PREDICTORS OF WEIGHT LOSS IN HIV-INFECTED WOMEN ON ANTIRETROVIRAL THERAPY IN RWANDA

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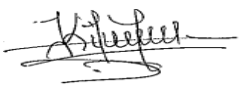
DECLARATION

I, **Jean Paul Kimenyi**, declare that this research report is my own work except to the extent indicated in the reference and acknowledgements. It is being submitted for the degree of Master of Science in Epidemiology in the field of Epidemiology and Biostatistics, University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

The University of the Witwatersrand Human Research Ethics Committee approved the study (clearance certificate number M120937).

Signature:



Name: Jean Paul Kimenyi

Date: 12 November 2013

DEDICATION

To my mom, Emerance Mukakamali, for the support rendered so that I should be where I am now.

To all my relatives for not worrying about all the hours spent away from them.

To my late father, Mvunabandi Cyprien.

To my late brothers and sister, Gustave Rumanyika, Olivier Nkeza and Eugenie Mvunabandi.

To my late uncles, Charles Karinijabo, Jean Chrysostome Kanyamuhungu and Jean Berchmas Kambanda.

To Women's Equity in Access to Care & Treatment (WE-ACT) organisation and Albert Einstein College of Medicine, for ably funding my studies.

To Lord God Almighty for giving me wisdom and knowledge and making it possible that my MSc degree should be a success.

ABSTRACT

Background: Highly Active Antiretroviral Treatment (HAART) has reduced the frequency of weight loss/wasting associated with HIV infection. However, weight loss remains a problem, even in the HAART era.

Objectives: This study was carried out to assess weight change in a cohort of HIV-infected women on HAART in Rwanda, from 2005 to 2008, and to identify factors that predict weight loss in this cohort.

Methods: Data from a cohort of 449 HIV-positive women on HAART enrolled in the Rwanda Women's Inter-association Study and Assessment (RWISA), starting in May 2005, and followed at six monthly intervals until December 2008, were analysed. The outcome assessed in this study was change in weight, measured in kilograms at 6, 12 and 24 months after HAART initiation. Nutritional status was recorded and laboratory measurements (weight, height and CD4 cell count) were taken prior and after HAART initiation. All covariates were time dependent, except for the history of weight loss which was recorded at baseline only. Generalized Estimating Equation (GEE) using the linear link (Gaussian [normal]), exchangeable covariance structure and robust standard error was used to assess the factors associated with changes in weight (weight loss or weight gain) and to control for potential confounders.

Results: Prior to HAART initiation, the mean weight of the study participants was 53.1 kg (SD 9.5). The mean BMI was 21.3 kg/m^2 (SD 3.6) and the mean CD4 cell count was 222.9 cells/µL (SD 120.6) [47.6% had CD4 cell counts <200 cells/µL, 52.2% had CD4 cell counts ≥200 cells/µL]. Overall, the participants gained weight from baseline to 12 months after HAART initiation. The mean weight change was 1.9 kg (SD 7.8) ($p<0.001$) 6 months after HAART

initiation, 2.9 kg (SD 5.9) (p <0.001) 12 months after HAART initiation, and 2.4 kg (SD 6.5) (p <0.001) 24 months after HAART initiation. Six months after HAART initiation, 48.3% of participants had gained weight, and 21.0% had lost weight. Twelve months after HAART initiation, 56.9% had gained weight, and 18.3% had lost weight, Twenty-four months after HAART initiation, 56.6% had gained weight, and 22.6% had lost weight. Participants with CD4 cell counts ≤ 200 cells/µL at baseline gained more weight than those with CD4 cell counts > 200 cells/µL at 6, 12 and 24 months after HAART initiation. Participants who were underweight (BMI <18.5 kg/m2) at baseline gained more weight than other participants three months after HAART initiation. Time-dependent diarrhoea for more than two weeks and a CD4 cell count of 200 - 350 cells/µL were significantly associated with weight loss (p≤ 0.05). Others factors, such as time-dependent education level (completion of secondary school), marital status (married legally and status other than married legally or widowed), and increases in CD4 cell counts, were associated with weight gain (p≤ 0.05).

Conclusion: Although the majority of participants gained weight during the first 12 months of being on HAART, a significant proportion of participants lost weight while on HAART. The findings on the predictors of weight change in HIV-positive women on HAART can be used to promote weight gain in women who start HAART. Clinicians who take care of HIV-infected patients on HAART should pay attention to those who lose weight, and those who present with diarrhoea or with CD4 cell counts of <350 cells/µL at follow-up visits, since these factors are associated with weight loss in the HAART era.

Keywords: Rwanda, women, HAART**,** HIV/AIDS, weight loss, weight gain, wasting, longitudinal study, secondary data.

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God bless you all.

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AIDS:	Acquired Immune Deficiency Syndrome
CD4:	4 Displaying T Lymphocyte Cells
HIV:	Human Immunodeficiency Virus
HAART:	Highly Active Antiretroviral Therapy
ART:	Antiretroviral Therapy
NNRTI:	Non-Nucleoide Reverse Transcriptase Inhibitor
NRTI:	Nucleoside Reverse Transcriptase Inhibitor
OI:	Opportunistic Infection
WHO:	World health Organization
VL:	Viral Load
BMI:	Body Mass Index
D4T:	Stavudine
RWISA:	Rwandan Women's Inter-association Study and Assessment
WIHS:	Women's Interagency HIV Study
PTSD:	Post Traumatic Stress Disorder
WE-ACT:	Women's Equity in Access to Care & Treatment

Outline of the research report

This report is organized into five chapters. The first chapter is the introduction which comprises the background and literature review. The second chapter is the methodology which provides a brief description of the study setting, study design, study population, data collection and statistical analysis. Chapter Three presents the study results and Chapter Four is a discussion of these results. Finally, Chapter Five is the conclusion of the results and includes remarks and policy recommendations based on the study findings.

CHAPTER 1: INTRODUCTION

1.1 Background

HIV/AIDS is a public health problem worldwide. At the end of 2010, an estimated 34 million people (31 600 000–35 200 000) were living with HIV globally (1). There were 2.7 million [2 400 000–2 900 000] new HIV infections in 2010. In mid-2010, about 68% of all people living with HIV resided in Sub-Saharan Africa, a region with only 12% of the global population(2). Globally, women constituted half (50%; 95% CI: 48–53%) of the adults (15 years and older) living with HIV in 2010, according to UNAIDS estimates (1). Women comprised 59% (95% CI 56–63%) of adults living with HIV in sub-Saharan Africa in 2010, as they have for most of the past decade.

The HIV/AIDS epidemic in Rwanda affects all segments of the population. The estimated adult HIV seroprevalence in Rwanda is 3.0% in the general population (3). HIV prevalence in urban areas is much higher than in rural areas (7.3% and 2.2%, respectively); and HIV prevalence in women (3.6%) is much higher than in men (2.3%). The Rwandan government is endeavouring to ensure access to Highly Active Antiretroviral Therapy (HAART) for all HIV-infected individuals. In 2008, an estimated 63 149 individuals were on HAART; this increased in 2009 to around 76 726 (61% of whom were women) (3).

Universal access to HAART has improved the health of people living with HIV infection and has reduced the occurrence of new infections. Globally, mortality associated with HIV/AIDS has decreased. By 2010, 1.7 million people initiated treatment; of these, 1.4 million were alive and on treatment at the end of 2010 (1). At the end of 2010, 6 650 000 people were receiving

HAART in low and middle income countries, an increase of over 1.4 million people or 27% from December 2009 (1). Sub-Saharan Africa had the greatest increase in the absolute number of people receiving HAART in 2010, from 3 911 000 in December 2009 to about 5 064 000 a year later. In low- and middle-income countries, after factoring in prevention of HIV transmission from HAART, treatment has averted an estimated 2.5 million deaths due to AIDS since 1995, the majority in the past few years (1). In countries that have achieved high levels of treatment coverage, new infections may be declining, even in the absence of any significant changes in patterns of sexual behaviour. In Zimbabwe, for example, there was a decline in new HIV infections from 1995 to 2000 (1). It is worth noting that Rwanda is among those countries that have achieved Universal Access to Treatment (defined as providing ART to at least 80% of patients in need) (4) .

Although HAART has changed the course of HIV infection it does not solve every problem that an HIV infected person has. For example, HIV infected persons on HAART still experience an increased incidence of Herpes Zoster, oral *candidiasis*, *Pneumocystis jirovecii Pneumonia* (PCP), Kaposi Sarcoma, tuberculosis (TB), and HIV wasting, compared to those who are not infected with HIV (5, 6). Clinicians monitoring patients on HAART need to be aware of this when evaluating health and treating patients.

This study focused on weight loss, as a high proportion of HIV-infected patients on HAART still lose weight, and severe weight loss is associated with increased mortality and morbidity (7-11).

1.2 Literature Review

Weight loss among HIV infected persons in the pre-HAART era was one of the challenges for health care providers and for researchers in the domain of HIV/AIDS treatment. Although HAART has reduced the frequency of weight loss/wasting associated with HIV infection, studies have shown that some patients still lose weight and are thus at risk of disease, and even death (5, 7, 8, 10, 11).

This literature review focuses on weight loss in the pre-HAART era, weight loss in the HAART era, the association between weight loss and survival in HIV-infected patients on HAART, and predictors of weight loss identified in previous studies.

1.2.1 Weight loss in the pre-HAART era

Weight loss was very common in HIV-infected patients before the advent of HAART (12). HIV-infected patients were undergoing severe depletion of both lean mass and fat in the pre-HAART era and nutrition alteration was associated with shortened survival and diminished quality of life due, in part, to physical debilitation (12, 13).

As pointed out by Hendricks et al. (12) most studies on weight loss in the pre-HAART era were conducted in developed countries in the late 1980s to mid-1990s, and the majority were cross sectional studies. Wasting syndrome was defined, at that time, as the unintentional loss of more than 10% of body weight (14). In the studies that Hendricks et al. cited (14-16), weight loss of any degree was reported at examination (prior time course of disease often unspecified) in up to

78% of patients with HIV infection and/or AIDS. More specifically, weight loss of more than 10% of usual body weight was reported in up to 31% of patients.

Few researchers have analysed changes in weight in longitudinal studies. One study reported that 66.5% of a large cohort of patients experienced weight loss over a median 43-month period of follow up after recruitment (17). A more in-depth study of longitudinal changes in weight in 30 males with stage IV HIV infection revealed two distinct patterns of weight loss: acute episodes, associated predominantly with non-GI opportunistic infections; and chronic episodes, predominantly associated with GI disease (18).

1.2.2 Weight loss in the HAART era

Weight loss remains one of the complications in HIV persons on HAART (13, 19). A study in participants enrolled in the Nutrition for Healthy Living Cohort in Boston, Massachusetts, reported that the total prevalence of weight loss in participants on HAART was 38% and that both weight loss and wasting occurred in those treated successfully with HAART, and in those for whom HAART failed (20). Wanke et al. conducted a longitudinal analysis of a prospective cohort of 469 HIV-infected individuals enrolled in a USA study, looking at the impact of HIV on nutrition, and found that 33.5% were in the category of wasting (any individual who had a loss of >10% of body weight since the baseline visit or who had a body mass index (BMI) that had fallen to <20 kg/m2 since the last clinic visit) (19). Other studies in the USA have reported similar results of weight loss in HIV patients on HAART (21). In a cross-sectional study in Australia, Marijka et al. reported that 40% of study participants on HAART lost weight (defined as a loss of ≥5% in weight) (22). Studies in developing countries show some similarities in

weight loss in HIV-infected patients on HAART with those in developed countries. In a cohort study in Tanzania, 31% of participants experienced an initial significant weight loss at three months after HAART initiation (23). In contrast with previous studies, Rwandan HIV-infected patients on *Stavudine*-containing HAART displayed a high prevalence of weight loss after the first year of HAART initiation (62% of all patients) (24).

1.2.3 Weight loss and mortality

Weight loss has been recognised as a prognostic indicator of increased mortality and morbidity since early in the HIV epidemic (7, 8, 10), and is associated with mortality in HIV-infected participants. Wheler et al. calculated the relative risk of death for those with 5% to 10% weight loss over four months to be 2.22 ($p< 0.001$), and 1.26 ($p< 0.01$) among those who lost 0% to 5% of their body weight, respectively, compared with those with no weight loss (25). Similar findings were reported in the Nutrition for Healthy Living Study which found weight loss to be the strongest independent predictor of mortality, despite the availability of HAART (20). A 4- to 6-fold increase in mortality was seen in patients with ≥10% weight loss from baseline or the previous visit. Similarly, other studies have shown weight loss to be associated with a higher risk of mortality, with hazard ratios ranging from 2 to 5 (8, 25, 26).

1.2.4 Predictors of weight loss during the HAART era

Weight loss progressing to wasting syndrome in patients with HIV appears to be a complex and multifactorial process (27). Wasting is defined by the Centers for Disease Control (CDC) as a loss of >10% of baseline body weight plus chronic diarrhoea (at least two stools per day for >30 days) or chronic weakness and documented fever (for >30 days, intermittent or constant) in the

absence of a concurrent condition/illness or conditions other than HIV infection that could explain the findings (e.g. tuberculosis, cancer, *isosporiosis*, *cryptosporidiosis*, or other specific enteritis) (28). Factors that have been identified as risks for weight loss include clinical factors which can be divided into three categories: i) caloric intake, ii) disturbed gastrointestinal function and, iii) metabolic abnormalities. Others factors that contribute to weight loss include socio-economic status, access to care, psychological factors, and medical complications of therapies for HIV infection (19, 29).

Many studies on predictors of weight loss have been conducted in developed countries. The Nutrition for Health Cohort Study in Boston found that calendar time (1995-1997; 1998-2003) , use of injection drugs, living below the federal poverty level, higher BMI ($\geq$25 kg/m^2), lower CD4 cell count, higher HIV viral load, and presence of diarrhoea, nausea or fever, were independently associated with weight loss (20). Another study in the USA, on clinical factors associated with weight loss, found AIDS and non-specific markers of progression (fever, thrush, CD4 cell count of <100 cells/µL) to be predictors of weight loss in HIV-infected individuals (30). In Australia, Marijka et al. reported similar findings: oral symptoms and trouble swallowing were associated with acute weight loss (22).

The few studies on predictors of weight loss that have been conducted in developing countries present some similarities with those in developed countries. A study in Vietnam among drug injection users found that moderate to heavy alcohol use and tobacco smoking were associated with negative weight changes (31). In Tanzania, being younger or older than the age group 30 to 39 years, lower socioeconomic status (SES), higher BMI, lower haemoglobin, difficulty in

breathing, loss of appetite, and nausea/vomiting at baseline, were associated with the risk of significant weight loss at three months after initiation of HAART (23). During a median follow-up period of 10 months [interquartile range (IQR) 4-20 months], 31% of patients had experienced an initial significant weight loss after HAART initiation. In addition to time-varying CD4 cell count and hemoglobin level, age, sex, baseline BMI and loss of appetite, and nausea/vomiting at baseline were associated with the risk of long-term significant weight loss. A Rwandan study found that weight loss was significantly associated with treatment-limiting lipo-atrophy (adjusted effect/kg/year -2.0 kg, 95% CI -0.6;-3.4 kg; $p<0.01$) after the first year of HAART initiation (24).

1.3 Objectives of the study

The objectives of the study were to assess weight change from initiation (baseline) to last visit, in a cohort of 449 HIV infected women on HAART in Rwanda, from 2005 to 2008; and to identify factors that predict weight loss in this cohort.

1.4 Justification for the study

Despite the burden of weight loss in HIV-infected individuals on HAART in developing countries, information on prevalence and predictors of weight loss is scarce. The limited knowledge concerning weight loss in HIV-infected patients contributes to inadequate clinical management. This study determined the frequency of weight loss and associated factors in a cohort of HIV-infected women. The results will help clinicians to take appropriate measures when assessing patients on HAART. Furthermore, researchers on nutrition in HIV-infected

individuals can use this information for improving nutrition management of HIV-infected individuals.

CHAPTER 2: METHODOLOGY

2.1 Description of primary study

RWISA (the Rwandan Women's Inter-association Study and Assessment) was a prospective observational cohort study, assessing the effectiveness and toxicity of HAART in HIV-infected Rwandan women. The cohort was established in May 2005 and was followed until 2008. The research team and activities were situated in central Kigali, with all research activities provided on-site. The cohort comprised 936 women, of whom 710 were HIV-positive and 226 HIV-negative. Volunteers were included if they were HAART naive except for possible exposure to single-dose *nevirapine* to prevent mother to child HIV transmission, if they were older than 25 years, had resided in Rwanda in 1994 and, if HIV-negative, would be willing to undergo voluntary counselling and testing for HIV at 6-month intervals. All participants provided information on medical history, demographic characteristics, psychosocial history, their experiences of trauma during the 1994 Rwandan genocide, and symptoms of depression and post-traumatic stress. A physical assessment was performed and specimens were taken for CD4 cell counts, full blood counts and other laboratory studies. More details on the design of RWISA can be found elsewhere (32).

The data collection instruments followed the format of the Women's Interagency Health Study (WIHS) forms, modified for Rwandan women. The questions included medical, psychosocial and behavioral information necessary to assess clinical status, disease progression, risks for exposure to HIV-1, quality of life, depression and Post Traumatic Stress Disorder (PTSD), and experience of trauma during the 1994 genocide. Height, weight and CD4 cell counts were also measured (32).

Follow-up (core) visits occurred every six months until December 2008. At each visit, the collection of interval historical data, physical examination data and biologic specimens, and assessment of adherence, alcohol use, depression and PTSD was recorded. Operationally, visits occurred in specific six-month calendar windows (e.g. Visit 1 from 15 May - 20 November 2005; Visit 2 from 1 December 2005 - 31 May 2006; Visit 3 from 1 June to 30 November 2006, etc.). An individual woman's follow-up visits occurred at approximately 6-month intervals within a 10-week window determined by her Visit 1 enrollment date; Visit 2 occurred from 5 to 7.5 months after Visit 1; Visit 3 from 11 to 13.5 months after Visit 1; Visit 4 from 17 to 19.5 months after Visit 1, etc.

Women initiating HAART were also seen three months after HAART initiation ('3-Month Visit' or Visit 1.5) unless their scheduled core visit occurred within the first three months of HAART initiation, for the collection of information on medication regimen, start dates, adherence, symptomatic toxicity, determination of complete blood count (CBC), and CD4 cell count; and for repositing of serum and plasma.

2.2 Study design

This was a longitudinal secondary data analysis of a cohort of HIV-positive women.

2.3 Study setting

The research team and activities were situated in central Kigali, with all research activities provided on-site. The women recruited in RWISA represented a community-based population

recruited and enrolled through the grassroots association partners in the research from Kigali-Rwanda. All specimens of blood were examined at the National Reference Laboratory or the King Faisal Hospital laboratory within one hour of blood-drawing.

2.4 Study population

The inclusion criteria for entry into the study were being older than 25 years old, on HAART, having completed at least two visit while on HAART. The study population thus comprised 449 HIV-infected women, older than 25 years, initiating HAART, enrolled in the RWISA cohort from May 2005, and followed until December 2008. Women with cancer and pregnant women were excluded. Participants with a missing date of HAART initiation and those who started HAART after Visit 4 were excluded from this analysis as well. Participants without a HAART initiation date were excluded because they had no evidence of ever being on HAART. Those who started HAART after Visit 4 were excluded because they had only one visit with a weight measurement and at least two visits were required to estimate change in weight.

In Rwanda, at the time Rwisa data were collected, adults and children were eligible for HAART if they were HIV-positive and had a diagnosis of: i) World Health Organization (WHO) clinical stage IV, irrespective of CD4+ cell count, or ii) WHO clinical stage III and a CD4+ cell count < 350 cells/mm3, or iii) WHO clinical stage I or II and a CD4+ T-lymphocyte count < 200 cells/mm3 (National Care and Treatment Guidelines, Rwanda, 2003). Patients also had to meet several socio-economic and adherence criteria, including the identification of a treatment guardian, or “buddy”, prior to being considered eligible for HAART (3).

2.5 Study procedures

Anthropometric measurements and laboratory procedures

Height and weight were measured at all visits while the participant wore light clothing and no shoes.

Blood specimens were collected at each regular visit and at the 3-month post-HAART visit if the woman had initiated HAART at this point. CD4 cell counts were determined with a FACS counter (Becton and Dickinson, immunocytometry Systems, San Jose, CA, USA) (32).

2.6 Measurement and data sources for variables

2.6.1 Outcome variable

The main outcome of interest was weight change in kg (loss or gain). Weight was measured at each visit (6, 12, 18 and 24 months-visits). Weight change was defined as weight in kg at each visit minus weight at baseline in kg:

$$\text{Weight Change} = [Yi - X]$$

Where Yi = post baseline visit for i = 6, 12 and 24 months and X = baseline weight.

2.6.2 Covariates

We included the following time-dependent covariates in the analysis: socio-demographic factors: age, income, marital status, education; self-reported opportunistic infections: TB, PCP, Oesophagus *Candidosis,* mouth *candidosis;* self-reported symptoms: diarrhoea for more than

two weeks, fever that lasted for more than two weeks; information on diet and weight: diet change and history of unexpected weight loss (taken at baseline); and CD4 cells count. These selected covariates were based on a careful literature review on HIV weight change in the HAART era. Age was grouped and included as a categorical variable (26-30; 31-35; 36-40; 41-45, 46-50 and older than 51 years). Income was categorised as <10 000 Rwandan francs (Frws) per month (in 2005, this was equivalent to $17), 10 000 to 35 000 Frws (equivalent to $18-$60), and more than 35 000 Frws (equivalent to > $ 60). Education was categorised as 'none', 'some primary school', 'completed primary school', 'some secondary school' or 'completed secondary school', marital status was categorized as 'married legally or living with a partner', 'widowed' or 'other ('divorced', 'separated', and 'never married'). Opportunistic infections and symptoms were categorised as 'Yes', if the participant had the condition and as 'No' if the participant did not. Similarly, unexpected weight loss, nutritional supplement and diet change were categorised as 'Yes' if the participant experienced the condition, and 'No' if the participant did not.

2.7 Data management and analysis

2.7.1 Data cleaning

Data cleaning and all data analysis were done using STATA version12. Standard data cleaning procedures to identify values on variables were carried out by conducting checks on all extracted variables to determine the extent of missing values and duplicated variables.

2.7.2. Data coding

CD4 cell count was categorised as <200 µ/L, 200-349 µ/L, and >350 µ/L.

Participants were categorized into three groups: those who lost weight (1 kg or more), those with no change in weight or weight stable (if weight changed by less than 1 kg), and those who gained weight (by 1 kg or more).

2.7.3 Data analysis

In the descriptive analysis, continuous variables, such as age, height, CD4 cell count and weight were summarised using means and standards deviations. Categorical variables, such as marital status, income, education level, symptoms (fever, thrush, diarrhoea, vomiting), opportunistic infections (TB, PCP, Candida) were described using proportions and percentages.

Paired t-tests were used to compare the means of two continuous variables between two visits (e.g. weight and CD4 cell counts).

The change in weight from baseline was calculated by subtracting weight at the baseline visit from weight at the current visit. Similarly, the change in CD4 cell count was calculated by subtracting the CD4 cell count at the baseline visit from the CD4 cell count at the current visit.

Participants were described according to their CD4 cell counts and BMI categories at baseline. Line graphs were used to depict changes in weight over time.

In the inferential analysis, Generalized Estimating Equation (GEE), using the linear link (Gaussian [normal]), exchangeable covariance structure, and robust standard error, was used to assess factors associated with changes in weight and to control for potential confounders. Covariates were entered into a multivariable model if they had a p–value of less than 0.20 in the univariable analysis. The final multivariable model was determined using a backward stepwise regression method and only included covariates with a two-sided p-value of 0.05 or less.

2.7.4 Ethical considerations

The primary study was approved by the Rwandan National Ethics Committee and the Institutional Review Board of Montefiore Medical Center (Bronx, NY). The reference numbers are FWA 00001973 and IRB 00001497, respectively. The participants were informed about the study and signed an informed consent form prior to data collection.

The secondary data analysis was approved by the University of the Witwatersrand Human Research Ethics Committee (clearance certificate number M120937). Permission to use the data was obtained from WE-ACT Rwanda (Women's Equity in Access to Care & Treatment). Patient confidentiality was maintained through the allocation of unique identifiers to individual participants and removal of any personal identifiers before analysis.

CHAPTER 3: RESULTS

3.1 Introduction

This chapter presents the results from the analysis of the dataset of HIV-infected women in two parts. The first part involves a description of the cohort and the weight changes at each of the follow up visits. The second part assesses the predictors of weight change.

3.2 Baseline characteristics of the study participants

3.2.1 Socio-demographic characteristics

A total of 449 HIV-positive women were included in the analysis. The baseline characteristics of the study participants are shown in Tables 1 and 2. The mean baseline age was 35.49 ± 6.64 years. The age groups 31-35 and 36-40 years were predominant, with 36.0% and 20.6% of the participants in each, respectively.

The majority of participants were widowed (41.0%), followed by women who were married legally or living with a partner (37.4%).

The level of education was low: only 1.8% had completed secondary school and 22.6% had no education. The majority (50.2%) of participants had a monthly income of 10 000-35 000 Frws ($ 18-60), followed by those with a monthly income of less than 10 000 Frws (18$) (34.9%), and those with a monthly income of >35 000 Frws (> $60) (14.9%).

3.2.2 Self-reported clinical characteristics at baseline

The participants reported the following histories with clinical symptoms and diseases prior to HAART initiation: oral Candida (*Candidosis)* with thrush in mouth (98.4%), Herpes Simplex (13.1 %), PCP (12.9 %), and oesophagus Candida with thrush (3.6 %). Almost one third of the participants reported (in their history) a fever for more than two weeks (27.0%) and diarrhoea for more than two weeks (26.7%). Those who reported a history of unexpected weight loss and diet change comprised 24.9% and 22.2% of the total participants, respectively.

3.2.3 Anthropometric and laboratory measurements at baseline

The mean weight at baseline was 53.1 ± 9.5 kg; the mean height was 1.5 ± 0.07 m and the mean BMI was 21.3 ± 3.5 kg/m^2. Most participants (69.0%) were of normal weight; 18.5% were underweight, and 12.4% were either overweight or obese at baseline (Table 1). The mean CD4 cell count at baseline was 216.9 ± 121.0 cells/µL. Most participants (47.69%) had CD4 cells counts of <200 cells/µL, followed by 200-349 cells/µL (38.9%), and ≥350 cells/µL (13.3%) (Table 2).

Most women (70.0%) started treatment between visits one and two. Sixty-three women (12.5%) started treatment between visits 2 and 3, 51 women (10.0%) between visits 3 and 4, and 40 women (7.9%) between visits 4 and 5. Participants were followed for a mean of 372 ± 215.35 (1-819) days while on HAART.

The number of lost to follow up at different was not high. For example on visit 1, 2, 3, 4 and 5, the number of women who were present is respectively 449, 444 (5 lost to follow up), 432 (17

lost to follow up), 430 (19 lost to follow up), 413 (36 lost to follow up). The difference between the first visit and the filth visit is 36, which corresponds to 15 drop outs, 15 stoppers(who stopped treatment without providing any reason) and 6 deaths.

Table 1: Socio-demographic characteristics of participants at baseline

Variable	HIV+ treated women (N=449)	
	n	%
Age category (years)		
26-30	72	20.6
31-35	126	36.0
36-40	78	22.3
41-45	41	11.7
46-50	20	5.7
51+	13	3.7
Marital status		
Married legally/ living with a partner	168	37.4
Widowed	184	41.0
Other *	97	21.6
Education		
No education	100	22.5
Some primary	157	35.4
Completed primary	133	30.9
Some secondary	46	10.4
Completed secondary	8	1.8
Monthly Income (Frws)		
<10000($ 18)	155	34.9
10000-35000($ 18-60)	223	50.2
>35000(>$ 60)	66	14.8
BMI category (kg/m^2)		
underweight <18.5	83	18.5
normal weight18.5-25	310	69.0
overweight 25-29.9	45	10.0
obese ≥30	11	2.4

Note: * Other includes divorced, separated, never married women.

Table 2: Self reported clinical and laboratory characteristics of participants at baseline visit

Characteristic	HIV+ treated women (N=449)	
	n	%
Opportunistic infections		
Tuberculosis	64	14.5
Herpes simplex	58	13.1
PCP	56	12.9
Candida-thrush-oesophagus	16	3.6
Candida-thrush-mouth	442	98.4
Symptoms		
Diarrhoea more than 2weeks	119	26.7
Fever more than 5weeks	121	27.0
Unexpected weight loss	105	24.9
Change in diet	99	22.2
Ingestion of nutritional supplement	61	86.2
CD4 cell count categories(cells/µL **)**		
≥350	60	13.3
200-349	175	38.9
<200	214	47.6

3.2.4 Weight change at follow up visits

3.2.4.1 Weight and CD4 cell count changes after 6, 12 and 24 months on HAART

Weight and CD4 cells count changes during the follow up time on HAART are described in Table 3. Overall, there were statistically significant increases in weight 12 months after HAART initiation compared to the baseline. There was a rapid increase in weight from baseline until 12 months after HAART initiation, when it reached a peak and then started decreasing until 24 months after HAART initiation (Figure 1). The mean weights (± SD) at baseline, 6 months, 12 months and 24 months after HAART initiation are also shown in Table 3. The mean weight

changes at each visit from baseline are shown in Table 3. The greatest mean weight change from baseline occurred at the 12 month visit.

Mean CD4 cell counts increased during the follow up period. The mean (± SD) CD4 cell counts at baseline, 6 months, 12 months and 24 months after HAART initiation are reported in Table 3. The greatest mean CD4 count change occurred at the 24 month visit.

Table 3. Weight and CD4 cells count changes

Mean change from baseline	**weight change (kg)**			**Cd4 cell count (cells/µl)**		
	n	mean±sd	p	n	mean ± sd	p
6 month	297	1.9 ±7.8	<0.001	297	60.5 ±117.3	<0.001
12 month	334	2.9 ±5.9	<0.001	334	73.7 ±131.9	<0.001
24 month	336	2.4 ±6.5	<0.001	336	104.7 ±117.5	<0.001

3.2.4.2 Description of weight change

Table 4 shows the weight change in HIV positive women on HAART at different visits.

Overall, most women gained weight during the follow up time on treatment. The majority of women gained weight at the 12 and 24 month visits (56.9% and 56.6% respectively). The mean

CD4 cell count increase was approximately the same at the 6, 12 and 24 month visits (6.2 ± 9.2 kg, 6.8 ± 4.1 kg, and 6.5 ± 4.3 kg, respectively).

Table 4: Classification and distribution of weight change at different visits in HIV infected women on treatment

hiv positive women on treatment				
visit at:	**weight change category**	**n**	**%**	**mean weight change (kg)**
6 months	Stable	83	30.6	0.6 ±3.8
	Gained	131	48.3	6.2 ±9.3
	Lost	57	21.0	-4.7 ±3.5
12 months	Stable	83	24.8	0.2 ±0.7
	Gained	190	56.9	6.8 ±4.1
	Lost	61	18.2	-5.3 ±3.7
24 months	Stable	71	20.8	-0.04 ±0.8
	Gained	193	56.6	6.5 ±4.7
	Lost	77	22.6	-5.3 ±3.9

3.2.4.3 Weight change over time, according to baseline CD4 cell count and BMI

Women with CD4 cell counts ≤200 cells/µL at baseline gained more weight than those with CD4 cell counts >200 cells/µL (Table 5). Weights in women with CD4 cell counts <200 cells/µL at baseline increased rapidly until 12 months after HAART initiation and then started decreasing slightly until 24 months (Figure 2). The mean weight changes at 6, 12 and 24 months after

HAART initiation compared to the baseline, in women with CD4 cell counts ≤200 cells/μL, were 3.0 kg, 4.2 kg, and 3.2 kg, respectively. All of these changes were statistically significant. The mean weight changes in women with CD4 cell counts >200 cells/μL were 1.2kg, 1.91kg, and 1.7 kg, respectively; all these changes were also statistically significant.

There was an increase in weight in women who were underweight (BMI <18.5 kg/m^2) and of normal weight (18.5-25 kg/m^2) at baseline, and 12 months after HAART initiation (Table 5). Women who were underweight at baseline gained more weight three months after HAART initiation (Figure 3). The mean weight gains achieved in underweight women at 6, 12, and 24 months after HAART initiation were 6.1 kg, 6.3 kg and 5.8 kg, respectively, and all these changes were statistically significant ($p<0.001$) compared to the baseline. The mean weight gains in women of normal weight at baseline were 1.4 kg, 2.8 kg and 2.2 kg, respectively; all these changes were statistically significant ($p<0.001$) compared to the baseline. However, both overweight and obese women lost weight at 6, 12 and 24 months after HAART initiation, in these cases, this loss was not statistically significant compared to the baseline.

Table 5: Change in weight after 6, 12 and 24 months on HAART in different BMI and CD4 Cell count categories at baseline

CD4 cell count at baseline (cells/µL)	Change at 6 months (Mean ± SD)	P *	Change at 12 months (Mean± SD)	P *	Change at 24 months (Mean± SD)	P *
≤200	3.0 ±10.1	<0.001	4.2 ±5.4	<0.001	3.2 ±6.2	<0.001
>200	1.2 ±5.3	0.004	1.9 ±6.1	<0.001	1.7 ±6.8	<0.001
BMI at baseline (kg/m^2)						
<18.5	6.1 ±13.7	<0.001	6.3 ±5.78	<0.001	5.8 ±7.1	<0.001
18.5-25	1.4 ±4.4	<0.001	2.8 ±5.35	<0.001	2.2 ±5.5	<0.001
>25-30	-1.7 ±6.0	0.153	-0.6 ±6.40	0.553	-1.2 ±8.2	0.386
>30	-3.0 ±3.5	0.034	-4.0 ±5.8	0.155	-4.6 ±5.5	0.139

* Paired t-test. Comparison of weight at baseline and weight at 6, 12 and 24 months, according to CD4 cell count and BMI.

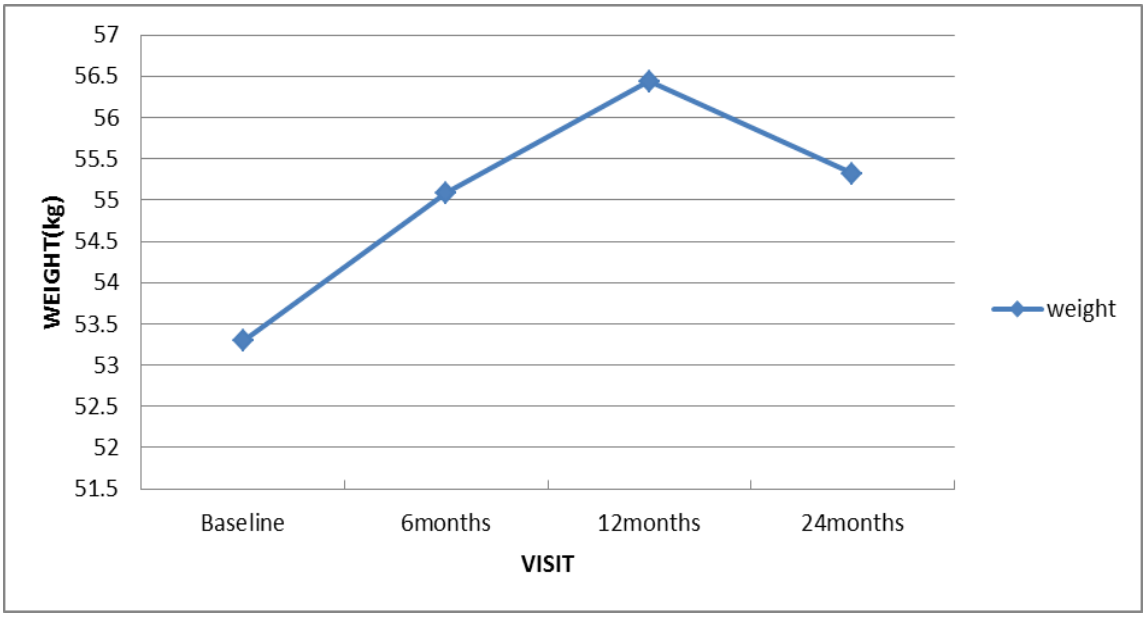

Figure 1: Weight change over time in women on HAART

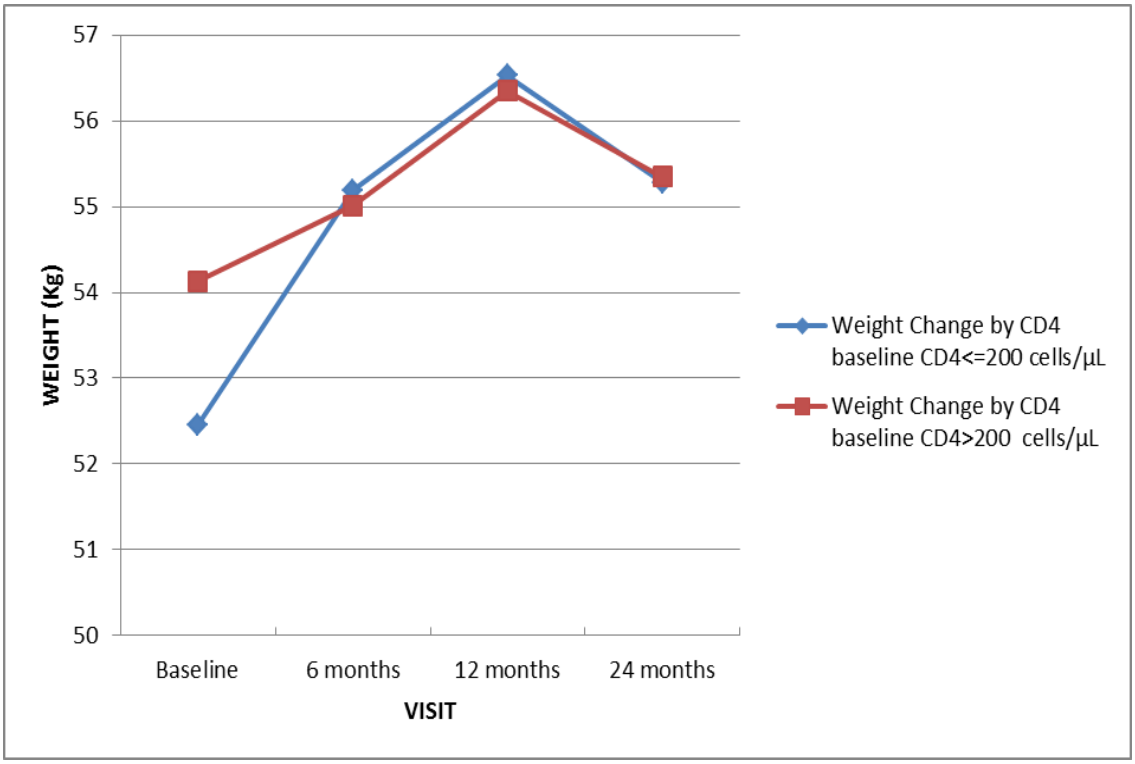

Figure 2: Weight change over time by baseline CD4 cell count in women on HAART

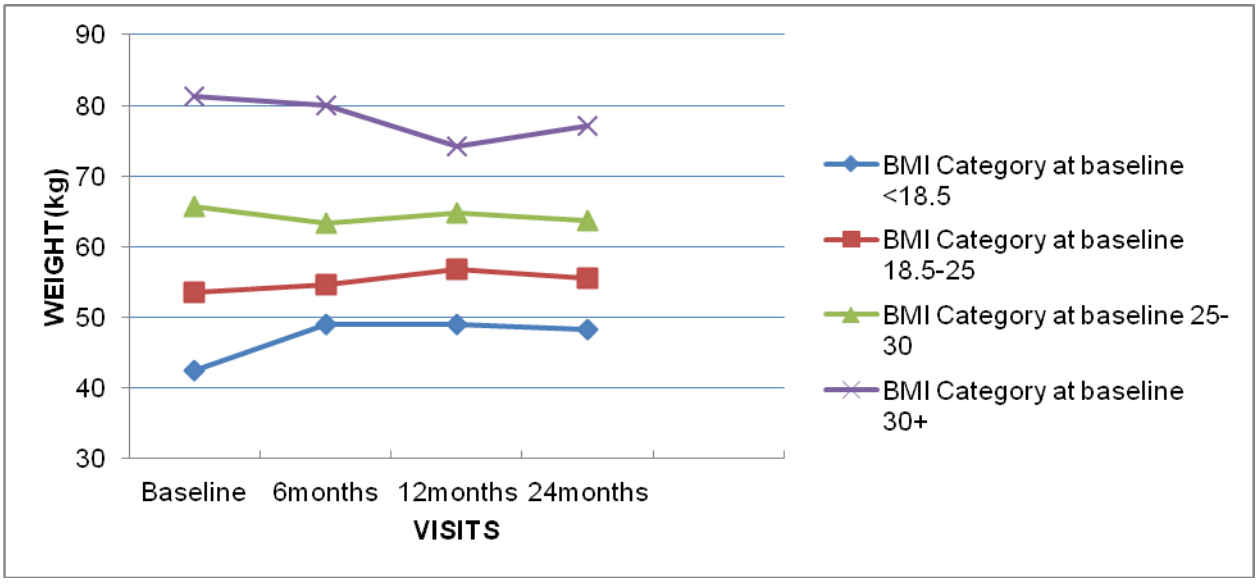

Figure 3: Weight change over time by baseline BMI in women on HAART

3.3 Predictors of weight change

The following time varying factors were investigated for possible associations with weight change: age, marital status, education level, income, opportunistic infections (PCP, Candida - thrush mouth, Candida - thrush oesophagus, TB), symptoms (diarrhoea for more than two weeks, high fever for more than two weeks), diet (change in diet, use of nutritional supplements), mean CD4 cell count, mean CD4 cell count change, time on treatment, study visit number while on follow up, and history of weight loss (at baseline). BMI was not added to the model to avoid multicollineality. The results of the univariable and multivariable analyses are presented in Tables 6 and 7.

3.3.1 Univariable analysis

In the following section, the predictors of weight change are subdivided into two categories: predictors of weight gain and predictors of weight loss.

3.3.1.1. Predictors of weight gain

In the univariable analysis, factors that were significantly associated with weight gain were marital status other than being married or widowed, completion of secondary education, and attendance at the 12-month visit. Weight increased by 1.67 kg (95% CI -0.192; 3.162) in women who were neither married nor widowed, compared to women who were married (Table 6). Weight change increased by 8.20 kg (95% CI 0.33; 16.05) in women who completed secondary school compared to women who had no education. Weight increased by 1.02 kg (95% CI 1.129; 1.925) in women who attended the 12-month visit compared to the baseline visit (reference).

3.3.1.2.. Predictors of weight loss

In the univariable analysis (where all of the visits were pooled), self-reported diarrhoea for more than two weeks and a history of unexpected weight loss were significantly associated with weight loss. The weight change decreased by 1.81 kg (95% CI -2.843; -0.784) among women who reported diarrhoea for more than two weeks before each visit (Table 7), and weight decreased by 1.24 kg (95% CI -2.42; -0.06) among women with a history of unexpected weight loss. Other factors, such as age (31-35, 36-40, 41-45), education level (completed primary school), opportunistic infections, diet changes, high fever for more than two weeks, and CD4 cell count of 200 - 349 cells/μL were also associated with weight loss, but the associations were not statistically significant.

3.3.2 Multivariable analysis

Variables with a p value of ≤0.20 in the univariable model were included in the multivariate model, viz. marital status, educational level, diarrhoea for more than two weeks, CD4 cell count, diet change, nutritional supplement, visit number attended, and time on treatment. Variables were retained in the final model if they had a p value of ≤ 0.05.

3.3.2.1 Independent predictors of weight gain

After adjusting for other factors, the time-variable, marital status (widowed category and other), education level (completed secondary school), and CD4 cell count increase were independently associated with weight gain (Tables 6 and 7).

Level of education (completed secondary school) remained associated with weight change ($p \leq 0.05$). Weight increased by 8.39 kg (95% CI 0.67; 16.11, p=0.03) among women who completed secondary school compared to women with no education. Similarly, weight increased by 1.24 kg (95% CI 0.06; 2.43, p=0.03) in widowed women compared to legally married women and weight increased by 1.62 kg (95% CI 0.14; 3.09, p=0.03) in women who were neither married nor widowed, compared to legally married women. In addition, time-variable CD4 cell count change (increase) was associated with weight gain (p<0.001). Weight increased by 0.005 kg (95% CI 0.001; 0.009) for every 1 cell/ µL increase in CD4 cell count change.

3.3.2.2 Independent predictors of weight loss

After controlling for other factors, diarrhoea for more than two weeks and CD4 cell count of 200 - 350 cells/µL were significantly associated with weight loss (p=0.020 and p=0.008, respectively). Weight decreased by 1.46 kg (95% CI -2.75; -0.17) in women who reported diarrhoea for more than two weeks before each visit; and decreased by 0.005 kg (95% CI -1.665; 0.100) in women with CD4 cell counts of 200 - 349 cells/µL, compared to women with CD4 cell counts of < 200 cells/µL.

Table 6: Predictors of weight change (socio-demographic predictors) in women on HAART

Variables:	Univariable analysis			Multivariable analysis		
	Coefficient	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Age (years):						
26-30	1(reference)					
31-35	-0.57	-2.35; 1.20	0.52			
36-40	-0.56	-2.53; 1.41	0.57			
41-45	-0.82	-2.88; 1.24	0.43			
46-50	1.05	-1.34; 3.45	0.38			
51+	1.67	-1.02; 4.38	0.22			
Marital Status:						
Married legally	1(reference)					
Widowed	1.17	-0.06; 2.41	0.06	1.24	0.06; 2.43	**0.03**
Other	1.67	0.19; 3.16	**0.02**	1.62	0.14; 3.09	**0.03**
Education Level:						
No Education	1(reference)					
Some Primary	0.09	-1.34; 1.54	0.89	0.41	-0.98;1.82	0.56
Complete primary	-0.60	-2.01; 0.81	0.40	-0.33	-1.73; 1.06	0.64
Some Secondary	0.28	-1.67; 2.24	0.77	0.51	-1.39; 2.43	0.59
Complete secondary	8.20	0.33; 16.05	**0.04**	8.39	0.67; 16.11	**0.03**
Income (Frws):						
<10000	1(reference)					
10000-35000	0.20	-0.61; 1.02	0.61			
>35000	0.23	-0.80; 1.26	0.66			

Table 7: Predictors of weight change (clinical and laboratory factors) in women on HAART

Variables	Univariable analysis			Multivariable analysis		
	Coefficient	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Opportunistic infection						
PCP:						
No	1(reference)					
Yes	-0.14	-4.31; 4.02	0.94			
Candida Thrush mouth:						
No	1(reference)					
Yes	-0.39	-2.21; 1.43	0.67			
Candida Thrush-oesophagus:						
No	1(reference)					
Yes	1.09	-1.11; 3.31	0.33			
TB:						
No	1(reference)					
Yes	-0.90	-3.02; 1.22	0.40			
Symptoms:						
Diarrhoea for more than 2weeks:						
No	1(reference)					
Yes	-1.81	-2.84; -0.78	**<0.001**	-1.46	-2.75; -0.17	**0.026**
High Fever-2weeks:	1(reference)					
No	-0.13	-2.20; 1.93				
Yes			0.90			
Diet change:						
No	1(reference)					
Yes	-0.43	-1.17; 0.30	0.24			

Nutritional Supplements:						
No	1(reference)					
Yes	0.29	-0.49;1.09	0.46			
Unexpected weight loss:						
No	1(reference)					
Yes	-1.24	-2.42; -0.06	**0.03**	-0.82	-2.11; 0.46	0.21
CD4 cells count:						
<200	1(reference)					
200-349	-0.50	-1.38; -0.36	0.20	-0.78	-1.66; 0.10	0.008
>=350	0.72	-0.34; 1.79	0.18	-0.05	-1.26; 1.16	0.930
Visits:						
6 months*	1(reference)					
12 months	1.02	0.12; 1.92	**0.02**	0.45	-0.81;1.73	0.48
18 months	0.31	-0.60;1.23	0.50	-0.59	-2.81; 1.62	0.59
24 months	0.42	-1.09;1.95	0.58	-0.95	-4.25; 2.34	0.57
Time on treatment:	0.0003	-0.001;0.002	0.115	0.0009	-0.003;0.005	0.679

Note: the six month visit is the reference (baseline)

CHAPTER 4: DISCUSSION

Making use of the Rwandan Women Inter-association Study Assessment data from a cohort study on the effectiveness and side effects of antiretroviral treatment, we evaluated weight changes (loss or gain) in HIV-infected women initiating HAART, and identified predictors of weight changes in the cohort. This chapter presents the discussions of the findings.

4.1. Change in weight after HAART initiation

The results suggested an increase in mean weight from the baseline visit until 12 months after HAART initiation, and a slight decrease in weight from 12 to 24 months. The findings of this study share some similarities with previous reports in Rwanda and other developing countries (23, 33-36). For example, a study done in HIV-infected participants on *Stavudine*-containing HAART in Rwanda found a rapid increase in weight during the first 6-12 months of treatment and a progressive decline of weight during the second year of HAART (24). Another study in a large cohort of HIV-infected adults on HAART in Tanzania found a rapid increase in weight in the first 12 months, followed by stabilisation or a decrease in weight after 12 months. (23). The same pattern of weight change was reported in other studies where participants were followed for six months while on HAART. In India, in a cohort of HIV-infected patients who initiated *Nevirapine*-based HAART, an overall mean increase in weight of 2.8 kg (range: -12.5 to 22.5 kg) occurred after six months (34). Similarly, a study in three east African countries (Rwanda, Uganda, and Kenya) and Ethiopia reported that weight increased by 3.9 kg after six months of

HAART initiation (37). Studies in developed countries have shown the same pattern of weight change in HIV patients initiating HAART (30, 38).

In accordance with other studies (34, 39), approximately 50% of the participants gained weight, a quarter (26%) remained stable, and 21% lost weight. Severe et al. found that 84% of their study participants gained weight, and 16% remained at the same weight or lost weight after six months on HAART (39); after 12 months, 85% had gained weight and 15% remained at the same weight or had lost weight. In Rwanda, the study mentioned above in HIV-positive patients on *Stavudine*-containing HAART, a rapid increase of weight during the first 6-12 months of treatment was reported. It was estimated that 62% of patients had a progressive decline in body weight during the second year of treatment with a median loss of -3.1kg/year (IQR -1.6; -5.6; $p<0.01$) (24). In Tanzania, nearly one-third of study participants on HAART experienced substantial weight loss in the first 10 months after starting HAART (23).

4.2 Change in weight according to baseline CD4 cell count and baseline BMI

Study participants who were underweight at baseline (BMI <18.5 kg/m^2) gained more weight compared to other participants. These findings support those from a cohort of patients initiating HAART in Zambia where underweight patients at baseline gained more weight than those in other categories (9). Similarly, Li et al. found that patients who were underweight at initiation of HAART had a better response to treatment at three months and gained more weight than other

BMI groups during the follow-up period (23). Furthermore, they found that close to 50% of underweight patients gained more than 10% of their baseline weight, compared to 19% and 8% among those of normal weight and those who were overweight or obese, respectively (40).

This study did not find a statistically significant change in weight during the follow-up period compared to the baseline in overweight and obese women. This may be due to the small number of women in those two categories. The fact that underweight participants gained more weight compared to other BMI categories may also be partially explained by the regression to the mean (41).

In this study, the immunosuppressed participants with CD4 cell counts <200 µL at baseline gained more weight than those with CD4 cell counts >200 cells/µL. This finding is in line with other studies in South Africa, USA, Brazil and Vietnam (31, 38, 42, 43) where a low CD4 cell count at baseline was associated with greater increase in weight in patients initiating HAART. Similarly, the gain in weight in the immunosuppressed underweight group , may be explained by the regression to the mean (41).

Thought in general women in underweight and normal weight categories gained rapidly weight compared to other categories after six month of HAART initiation, some of women in both categories lost weight during different visits. For example in those two categories mentioned above, 30% of women lost weight six month after HAART initiation (Appendix A). As well around 35% of obese and overweight women gained weight during twelve months after HAART

initiation. Similarly some of women who lost weight at different visits had CD4 cell count of <=200 cells/µL.

4.3 Independent predictors of weight change

4.3.1 Independent predictors of weight loss

Time-varying diarrhoea for more than two weeks and CD4 cell counts of 200-349 cells/µL were independent predictors of weight loss. According to the literature, diarrhoea is common in HIV patients and is caused by organisms or drugs. Diarrhoea will negatively affect the nutritional status of the HIV/AIDS patient, thus further compromising the immune system (27). The findings of this study support those from the Nutritional for Living Study in Boston which found diarrhoea to be associated with a risk of ≥ 5% weight loss in HIV patients initiating HAART (20). In Tanzania, diarrhoea was also a predictor of weight loss in a cohort of HIV patients initiating HAART (23). Graham et al. also showed diarrhoea to be a predictor of weight loss, as well as a low CD4 cell count of 200-350 cells/mL. This result is in line with the Tanzanian study in patients on HAART, where a time-varying low CD4 cell count was found to be associated with weight loss (23).

4.3.2 Independent predictors of weight gain

After adjusting for other factors, the time-varying variables, education level (completion of secondary school), marital status (married legally and other), and CD4 cell count (200-349 µ/L) were associated with weight gain. The association of socio-demographic factors (educational

level and marital status) with weight gain has also been reported in other studies in Africa in patients on HAART (23). The finding that a high education level is associated with weight gain can also be explained by high adherence of patients to treatment, and better diets in educated women. This study showed an increase in CD4 cell count to be associated with weight gain, supporting the findings of a study conducted in Rwanda which found that higher on-treatment CD4 cell counts were protective against weight loss (24).

4.3.3 Implications

The results from this study show the importance of measuring weight during follow-up visits in patients starting antiretroviral treatment, as well potential areas of intervention in order to prevent weight loss and promote weight gain in patients on HAART. In the HAART era, physicians need to remain vigilant about weight changes in patients on HAART, whether they are starting treatment or have been on it for some time. In addition, it is important for clinicians who take care of HIV-infected patients on HAART to pay attention to patients who lose weight, and those who present with diarrhoea or CD4 cell counts at follow-up visits (<350 cells/µL) since these factors have been associated with weight loss during the HAART era.

4.3.4 Limitations of the study

The main limitation of the study was due to the fact that secondary data were used. Other potential factors associated with weight change, identified in other studies, such as viral load, haemoglobin, and HAART regimen, were missing from the dataset. In addition, it was not possible to analyse data on body weight composition, such as lean and fat mass, as these data

were not collected in the primary study. Thus, we were unable to identify which component of body composition was associated with weight change.

A further limitation is that the study participants were women from Kigali city and, as such, are not necessarily representative of the HIV population receiving HAART in the entire country. Therefore, the results of this study may not be generalised to all women in Rwanda, and certainly cannot be generalised to males.

The analysis did not include the covariates, alcohol intake and psychosocial factors. A history of alcohol use was recorded at baseline only, when participants were asked about their alcohol intake in the last six months; 141 (30%) women reported alcohol intake. The majority (109; 24 %) drank alcohol less than once a week; only a very small number 12 (2.6%) drank alcohol every day. For this reason, alcohol intake was not considered as a covariate in the analysis. It would have been interesting to include psychosocial factors, such as depression or PTSD, however, a previous unpublished study using the RWISA data set showed no effect of these psychosocial factors on weight change (44) which is why they were not included as covariates in the study reported here.

4.3.5 Strengths of the study

To our knowledge, this is one of the few studies to specifically examine predictors of weight change in women on antiretroviral treatment in Rwanda using longitudinal data. This was also a relatively large study of almost 500 women. The data used for the analysis were obtained by

trained health professionals, which minimised reporting bias. The participants of this study were HAART-naïve which avoided confounding of the results due to previous exposure to HAART.

CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

5.1. Conclusion

The results of this study demonstrated that the majority of participants showed significant weight gain after the initiation of HAART. Relationship between baseline characteristics, such as CD4 cell count and BMI, and weight change, were identified. The predictors of weight loss were: diarrhoea for more than two weeks and CD4 cell counts of 200 to 349 cells/mL , while socio-demographic factors such as marital status, high education level, and an increase in CD4 cell count were predictors of weight gain.

This study has shown the importance of taking weight measurements during follow-up visits, especially in patients starting antiretroviral treatment. It also identified potential areas of intervention in order to promote weight gain in patients on antiretroviral treatment. HIV/AIDS clinicians need to adequately follow up all patients who start antiretroviral treatment, especially those who present with diarrhoea for more than two weeks, and those with a CD4 cell count of 200 - 349, since some of them will still lose weight, even while on treatment.

5.2. Recommendations

The predictors of weight change, viz. diarrhoea for more than two weeks, CD4 cell count of 200 - 349 cells/µL, marital status (married legally and other), and educational level (complete secondary school), provide information that can be used while planning HIV care programmes and during HIV patient management in the clinic.

The methods used in this study and the information generated can be used to guide the planning and design of future studies to investigate changes in nutritional status after the initiation of HAART.

There is a need for further studies that consider women's body mass composition (lean and fat mass) in order to identify which component of body composition is associated with weight change while on HAART.

APPENDICES

Appendix A: Weight change according to CD4 cell count and BMI at baseline.

BMI at baseline		**Weight Change at 6months**		**Weight Change at 12 months**		**Weight Change at 24 months**	
		Gained	**Lost**	**Gained**	**Lost**	**Gained**	**Lost**
cd4 <=200	**<18.5**	6.4±3.9 (n=7)	-1.8±0.9 (n=6)	**3**±1 (n=3)	**-4.6**±3.7 (n=5)	**4**±2.8 (n=2)	**-3.9**±2.7 (n=11)
	18.5-25	3.9±2.9 (n=31)	-5.4±5.0 (n=18)	**6**±4.3 (n=45)	**-2.5**±1.2 (n=12)	**5.6±4.1 (n=27)**	**-3.9**±2.7 (n=11)
	>25-30	2.5±2.1 n=2)	-2±1 (n=6)	8.0±4.9 (n=45)	**-10(1)**	**7.5**±4.9 (n=4)	**-4(1)**
	>30	0	0	0	0	**6.5**±6.3 (n=2)	0
cd4 >200	**<18.5**	**3.3**±1.8 (n=14)	**-4.0**±1.7 (n=16)	**3.4**±2.9 (n=12)	**-4**±4.8 (n=7)	**4.0**±4.4 (n=18)	**-5.6**±5.9 (n=15)
	18.5-25	**4.5**±3.5 (n=95)	**-3.4**±3.2 (n=41)	**5.4**±3.5 (n=96)	**-5.5**±4.6 (n=46)	**5.0**±3.9 (n=116)	**_4.5**±3.5 (n=61)
	>25-30	**6**±4.1 (n=21)	**-4**±2.1 (n=7)	**8.1**±5.2 (n=38)	**_3.5**±1.2 (n=4)	**10.3**±7.6 (n=25)	**-2.5**±1.8 (n=6)
	>30	**9**±7 (n=2)	**-4**±3 (n=3)	**11**±3.4 (n=3)	**-5**±4.2(n=2)	**15.8**±4.5 (n=6)	**-9.5**±2.1 (n=2)

Appendix B: University of the Witwatersrand Human Research Ethic Clearance Certificate for the study

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Jean Paul Kimenyi

CLEARANCE CERTIFICATE	**M120937**
PROJECT	Predicators of Weight Loss in HIV-Infected Women on Antiretroviral Therapy in Rwanda
INVESTIGATORS	Dr Jean Paul Kimenyi.
DEPARTMENT	School of Public Health
DATE CONSIDERED	28/09/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 28/09/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr Gill Nelson

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix C: Rwanda Republic National Ethics Committee Clearance Certificate for the study

REPUBLIQUE DU RWANDA

NATIONAL ETHICS COMMITTEE / COMITE NATIONAL D'ETHIQUE

Telephone: (250) 55 10 78 84
E-mail: rnec@moh.gov.rw

Ministry of Health
P.O. Box 84
Kigali, Rwanda.

Assurance No. FWA 00001973
IRB 00001497 of IORG0001100

Dr Francois NDAMAGE
Principal Investigator
WE-Actx
Rwanda

Re: Rwandan women's Interassociation Study and Assessment (RWISA) : Effectiveness and Toxicity of Antiretroviral therapy in HIV- Infected Rwandan Women

After reviewing your Protocol and revision made on the advice of the RNEC on 19 July 2008, we hereby provide approval for the above mentioned protocol.
Please note that approval of the protocol and consent form is valid for 12 months.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrollment of participants
3. All consent forms signed by subjects should be retained on file. The RNEC may conduct audits of all study records, and consent documentation may be part of such audits.
4. Please present nutritional aspects as a separate protocol
5. Provide Material Transfer Agreement (MTA)before shipment of samples to the USA
6. A continuing review application must be submitted to the RNEC in a timely fashion and before expiry of this approval.
7. Failure to submit a continuing review application will result in termination of the study.

Sincerely,

Dr. Kayitesi KAYITENKORE.
CHAIR, Rwanda National Ethics Committee.

P.O Dr Emmanuel Nkeramihigo
Secretary

C.P.I.
- Hon. Minister of Health.
- The Permanent Secretary, Ministry of Health.

RWANDA NATIONAL ETHICS COMMITTEE
DATE: 24/7/2008
COMITE NATIONAL D'ETHIQUE

Appendix D: Approval for data set use from Rwanda Women's Equity in Accesss to Care and Treatment (WE_ACTx).

Women's Equity in Access to Care and Treatment (WE-ACTx)

P.O.BOX 5141 Kigali- Rwanda
www.we-actx.org

September 5, 2012

Christine Mutaganzwa, MD
Aline Aurore Niyibizi, MD
Jackline Umunyana, MD
Jean Paul Kimenyi, MD

Dear Christine, Aline, Jackline and Jean Paul,

Subject: **Availability of RWISA database for your studies.**

I am writing to confirm that you are permitted use of RWISA (Rwanda Women's Interassociation Study and Assessment) database for your Masters degree studies at the University of the Witwatersrand.

I take the opportunity to request all assistance required from the database keeper to avail the dataset and all details you require for successful analyses to meet your study goals.

I am also attaching the Rwanda National Ethics Approval letter and other approvals for RWISA study.

I wish you the best of good luck in your studies.

Sincerely,

WE-ACT, RWANDA

Eugene MUTIMURA, Ph.D
Director of Research & Professional Training
Women's Equity in Access to Care & Treatment (WE-ACTx)
Dorona House, Avenue Kalisimbi; P.O.BOX 5141 Kigali Rwanda
Phone: +250 078 830 2774; e-mail: eugene.mutimura@gmail.com

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