Golden & Earp, 2012). PLHIV on treatment

should know to ask HCPs about their BMI, in addition to their weight, at every clinic visit, even if the HCP forgets to mention it. Additionally, and more importantly, PLHIV should learn, or be taught, how to compute their BMI, access a BMI chart (online), and interpret their own BMI by themselves.

Second, at the interpersonal level, the support of friends and family cannot be overemphasized. Family and friends provide the primary support structure, hence they should ensure that they provide an environment that is stigma-free, both as regards stigma against HIV or stigma against obesity. More importantly, PLHIV who are obese should not be treated any differently from HIV-negative obese people. Additionally, family and friends provide the critical social network that will support the lifestyle changes (diet, physical activity, and behavioral skills) that may be adopted by the PLHIV on his or her path to optimal BMI and better quality of life (Golden & Earp, 2012; Panza et al., 2019).

Third, at the institutional level, HCPs play a core role towards improving the quality of life of PLHIV on treatment. Starting from their perceptions of obesity among PLHIV, attitudes towards obese PLHIV, and their capacity to render high quality care, they provide a critical link to information and treatment options for the PLHIV. HCPs will need to educate PLHIV about excess weight gain while on treatment and provide links to information, care, and treatment, either on-site or by referral. Internal processes within the clinic also need to be put in place. A quality improvement program to address documentation issues for BMI, weight, and height is critical. Additionally, continuous medical education for the HCPs will ensure that they are abreast of current information or are provided a refresher of what they have already learned.

In addition, dietitians need to be integrated into the normal clinic routine (Willig, Wright, & Galvin, 2018). In the early days, dietitians may have been integrated into HIV clinics because

of wasted and underweight clients, but now their roles should begin to shift to address needs related to overweight and obesity. Dietitians will also need to provide support to other HCPs on how to structure messages on weight gain that can be delivered to PLHIV at commencement of treatment and all through the continuum of care (Panza et al., 2019; Willig et al., 2018).

Finally, at the level of the larger community and public policy, stigma issues need to be addressed, both culturally, and with legal frameworks. PLHIV who are obese may be subject to multiple layers of stigma, either due to the HIV (if their status is known), due to obesity (which is obvious), or due to both HIV and obesity. The availability of community resources that can support lifestyle changes (diet, physical activity, and behavioral skills) are critical (Golden & Earp, 2012; Panza et al., 2019). The same goes for enforcement of anti-stigma and anti-discrimination laws that can help reduce the challenges that PLHIV with obesity face.

Chapter 6: Conclusion

Future Implications for Public Health

To the investigator's knowledge, this is the first study in sub-Saharan Africa that explores the interface between HIV and obesity using a mixed-methods design. The results will help HCPs and PLHIV to further understand the trends of obesity and overweight among PLHIV on treatment and how best to support obese PLHIV on treatment. The results also provide more in-depth understanding of this emergent phenomenon through the lens of the healthcare providers who care for PLHIV.

The findings of increasing BMI among three-quarters of the study participants, which was further corroborated by the HCPs, raises several concerns and questions for future consideration. One, how do HCPs construct and communicate messages about the potential future weight gain challenges that PLHIV on treatment may face? Two, in constructing these messages, how do HCPs communicate culturally-appropriate weight gain and BMI messages? Three, how much weight gain is too much? And, finally, how do the clinical and public health communities begin to educate about and address the numerous cardio-metabolic issues associated with HIV and ART, especially in the context of an aging population of PLHIV?

The answers to these questions will require a committed effort of everyone concerned, to raise awareness, remove complacency, and actively address an emerging problem within sub-Saharan Africa. This region of the world simply cannot afford to pile on more health challenges. All partners, first among whom are the PLHIV themselves, in addition to the HCPs, friends and family, the community, and the government, need to collaborate to address this double epidemic. A cooperative effort will ensure that PLHIV who are on treatment will receive services that will help them to achieve the highest possible quality of life (QoL).

Limitations to the Study

This study is not without its limitations. First, the quantitative study was based on secondary data which had some degree of missing data, which is also a problem with longitudinal studies. Missing data could have decreased the power to detect differences, and underestimate or overestimate effect sizes (Ayilara, Zhang, Sajobi, Sawatzky, Bohm, & Lix, 2019). Additionally, time and resource constraints did not allow a more elaborate design to study this topic. A prospective cohort study would have yielded better results as data on diet, physical activity levels, and adverse events could have been collected from the participants. These data would have provided additional information which could have been connected to the qualitative study.

Second, the quantitative data and the qualitative data were not collected concurrently. The quantitative data covers 4 years (2012 to 2016), while the qualitative data was collected in 2019 (June – August) from HCPs with 1 – 12 years of experience in the HIV clinics. This non-concurrence may have affected the mixed-methods study, not allowing adequate number of connections to be tested and described. However, the investigator has worked within these limitations to expand the scope of the qualitative phase beyond what the quantitative phase tested. This expansion has generated very deep insights and unexpected findings, thereby meeting the broad aims of this mixed-methods study.

Third, the investigator planned to travel to Nigeria in June 2019 to conduct the qualitative interviews in-person. However, delays in travel plans and other mitigating factors prevented this. Hence, the interviews were conducted over the telephone. Some researchers believe phone interviews are inferior (Irvine et al., 2013; Novick, 2008). However, other researchers have showed that despite some of the perceived disadvantages, phone interviews have numerous selling points,

like the ability to transcend distance, cost and resource savings, convenience, and the preservation of participants' anonymity (Cachia & Millward, 2011; Sturges & Hanrahan, 2004).

Finally, the investigator would have preferred to interview PLHIV who are obese/overweight instead of, or in addition to, the HCPs. The information from the PLHIV on treatment would have probably been more explanatory. However, potential IRB delays, access to this population, and the sensitive nature of the topic, would have made recruitment into the study very difficult for the investigator and increased the time to complete the study. To address these issues, the data from the HCPs will serve as a sturdy platform to define constructs to be tested when engaging directly with the PLHIV in the follow-up phase of this research.

Conclusion

The increasing prevalence of overweight/obesity seen among PLHIV on treatment is a cause for concern. Healthcare providers (HCPs) who deliver the needed care for PLHIV should be aware of the clients' individual and collective needs so as to ensure that the clients achieve the maximum possible quality of lived experience. The perceptions of HCPs on the QoL of obese/overweight PLHIV on treatment is paramount to supporting the PLHIV in their bid for higher QoL. HCPs, who render care to PLHIV, and the families of PLHIV, will benefit from further understanding the needs of this population to support them towards achieving their individual QoL goals.

Appendices

Appendix A: Summary table of 30 eligible studies for the systematic review

Studies Reporting Mean BMI (20 Studies)							
Author	**Country**	**Study Design**	**Study Participants (% Female)**	**Age (Years)**	**Follow-up Time (Years)**	**Baseline BMI (kg/m^2) – change to difference**	**Baseline CD4 (cells/µl)**
Akinboro et al., 2013	Nigeria	Cohort (Prospective)	55	35 ± 8.8	1	20.65 ± 2.89	121.5 ± 84.83
Bala et al., 2016	India	Cohort (Prospective)	120	33.2	1	17.33 ± 3.33	
Bezabhe et al., 2015	Ethiopia	Cohort (Prospective)	211 (60)	32** (IQR: 27,38)	1	20.0*	183 (IQR: 94, 252)
Bonnet et al., 2013	France	Cohort (Prospective)	35 (37)	39.2*	1.75	23.8*	240*
Denue et al., 2013	Nigeria	Cohort (Prospective)	120 (61)	39.0*	2.5	21.39 ±3.96	224
Erlandson et al., 2015	Multi-country	RCT	1045 (46)	34** (IQR: 29,41)	3	23.2 ±4.4	167 (IQR: 89, 228)
Gil et al., 2011	Cuba	Cohort (Prospective)	56	Range: 30-50	0.5	24.1 (SEM=7.2)	
Gupta et al., 2011	India	Cohort (Prospective)	68 (16)	35.9 ±9.4	0.5	18.3 ±2.8	109
Herrin et al., 2016	USA	Cohort (Retrospective)	7177 (3)	50** (IQR: 43,56)	1	25.1 ±4.6	218 (IQR: 85, 338)

Author	Country	Study Design	Study Participants (% Female)	Age (Years)	Follow-up Time (Years)	Baseline BMI (kg/m^2)	Baseline CD4 (cells/µl)
Hurley et al., 2011	South Africa	Cohort (Prospective)	230 (63).	35** (IQR: 29,39)	1	23.8*	97 (IQR: 44, 169)
Lakey et al., 2013	USA	Cohort (Retrospective)	92 (16)	38.2 ±10.5	1	26.4 ±6.8	219.3 ±181.0
Moyle et al., 2014	Multi-country	RCT	224 (32)	36*	2	23.6*	203.5*
Mutimura et al., 2015	Rwanda	Cohort (Prospective)	371 (100)	35.2 ±7.1	2.7	21.3 ± 3.9	
Ncube et al., 2008	Zimbabwe	Cohort (Prospective)	72 (54)	38** (IQR: 32,43)	0.5	20.4	80
Saghayam et al., 2007	India	Cohort (Prospective)	190 (15)	35 ±7	0.5	20.1 ± 3.3	175 ± 102
Sarna et al., 2008	Kenya	RCT	234 (64)	37.1*	1.5	20.7*	96
Tang et al., 2011	Vietnam	Cohort (Prospective)	99 (None)	31.7 ± 4.8	1	19.1 ± 2.1	96.7 ± 67.6
Tate et al., 2012	USA	Cohort (Retrospective)	681 (22)	38	2	25.4 ± 6.1	
Tieno et al., 2015	Burkina Faso	Cohort (Prospective)	144	37.4 ±9.4	0.75	19.6	143.7 ±108.5
van Oosterhout et al., 2010	Malawi	Cohort (Retrospective)	104 (48)	36	0.5	16.6 ±1.5	112 ±101

Studies Reporting Median BMI (10 Studies)							
Author	**Country**	**Study Design**	**Study Participants (% Female)**	**Age (Years)**	**Follow-up Time (Years)**	**Baseline BMI (kg/m^2)**	**Baseline CD4 (cells/µl)**
Abrahams et al., 2016	South Africa	Cohort (Prospective)	187 (71)	33** (IQR: 27,39)	2	24.8	156 (IQR: 110,196)
Achhra et al., 2016	Multi-country	Cohort (Prospective)	9321 (25)	39.6 ±10.1	5	23 (IQR: 20.9, 25.5)	254 (IQR: 154,342)
Dirajlal-Fargo et al., 2016	USA	RCT	328 (10)	36	2	25	349
Evans et al., 2013	South Africa	RCT	19 (63)	34** (IQR: 30,43)	0.5	19.3 (IQR: 18.4, 21.3)	107 (IQR: 63, 165)
George et al., 2009	South Africa	Cohort (Prospective)	42 (64)	34.4	2.1	22.7 (IQR = 2.55)	93 (IQR=107)
Grant et al., 2016	USA	Cohort (Prospective)	97 (14)	40** (IQR: 31,44)	7.5	24 (IQR: 22, 27)	247 (IQR: 130,333)
Guehi et al., 2016	Côte d'Ivoire	RCT	755 (78)	35** (IQR: 29,42)	2	22.3 (IQR: 20, 25.2)	442 (IQR: 348,541)
Huisin 't Veld et al., 2015	Multi-country	Longitudinal data analysis	205,571 (61).	35** (IQR: 30,42)	2	20.0 (IQR: 17.9, 22.5)	128 (IQR: 61, 199)
Koethe et al., 2016	Canada and USA	Cohort (Prospective)	14,084 (17)	40** (IQR: 33,47)	3	23.8 (in 1998); 24.8 (in 2010)	241 (IQR: 94, 377)
Messou et al., 2008	Côte d'Ivoire	Cohort (Prospective)	622 (76)	34** (IQR: 29,39)	0.5	20.8 (IQR: 19.1, 22.6)	250 (IQR: 185,315)

*Weighted mean ** Median values reported

Appendix B. Quality ratings for 30 eligible studies using the Effective Public Health Practice Project (EPHPP) tool.

Author	Selection Bias	Study Design	Confounders	Blinding	Data Collection	Withdrawals	Global Rating
Abrahams et al., 2016	Moderate	Moderate	Strong	Moderate	Moderate	Weak	Moderate
Achhra et al., 2016	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Strong
Akinboro et al., 2013	Moderate	Moderate	Weak	Moderate	Strong	Moderate	Moderate
Bala et al., 2016	Moderate	Moderate	Weak	Moderate	Moderate	Strong	Moderate
Bezabhe et al., 2015	Moderate	Moderate	Weak	Moderate	Moderate	Strong	Moderate
Bonnet et al., 2013	Strong	Strong	Strong	Moderate	Moderate	Weak	Moderate
Denue et al., 2013	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Strong
Dirajlal-Fargo et al., 2016	Moderate	Strong	Strong	Moderate	Moderate	Strong	Strong
Erlandson et al., 2015	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Evans et al., 2013	Moderate	Strong	Strong	Moderate	Moderate	Weak	Moderate
George et al., 2009	Moderate	Moderate	Weak	Moderate	Strong	Strong	Moderate

Author	Selection Bias	Study Design	Confounders	Blinding	Data Collection	Withdrawals	Global Rating
Gil et al., 2011	Moderate	Moderate	Weak	Moderate	Moderate	Weak	Weak
Grant et al., 2016	Moderate	Moderate	Strong	Moderate	Moderate	Weak	Moderate
Guehi et al., 2016	Moderate	Strong	Strong	Moderate	Strong	Moderate	Strong
Gupta et al., 2011	Moderate	Moderate	Weak	Moderate	Moderate	Weak	Weak
Herrin et al., 2016	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Strong
Huisin 't Veld et al., 2015	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Strong
Hurley et al., 2011	Moderate	Moderate	Strong	Moderate	Strong	Moderate	Strong
Koethe et al., 2016	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Strong
Lakey et al., 2013	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Strong
Messou et al., 2008	Moderate	Moderate	Strong	Moderate	Strong	Strong	Strong
Moyle et al., 2014	Moderate	Strong	Strong	Moderate	Moderate	Strong	Strong
Mutimura et al., 2015	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Strong

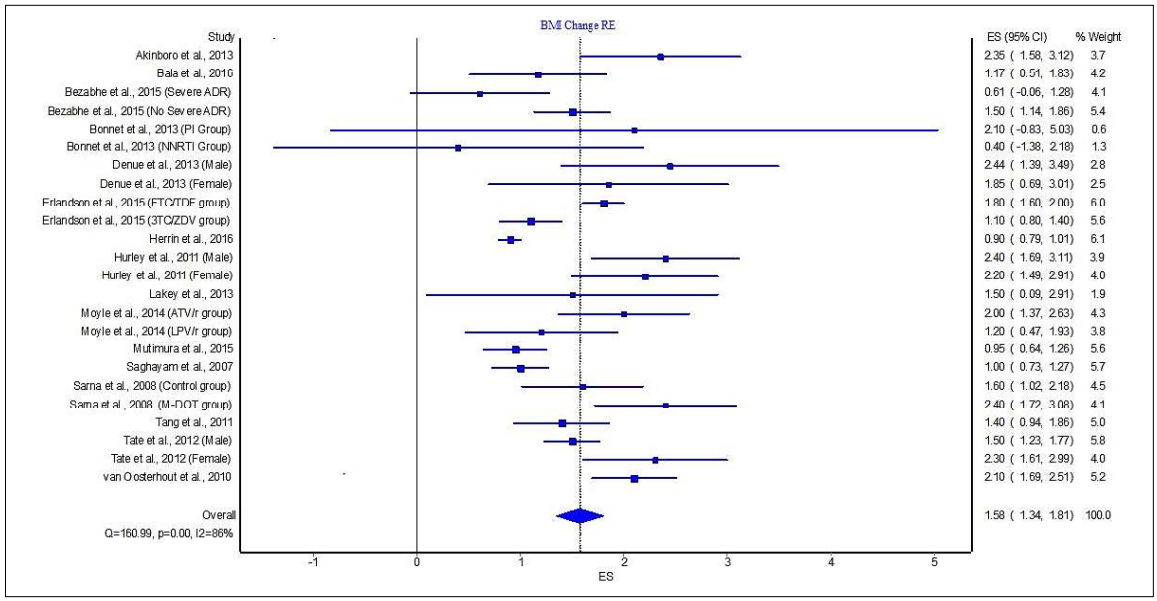
Author	Selection Bias	Study Design	Confounders	Blinding	Data Collection	Withdrawals	Global Rating
Ncube et al., 2008	Moderate	Moderate	Weak	Moderate	Moderate	Moderate	Moderate
Saghayam et al., 2007	Moderate	Moderate	Moderate	Moderate	Strong	Weak	Moderate
Sarna et al., 2008	Strong	Strong	Strong	Moderate	Moderate	Moderate	Strong
Tang et al., 2011	Moderate	Moderate	Strong	Moderate	Strong	Moderate	Strong
Tate et al., 2012	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Strong
Tieno et al., 2015	Moderate	Moderate	Weak	Moderate	Moderate	Moderate	Moderate
van Oosterhout et al., 2010	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Strong

Appendix C. Sensitivity analysis for meta-analysis of 18 studies on HAART and BMI changes

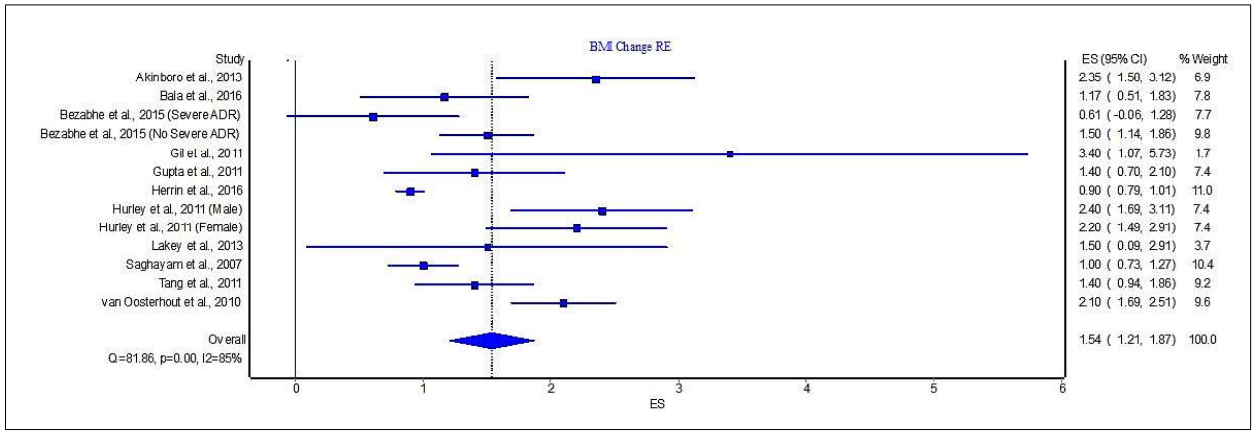
Excluded Study	Pooled Effect Size	LCI 95%	HCI 95%	Cochran Q	P-Value	I^2	I^2 LCI 95%	I^2 HCI 95%
Akinboro et al, 2016	1.55	1.33	1.78	156.68	<.001	84.68	78.50	89.09
Bala et al., 2016	1.60	1.37	1.84	164.35	<.001	85.40	79.60	89.55
Bezabhe et al., 2015 (Severe ADR group)	1.62	1.39	1.85	160.82	<.001	85.08	79.11	89.34
Bezabhe et al., 2015 (No Severe ADR group)	1.59	1.35	1.83	162.62	<.001	85.24	79.36	89.45
Bonnet et al., 2013 (PI Group)	1.58	1.35	1.81	164.10	<.001	85.37	79.56	89.53
Bonnet et al., 2013 (NNRTI Group)	1.60	1.37	1.83	163.53	<.001	85.32	79.48	89.50
Denue et al., 2013 (Male)	1.56	1.33	1.79	159.49	<.001	84.95	78.91	89.26
Denue et al., 2013 (Female)	1.58	1.35	1.81	163.40	<.001	85.31	79.47	89.49
Erlandson et al., 2015 (FTC/TDF group)	1.57	1.34	1.79	132.14	<.001	81.84	74.08	87.27
Erlandson et al., 2015 (3TC/ZDV group)	1.61	1.37	1.85	163.33	<.001	85.31	79.46	89.49
Gil et al., 2011	1.57	1.34	1.79	161.16	<.001	85.11	79.15	89.36
Gupta et al., 2011	1.59	1.36	1.82	164.25	<.001	85.39	79.58	89.54
Herrin et al., 2016	1.62	1.40	1.83	94.10	<.001	74.49	62.32	82.74
Hurley et al., 2011 (Male)	1.55	1.32	1.78	154.33	<.001	84.45	78.14	88.94
Hurley et al., 2011 (Female)	1.56	1.33	1.79	157.49	<.001	84.76	78.62	89.14
Lakey et al., 2013	1.59	1.36	1.82	164.30	<.001	85.39	79.59	89.55
Moyle et al., 2014 (ATV/r group)	1.57	1.33	1.80	159.05	<.001	84.91	78.85	89.23

Moyle et al., 2014 (LPV/r group)	1.60	1.37	1.83	164.39	<.001	85.40	79.60	89.55
Mutimura et al., 2015	1.62	1.38	1.86	160.40	<.001	85.04	79.05	89.32
Saghayam et al., 2007	1.62	1.38	1.86	160.78	<.001	85.07	79.10	89.34
Sarna et al., 2008 (Control group)	1.58	1.35	1.82	163.06	<.001	85.28	79.42	89.47
Sarna et al., 2008 (M-DOT group)	1.55	1.32	1.77	153.44	<.001	84.36	78.00	88.88
Tang et al., 2011	1.59	1.36	1.83	164.03	<.001	85.37	79.55	89.53
Tate et al., 2012 (Male)	1.59	1.35	1.83	160.96	<.001	85.09	79.13	89.35
Tate et al., 2012 (Female)	1.55	1.33	1.78	155.62	<.001	84.58	78.34	89.02
van Oosterhout et al., 2010	1.55	1.33	1.78	147.50	<.001	83.73	77.03	88.47

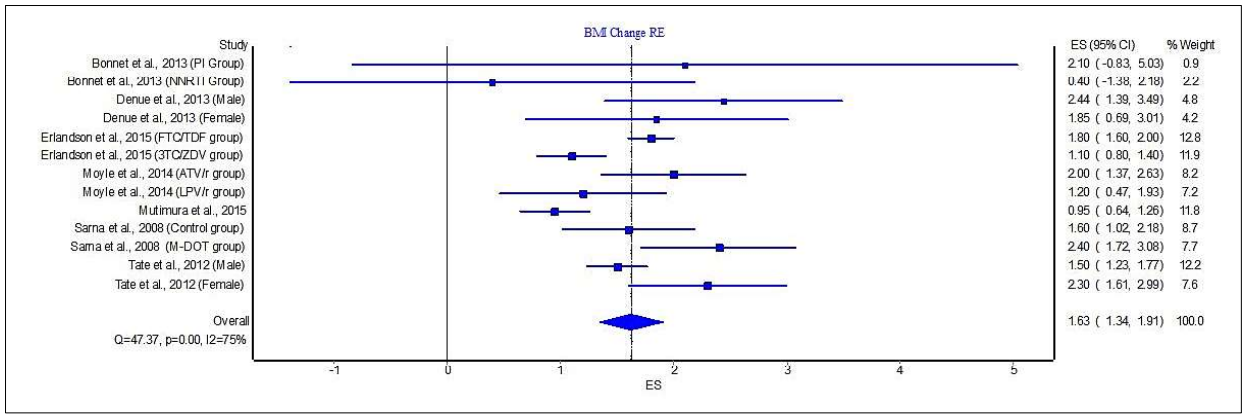
Appendix D. Supplementary Forest plots



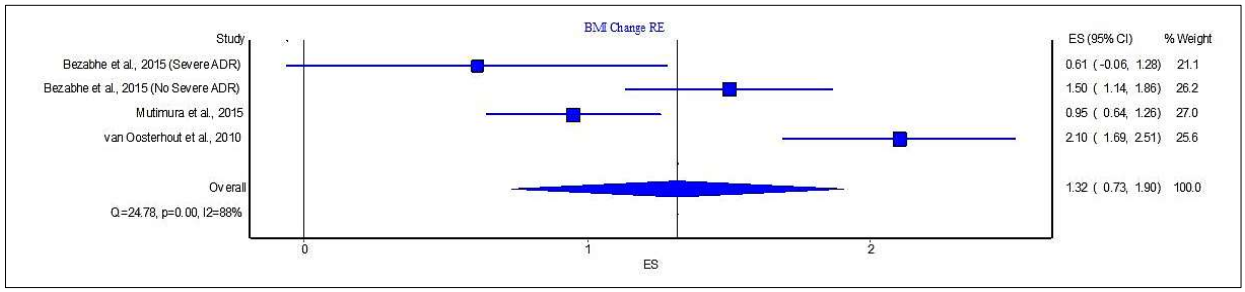
Supplementary Figure 1: Forest plot for HAART and BMI change (without the 2 weak studies)



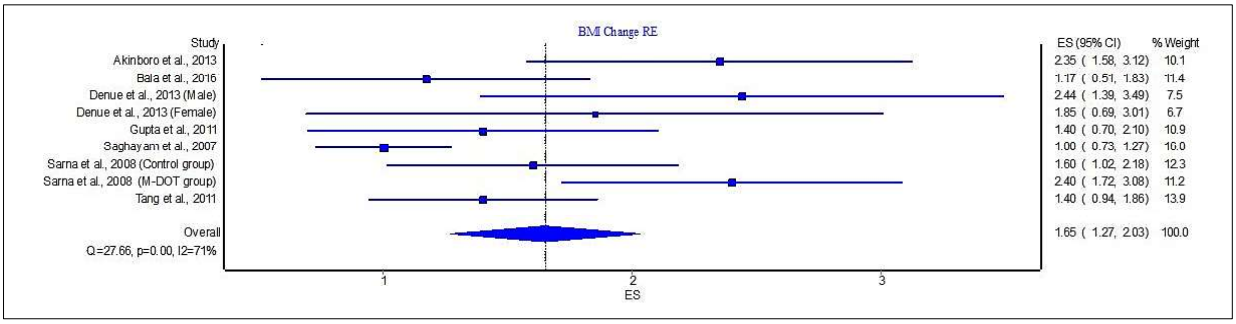
Supplementary Figure 2: Forest plot for HAART and BMI change (studies less than 1 year follow-up)



Supplementary Figure 3: Forest plot for HAART and BMI change (studies greater than 1 year follow-up)



Supplementary Figure 4: Forest plot for HAART and BMI change (low-income countries only)



Supplementary Figure 5: Forest plot for HAART and BMI change (low-middle income countries only)

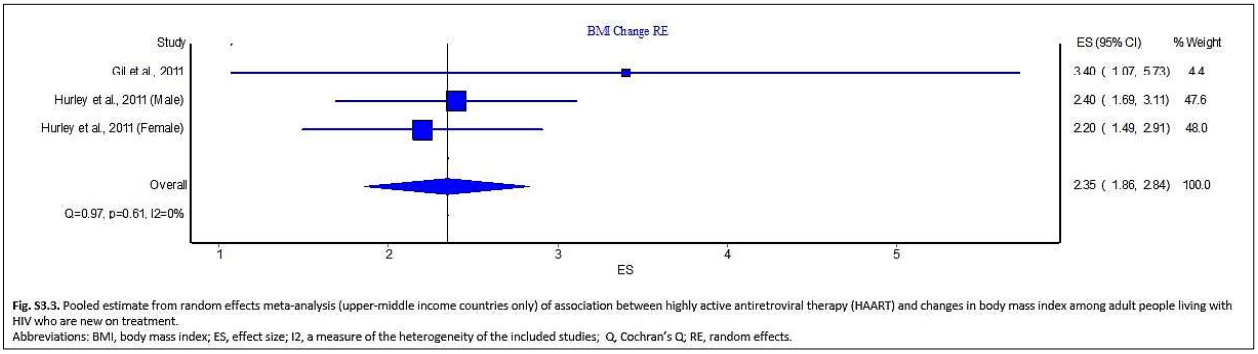


Fig. S3.3. Pooled estimate from random effects meta-analysis (upper-middle income countries only) of association between highly active antiretroviral therapy (HAART) and changes in body mass index among adult people living with HIV who are new on treatment.
Abbreviations: BMI, body mass index; ES, effect size; I2, a measure of the heterogeneity of the included studies; Q, Cochran's Q; RE, random effects.

Supplementary Figure 6: Forest plot for HAART and BMI change (upper-middle income countries only)

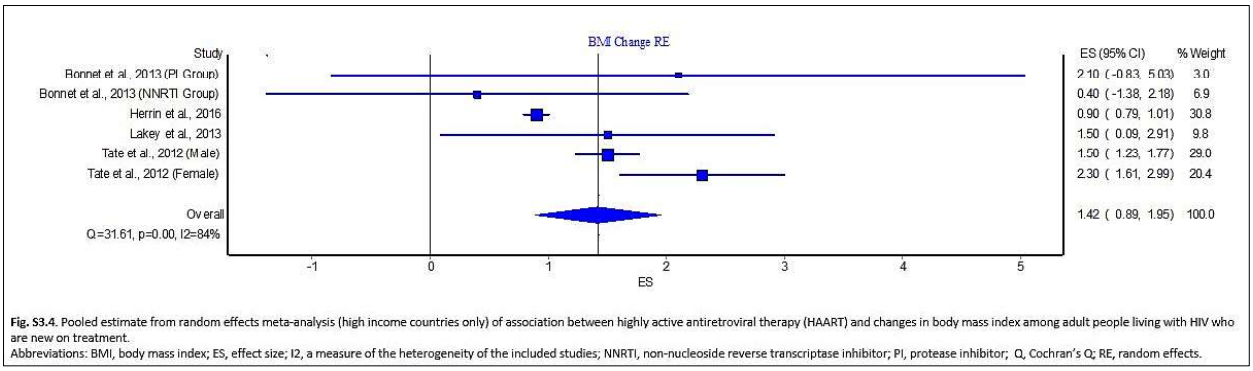


Fig. S3.4. Pooled estimate from random effects meta-analysis (high income countries only) of association between highly active antiretroviral therapy (HAART) and changes in body mass index among adult people living with HIV who are new on treatment.
Abbreviations: BMI, body mass index; ES, effect size; I2, a measure of the heterogeneity of the included studies; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Q, Cochran's Q; RE, random effects.

Supplementary Figure 7: Forest plot for HAART and BMI change (high-income countries only)

Appendix E. Semi-structured Interview Guide

RESEARCH PROTOCOL TITLE: Perceptions of health care providers about overweight/obesity among people living with HIV who are on treatment in Nigeria.

Introduction: Hello, my name is John Olawepo. I am a medical doctor from Nigeria currently doing my PhD at the University of Nevada Las Vegas. I would like to have a discussion about changes in weight and body mass index (BMI) among people living with HIV (PLHIV) who are on treatment in Nigeria. BMI is usually measured by dividing a person's weight (in kilograms) by the square of the person's height (m^2). This result is then classified as either underweight (BMI <18.5 kg/m^2); normal weight (BMI 18.5-24.9 kg/m^2); overweight (BMI 25.0-29.9 kg/m^2); or obese (BMI ≥30 kg/m^2).

Preliminary Questions

1. What is your profession?
2. What is your gender?
3. How many years' experience do you have in a HIV clinic?

Interview Questions

1. Explain your daily routine managing HIV clients?
2. What are some of the hurdles or barriers to providing care for people living with HIV (PLHIV)?
3. In your opinion, why do you think PLHIV want to gain weight or lose weight?
    a. Why? Please explain.
4. From your years of caring for PLHIV, do you encourage or discourage PLHIV about gaining or losing weight?
    a. Please describe your experiences.
    b. What might that discussion sound like?

5. What types of concerns do you have about PLHIV gaining too much weight?
    a. Can you elaborate?
6. What types of long term health issues could PLHIV face due to being overweight or obese?
    a. How do you address these health issues?
7. We know that there is stigma against obese or overweight people in the general population. Do you have concerns about stigma against PLHIV who are overweight or obese?
8. What discussions have healthcare providers had concerning PLHIV who are overweight or obese?
9. From your interactions with PLHIV who are overweight/obese, how do you think they perceive themselves as regards having a weight issue?
    a. Do they ever bring up weight as a concern? Please elaborate
10. When you consult with PLHIV who are overweight/obese, can you kindly describe how you counsel them about weight issues?
11. How could family members support PLHIV who are overweight or obese?
12. How could healthcare providers support PLHIV who are overweight or obese?
13. There are cases of PLHIV who also have other chronic illnesses (like diabetes, hypertension etc.) for which they are on medications. In your opinion, how do you think these PLHIV cope with their medications for both the HIV and the other illnesses at the same time?
14. Culturally, we tend to see slim/thin people as sick people. How do you think we can change this?
15. Is there anything else you can think of that you would like to share on the topic that I haven't asked you about?

Appendix F. Glossary of Colloquial Terms from Key Informant Interviews

1. *Abacha*: Local snack made from cassava.
2. *Abeg*: Please or kindly.
3. *Akpu*: Traditional food made from cassava. A major staple diet in Nigeria. Same as *fufu*.
4. *Belle:* Local slang for tummy or abdomen. Also used to describe truncal obesity.
5. Chemist shop: A local dispensary where people buy over-the-counter medications. It is usually privately owned.
6. Chief: Used colloquially as a sign of respect. It can mean sir or boss.
7. *Corper:* A participant in the mandatory one-year post-bac national service program in Nigeria
8. *Ehehn:* 'Really?' or 'Okay, so'
9. *"e no dey show for face":* A common phrase associated with the HIV epidemic. When translated, it means, HIV "does not show on people's faces". The only way to know who has HIV is to get tested.
10. Flash: To dial someone on the phone and immediately terminate the call when it starts ringing or when the person picks the call. It is usually used as a reminder or as a prank.
11. *Fufu:* Cassava flour paste. A major food staple in Nigeria. Same as *akpu*.
12. *Garri*: A coarse flour made from cassava. A major food staple in Nigeria.
13. *GoTv:* A subscription-based cable TV company in Nigeria.
14. *Lepa*: Used to refer to someone that is very thin or severely underweight.
15. Matron: A senior nurse in a hospital ward or clinic, usually the head nurse.
16. *Na:* Usually used for emphasis.
17. Naira: The official currency used in Nigeria.

18. *Nna*: A friendly way to address someone. It could mean ‘my brother’. It is commonly used in the southwestern part of Nigeria.
19. *Oga:* Mister or boss or leader.
20. *OND:* Ordinary National Diploma. A college degree similar to a 2-year associate’s degree.
21. *Omugo*: When a family member (usually the mother or mother-in-law), friend, or relative stays with a woman who has recently been delivered of a baby. The family member or friend provide care and support for the new mother and baby during this period. Also called *mugomugo*.
22. *Ooo*: Usually used to emphasize the preceding word or phrase.
23. *Orobo*: Used to refer to someone that is very fat or obese.
24. *Oya:* Go ahead or go on or let’s go or come on.
25. *Plumpy:* Plump.
26. Plumpy nuts: A ready-to-use-food (RTUF) that is very dense in nutrients. Usually used to treat malnutrition. It is often supplied by donor funded projects.
27. *Purging*: Passing water stool or bouts of diarrhea.
28. *Sef:* Another way of saying ‘even’.
29. *Semo*: A fine flour made from durum wheat. A major food staple in Nigeria.
30. Soyaplus: Nutritional food made locally from soya beans. Usually used to treat malnutrition.
31. *Uhn uhn uhn uhn*: No, no, no, no.
32. *Wahala*: Trouble or problem or challenge.
33. *Yab*: To insult or to make fun of or to tease.

Appendix G. A joint display showing integration of results from a mixed method study of obesity among people living with HIV

	Quantitative findings		**Qualitative findings (data fit, with exemplar quotes)**		
	Proportion at Baseline	Proportion at 24 months	Confirmation	Discordance	Expansion
Under-weight	17.0%	5.8%	I encourage them to gain…not to gain too much weight, but to be of moderate weight. (**Interviewee #3**)	…. 55% of them come in with that underweight because they are already emaciated because of that chronic illness. (**Interviewee #13**)	Well, the category of the patient's weight at the time they... commence treatment depends on the route through which the person was enrolled ... For those of them who are positive and pregnant, most of them will not likely be underweight or wasted, such people will usually have a normal weight...people who come to do basic pre-marital screening test including HIV. Some of them are diagnosed as positive... Such people would not usually have very low weight, it may be normal and or overweight. But for some patients...they come to screen for HIV because they seem to be showing symptoms suggestive of HIV. They have lost a lot of weight, they have tried to treat other medical conditions but have not gotten better, so they come in a very bad way, severely wasted. Such patients will usually start treatment and will be very very low weight. (**Interviewee #15**)

Normal weight	61.0%	56.9%	Okay, so I will say I see more of normal weight, then underweight, and then overweight. In that order. But more of normal weight. (**Interviewee #10**)		Usually most people come within the normal weight or just overweight range. By the time they start treatment and they start getting tilted towards the level of obesity. (**Interviewee #14**)
Over-weight	17.0%	27.8%	There are more people gaining weight than people losing weight. (**Interviewee #1**)	Well, gaining weight while on treatment, we would appreciate it. But if it is becoming too much, which is rare, if somebody is really underweight and is gaining weight to get to the point of being overweight within the timeframe of initiation of therapy, it's really rare. I have not really seen much of that. (**Interviewee #10**)	
Obese	3.7%	9.5%			They are few and far between. They are not many. It is not that one person is not important, but it has not gotten to that alarming proportion, or significant proportion. (**Interviewee #5**)

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UNLV Biomedical IRB - Exempt Review
Exempt Notice

DATE:	January 8, 2019
TO:	Jennifer Pharr
FROM:	Office of Research Integrity - Human Subjects
PROTOCOL TITLE:	[1362106-1] Prevalence and trends of obesity among HIV positive clients on treatment
ACTION:	DETERMINATION OF EXEMPT STATUS
EXEMPT DATE:	January 8, 2019
REVIEW CATEGORY:	Exemption category # 4

Thank you for your submission of New Project materials for this protocol. This memorandum is notification that the protocol referenced above has been reviewed as indicated in Federal regulatory statutes 45CFR46.101(b) and deemed exempt.

We will retain a copy of this correspondence with our records.

PLEASE NOTE:
Upon final determination of exempt status, the research team is responsible for conducting the research as stated in the exempt application reviewed by the ORI - HS and/or the IRB which shall include using the most recently submitted Informed Consent/Assent Forms (Information Sheet) and recruitment materials.

If your project involves paying research participants, it is recommended to contact Carisa Shaffer, ORI Program Coordinator at (702) 895-2794 to ensure compliance with the Policy for Incentives for Human Research Subjects.

Any changes to the application may cause this protocol to require a different level of IRB review. Should any changes need to be made, please submit a **Modification Form**. When the above-referenced protocol has been completed, please submit a **Continuing Review/Progress Completion report** to notify ORI HS of its closure.

If you have questions, please contact the Office of Research Integrity - Human Subjects at IRB@unlv.edu or call 702-895-2794. Please include your protocol title and IRBNet ID in all correspondence.

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UNLV Biomedical IRB - Exempt Review
Exempt Notice

DATE:	April 23, 2019
TO:	Jennifer Pharr, PhD
FROM:	Office of Research Integrity - Human Subjects
PROTOCOL TITLE:	[1425703-1] Perceptions of health care providers about overweight/obesity among people living with HIV who are on treatment in Nigeria
ACTION:	DETERMINATION OF EXEMPT STATUS
EXEMPT DATE:	April 23, 2019
REVIEW CATEGORY:	Exemption category # 2

Thank you for your submission of New Project materials for this protocol. This memorandum is notification that the protocol referenced above has been reviewed as indicated in Federal regulatory statutes 45CFR46.101(b) and deemed exempt.

We will retain a copy of this correspondence with our records.

PLEASE NOTE:
Upon final determination of exempt status, the research team is responsible for conducting the research as stated in the exempt application reviewed by the ORI - HS and/or the IRB which shall include using the most recently submitted Informed Consent/Assent Forms (Information Sheet) and recruitment materials.

If your project involves paying research participants, it is recommended to contact Carisa Shaffer, ORI Program Coordinator at (702) 895-2794 to ensure compliance with the Policy for Incentives for Human Research Subjects.

Any changes to the application may cause this protocol to require a different level of IRB review. Should any changes need to be made, please submit a **Modification Form**. When the above-referenced protocol has been completed, please submit a **Continuing Review/Progress Completion report** to notify ORI HS of its closure.

If you have questions, please contact the Office of Research Integrity - Human Subjects at IRB@unlv.edu or call 702-895-2794. Please include your protocol title and IRBNet ID in all correspondence.

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Curriculum Vitae

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EDUCATION

May 2020 **PhD Public Health**

University of Nevada Las Vegas (UNLV), United States

Nov. 2014 **MSc Public Health**

London School of Hygiene & Tropical Medicine, United Kingdom

Feb. 2008 **Bachelor of Medicine and Surgery (MBBS)**

College of Medicine, University of Ilorin, Nigeria

PROFESSIONAL EXPERIENCE

2019 - Date Part-Time Instructor, UNLV School of Public Health

2019 Graduate Research Assistant, Health for Nevada Initiative, UNLV

2018 - 2019 Graduate Research Assistant, Urban Air Quality Lab, UNLV

2018 Volunteer, Immunize Nevada

2017 - 2019 Graduate Research Assistant, Global Health Initiative, UNLV

2016 – 2017 Research Manager, Caritas Nigeria

2013 – 2017 Program Lead, Caritas Nigeria

2011- 2012 Clinical HIV Services Specialist, Management Sciences for Health (MSH)

2010 – 2011 Medical Officer, Ahmadiyya Hospital, Kano, Nigeria

2009 – 2010 Volunteer Physician, Pro-Health International, Nigeria

2008 – 2009 Medical Intern, National Hospital Abuja, Nigeria

PEER REVIEWED JOURNAL PUBLICATIONS

1. **Olawepo, J.O** & Chen, L.-W.A. (2019). Health benefits from upgrading public buses for cleaner air: A case study of Clark County, Nevada and the United States. *Int J Environ Res Public Health*, *16*(5), 720.
2. Olakunde, B.O., Adeyinka, D.A., **Olawepo, J.O**., & Pharr, J.R. (2019). HIV testing among men in Nigeria: Comparative analysis between young people and adults. *AIDS Care*, DOI: 10.1080/09540121.2019.1622642.
3. Olakunde, B.O., Adeyinka, D.A., **Olawepo, J.O**., Pharr, J.R., Ozigbu, C., Wakdok, S., Oladele, T., & Ezeanolue, E.E. (2019). Towards the elimination of mother-to-child transmission of HIV in Nigeria: a health system perspective of the achievements and challenges. *Int Health, 11*(4), 240-249.
4. Gbadamosi, S.O., Itanyi, I.U., Menson, W.N.A., **Olawepo, J.O.**, Bruno, T., Ogidi, A.G., Patel, D.V., Oko, J., Onoka, A.O., & Ezeanolue, E.E. (2019). Targeted HIV testing for male partners of HIV positive pregnant women in a high prevalence setting in Nigeria. *PLoS ONE, 14*(1): e0211022.
5. Olakunde, B.O., Adeyinka, D.A., Ozigbu, C.E., Ogundipe, T, Menson, W.N.A, **Olawepo, J.O.**, Olakunde, O.A., & Ezeanolue, E.E. (2019). Revisiting aid dependency for HIV programs in Sub-Saharan Africa. *Public Health, 170*, 57-60.
6. **Olawepo, J.O.**, Pharr, J.R., & Kachen, A. (2018). The use of social marketing campaigns to increase HIV testing: A systematic review. *AIDS Care*, *31*(2), 153-162.
7. Menson, W.N.A., **Olawepo, J.O**., Bruno, T., Gbadamosi, S.O., Nalda, N.F., Anyebe, V., Ogidi, A., Onoka, C., Oko, J.O., & Ezeanolue, E.E. (2018). Reliability of self-reported mobile

phone ownership in rural north-central Nigeria: Cross-sectional study. *JMIR Mhealth Uhealth*, *6*(3):e50.

8. Gbadamosi, S.O., Eze, C., **Olawepo, J.O**., Iwelunmor, J., Sarpong, D.F., Ogidi, A.G., Patel, D., Oko, J.O., Onoka, C., & Ezeanolue, E.E. (2018). A patient-held smartcard with a unique identifier and mHealth platform to improve the availability of prenatal test results in rural Nigeria: Demonstration study. *J Med Internet Res*, *20*(1):e18.
9. Ezeanolue, E.E., Gbadamosi, S.O., **Olawepo, J.O.**, Iwelunmor, J., Sarpong, D., Eze, C., Ogidi, A., Patel, D., & Onoka, C. (2017). An mHealth framework to improve birth outcomes in Benue State, Nigeria: A study protocol. *JMIR Res Protoc, 6*(5):e100.
10. Ihekuna, D., Rosenburg, N., Menson, W.N-A, Gbadamosi, S.O., **Olawepo, J.O.**, Chike-Okoli, A., Cross, C., Onoka, C., & Ezeanolue, E.E. (2017). Male partner involvement on initiation and sustainment of exclusive breastfeeding among HIV-infected post-partum women: Study protocol for a randomized controlled trial. *Matern Child Nutr*., *14*(2): e12545.

TRAININGS/CERTIFICATIONS

July 2019 27th Annual Principles of STD/HIV Research Course
University of Washington, Department of Global Health

2018 - 2019 Graduate College Research Certification
University of Nevada Las Vegas

2018 - 2019 Graduate College Communication Certification
University of Nevada Las Vegas

Aug. 2018 Intensive Course on Fundamentals of Implementation Science
University of Washington, Department of Global Health

Nov. 2015 Certificate in Advanced Clinical HIV Management

Wits Reproductive Health and HIV Institute, Johannesburg

Aug. 2015 Dale Carnegie Leadership Training for Managers

Dale Carnegie Training

Nov. 2014 Project Management for Development Professionals-Training of Trainers

APM Group

AWARDS AND HONORS

2020 Graduate and Professional Student Association (GPSA) Merit Award, UNLV

2020 Graduate and Professional Student Association (GPSA) Service Award, UNLV

2019 President's UNLV Foundation Graduate Research Fellowship, UNLV

2019 Summer Doctoral Research Fellowship, UNLV

2019 Chino Dissertation Award, School of Public Health, UNLV

2018 Summer Doctoral Research Fellowship, UNLV

2018 Book Scholarship, Graduate and Professional Student Association, UNLV

PROFESSIONAL AFFILIATIONS

2018 – Date American Public Health Association (APHA)

2018 - Date Nevada Public Health Association (NPHA)

2018 - Date Delta Omega (Public Health Honor Society), Delta Theta Chapter, UNLV

2017 - Date International AIDS Society (IAS)

2017- Date Consortium of Universities in Global Health (CUGH).