CHAPTER ONE: INTRODUCTION AND MOTIVATION FOR THE STUDY

1.1 Introduction

The Centers for Disease Control and Prevention first described acquired immune deficiency syndrome (AIDS) in 1981 (Fee and Brown, 2006). HIV (human immunodeficiency virus) and AIDS have reached epidemic proportions since then. Affecting millions of people globally, HIV and AIDS threaten the quality of health of vulnerable populations (Tabi and Vogel, 2006), including South Africa. Trends indicate that in Africa HIV prevalence in females is notably higher than in males, and females have a less accurate, comprehensive knowledge of HIV (UNAIDS, 2008). The largest proportion of new HIV cases is among youth and woman who are often economically disadvantaged and have experienced barriers when trying to access HIV care (Fields-Gardener *et al*., 2004).

HIV is spread from human to human through direct sexual contact with sexual fluids and blood or blood products (Schreibman and Friedland, 2003). Infants can also be exposed to the virus through pregnancy and lactation (Schreibman and Friedland, 2003). The virus targets the immune system, in particular, CD4 lymphocytes, (Rosenberg and Walker, 1998) also referred to as T-helper lymphocyte cells which are involved in protecting the body against infection (Fenton and Silverman, 2008, 992).

According to the UNAIDS Report on the global AIDS epidemic (2008) there were an estimated 33 million people living with HIV in 2007. Although the global percentage of people living with HIV has stabilized since 2007, the overall number of people living with HIV has increased due to new infections (UNAIDS 2008). Sub-Saharan Africa, the geographical region most heavily affected (Merson, 2006; Fawzi, *et al*, 2005; Anabwani and Navario, 2005) by this epidemic accounts for 67% of all people living with HIV (UNAIDS, 2008). Famine, droughts, floods, poverty, food insecurity, war and political insecurities are

common factors that affect the lives of people living in this region (Spencer, *et al*., 2007). Reports have shown that during 2007 72% of AIDS deaths occurred in Sub-Saharan Africa (UNAIDS, 2008).

Poor nutrition, access to suitable amounts of good quality food (Spencer *et al*, 2007), and disease progression are involved in the vicious cycle that contributes to the deterioration of the health of HIV patients and ultimately leads to increased mortality (Fawzi, *et al*, 2005). The relationship between HIV / AIDS, malnutrition and wasting is well described, with nutritional status being compromised by various factors including reduced food intake; malabsorption caused by gastrointestinal involvement; increased nutritional needs as a result of fever and infection; increased nutrient losses and medication related side effects (Kennedy and MacIntyre, 2003; Earthman, 2004; Fawzi *et al*, 2005).

Malnutrition, weight loss, body cell mass depletion and micronutrient deficiencies are often observed in individuals with HIV / AIDS and are associated with increased morbidity and mortality (Earthman, 2004; Fawzi *et al.*, 2005). According to Kennedy and MacIntyre (2003), malnutrition is a common consequence of HIV infection and contributes to the frequency and severity of opportunistic infections seen in HIV / AIDS. Many studies have indicated that malnutrition develops due to multiple factors and is influenced by the disease stage, as well as by the nature of specific disease complications (Donald, 2001).

Nutritional status is a major factor in survival, and failure to maintain body cell mass at 54% of ideal body weight leads to death (Kennedy and MacIntyre, 2003). Effective nutrition intervention including dietary counseling and support to improve nutritional status is considered critical in the treatment of HIV / AIDS (Kennedy and MacIntyre, 2003; Donald, 2001). Adequate nutrition is also necessary to optimize the benefits of antiretroviral drugs which are essential to prolong the lives of people infected with HIV (Tomkins, 2005).

According to Montessori *et al*. (2004), the introduction of highly active antiretroviral therapy (HAART) has led to a significant reduction in AIDS-related morbidity and mortality. Long-term remission of HIV can be achieved by using combinations of antiretroviral therapy (Montessori, *et al*., 2004).

According to Fenton and Silverman, (2008) HAART usually consists of a combination of at least three antiretroviral agents used with the intent to suppress viral replication and progression of HIV disease. HAART therapies consider viral load levels, current and lowest CD4 counts, current and past clinical conditions and life stage (Grinspoon, 2005; Fenton and Silverman, 2008, 999).

Current antiretroviral therapy (ART) consists of 4 major treatment modalites, including nucleoside reverse transcriptase inhibitors (NRTIs), non nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs) and fusion or entry inhibitors (Grinspoon, 2005). NRTI's commonly form the "backbone" of the antiretroviral therapy cocktail, two NRTI's are usually combined with one medication from either of the two remaining classes, namely the NNRTI's or the PI's (Montessori *et al*., 2004). According to the UNAIDS Report on the global AIDS epidemic (2008) "in sub-Saharan Africa, only about half of national HIV strategies meet UNAIDS quality criteria".

After pressure from local and international organizations, the South African Government made antiretroviral therapy available to people living with HIV and AIDS in 2003 (Anabwani and Navario, 2005). At that time South Africa had the largest prevalence of HIV infected persons world wide (Anabwani and Navario, 2005). In South Africa two adult regimens are currently available at Comprehensive Care, Management and Treatment (CCMT) of HIV / AIDS sites. The uptake of antiretroviral therapy in South Africa is far below what is required (Hasen and Bosch, 2006) and weaknesses in health care systems are slowing the implementation of HIV treatment programmes (UNAIDS, 2008). The adult regimens in South Africa include the following (Table 1).

Table 1: ART Regimens used in SA (Fomundan *et al.,* 2006)

Regimen	Drugs
1a	Lamivudine(3TC) + Stavudine (d4T) + Efavirenz
1b	Lamivudine(3TC) + Stavudine (d4T) + Nevirapine
2 (second line)	Didanosine (ddI) + Zidovudine (ZDV) + Lopinavir / Ritonavir

Due to HAART, HIV has become a manageable chronic condition, which results in an increase in life expectancy. The use of ART is however, often accompanied by several clinical and metabolic complications (Oh and Hegele, 2007; Montessori *et al*., 2004).

Metabolic complications including insulin resistance, glucose intolerance, lactic acidosis, liver enzyme abnormalities, anemia, osteopenia and fat abnormalities (lipodystropy and dyslipidemia) have been associated with HIV–1 infection and long-term usage of antiretroviral medications and occur in approximately half of all HAART-treated patients, (Valcour *et al.,* 2005; Donald, 2001; Oh and Hegele, 2007; Jain *et al*., 2001; Montessori *et al*., 2004). Apart from underlying metabolic conditions, patients often have difficulties eating due to side effects like nausea, vomiting and loss of appetite and coupled with increased incidence of diarrhea these patients are at a high risk of becoming malnourished (Spencer *et al*., 2007).

HAART-associated dyslipidemia is characterized by hypertriglyceridaemia with low levels of high-density lipoprotein (HDL) cholesterol and increased total cholesterol, with or without increased low-density lipoprotein (LDL) cholesterol. A proposed mechanism underlying dyslipidemia is HAART-induced mitochondrial alterations (Oh and Hegele, 2007).

Insulin resistance is characterized by the reduced ability of insulin to inhibit hepatic gluconeogenesis and to increase muscle uptake of glucose. The pathophysiologic basis of insulin resistance in patients on potent antiretroviral therapy is unknown (Schambelan *et al.*, 2002). Potential mechanisms include direct effects of antiretroviral drugs that impair cellular glucose uptake, or indirect

mechanisms related to body fat changes, including central obesity and peripheral lipoatrophy (Schambelan *et al.*, 2002). New-onset diabetes mellitus, clinically similar to type 2 diabetes, affects a small population (1-6%) of HIV-infected patients treated with PI-based antiretroviral regimens (Montessori *et al*, 2004). However, insulin resistance may also be associated with HIV infection itself in patients not receiving PI therapy, perhaps resulting from direct effects of the HIV on pancreatic beta cell function and insulin secretion (Montessori *et al*, 2004). Insulin resistance and dyslipidemia are associated with an increased risk of obesity and cardiovascular disease, all of which are a growing concern in HIV infected patients (Engelson *et al*., 2006).

According to Andrade *et al.* (2002), "a substantial proportion of HIV infected men, woman and children undergo body fat redistribution, characterized by depletion of subcutaneous adipose tissue or accumulation of adipose tissue in the visceral compartment". PI therapy is most strongly linked to lipodystropy syndrome; NRTI's especially d4T has been associated with lipodystropy (Montessori *et al*, 2004). Factors which increase risk for lipodystropy include advanced HIV disease, increased duration on PI therapy and increasing age (Schwenk *et al*., 2000; Martinez *et al*., 2001).

Viral resistance can occur and more new HIV infections involve strains resistant to at least one class of medications, leaving fewer treatment options (Kuritzkes *et al,* 2003). Not all patients tolerate antiretroviral drugs, and although some side effects diminish after the start of medication treatment, some persist, and HIV-related side effects continue (Fenton and Silverman, 2008, 1001).

According to Fomundan *et al*. (2006), "Prevention and management of side effects of drugs used to manage HIV and AIDS are a challenge to clinicians, patients, drug regulators, researchers, government, health care workers, family members and all those affected. Side effects and reactions continue to affect patients' decisions to start treatment, to continue treatment and to adhere to prescribed regimens".

This study will assist in describing the nutritional status of HIV infected people on HAART in a typical CCMT site in South Africa, thus highlighting areas that need to be focused on in nutrition interventions to improve the nutritional status and quality of life for HIV infected individuals.

1.2 Objectives and aims

1.2.1 Aims

The aim of the study was to determine the nutritional status of HIV / AIDS infected adults on HAART.

1.2.2. Objectives

To achieve the aim of the study the following parameters needed to be determined:

1. Anthropometric status (BMI, waist circumference, waist to hip ratio, body fat percentage)
2. Dietary intake
3. Lifestyle factors and family history of chronic disease
4. Biochemical parameters (fasting glucose concentrations, total cholesterol levels, HDL cholesterol, LDL cholesterol, triglyceride levels, CD 4 counts and viral load) and blood pressure
5. Associations between variables listed in sub-aims 1- 4

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) epidemic affects many people globally, impacting on health, nutrition, food security and socioeconomic development (WHO, 2003; Spencer, *et al*., 2007). According to the UNAIDS Report on the global AIDS epidemic (2008), "the global HIV epidemic cannot be reversed."

HIV/ AIDS is most prevalent in Sub-Saharan Africa (Spencer *et al*., 2007; Pratt, 2003, 9), and is exacerbated by the presence of malnutrition, opportunistic infections, (Anabwani and Navario, 2005), widespread poverty, unemployment (ASSAf, 2007), discrimination and inadequate health care systems (Steinbrook, 2008; Morris and Cilliers, 2008). Improvement of the nutritional status of HIV infected individual's can only be achieved by utilizing local resources, learning from clinical experience and applying scientific based evidence to treatment programmes (WHO, 2003).

Chapter two highlights current literature on various aspects that affect nutritional status in HIV infected adults. Pathophysiology, etiology, antiretroviral therapy, HAART side affects, nutrition assessments and requirements that can impact on HIV, as well as lifestyle factors will be discussed in this chapter.

2.2 Pathophysiology and etiology

The Centers for Disease Control and Prevention (CDC) first described AIDS in 1981(Hubley, 2002, 2; Fenton and Silverman, 2008, 992; Pratt, 2003, 2). HIV infection is the underlying cause of AIDS and targets principal agents called CD4 cells (T-helper lymphocyte) that are involved in protection against infection (Rosenberg and Walker, 1998; Morris and Cilliers, 2008, 79: Fenton and Silverman, 2008, 992; Visagie, 1999, 9). HIV works by encoding the enzyme

reverse transcriptase and thereby making a DNA copy of the viral RNA, which can remain in the nucleus of the infected cell for a long time (Hubley, 2002, 14; Morris and Cilliers, 2008, 81; Pratt, 2003, 19; Visagie, 1999, 9; Spencer, 2005, 8). The virus attacks and replicates in CD4 cells and macrophages (Spencer *et al*., 2007; Morris and Cilliers, 2008, 81; Hubley, 2002, 14; Spencer, 2005, 5). CD4 cells diminish in number, increasing patients' susceptibility to opportunistic infections. As a result CD4 cell count together with viral load is frequently used to assess HIV disease progression (Spencer, 2005, 8; Fenton and Silverman, 2008, 992; Morris and Cilliers, 2008, 85; Visagie, 1999, 9).

Lymph glands, semen, vaginal secretions, and the central nervous system (CNS) all contain HIV which evolves quickly, depleting CD4 cells, causing immunodeficiency, neurologic complications, opportunistic infections, and constitutional disease (high temperatures, thrush, shingles, night sweats, chronic fatigue, malaise and diarrhea) (Fenton and Silverman, 2008, 992; Pratt, 1999, 12).

Viral load is a major determinant in HIV progression (Spencer *et al.,* 2007; Fenton and Silverman, 2008, 992; Spencer, 2005, 8). Sharing contaminated needles and injecting contaminated blood products are both ways of transmitting HIV (Hubley, 2002, 3; Spencer *et al*., 2007; Fenton and Silverman, 2008, 992), the virus is however most commonly transmitted via blood or semen during unprotected intercourse with an HIV-infected individual (Spencer *et al*., 2007; Fenton and Silverman, 2008, 992).

Other body fluids that contain blood, pre-semenal fluid, vaginal fluid and breast milk all contain HIV and are possible routes for transmission of the virus (Spencer *et al*., 2007; Fenton and Silverman, 2008, 992; Semba, 2006, 1406). Mother to child transmission of HIV is a major global concern and can occur before or during birth or through breast-feeding (Dreyfuss and Fawzi, 2002; Semba, 2006, 1406).

According to Fenton and Silverman (2008, 992) HIV-1 mutates readily and is the most common type of HIV distributed globally (Hubley, 2002, 15) in various strains, subtypes and groups. HIV-2 is less easily transmitted and takes longer to develop in infected individuals; both types of HIV are transmitted in the same way (Hubley, 2002, 15; Fenton and Silverman, 2008, 992; Pratt, 2003, 23).

2.3 Stages of HIV infection

HIV spreads throughout the body and decreases blood CD4 cell count after exposure and transmission of HIV into the host (Fenton and Silverman, 2008, 996; Spencer *et al*., 2007; Morris and Cilliers, 2008, 81; Hubley, 2002, 14). Even with HIV replication, equilibriums can be reached, returning CD4 cell counts to almost normal and reducing the virus in the blood, at a later stage the host cell can be triggered to produce the virus (Hubley, 2002, 14; Fenton and Silverman, 2008, 996). The central nervous system and gastrointestinal tract are reservoirs for the virus and years can pass until the active HIV replication affects CD4 cell count and increases risk for opportunistic infections (Fenton and Silverman, 2008, 996). HIV has four stages including acute HIV infection, asymptomatic, symptomatic and AIDS (Visagie, 1999, 14: Fenton and Silverman, 2008, 998).

Acute HIV infection presents with flu like symptoms (including loss of appetite, weight loss, fever, maculopapular rash, inflamed lymph nodes, oral ulcers, malaise and pharyngitis) and occurs within 2-4 weeks after infection during which time rapid viral replication occurs (Fenton and Silverman, 2008, 998). HIV diagnosis is often missed at this point as there may be no symptoms (SA, DOH, 2001; Visagie, 1999, 13) and only after seroconversion (development of HIV antibodies) will antibodies become apparent in the blood at which point individuals will test positive for HIV (Fenton and Silverman, 2008, 998; Visagie, 1999, 14). During this time, patients are extremely infectious (Visagie, 1999, 13) and viral loads extremely elevated (Fenton and Silverman, 2008, 998).

Asymptomatic chronic HIV infection varies in duration lasting between a few months to 10 years, often with little or no symptoms (Visagie, 1999, 14; Fenton and Silverman, 2008, 998). Decreases in lean body mass and vitamin B_{12} are evident, thereby increasing susceptibility to water and food borne pathogens (Fenton and Silverman, 2008, 998).

Symptomatic HIV infection is characterized by non-AIDS defining symptoms such as fever, thrush, bacterial pneumonia, skin problems, sweats and fatigue along with a decline in body composition and nutritional status (Fenton and Silverman, 2008, 998; Visagie, 1999, 14). AIDS or advanced HIV disease also know as "full blown AIDS" (SA, DOH, 2001; Visagie, 1999, 14) is used to diagnose patients who present with at least one well-defined, life threatening clinical conditions (as seen in table 2.2) (Fenton and Silverman, 2008, 998; Visagie, 1999, 16).

2.3.1 Classification system of HIV / AIDS

Table 2.1 CDC Classification System for HIV Infection according to clinical categories (CDC, 1993)

Cell Categories	Clinical Categories		
	A	**B**	**C**
	Asymptomatic, Acute HIV,	Symptomatic, not A or C	AIDS-Indicator
(1) ≥500 cells/µL	A1	B1	C1
(2) 200-499 cells/µL	A2	B2	C2
(3) <200 cells/µL	A3	B3	C3

Table 2.2 Classification system for HIV infection (CDC, 1993)

Classification System for HIV Infection and Expanded AIDS Surveillance Case Definition for Adolescents and Adults

CLINICAL CATEGORIES

Clinical categories are defined as follows:

Category A – one or more of the conditions listed here occurring in an adolescent or adults with documented HIV. Conditions listed in categories B and C must not have occurred

- Asymptomatic HIV infection
- Persistent generalized lymphadenopathy
- Acute (primary) HIV infection with accompanying illness or a history of acute HIV infection

Category B – symptomatic conditions occurring in an HIV infected adolescent or adult that are not included among conditions listed in clinical category C and that met at least one of the following criteria:

a) The conditions are attributed to HIV infection and/or indicate a defect in cell-mediated immunity.

b) The conditions are considered by physicians to have a clinical course or management that is complicated by HIV infection.

Examples include, but are not limited to, the following:

- Bacillary angiomatosis
- Oropharyngeal candidiasis (thrush)
- Vulvovaginal candidiasis, persistent or resistant
- Pelvic inflammatory disease (PID)
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Hairy leukoplakia, oral
- Idiopathic thrombocytopenic purpura
- Constitutional symptoms, such as fever (>38.5°C) or diarrhea lasting >1 month
- Peripheral neuropathy
- Herpes zoster (shingles), involving >2 episodes or >1 dermatome

Category C – any condition listed in 1987 surveillance case definitions for AIDS and affecting an adolescent or adult. The conditions in clinical category C are strongly associated with severe immunodeficiency, occur frequently in HIV- infected individuals, and cause serious morbidity and mortality. Among the conditions listed in the 1993 AIDS surveillance case definition (assuming HIV positivity) are the following:

- Candidiasis of the bronchi, trachea, or lungs
- Candidiasis, esophageal
- CD4 lymphocyte counts <200 or a CD4 % total lymphocytes <14 if the absolute count is not available
- Cervical cancer, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1-month duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Cytomegalovirus retinitis (with loss of vision)
- HIV encephalopathy
- Herpes simplex: chronic ulcers (>1-month duration), or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1-month)
- Kaposi sarcoma
- Lymphoma, Burkitt, immunoblastic, or primary central nervous system
- Lymphoma, primary in brain
- *Mycobacterium avium* complex (MAC) or *M kansasii* , disseminated or extrapulmonary
- *Mycobacterium tuberculosis* , pulmonary or extrapulmonary
- *Mycobacterium* , other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis jiroveci* pneumonia
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent (nontyphoid)
- Toxoplasmosis of brain
- Wasting syndrome secondary to HIV

2.4 Antiretroviral therapy

According to the UNAIDS Report on the global AIDS epidemic (2008), effective prevention strategies are available to reduce the risk of HIV exposure. Post-exposure prophylaxis, experimental regimens for pre-exposure prophylaxis and prevention of mother to child transmission are all strategies centered on antiretroviral therapy (UNAIDS, 2008). The application and overall goals of initiating highly active antiretroviral therapy (HAART) includes optimizing the suppression of viral replication (Hammer *et al.,* 2008; Fenton and Silverman, 2008, 999; Barth *et al*., 2008), reducing the incidence of malnutrition (Valcour *et al.,* 2005; Donald, 2001), improving immunity and delaying disease progression, as well as extending life expectancy (Tomkins, 2005; Coyne-Meyers and Trombley, 2004). The pattern of infection by HIV and AIDS has been changed by HAART (Tomkins, 2005) through a reduction in viral burden and better prognosis (Ware *et al*., 2002) that significantly reduces AIDS-related morbidity and mortality (Fenton and Silverman, 2008, 999; Montessori *et al.,* 2004; Nerad *et al*., 2003).

Current HAART regimens have the ability to reduce viral load to undetectable levels, consequently increasing CD4 counts (Nerad *et al*., 2003). Long-term use of antiretroviral medications is costly (Levy, 2009) and does result in altered body fat distribution and metabolic complications, which include hyperlipidemia and insulin resistance (Valcour *et al.,* 2005; Donald, 2000).

According to Montessori *et al*., (2004), the implementation of HAART together with adequate nutrition, are essential components required to ensure an effective response to the HIV / AIDS pandemic in Africa as well as globally.

Despite intensive efforts, millions of HIV-infected patients do not access antiretroviral therapy, even when they are available (Tomkins, 2005). Several countries have shown an increase in the uptake of antiretroviral therapy

(Tomkins, 2005). By the end of 2007, almost 3 million people were receiving HAART in low and middle-income countries, accounting for a ten-fold increase in the last six years (UNAIDS, 2008). Even with this increase it was reported by WHO that in 2007 an estimated 7 million HIV infected individuals in Sub-Saharan Africa still required antiretroviral therapy (Steinbrook, 2008). According to UNAIDS (2008) "This rapid expansion of treatment is saving lives, improving quality of life and contributing to the rejuvenation of households, communities and entire societies".

2.4.1 Types of antiretroviral therapy

Four major treatment modalities are available; they include the following drug groups; (1) nucleoside reverse transcriptase inhibitors (NRTIs), (2) non nucleoside reverse transcriptase inhibitors (NNRTIs), (3) protease inhibitors (PIs) and (4) fusion or entry inhibitors (Grinspoon, 2005; Fields-Gardener *et al*., 2004). NRTIs were the first drugs given as antiretroviral agents (Grinspoon, 2005), however one antiretroviral doesn't suppress viral activity and a combination of drugs are required (Fenton and Silverman, 2008, 999).

NRTIs commonly form the "back bone" of antiretroviral cocktails and often two NRTI's are combined with a medication from either of the remaining drug classes (Montessori *et al*., 2004). According to Fenton and Silverman (2008, 1001), there are now 27 antiretroviral agents approved by the FDA (Food and Drug Administration).

In South Africa, two adult regimens are currently available at Comprehensive Care, Management and Treatment of HIV / AIDS (CCMT) sites. The adult regimens include the following (Table 2.3).

Table 2.3 HAART Regimens used in South Africa (Fomundan, 2006, 2)

Regimen	Drugs
1a	Lamivudine(3TC) + Stavudine (d4T) + Efavirenz
1b	Lamivudine(3TC) + Stavudine (d4T) + Nevirapine
2 (second line)	Didanosine (ddI) + Zidovudine (ZDV) + Lopinavir / Ritonavir

Not all HIV-infected patients tolerate HAART (Fenton and Silverman, 2008, 1009). Ninety five percent adherence is necessary to ensure that medications work correctly and drug resistance does not occur (Carpenter *et al*., 2000). Viral resistance can influence the effectiveness of the antiretroviral agents (Kuritzkes *et al.*, 2003), drug mutations occur and patients' drug regimens will need to be adjusted (Long *et al*., 2009), therefore reducing available treatment options (Kuritzkes *et al.*, 2003).

2.4.1.1 Nucleoside reverse transcriptase inhibitors

Nucleoside reverse transcriptase inhibitors (NRTI) are structurally diverse (Grinspoon, 2005) nucleoside analogues that prevent DNA elongation and viral reproduction by incorporating into the viral DNA chain thus stopping DNA transcription (Montessori *et al*., 2004).

Nucleoside reverse transcriptase inhibitors were the first class of antiretroviral drug approved by the FDA (Long *et al*., 2009) and include emtricitabine, zalcitabine, zidovudine (AZT), lamivudine (3TC), didanosine (ddI), stavudine (d4T), abacavir (ABC) (Fenton and Silverman, 2008, 1002; Montessori *et al.*, 2004) and the nucleotide analogue tenofovir (Montessori *et al*., 2004). NRTI's can theoretically function as substrates for other enzymes involved in mitochondrial replication that can cause subsequent adverse events (Montessori *et al.*, 2004).

2.4.1.2 Non-nucleoside reverse transcriptase inhibitors

The NNRTI class comprises of nevirapine (NVP), delavirdine (DLV) and efavirenz (EFV) (Montessori *et al*., 2004). NNRTI's inhibit reverse transcriptase enzyme by binding near the active site and causing allosteric changes in the enzyme (Long *et al*., 2009). NNRTI-based HAART is more effective due to its extended half life and is preferred rather than protease inhibitor (PI) based regiments for initial treatment (Long *et al*., 2009). The low genetic barrier for class-wide resistance is the major drawback when using NNRTI's (Long *et al*., 2009).

2.4.1.3 Protease inhibitors

PIs act by binding and inhibiting the HIV protease enzyme, which cleaves polyprotiens to release structural proteins that are necessary for viral replication (Long *et al*., 2009; Grinspoon, 2005). According to Grinspoon (2005), protease enzyme inhibition doesn't prevent production of new viral copies, but produces copies that are unable to infect new cells. Currently there are nine protease inhibitors in use: atazanavir, indinavir, darunavir, fosamprenavir, lopinavir, ritonavir, nelfinavir, tipranavir and saquinavir (Long *et al*., 2009).

PI associated side effects include; abnormal accumulation (lipodystropy) of intramyocellular fat, leading to insulin resistance with resulting increases in plasma triglycerides and LDL concentrations (Oh and Hegele, 2007; Shah *et al*., 2005).

2.4.2 Adverse effects

In spite of the benefits of antiretroviral therapy, a wide range of adverse reactions are linked to HAART (Stein, 2009; Montessori *et al*., 2004; Nerad *et al.,* 2003; Almeida *et al*., 2009; Crane *et al*., 2006). These adverse reactions have been one of the leading causes for hesitation to begin antiretroviral therapy (Fomundan *et al*., 2006). Adverse effects can lead to non-adherence and

interruption or discontinuation of HAART (Stein, 2009; Nerad *et al.,* 2003), which increases risk for cardiovascular disease, renal and hepatic complications (Hammer *et al*., 2008), opportunistic infections and death (Stein, 2009).

The adverse affects of HAART can range from mild (gastrointestinal effects such as bloating, nausea and diarrhea) to life threatening conditions, side effects differ depending on the group of drugs (Montessori *et al*., 2004; Fomundan *et al*., 2006). Zidovudine (AZT) which is commonly used in the second line regimen in South Africa is associated with anemia, headaches, fatigue and elevated lactic acid levels (Montessori *et al*., 2004; Fomundan *et al*., 2006). Stavudine (d4T) is known to cause peripheral neuropathy and lactic acid level increases, protease inhibitor therapy-associated retinoid toxicity and NNRTI-associated hypersensitivity are common class specific side effects (Fomundan *et al*., 2006; Montessori *et al*., 2004). Lactic acidosis caused by mitochondrial toxicity, characterized by increased level of venous lactate (Salomon *et al*., 2002) is associated with Didanosine (ddL), AZT and d4T usage (Montessori *et al*., 2004). Complaints related to this condition include nausea, vomiting, malaise and fatigue (Montessori *et al*., 2004; Salomon *et al*., 2002). If lactic acidosis is not treated timeously is can be fatal, causing cardiac dysrhythmias, liver failure and death (Montessori *et al*., 2004). Total cholesterol and low density cholesterol levels are increased more by protease inhibitors (Grover *et al*., 2005) than by non-nucleoside reverse-transcriptase inhibitors (DAD study group, 2007), thereby increasing risks for future cardiovascular events (Grover *et al*., 2005; Kaplan *et al*., 2007; Baekken *et al*., 2008).

Treatments for adverse affects are managed using the same accepted medical therapy that would be used to treat similar conditions in patients not receiving HAART (Montessori *et al*., 2004). Understanding and managing the adverse affects of HAART are however a challenge (Fomundan *et al*., 2006) and the development of new antiretroviral agents continues in the hopes of maximizing the effectiveness of current available treatments (Montessori *et al.,* 2004).

2.4.2.1 Lipodystrophy and metabolic abnormalities

The use of HAART often results in metabolic changes (Kotler, 2000; Ware *et al*., 2002; Salomon *et al*., 2002) such as generalized lipodystropy and associated metabolic abnormalities (Salomon *et al*., 2002; Grinspoon, 2005). These metabolic abnormalities include changes to organs and tissue function that can lead to altered utilization, storage and excretion of nutrients (Fields- Gardener *et al*., 2004).

2.4.2.1.1 Fat maldistribution

The causes of fat maldistribution, also known as HIV-associated lipodystrophy syndrome (HALS) (Marcason, 2009) are poorly understood and multifactorial aspects including both endocrine and metabolic abnormalities influence body fat redistribution (Montessori *et al.*, 2004). HALS may occur within 20 months of starting antiretroviral therapy (Skipper, 2008). HAART has resulted in a substantial proportion of HIV infected individuals undergoing body fat redistribution (Andrade *et al*., 2002; Montessori *et al.*, 2004 Fenton and Silverman, 2008, 1009; Justman *et al*., 2008). Altered fat distribution is characterized by visceral fat accumulation (Andrade *et al*., 2002; Marcason, 2008; Kotler, 2000; Montessori *et al*., 2004; Fenton and Silverman, 2008, 1009) in the central regions such as the abdomen, breasts and the dorsocervical fat pad ("buffalo hump")(Montessori *et al*., 2004; Fenton and Silverman, 2008, 1009; Marcason, 2009). This increase in visceral and abdominal fat is associated with an increased risk for the development of glucose intolerance (Montessori *et al.*, 2004) and metabolic abnormalities (Marcason, 2008). Depletion of subcutaneous fat (Andrade *et al*., 2002; Kotler, 2000) in the face, limbs and buttocks are main clinical features of lipoatrophy (peripheral fat loss) (Montessori *et al*., 2004), ingrown toenails and prominent veins have been reported as a result of subcutaneous fat loss (Fenton and Silverman, 2008, 1009).

Patients are often hesitant to start HAART due to fear of developing fat-redistribution syndrome (Nerad *et al*., 2003; Fenton and Silverman, 2008, 1009), as cosmetic changes due to lipodystrophy compromise the confidentiality of their HIV status (Montessori *et al.*, 2004). Risk factors associated with the development of lipodystophy include increased duration on protease inhibitors, advanced HIV disease and age (Marcason, 2008; Martinez *et al*., 2001; Schwenk *et al*., 2000). Specific HAART drug classes, combinations of HAART and medications have been known to affect body shape differently (McDermott *et al*., 2005), protease inhibitors and NRTI's, stavudine and zidovudine (Fenton and Silverman, 2008, 1009) are known to cause lipodystrophy syndrome (Montessori *et al.*, 2004; Jain *et al*., 2001).

Hypertriglyceridemia, hypercholesterolemia and insulin resistance (Kosmiski *et al.,* 2001; Marcason, 2008) are also commonly seen in these patients who present with fat redistribution syndrome (Kotler, 2000). Failure to manage lipodystrophy and its associated risks, influence antiretroviral therapy and its effectiveness, thereby discouraging patients to continue with HAART (Montessori *et al.*, 2004). HALS is similar to dyslipidemia seen in the metabolic syndrome and only limited, often conflicting studies are available in this population group (Marcason, 2008). Nutrition therapy for HIV infected individuals may need to include nutrition applications that are applicable for metabolic syndrome (Marcason, 2008).

2.4.2.1.2 Dyslipidemia

Dyslipidaemia is defined as either elevated triglyceride levels ($\geq$1.7mmol/l) or low HDL (high density lipoprotein) cholesterol (<0.9mmol/l for men and <1.29mmol/L for women) (Alberti *et al*., 2006; Oh and Hegele, 2007; Montessori *et al*., 2004; Krummel, 2008, 833). Dyslipideamia is linked to insulin resistance and fat redistribution syndromes (Grover *et al*., 2005; Oh and Hegele, 2007) and occurs more commonly in patients receiving protease inhibitor therapy (Montessori *et al*., 2004; Stein, 2009; Grinspoon, 2005), thereby increasing risk for myocardial

infarction (Stein, 2009). Not only caused by HAART alone, the pathogenesis of dyslipedimia is poorly understood (Montessori *et al*., 2004) and HIV-associated dyslipidemia have been recognized for years before the use of protease inhibitor-based HAART (Grover *et al*., 2005; Oh and Hegele, 2007).

The pathogenesis of HIV-associated dyslipidemia is multifactorial (Brown, 2008). Immune activation early in HIV infection affects HDL levels by impairing cholesterol influx from macrophages and increased enzyme stimulus as a result of inflammation. High triglycerides occur due to impaired clearance of lipoproteins. Inflammatory cytokines interfere with lipid oxidation and free fatty acid metabolism changes, leading to suppression of lipolysis. Weight loss, protein depletion and nutritional status of HIV-infected patients can contribute to reduced HDL and LDL cholesterol levels (Oh and Hegele, 2007).

Antiretroviral-induced dyslipidemia is complex and may be difficult to treat (Brown, 2008). It is associated with various hormonal and immunological factors influenced by individual genetic predispositions (Oh and Hegele, 2007). Abnormal lipoprotein concentrations are worsened after HAART is started (Grover *et al*., 2005), mitochondrial alterations are one of the proposed mechanisms contributing to dyslipidemia (Oh and Hegele, 2007). Protease inhibitor therapy may interfere with LDL receptor regulatory proteins (Montessori *et al*., 2004) and mitochondrial dysfunction in skeletal muscle that can cause insulin resistance, with secondary dyslipidemia (Oh and Hegele, 2007). Cellular and mitochondrial interactions with protease inhibitors could also underlie metabolic alterations, causing pro-atherogenic changes that can further increase small dense LDL particles (Oh and Hegele, 2007). Lipid abnormalities may increase the risk of diabetes, heart disease and stroke (Nerad *et al*., 2003). A three fold increase in risk for coronary heart disease was noted in the DAD study for patients (that were on protease inhibitor therapy) who had changes in blood glucose, blood pressure and lipid levels (Grover *et al*., 2005; DAD study group, 2007).

HIV infected individuals often consume poor quality atherogenic diets, which might also affect plasma lipoproteins (Oh and Hegele, 2007). Non-drug interventions should be included in the management of dyslipidemia and additional focus should be placed on reducing cardiovascular disease risk (Alberti *et al*., 2006) through dietary changes, reduced total caloric intake, attaining ideal body weight and increased physical activity (Oh and Hegele, 2007).

2.4.2.1.3 Insulin resistance

Patients on HAART are living longer, but becoming commonly overweight and obese (Bhavan *et al*., 2008) contributing to the increasing incidence of insulin resistance (Tomazic *et al*., 2004). HIV-infected patients often develop metabolic abnormalities such as insulin resistance, hyperlipidemia and fat redistribution due the direct effects of the HIV infection or HAART (Arendt *et al*., 2008; Salomon *et al*., 2002; Jacobson *et al*., 2006).

Insulin resistance is strongly associated with atherogenic dyslipidaemia (Haffner and Miettinen, 1997) and a pro inflammatory state (Alberti *et al*., 2005). It is characterized by a reduction of insulin to inhibit hepatic gluconeogenesis and increase muscle uptake of glucose (Schambelan *et al.*, 2002). HIV infection affects pancreatic beta cell function and insulin secretion even in the absence of PI therapy (Montessori *et al*., 2004). According to Schambelan *et al.* (2002) the pathophysiologic basis of insulin resistance in patients on HAART is unknown. Potential mechanisms include direct effects of antiretroviral drugs (impaired cellular glucose uptake) or indirect mechanisms related to body fat changes (including central obesity and peripheral lipoatrophy) (Schambelan *et al*., 2002). NRTI's and PI's have been shown to cause insulin resistance via mitochondrial toxicity and through direct effects on glucose transport, respectively (Engelson *et al*., 2006).

New-onset diabetes mellitus affects a small population (1%-6%) of HIV-infected patients on PI-based antiretroviral regimens (Montessori *et al*., 2004: Blass *et al*., 2008) while 16% of patients in this group present with impaired glucose tolerance (Salomon, *et al*., 2002). A number of patients receiving PI therapy present with insulin resistance without diabetes (Montessori *et al*., 2004).

2.4.3 Drug and nutrient interactions

Effectiveness, tolerability and bioavailability of HAART are all affected by food and drug interactions (Nerad *et al*., 2003; Spencer *et al*., 2007). Food in the gastrointestinal tract can influence the absorption of several HIV medications (Spencer *et al*., 2007; Nerad *et al*., 2003). Drug-food interactions can alter serum drug concentrations, high serum concentrations increase the risk for viral resistance and low drug concentrations can cause loss of durable viral suppression (Nerad *et al*., 2003). Complicated medical and food schedules in combination with side effects of the medications can affect tolerability to drug regimens and compromise adherence to HAART (Nerad *et al*., 2003). Table 2.4 indicates possible HIV drug nutrient interactions.

Table 2.4 HIV medications and food interactions (Nerad *et al*., 2003)

Antiretroviral medication & Adult daily dosage	Food effect	Dietary recommendation
	NRTI	
Zidovudine (Retrovir / AZT / ZDV), Glaxo Wellcome, 300 mg b.i.d.	Administration of zidovudine capsules with food decreased peak plasma concentration by >50%; however, AUC may not be affected; or AUC decreased by 25% after meal. Avoid alcohol.	Take on empty stomach, if possible. If this is not possible because of GI side effects, recommend taking with low fat meal.
Lamivudine (epivir / 3TC), Glaxo Wellcome, 150 mg b.i.d. or 300 mg q.d.	Food has little effect on the extent of absorption. Avoid alcohol.	Can be taken without regard to meals. If taken with meals, may decrease GI side effects.
Zidovudine / lamivudine (Combivir, AZT / 3TC), Glaxo Wellcome, 1 tablet b.i.d.	Administration of zidovudine capsules with food decreased peak plasma concentration by >50%; however, AUC may not be affected; or AUC decreased by 25% after meal. Avoid alcohol.	Take on empty stomach, if possible. If this is not possible because of GI side effects, recommend taking with low fat meal.

Antiretroviral medication & Adult daily dosage	Food effect	Dietary recommendation
Zidovudine / lamivudine / abacavir (Trizivir,AZT / 3TC / ABC), Glaxo Wellcome, 1 tablet b.i.d.	Administration of zidovudine capsules with food decreased peak plasma concentration by >50%; however, AUC may not be affected; or AUC decreased by 25% after meal. Alcohol increased AUC of ABC by 41%.	Take on empty stomach, if possible. If this is not possible because of GI side effects, recommend taking with low fat meal. Avoid alcohol.
Didanosine (Videx EC / ddI), Bristol Myers–Squibb, 400 mg tablets q.d. for >60 kg and 250 mg tablets q.d. for <60 kg	Food decreases absorption. Administration with food results in approximately 55% decrease in AUC. Avoid alcohol as it exacerbates toxicity. Avoid antacids containing magnesium and aluminum.	Take on empty stomach, at least 30 min before or 2 h after a meal. Take only with water.
Stavudine (zerit / d4T), Bristol Myers–Squibb, 40 mg b.i.d. for >60 kg 30 mg b.i.d. for <60 kg	Food has little effect on absorption. Avoid alcohol.	Can be taken without regard to meals.
Tenofovir (Viread), Gilead Sciences, 300 mg qd	Administration with high fat meal increased AUC by 40%. If taking didanosine, must take tenofovir 2 h before or 1 h after didanosine.	Take with food.
Zalcitabine (Hivid / ddC), Roche Laboratories, 0.75 mg q8h	Administration with food decreases AUC by 14% (not clinically significant). Do not take antacids containing magnesium and aluminum at the same time as medication. Avoid alcohol. Do not take with metoclopramide (decreases AUC by 10%).	Can be taken without regard to meals.
NNRTI		
Delavirdine (Rescriptor / DLV), Pharmacia and Upjohn, 400 mg t.i.d.	Concentrations similar in fasting and fed states in steady state dosing. Medications such as antacids containing aluminum and magnesium and didanosine should be taken at least 1 h after, they can decrease absorption. Avoid St. John's wort (*Hypericum perforatum*), alcohol.	Can be taken without regard to meals.
Efavirenz (Sustiva / EFV), Dupont Merck, 600 mg/d	Low fat meal improves tolerability. High fat meal increased bioavailability by 50%. Take in the evening or bedtime to minimize side effects. Alcohol may increase side effects. Avoid St. John's wort.	Can be taken without regard to meals; however, avoid high fat meal.
Nevirapine (Viramune / NVP), Roxane, 200 mg/d for 14 d, then 200 mg b.i.d.	Absorption not affected by food, antacids, or didanosine. Avoid St. John's wort, alcohol.	Can be taken without regard to meals.

Antiretroviral medication & Adult daily dosage	Food effect	Dietary recommendation
Protease inhibitor		
Amprenavir (Agenerase / APV), Glaxo Wellcome, 1200 mg b.i.d.	Take with or without food. If taken with food, avoid high fat meal (>67 g fat), as high fat decreases absorption (decreases C_{max} and AUC). Avoid grapefruit juice. Increase fluid intake. Avoid extra vitamin E supplements (872 IU vitamin E /1200 mg amprenavir). Avoid St. John's wort. Do not take antacids within 1 h of this medicine.	Can be taken without regard to meals; however, avoid high fat meal.
Indinavir (Crixivan / IDV), Merck, 800 mg q8h	Administration with high fat, high protein meal decreased serum concentrations by 84% and decreased AUC by 77%. It can be taken with a nonfat snack. Avoid grapefruit juice. Drink an additional 48 ounces of liquid daily to avoid kidney problems. Avoid St. John's wort. Ritonavir indinavir combination (400 mg q12h each) significantly increases the drug level of indinavir and eliminates the need to fast.	Take on empty stomach at least 1 h before or 2 h after a meal or with a low/non fat meal (juice, skim milk, etc.). Take 1 h before or after ddI as buffer impairs IDV absorption.
Saquinavir (soft / gel capsule) (Fortovase / SQVsgc), Roche Laboratories, 1200 mg t.i.d.	Administration with food (i.e., fatty meal) increases AUC 67%. Store capsules in refrigerator. Avoid alcohol, St. John's wort.	Take with meal or up to 2 h after a full meal.
Saquinavir (hard gel capsule) (Invirase / SQV), Roche Laboratories, 600 mg t.i.d.	Administration with food (i.e., fatty meal) increases AUC 200%. Taking with grapefruit juice will also increase absorption by 40%–100% as a result of inhibition of gut CYP3A4. Avoid alcohol, St. John's wort.	Take with meal or up to 2 h after a full meal with high calories and high fat foods for better absorption.
Lopinavir / ritonavir(Kaletra, LPV / RTV), Abbott, 3 capsules b.i.d.	Take with high fat food for better absorption. Store the capsules in the refrigerator. Avoid St. John's wort.	Take with meals, especially with high fat content.
Ritonavir (Norvir / RTV), Abbott, 600 mg b.i.d.	Extent of absorption of ritonavir from the soft□gel capsule formulation was 13%–15% higher when administered with a meal. Store capsules in refrigerator. Avoid St. John's wort.	Take with meals if possible. Mix oral solution with chocolate milk or oral supplements to improve taste.
Nelfinavir (Viracept / NLF), Agouron, 750 mg t.i.d. or 1250 mg b.i.d.	Plasma concentrations and AUC were 2–3 fold higher under fed versus fasting conditions. Increase fluid intake. Lactose free dairy products or lactase may be needed to minimize diarrhea. Avoid acidic food or liquid. Avoid St. John's wort.	Take with a meal or light snack that includes a high protein food to increase absorption and to decrease GI side effects.

2.5 Alternative therapies

HIV-infected individuals often become frustrated with the lack of definitive medical therapies and turn to unconventional therapies, such as herbal medicines, oral nutritional supplements and micronutrient supplements (Fenton and Silverman, 2008, 1017; NICUS, 2009), many of which have not been subjected to scientific evaluation and peer review (Tomkins, 2005). HIV is a complex disease and recommending treatments that are not scientifically sound is unethical (ASSAf, 2007).

Unconventional treatments that have been highlighted by the South African HIV Clinical Society include African potato, virgin olive oil, onion, spirulina, garlic, sutherlandia, frutescens and certain phytosterols (ASSAf, 2007). Various herbs including, St John's wort and milk thistle (Venterataramanan *et al*., 2000) have been contraindicated when used with HAART (Fenton and Silverman, 2008, 1017; Spencer *et al*., 2007). St John's wort decreases the effectiveness of drugs metabolized via the P450 enzyme system and can also cause haemorrhage in surgical patients (NICUS, 2009). Garlic supplementation can reduce blood concentrations of saqunavir by 50% (Piscitelli *et al*., 2001; NICUS 2009), cause adverse side effects and should be discouraged among HIV patients (ASSAf, 2007). African potato was given to HIV infected adults to determine the effects of this alternative therapy. The study had to be discontinued and reported to the Medicines Control Council, as most of the patients included in the study showed severe bone marrow depression, decreases in CD4 count and total lymphocyte count (NICUS, 2009). The use of African potato should be discouraged amongst HIV patients (NICUS, 2009). All "cures" need to be tested to verify safety and efficacy before being recommended to HIV infected patients and raising false hopes (Hubley, 2002, 36).

2.6 Relationship between malnutrition and HIV / AIDS

Poor nutrition is part of the vicious cycle that contributes to a deterioration of HIV-infected individuals' health, which ultimately leads to increased morbidity and mortality (Nerad *et al.*, 2003). In the era of HAART, it is vital to acknowledge that adequate nutrition is necessary to optimize the benefits of antiretroviral (Marcason, 2009) drugs that essentially prolong the lives of individuals who are HIV-positive (Tomkins, 2005; Wanke, 2005).

Malnutrition, weight loss, body cell mass depletion and micronutrient deficiencies have long been observed in individuals with HIV/ AIDS and are associated with increased morbidity and mortality (Earthman, 2004; Fawzi *et al.,* 2005; Malvy *et al*., 2001; Kotler, 2000). According to Kotler (2000), malnutrition is the earliest, most common AIDS complication to be recognized and reported to public health authorities.

According to Kennedy and MacIntyre (2003), malnutrition is a frequent consequence of HIV infection (Malvy *et al*., 2001; Salomon *et al*., 2002) and weight loss is a diagnostic criterion that is often used for HIV / AIDS. Malnutrition contributes to the severity of opportunistic infections seen in HIV / AIDS and nutritional status is a major factor in survival (Kennedy and MacIntyre, 2003; Donald, 2001). Failure to maintain body cell mass at 54% of ideal body weight can lead to death (Kennedy and MacIntyre, 2003; Donald, 2001).

An increased immunocompromised state can occur due to malnutrition (Nerad *et al.,* 2003; Salomon *et al*., 2002). The relationship between HIV / AIDS and malnutrition is well described, with nutritional status compromised by reduced food intake, increased nutrient losses, drug-nutrient interactions (Stambullian *et al*., 2007; DOH SA, 2001) and malabsorption caused by gastrointestinal involvement and increased nutritional needs as a result of fever and infection (Kennedy and MacIntyre, 2003; Malvy *et al*., 2001; Earthman, 2004; Fawzi *et al.,* 2005).

Additional confounding factors are resource-limited situations where substandard nutritional status is the norm and insufficient food availability is a common occurrence (Tomkins, 2005; Faintuch *et al*., 2006).

2.6.1 Wasting and weight loss

According to Mangili *et al*., (2006) "In 1987, the Centers for Disease Control and Prevention included HIV associated wasting as an AIDS-defining condition; it is defined as an involuntary weight loss of >10% of baseline body weight plus either diarrhea, fever, or weakness for ≥30 days in the absence of concurrent illness".

Defining the pathophysiology of AIDS wasting is complex due to multiple pathologic processes that operate concurrently in an HIV-infected patient (Macallan, 1999). Opportunistic infections, socioeconomic status, access to care, cultural practices, psychological factors, production of inflammatory cytokines and medical complications related to HIV infection all influence the prevalence of wasting (Mangili *et al*., 2006; Macallan, 1999).

With every 1% decrease in body mass since the previous visit, the risk of death increases significantly (Wheeler *et al.,* 1998), by up to 11% (Mangili *et al*., 2006). In a study by Mangili *et al*., (2006), BMI was inversely associated with risk of death; individuals with a baseline BMI of ≥25 had much lower risk of dying that those with baseline BMI of <25. Weight loss is a stronger predictor of death than loss of lean body mass (Mangili *et al*., 2006). According to Testa and Lenderking (1999), the implications of AIDS wasting on quality of life are striking.

According to Mangili *et al*. (2006), "Cachexia describes a preferential loss of lean body mass, which implies metabolic derangement rather than a nutrient deficiency, while wasting is a less precise term that suggests weight loss due to inadequate nutrition intake." Lower oral intake is common and can occur as a result of infections, depression, anorexia (secondary to medications), symptoms such as vomiting, diarrhea, nausea, dyspnea, fatigue and neurologic disease which can affect nutrient intake (Fenton and Silverman, 2008, 1008). Infections

and fever can increase protein and energy requirements (Fenton and Silverman, 2008, 1008). Combined with low energy intake, these factors are known to increase the incidence of HIV wasting and weight loss (WHO, 2003).

Weight loss is associated with lower CD4 counts (Mangili *et al*., 2006) and includes variable proportions of fat and fat-free mass (Maia *et al*., 2005). HIV-infected patients who are on antiretroviral agents may have a decrease in subcutaneous fat (lipoatrophy) while fat-free mass depletion is absent leading to confounding clinical interpretation of weight loss (Maia *et al.,* 2005). According to Nerad *et al*., (2003), the incidence of wasting has been reduced since the initiation of HAART.

Various pharmacological therapies and effective treatments for HIV-associated weight loss and wasting are available (Mangili *et al*., 2006; Nerad *et al*., 2003). These include prescription drug treatments, appetite stimulants, anabolic agents and cytokine inhibitors (Fenton and Silverman, 2008, 1009). Anabolic steroid use is still controversial due to the increased risk for hepatotoxicity (Fenton and Silverman, 2008, 1009). Shevitz *et al*. (2005) found that nutrition intervention along with resistance training was more cost effective and induced similar body composition results than oxandrolone (an anabolic agent). Nutrition counseling is a vital component when treating HIV-associated wasting (Fisher, 2001) and individualized intervention is a necessity (Mangili *et al*., 2006).

2.6.2 Malabsorption

According to Fields-Gardener *et al*., (2004) malabsorption can lead to starvation induced malnutrition, with fat malabsorption occurring throughout HIV disease progression with or without various symptoms, such as diarrhea. Malabsorption can cause villous atrophy, intestinal cell maturation defects, increases in gastrointestinal pathogens and gut permeability have been suggested to be brought on by activation of gut immunity and inflammation (Fields-Gardener *et al*., 2004).

2.7 Assessment of nutritional status

Nutritional assessment is necessary to establish nutritional status and provides the key to effective patient management in HIV infection (Earthman, 2004; Nerad *et al*., 2003). Nutrition assessment should include diet history (Spencer *et al*., 2007), anthropometric measurements, selected laboratory tests (Gerrior and Neff, 2005) and thorough family and medical history, where risk for diabetes, coronary artery disease, hypertension and other cardiac risk factors need to be established (Nerad *et al.*, 2003).

During initial visits, new HIV-infected patients should be screened to establish nutritional risk (Nerad *et al*., 2003; Spencer *et al.,* 2007). Validated screening tools can be used for nutritional risk assessment (Nerad *et al*., 2003) and should be carried out at all HIV care institutions even in the absence of a registered dietitian (Spencer *et al*., 2007). Screening is needed to categorize patients according to nutritional needs and refer to a registered dietician for nutrition assessment and individualized medical nutrition therapy (Nerad *et al*., 2003).

Anthropometric measurements are easily performed, inexpensive techniques for estimating total body fat and regional fat contents and include measurements such as waist to hip ratio, waist circumference and body composition testing (Andrade *et al*., 2002; Spencer *et al*., 2007).

Bioelectrical impedance analysis (BIA) is a body composition technique (Kolter *et al*., 1996: Schwenk *et al*., 1999) that is inexpensive, noninvasive, quick and can fairly accurately measure fat free mass in HIV infected individuals (Batterham *et al*., 1999; Forrester *et al.,* 2008). This method however is unreliable in detecting changes in fat redistribution (Schwenk *et al*., 1999). BIA was shown by Aghdassi *et al.* (2007) to have a relatively small margin of error when compared to the dual energy x-ray absorptiometry (DEXA) scan and can therefore be used for routine monitoring in HIV infected patients with normal hydration.

Dietary intake reflects economic and lifestyle factors (Mangili *et al*., 2006), and is the best means of establishing dietary intake information with regards to an individual's usual food intake, selection and eating pattern (Hammond, 2008, 395).

Biochemical measurements are useful markers of human nutrition (Spencer *et al*., 2007). Valuable biochemical markers in HIV-infected patients include fasting lipids, blood glucose, insulin, serum albumin, C-reactive protein, serum alkaline phosphatase and liver functions tests (Fenton and Silverman, 2008, 1011).

Social factors within households and entire communities (Tomkins, 2005) can limit access to proper food and nutrition (Nerad, *et al*., 2003). Socioeconomic, literacy level, financial status, cultural and ethnic background are important factors that need to be assessed to ensure optimal medical nutrition therapy that is tailor made to utilize available resources and access to care (Nerad *et al.*, 2003).

Since HIV is now often considered to be a chronic illness in patients on HAART (Stein, 2009; Gerrior and Neff, 2005), assessment of nutritional status and medical nutrition therapy assists in maintaining nutritional health and overall well-being (Gerrior and Neff, 2005).

2.8 Medical nutrition therapy

Nutrition management is a vital component for all patients infected with HIV (Nerad *et al.*, 2003) throughout all stages of disease progression (DOH SA, 2001). The effectiveness of nutrition intervention has been documented and dietary nutrition counseling and support to improve nutritional status is considered critical in the treatment of HIV / AIDS (Kennedy and MacIntyre, 2003; Donald, 2000). Nutritional disorders are often present in HIV infected individuals (Stambullian *et al*., 2007) and can result in complicated nutritional issues (Nerad *et al.*, 2003).

There is growing evidence that nutritional interventions influence disease progression and health outcomes in HIV-infected patients (Nerad *et al.*, 2003; Fawzi *et al*., 2005). Specific HIV medical nutrition therapy is based on established and emerging nutritional science (Fenton and Silverman, 2008, 992) and requires specialized knowledge of nutrition, medications and complications associated with HIV (Nerad *et al*., 2003). Early ongoing medical nutrition therapy is a must for all individuals with HIV-infection and AIDS (Fenton and Silverman, 2008, 1011).

Nutritional assessment, support and counseling has been shown to positively influence health outcomes and improve nutritional status in HIV infection (Kotler, 2000; Nerad *et al*., 2003; Gerrior and Neff, 2005) as well as enhance the effectiveness of HAART through better adherence and acceptability (WHO, 2003).

According to Fenton and Silverman (2008, 1010) medical nutrition intervention should aim to improve patients' nutritional knowledge by educating patients about their condition, thereby enhancing their sense of empowerment and improving and prolonging their quality of life. Nutritional status assessment forms a part of nutrition intervention strategies and should address any nutrient deficiencies, metabolic disorders, maintain protein status and encourage adherence to HAART (Fenton and Silverman 2008, 1010).

Attention to nutritional status and medical nutrition therapy is critical in all HIV treatment programs to ensure treatment success (WHO, 2003; Fenton and Silverman, 2008, 1010; Duran *et al.,* 2008) and may assist in reducing the burden of disease and promoting an enhanced quality of life (Gerrior and Neff, 2005). According to Coyne-Meyers and Trombley, (2004) the benefit of providing adequate macro and micro nutrients is well accepted, though exact amounts of nutrients to be prescribed for HIV infected individuals is less clear.

2.8.1 Macronutrient requirements in HIV / AIDS

Even though the relationship between nutrition and immune function is well established, nutritional intake is often over-looked in the progression of HIV (Kim *et al*., 2001). Macronutrient metabolism is altered by HIV infection (Ware et al., 2002), while inadequate macronutrient intake and poor nutritional status can lead to an impaired immune response (Cunningham-Rundles *et al*., 2005; Kim *et al*., 2001). Adequate macro and micronutrients are necessary to maintain and restore malnutrition related immune dysfunction (Fields-Gardener *et al*., 2004), and wasting in infected adults is a clear indication that macro nutrient requirements are not being met (ASSAf, 2007).

2.8.1.1 Energy and protein

Energy expenditure and caloric intake are affected by the progression of HIV through pathogenic mechanisms (Kotler, 2000), often increasing energy requirements (WHO, 2003). Energy and protein requirements should be calculated according to individual requirements, taking into consideration the stage of HIV progression as well as any factors that will affect nutrient intake and use (Fenton and Silverman, 2008, 1011). A 10% increase in energy is required during the asymptomatic HIV stage to maintain body weight and physical activity (WHO, 2003). These requirements are increased to 20-30% during the symptomatic stage and the stages thereafter that progress to AIDS (WHO, 2003).

Batterham *et al*., (2003) found that resting energy expenditure increased in HIV-infected males. Resting energy expenditure is elevated by opportunistic infections (Nerad *et al*., 2003) and can increase energy requirements by up to 50-100% above normal recommendations (WHO, 2003).

According to McDermott *et al*., (2003), HIV wasting can be improved, if not reversed by increasing energy requirements to 500 kcal above estimated energy requirements (40 to 50 kcal/kg of current weight). According to WHO (2003)

there is insufficient data to support increased protein requirements in HIV infection. However current literature suggest a positive nitrogen balance and lean body mass repletion can be achieved by increasing protein intakes (Mc Dermott *et al*., 2003; Fenton and Silverman, 2008, 1011) (1-1.4 g/kg for maintenance and 1.5-2 g/kg for repletion), the exception being patients with renal or hepatic disease (Fenton and Silverman, 2008, 1011).

Weight loss and negative nitrogen balance are correlated and 80-90% of weight losses during acute events are usually protein losses, while less protein is lost during the starvation process (Fields-Gardener *et al*., 2004). Maintenance of body protein stores (body cell mass) is a crucial factor that affects an HIV infected person's ability to survive (Bogden *et al*., 2000)

2.8.1.2 Fat

Tolerance to fat varies from person to person and individual symptoms, such as fat malabsorption and persistent diarrhea (WHO, 2003) need to be taken into consideration when establishing fat requirements (Fenton and Silverman, 2008, 1011). Fat tissue losses can change metabolic stability (Fields-Gardener *et al*., 2004). Readily available fats such as medium chain triglycerides are preferred as they assist in improving abdominal symptoms, reduce the number of bowel movements, decrease stool fat and stool nitrogen content (Fenton and Silverman, 2008, 1011), there is however no evidence to support specific fat requirements for HIV infected individuals (WHO, 2003). Omega-3 fatty acids that are found in fish oils such as sardines, salmon, mackerel and herring (Sadovsky *et al*., 2008) improve immune function through reducing inflammation caused by higher consumptions of omega-6 fatty acids (Fenton and Silverman, 2008, 1011). According to WHO (2003), specific recommendations regarding fat intake for patients receiving HAART might be necessary. Omega-3 fatty acids and monounsaturated fatty acids are useful in the treatment of hypertriglyceridemia and for the prevention of cardiovascular disease (Mechanick *et al*., 2003; Marcason, 2009), both being common occurrences in HIV infected individuals on HAART.

2.8.2 Micronutrient requirements in HIV / AIDS

Micronutrient deficiencies occur commonly with advanced HIV disease (Tomkins, 2005) and increase the risk for disease progression and mortality (Drain *et al*., 2007; WHO, 2003; Semba, 2006, 1406).

Minerals and vitamins play essential metabolic roles and have an impact on immune function (Oguntibeju *et al*., 2007; Dreyfuss and Fawzi, 2002; Wintergerst *et al*., 2007). Mineral and vitamin deficiencies are associated with adverse outcomes (Nerad *et al.,* 2003; WHO, 2003). Micronutrient deficiencies are common amongst HIV infected patients (Drain *et al*., 2007), and often caused by decreased food intake, gastrointestinal malabsorption, increased utilization of nutrients and excretion of nutrients (Drain *et al*., 2007; Fawzi *et al*., 2005) which are known to complicate malnutrition as well as systemic diseases (Oguntibeju *et al*., 2007).

According to Woods *et al*. (2002) recommendations suggest that HIV infected patients use a multivitamin mineral supplement that provides 100% of the recommended daily allowances (WHO, 2003) and specific supplementation when required to treat micronutrient deficiencies (Nerad *et al.,* 2003). Micronutrients are an inexpensive, easy therapy that can be used in conjunction with HIV medications to improve clinical outcomes in developing and developed countries (Drain *et al*., 2007)

The HIV-infected population spends large amounts of money on over-the-counter minerals, vitamins, phytotherapeutic preparations and alternative therapies (refer to 2.6 Alternative therapies) which often do not have substantiated scientific evidence to support their use (Faintuch *et al*., 2006; ASSAf, 2007).

To ensure optimal immune system functioning vitamins and minerals are vital (Arendt *et al*., 2008; Drain *et al*., 2007). Deficiencies in vitamin A, B_1, B_2, B_6, B_{12}, and E in addition to folic acid, zinc and iron can impair host resistance and

lymphocyte function (Arendt *et al*., 2008; WHO, 2003). Vitamin A deficiency leads to impaired neutrophil function (Dreyfuss and Fawzi, 2002) and reductions in lymphocyte response, cell mediated immune response is reduced by vitamin C deficiency and vitamin E deficiency leads to lymphocyte proliferation and impairs T-cell mediated function (Drain *et al*., 2007). These antioxidants reduce oxidative stress, which can contribute to decreased CD4 counts and increased viral replication in HIV-infected patients (Arendt *et al*., 2008; Drain *et al*., 2007; Faintuch *et al*., 2006). According to the WHO (2003) supplementation with vitamin A, zinc and iron has raised concerns regarding adverse outcomes in HIV infected patients. Safe upper limits need to be established for daily micronutrient intakes for HIV infected individuals (WHO, 2003).

Minerals play important roles in immune functioning. Folic acid deficiency depresses the cell mediated responses; zinc deficiency reduces lymphocyte concentrations; cytokine response is reduced by copper deficiency; and low selenium concentrations affect the functioning of neutrophils and T-lymphocytes (Drain *et al*., 2007). Food sources containing vitamin K and C, as well as *zinc* are vital for bone formation and should be included during nutrition counseling (Fields-Gardener *et al*., 2004). According to Irlam, *et al*., (2005) evidence that micronutrient supplementation affects HIV morbidity or mortality is inconclusive. In the absence of such evidence micronutrient supplementation should be used in accordance with RDA levels as suggested by the WHO (Irlam *et al*., 2005).

According to Fawzi *et al*. (2005), multivitamin supplementation should not be seen as an alternative to HAART in developing countries, but rather as a complementary intervention as part of comprehensive care package. HIV infected patients that qualify for HAART (as per national guidelines) should be provided with HAART, patients who don't qualify for HAART should use a daily multivitamin supplement (Drain *et al*., 2007) to slow disease progression (Fawzi *et al*., 2005).

2.9 Lifestyle factors that can impact on HIV / AIDS

Various lifestyle factors have an impact on HIV infected individuals. Smoking habits, alcohol consumption and physical activity levels can have possible effects on HIV disease progression and quality of life.

2.9.1 Smoking

The prevalence of smoking is high amongst HIV infected patients, specifically in low socioeconomic groups (Feldman *et al*., 2006; Duval *et al*., 2008; Murdoch *et al*., 2008) and is associated with an increased risk for cardiovascular disease (Stein, 2009; Duval *et al*., 2008; Bazoes *et al*., 2008) and altered immunity (Wojna *et al*., 2007). Adherence to HAART is lower in smokers than in non smokers and is associated with adverse outcomes (Feldman *et al*., 2006; Shuter and Bernstein, 2008). Smokers on HAART have a higher morbidity and mortality rate than non smokers (Feldman *et al*., 2006) and greater efforts should be made to assist patients with smoking cessation (Feldman *et al*., 2006; Duval *et al*., 2008; Cook *et al*., 2009) to reduce their cardiovascular disease risk (Stein, 2009; Marcason, 2009; Salomon *et al.,* 2002).

2.9.2 Alcohol consumption

In 1998, the South African Demographic and Health Survey found that 50% of males and 17% of South Africans over the age of 15 years old consumed alcohol (van Heerden and Parry, 2001). Alcohol ingestion in large quantities can affect health and social factors negatively, despite the fact that research findings indicate potential benefits of moderate alcohol consumption in specific sectors of the population (Standridge *et al*., 2004; van Heerden and Parry, 2001).

Alcohol usage is common amongst HIV infected individuals (Cheng *et al*., 2009; Chander *et al*., 2008) and is associated with various social and demographic factors (Chander *et al*., 2008) as well as reduced adherence to HAART (Samet *et*

al., 2004). Alcohol intake is a modifiable risk for adverse HIV-associated outcomes and routine screening should form part of comprehensive care for HIV infected patients (Chander *et al*., 2008). Alcohol intake may further affect the development of lipodystrophy (Cheng *et al*., 2009). Long term studies are however required to fully establish the association (Cheng *et al*., 2009).

2.9.3 Physical activity

According to Lindegaard *et al*. (2008), insulin sensitivity is improved by both strength and endurance training, but strength training results in total body fat reduction in HIV infected individuals. A study conducted by Dolan *et al.* (2006) found that HIV infected women that completed a 16 week home based exercise regimen improved physical fitness, endurance and body composition. According to Johnson *et al*. (2007) a modest amount (30 minutes daily) of exercise significantly improved metabolic syndrome and risk for cardiovascular disease (Lakka and Laaksonen, 2007) both of which are associated with HIV infected patients on HAART. Physical activity is protective against the development of fat redistribution (Domingo *et al*., 2003; Florindo *et al*., 2007). Exercise that is of a moderate intensity seems to be more beneficial than vigorous intensity for improving metabolic syndrome (Johnson *et al*., 2007). Walking improves health, it is the most common form of exercise and generally regarded as safe (Lakka and Laaksonen, 2007). A brisk walk for 30 minutes daily should be recommended to improve health benefits with resistance training if contraindications are absent (Lakka and Laaksonen, 2007; WHO, 2006; Ramirez-Marrero *et al*., 2004). Diet and exercise are recommended therapies for type 2 diabetes and are also appropriate for HIV-related insulin resistance (Salomon *et al*., 2002).

2.10 Conclusion

According to Tomkins (2005) “once effective nutrition interventions for HIV / AIDS are introduced, substantially fewer infants will become infected with HIV, fewer children will die or become malnourished, HIV infected mothers and their partners will live longer, healthier lives and the time before they need ARV’s will be extended. These are all possible if only governments and agencies support nutrition intervention programmes and research more vigorously.” HIV negatively impacts on individual human development, entire households and also on a larger scale, affecting communities and nations (Colecraft, 2008).

Nutritional issues will remain clinically important in HIV infection (Mangili *et al*., 2006; Fields-Gardener *et al*., 2004) and practical issues such as food insecurity need to be addressed within nutrition intervention strategies (Fields-Gardener *et al*., 2004). Timely, effective (Fields-Gardener *et al*., 2004), sound nutritional counseling are interventions that can assist in improving health outcomes for HIV positive patients, particularly in Africa and other developing countries (Vogel, 2006; Colecraft, 2008). All HIV-infected people should have the benefit of receiving nutrition care plan that includes nutrition education and medical nutrition therapy (Fields-Gardener *et al*., 2004).

CHAPTER THREE: METHODOLOGY

3.1 Introduction

A descriptive cross sectional study was conducted to achieve the main aim of the study, which was to determine the nutritional status of HIV infected adults on HAART.

To achieve the above mentioned objective, the following information was collected: anthropometric measurements (body mass index (BMI), waist circumference, waist to hip ratio, body fat percentage), dietary intake (food, energy and macronutrient intakes) lifestyle factors (smoking and alcohol consumption), family history of chronic disease, biochemical parameters (fasting glucose concentrations, total cholesterol levels, high density lipoproteins (HDL), cholesterol, low density lipoproteins (LDL) cholesterol, triglyceride levels, CD 4 counts and viral load) and blood pressure. Associations between various parameters were also established.

3.2 Ethical considerations

Ethical approval was obtained from all relevant parties, including the Ethics Committee of the Faculty of Health Sciences, University of the Free State (Etovs no: 31/08) and WITS. Approval was obtained from the Helen Joseph Clinic prior to starting the study. All participants completed informed consent (Appendix A) and an information document (Appendix B) was given to each patient. The information document explained procedures that would be followed during the study, as well as risks, benefits, voluntary participation and guaranteed confidentiality.

3.3 Sample selection

3.3.1 Population

The total number of patients treated at the Helen Joseph CCMT site at the time that the study commenced was 9569. A total of 3867 patients were on the first line HAART regimen and 265 patients were on the second line HAART regimen. These included 3262 male patients and 6276 female patients.

3.3.2 Sample

A convenience sample was used, as the patients had to comply with the specific criteria set by the Department of Health for patients to qualify for HAART. The sample size included 61 patients on the first line HAART regimen and 50 patients on the second line HAART regimen. Inclusion and exclusion criteria were used on the therapy edge system to differentiate patients who were suitable candidates for the study. This was done for each day that the researcher collected data.

3.3.2.1 Inclusion criteria

HIV infected adults between the ages of 18 and 60 years old who were currently (for longer than 6 months) on HAART at the Helen Joseph CCMT site.

3.3.2.2 Exclusion criteria

Patients who did not complete the drug readiness counseling at the Helen Joseph CCMT and/or did not comply with the Department of Health criteria for initiation of HAART, were not be included in the study. Patients who were pregnant and patients who did not sign informed consent were excluded from the study.

3.4 Operational definitions

For the purpose of the study the following definitions were compiled and used to achieve the objectives of the study:

3.4.1 Dietary intake

For the purpose of this study, dietary intake included total intake of food, energy and macronutrient intakes. To determine patients dietary intakes a 24 hour recall of foods eaten the previous day together with a short food frequency questionnaire (Appendix C) were completed. The food frequency questionnaire was used to ensure that patients had reported all additional drinks and other foods not reported in the 24 hour recall. Macronutrient distributions relevant to total energy intake were analysed in accordance with prevalence of HAART related chronic disease. Food intake was compared to the recommendations of the American Dietetics Association (ADA) Food Guide Pyramid (United States Department of Agriculture (USDA), 1992) and then classified as either inadequate, higher or within the range of the specified guidelines (Summerfield, 2001). The Food Guide Pyramid includes seven food groups and is a standard used to evaluate dietary intake. The recommended servings per day for each group are listed below in table 2.1 and were used as cut off points when the data was analyzed.

Table 3.1: Food guide pyramid recommended servings (Earl, 2004)

Food Groups	Recommended Servings
Bread, cereal, rice and pasta group	6-11 Servings
Fruit group	2-4 Servings
Vegetable group	3-5 Servings
Milk, yoghurt and cheese group	2-3 Servings
Meat, poultry, fish, dry beans, eggs and nut group	2-3 Servings
Fats, oils and sweets	Use sparingly

3.4.2 Anthropometry

For the purpose of this study anthropometric indicators included height, weight, waist circumference, hip circumference, waist to hip ratio and body fat percentage.

3.4.2.1 Body Mass Index

BMI was calculated by dividing the patient's current weight in kilograms (kg) by their height squared. Body mass index results were categorized into groups, <18.5 kg/ m^2 (underweight), 18.5-24.9 kg/ m^2 (normal weight), 25-29.9 kg/ m^2 (overweight) and ≥ 30 kg/ m^2 (obese) (Lee and Nieman, 2003, 272).

3.4.2.2 Waist circumference

For the purpose of this study waist circumference referred to the minimal abdominal circumference located midway between the lower rib margin and the iliac crest (Lee and Nieman, 2003, 245). The cut off for waist circumference in women is > 80cm and > 94cm in men (Alberti *et al.*, 2006).

3.4.2.3 Waist to hip ratio

Waist to hip ratio was calculated by dividing waist circumference by hip circumference. For the purpose of this study values above 0.8 in women and 0.9 in men were indicative of a tendency for central fat deposition and a possible increased risk for chronic disease (Barasi, 2003, 12). The area where fat is deposited is defined as gynoid distribution (fat in the buttocks and thighs or "pear shape") and android distribution (fat around the waist and upper abdomen, or "apple shape") (Hammond, 2000, 372).

3.4.2.4 Body fat percentage

For the purpose of this study body composition refered to body fat percentage (determined using bioelectrical impedance) (Bodystat R 1500 – Bodystat, Isle of Man, Limited). Fat percentage referred to the percentage of fat tissue in the body (Lee and Nieman, 2003, 203). The cut off points for fat percentage results from the bioelectrical impedance are as follows:

- < 20 % : Low
- 20 – 25 % : Normal
- > 25 % : High (Laquatra, 2004, 599)

3.4.3 Lifestyle factors

3.4.3.1 Smoking

For the purpose of this study smoking referred to the number of cigarettes smoked per day. Smoking was categorized as follows (Russo *et al*., 2001; Hill *et al*., 1998):

- Non smokers: Patient who has never smoked;
- Former smoker: Patient who had smoked before, but who has stopped smoking for at least a year before entering the study.
- Current smoker: Patient that smoked at least one cigarette, pipe, or cigar per day for at least a year prior to entering the study.

3.4.3.2 Alcohol consumption

For the purpose of this study alcohol consumption referred to whether or not the participants were currently drinking alcohol, never used alcohol or formerly used alcohol.

3.4.3.3 Physical activity

For the purpose of this study physical activity was defined as any form of muscular activity, which resulted in the expenditure of energy (Power and Howley, 2001, 294). The amount of time spent on sport and leisure activities was established using the previous day physical activity recall (PDPAR) as validated by Weston *et al.* (1997). Patients were asked to list all the activities they performed during the previous day. In addition to the 24 hour physical activity recall, a frequency of activities not recorded in the 24 hour recall was documented. The average between the 24 hour recall and the frequencies from the other activities were calculated. From this information, the researcher calculated the level of physical activity for each patient. The level of physical activity for the various activities performed throughout the day was determined by adding the level of physical activity for each activity.

The level of physical activity refers to those activities structured around the household, as well as extra mural activities. The levels of physical activity were categorized as follows: (Frary and Jonson, 2004, 32).

- Sedentary: 1-1.39
- Low activity: 1.4-1.59
- Active: 1.6-1.89
- Very active: 1.9-2.5

3.4.3.4 Family history of chronic disease

For the purpose of this study reported family history was recorded to determine genetic predisposition for lifestyle associated chronic diseases including diabetes, hypertension, stroke and cardiovascular disease.

3.4.4 Biochemical parameters

Biochemical parameters that were needed for the study are not routinely measured in government CCMT sites. Funding for the processing of blood results was needed and a collaboration was formed with the Department of Chemical Pathology at the University of the Witwatersrand (WITS). The Department of Chemical Pathology will make use of the information collected in this study to investigate genetic links to specific findings from this study. The following biochemical markers were measured. Ranges or cut-off points for biochemical parameters that are used at the Chemical Pathology lab at WITS are indicated below:

- Fasting glucose concentrations — 4.1 – 5.9mmol/L
- Total cholesterol levels — < 5.0mmol/L
- HDL cholesterol — >1.0mmol/L
- LDL cholesterol — <2.5mmol/L
- Triglyceride levels — <1.5mmol/L
- Changes in viral load — > 25 - Detectable; < 25 – Undetectable
- CD4 count — 500 – 2000mm^3

3.4.5 Blood pressure

For the purpose of this study a blood pressure value was considered high if the systolic value $\geq$130mm Hg and/or diastolic $\geq$ 85mm Hg (Appel *et al*., 2006)

3.5 Pilot Study

A pilot study was conducted prior to commencing the main study to determine if the respondents understood the questions and to determine the duration needed to complete the necessary interviews, anthropometric measurements and collect

blood samples from respondents. The pilot study was conducted at the Helen Joseph Clinic by the researcher herself, using five patients.

3.6 Data collection process

Step 1

- Approval was obtained from the Research Evaluation Committee of the School of Allied Health Professionals, UFS.

- Approval was obtained from the Ethics Committees of the University of the Free State and WITS.

- Approval was obtained from the CCMT directorate and Project Manager at the Helen Joseph CCMT Site (Appendix D)

- Informed consent (Appendix A) was obtained from the participating patients. The information document (Appendix B) was discussed with each patient and informed consent was completed by patients before taking part in the study.

- The pilot study was undertaken

Step 2

- Patients attending the CCMT site completed the consent forms at Helen Joseph Clinic with the help of an assistant. There are assistants at the CCMT who help with research, specifically with translating and explaining the procedure of the study to patients in their own language. The information document was given to patients to provide them with more information regarding the study.

- Patients that where included in the study completed the questionnaires and assessments at the CCMT site on the day that they would normally have come to the clinic for their follow ups.

- Questionnaires (including; 24 hour recall, food frequency questionnaire, physical activity questionnaire, lifestyle and self reported medical history, family medical history and body composition questionnaire) were completed with each patient through a structured interview with the researcher. The interviews took place in a private room.

- The researcher conducted anthropometric measurements on all the patients, including weight, height, waist circumference measurements and body composition tests.

- Blood samples were collected by registered phlebotomists at the clinic from each patient to establish biochemical values.

Step 3

- The reliability interviews were conducted one month after the initial interviews on 12 patients.

- All the blood results were placed in patients files so that patients had access to their results. Patients had the opportunity to discuss these results with their doctor and necessary medical and nutrition therapy interventions were recommended.

- A feed back report was given to the health care professionals at the clinic to highlight the results of the study and help the clinic to improve in areas that warrant intervention strategies.

3.7 Techniques

3.7.1 Dietary intake

Dietary intake was determined by a food frequency questionnaire and 24 hour recall of foods usually eaten (Appendix C), completed by the researcher in a personal interview with each participant. Household measures were used to ensure accurate estimates of portion sizes. These results were interpreted according to the inclusion of the recommended number of daily servings from various food groups as recommended by the Food Guide Pyramid (UDSA, 2001).

The results from the dietary intake questionnaires were analysed using Food Fundi (MRC) to establish macronutrient splits of total energy intake.

3.7.2 Anthropometric measurements

3.7.2.1 Weight

Weight was determined using an electronic scale. Subjects wore minimal clothing (remove jacket, shoes and jewelry), and stood still in the middle of the scale without touching anything and with their body weight equally distributed on both feet. The patient's weight was recorded to the nearest 100g as recommended by Lee and Nieman (2003, 167).

3.7.2.2 Height

Height was measured using an anthropometer with a vertical scale of 2 meters and a sliding head-piece, to the nearest 0.5 cm. Subjects were measured without shoes on, heels together, arms to the side, legs straight, shoulders relaxed and head in the Frankfort horizontal plane (looking straight ahead). Heels, buttocks, scapulae (shoulder blades), and the back of the head were against the vertical

surface of the anthropometer. Patient's inhaled deeply, holding their breath in and maintaining an erect position ("stand up tall") while the sliding-headpiece was lowered on the highest point of the head with enough pressure to compress their hair (Lee and Nieman, 2003, 167).

3.7.2.3 Waist circumference

Waist measurements were taken, with subjects wearing little clothing, standing straight up with their abdomen relaxed, arms at their sides and feet together. The researcher measured the subjects by placing an in-elastic tape measure around the subject's waist, in a horizontal plane, at the level of the natural waist, which is the narrowest part of the torso. The measurement was taken at the end of a normal expiration, without the tape compressing the skin and was recorded to the nearest 0.1cm (Callaway *et al*., 1991, 44-45).

3.7.2.4 Hip circumference

Hip circumference was measured using an in-elastic tape which is placed around the patient's buttocks in a horizontal plane without compressing the skin. The hip circumference measurement was recorded to the nearest 0.1cm (Callaway *et al*., 1991, 46).

3.7.2.5 Body fat percentage

Body composition measurements were completed using bio-electrical impedance while patients lay down on a flat surface with their feet slightly apart, their arms by their sides and all jewelry removed. Patients were asked to empty their bladder before conducting the body fat composition measurements (Lee and Nieman, 2003, 203).

3.7.3 Lifestyle factors that can impact on HIV / AIDS

Lifestyle factors including smoking habits and alcohol consumption were measured by means of a questionnaire (Appendix E), completed in a personal interview with each patient.

3.7.4 Physical activity levels

Physical activity levels were determined by conducting an interview to obtain a 24 hour recall of physical activity for the previous day as well as frequency of activities not necessarily performed every day. The interview was conducted by the researcher with each patient.

3.7.5 Biochemical parameters

Biochemical parameters (fasting glucose concentrations, total cholesterol levels, HDL cholesterol, LDL cholesterol, triglyceride levels, CD 4 counts and viral load) were determined using standard laboratory techniques. Venous blood samples were collected from each patient. All the biochemical values where analysed by the Department of Chemical Pathology at WITS as part of a collaborative project.

3.7.6 Blood pressure

Blood pressure was measured using a sphygmomanometer by the nurse practitioner at the clinic. The patient was seated, with their arm resting on a table and slightly bent so that it is at the same level as the heart (Perloff *et al.*, 1993).

3.8 Statistical analysis

Descriptive statistics, namely frequencies and percentages for categorical data, medians and percentiles for continuous data was calculated. Associations

between variables were calculated and described by means of 95% confidence intervals for relative risks, differences in medians or percentages. The significance of differences between the patients in the first and second line regimen were compared using statistical analysis. All analyses were completed by the Department of Biostatistics at the University of the Free State.

3.9 Reliability and validity

Reliability refers to the degree of similarity of the information obtained when measuring a group. Reliability assesses whether the same value is arrived at every time a measurement is repeated, or if discrepancies occur (Monsen, 1992, 188). Validity refers to the extent to which a measure actually measures what it is meant to measure (Katzenellenbogen, 1997, 90).

3.9.1 Dietary intake questionnaires

3.9.1.1 Validity

To ensure that the questions related to dietary intake were valid, only information related to food intake were included in this questionnaire.

3.9.1.2 Reliability

To ensure reliability, only the researcher interpreted and coded the 24-hour recall and food frequency questionnaires.

3.9.2 Anthropometry

3.9.2.1 Validity

Anthropometric validity was ensured by using standardized methods and calibrated equipment to ensure the accuracy of measurements.

3.9.2.2 Reliability

To ensure reliability of the results, weight, height, waist circumference, hip circumference and body composition were measured in duplicate by the researcher according to standard procedures, as recommended by Lee and Nieman (2003, 65).

3.9.3 Lifestyle factors

3.9.3.1 Validity

All issues addressed by the questionnaire are directly related to the aim and objectives of the study. The content of the lifestyle questionnaire was chosen in accordance with recommended measurements for lifestyle factors as discussed in the literature.

3.9.3.2 Reliability

Reliability was ensured by repeating the lifestyle questionnaires on 10% of the study population 1 month after the study was complete. Where the answers to questions asked during the two interviews differed with more than 20%, the question was considered unreliable. No questions were found to be unreliable.

3.9.4 Biochemical parameters

3.9.4.1 Validity

The biochemical tests are valid due to the fact that they were analysed at an accredited lab (Department of Chemical Pathology Lab at the University of the Witswatersrand).

3.9.4.2 Reliability

The blood tests are reliable, because they were analysis using standardized laboratory procedures and controls at the Department of Chemical Pathology at the University of the Witwatersrand. Cut-off points for biochemical parameters that are used at the Chemical Pathology lab at the University of the Witswaterand are indicated below:

- Fasting glucose concentrations — 4.1 – 5.9mmol/L
- Total cholesterol levels — < 5.0mmol/L
- HDL cholesterol — >1.0mmol/L
- LDL cholesterol — <2.5mmol/L
- Triglyceride levels — <1.5mmol/L
- Changes in viral load — > 25 - Detectable
  < 25 – Undetectable
- CD4 count — 500 – 2000mm^3

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter includes the findings of the research study. The descriptive results that will be discussed include dietary intake, anthropometric measurements, lifestyle factors (including smoking habits, alcohol consumption, patient medical history and family medical history) and biochemical markers. Comparisons have been made between the group on regimen 1 and the group on regimen 2 and significance of differences in the medians are given as 95% CIs for the median differences. Associations between variables are also discussed and significance of differences in the percentages are given as 95% CIs for the percentage differences.

4.2 Socio-demographic information

The study population total was 111 patients, 54.95% of the patients (61 patients) were on HAART 1st line regimen and 45.05% (50 patients) were on HAART 2nd line regimen. The median age in the 1st line regimen group was 38 years and 39.5 years in the 2nd line regimen group. The study population included both genders and included 39 females (63.93%) and 22 males (36.07%) in the first line regimen group. In the second line regimen group 36 participants (72.00%) were females and 14 (28.00%) were males.

4.3 Dietary intake

4.3.1 24–hour recall

Table 4.1 indicates patients' dietary intake in various food group classifications. The following groups were included: the bread group, meat group, milk group, sweet group and fats group, fruit group and vegetable group.

Table 4.1: Evaluation of dietary intake expressed as food groups (n=111)

Food group (Recommended servings)	1st line regimen		2nd line regimen	
	% below	% equal to or higher	% below	% equal to or higher
Bread group (6-11)	95.08	4.92	88.00	12.00
Meat group (2-4)	75.41	24.59	70.00	30.00
Milk group (3-5)	96.72	3.28	96.00	4.00
Fruit group (2-4)	73.77	26.23	66.00	34.00
Vegetable group (3-5)	98.36	1.64	94.00	6.00

A large percentage of all participants had intakes below the recommended intakes for all the above mentioned categories (recommended by the Food Guide Pyramid) in both the 1st and 2nd line regimen groups. Within the bread group consumption was below the recommended intake of 6-11 servings daily in 95.08% and 88.00% of patients in the 1st and 2nd line regimens respectively. The milk group, fruit group and vegetable group indicated similar trends. Milk intake was below the recommended intake of 3-5 servings daily in 96.72% (1st line regimen group) and 96.00% (2nd line regimen group) of the patients.

Almost 74 % (1st line regimen group) and 66.00% (2nd line regimen group) of patients had low fruit intakes when compared to the recommended 2-4 servings daily. Overall vegetable consumption in both groups was low; with 98.36% of patients in the 1st line regimens and 94.00% of patients in the 2nd line regimen not meeting the recommended intake of vegetables. Meat intake was high in 11.48% and 12.00% of patients in the 1st and 2nd line regimen respectively, but 75.41% (1st line regimen group) and 70.00% (2nd line regimen group) of patients had a meat intake that was below the recommended intake of 2-4 servings daily.

4.3.2 Energy and macronutrient intakes

Tables 4.2 and 4.3 indicate the median energy and macronutrient intakes and median macronutrient intakes expressed as a percentage of total energy (TE) respectively.

Table 4.2: Median energy and macronutrient intakes (n = 111)

	1st line regimen			2nd line regimen			
	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	95% CI for med diff
Carbohydrate (g)	226	310	391	159	221	316	-1.8; 7.6
Protein (g)	62	77	103	53	68	95	-3.7; 0.5
Fat (g)	37	54	76	33	45	66	-3.4; 3.7
Total energy (kJ)	6988	7968*	9577	5011	6406*	9233	378; 2561*

Median intakes in grams for carbohydrates, proteins and fat were 310g, 77g and 54g respectively for regimen 1. Median energy intake for patients on regimen 1 was 7968kJ per day. In the 2nd line regimen group median intake in grams were 221g for carbohydrates, 68g for protein and 45g for fat. Median energy intake of patients on regimen 1 was significantly higher than that of patients on regimen 2 at 6406kJ per day (95% CI for median difference [378;2561]).

Table 4.3: Macronutrient intakes expressed as percentage of total energy (n = 111)

	1st line regimen			2nd line regimen			
	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	95% CI for med diff
Carbohydrate (%)	52	66*	70	48	59*	69	23; 117*
Protein (%)	14	16	21	14	18	24	-1; 22
Fat (%)	19	25	31	19	27	31	-2; 17

Median percentages of energy from macronutrients were as follows: 66 % of total energy from carbohydrate, 16 % energy from protein and 25 % energy from fat in the 1st line regimen group. In the 2nd line regimen the percentage energy from carbohydrates was significantly lower than that of the patients in the first regimen at 59% of total energy (95% CI for median difference [23; 117]. In the 2nd line regimen group 18 % of total energy came from protein and 27 % from fat.

4.3.3 Food types and frequency of consumption

The results of the food frequency questionnaire are shown in table 4.4.

Table 4.4: Food types and frequency of consumption (n=111)

	1st line regimen (n=61)						2nd line regimen (n=50)					
Food Types	**Never**		**Daily**		**Weekly**		**Never**		**Daily**		**Weekly**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Sweets/Chocolate	20	33	41	67	0	0	12	24	38	76	0	0
Chips (crisp)	14	23	47	77	0	0	12	24	38	76	0	0
Cake / biscuits	17	28	43	71	1	2	16	32	34	68	0	0
Cool drinks	14	23	46	75	1	2	10	20	35	70	5	10
Cremora	43	71	18	30	0	0	35	70	14	28	1	2
Coffee	36	59	24	40	1	2	33	66	16	32	1	2
Tea	8	13	43	71	10	16	9	18	33	66	8	16
Sugar	2	3	26	43	33	54	3	6	22	44	25	50
Full-cream milk	17	28	43	71	1	2	18	36	31	62	1	2
Low fat / skim milk	53	87	8	13	0	0	36	72	12	24	2	4
Eggs	9	15	47	77	5	8	5	10	39	78	6	12
Peanut butter	21	34	40	66	0	0	19	38	31	62	0	0
Soya mince / legumes	20	33	41	67	0	0	8	16	41	82	1	2
Chicken	0	0	61	100	0	0	0	0	50	100	0	0
Red meat	10	16	51	84	0	0	6	12	43	86	1	2
Fish	12	20	49	80	0	0	5	10	45	90	0	0
Bread	1	2	34	56	26	43	1	2	19	38	30	60
Porridge	1	2	59	97	1	2	6	12	42	84	2	4
Cereal	32	52	29	48	0	0	19	38	31	62	0	0
Samp / mielie rice	11	18	50	82	0	0	13	26	37	74	0	0
Margarine / oil/ fat	3	5	56	92	2	3	2	4	40	80	8	16
Fruit juice	9	15	51	84	1	0	7	14	40	80	3	6
Fruit	6	10	39	64	16	26	2	4	31	62	17	34
Vegetables	1	2	52	85	8	13	1	2	41	82	8	16
Salt / Stock / Royco	4	7	57	93	0	0	0	0	47	94	3	6
Alcohol	48	79	13	21	0	0	35	70	15	30	0	0

The food item that was consumed most often was chicken, with 100% of patients in both groups indicating that they consumed chicken daily. Other foods that were consumed most frequently included porridge, margarine, tea, oil, red meat, fish, fruit juice, vegetables and salt. The frequencies for both groups are shown below and are separated into three groups, namely weekly consumption, daily consumption and no consumption (never).

4.4 Anthropometric information

4.4.1 Body mass index

The median BMI values of the patients included in the study are shown in table 4.5.

Table 4.5: Median BMI of patients on 1st and 2nd HAART regimens (n=111)

	1st line regimen (n=61)			2nd line regimen (n=50)			
	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	95% CI for med diff
BMI (kg/m^2)	17.86	22.80	39.67	17.09	25.34	42.15	-3.62; 0.07

In the group of patients on the 1st line HAART regimen, median BMI was 22.80kg/m^2 (range 17.86kg/m^2 to 39.67kg/m^2). For the 2nd line HAART regimen group the median BMI was 25.34kg/m^2 (range 17.09kg/m^2 to 42.15kg/m^2). Median BMI of patients on regimen 2 was close to significantly higher than that of patients on regimen 1, with a 95% CI of [-3.62; 0.07].

Table 4.6: BMI categories of patients on 1st and 2nd HAART regimens (n=111)

		Regimen 1 (%)	Regimen 2 (%)
<18.5	Underweight	6.56	4.00
18.5 - 24.9	Normal weight	60.66	40.00
25-29.9	Overweight	21.31	34.00
>30	Obese	11.48	22.00

Table 4.6 shows the percentages of patients with BMI values in the underweight, normal weight, overweight and obese categories. Almost seven percent of the patients on the 1st line regimen and 4.00% of the patients on the 2nd line regimen were underweight. The majority of the patients had a BMI that was within the normal range (60.66% of patients on the 1st line regimen and 40.00% of patients on the 2nd line regimen). Twenty one percent of the patients on the 1st line regimen were overweight and 11.48% obese. Thirty four percent of patients on the 2nd line regimen where overweight and 22.00% were obese.

4.4.2 Waist circumference

Table 4.7: Median waist circumference of patients on Regimen 1 and 2 (n=111)

	Minimum value	Median	Maximum value	95% CI for med diff
Regimen 1	66 cm	80 cm	113 cm	-9; 0
Regimen 2	63 cm	86 cm	126 cm	

Table 4.7 indicates the median waist circumference measurements for patients on regimen 1 and 2. Median waist circumference for patients in the 1st and 2nd groups were 80.00cm and 86.50cm respectively. The patients in the 2nd regimen group had a very near to significantly higher waist circumference compared to patients in the 1st regimen group with a 95% CI for the median difference of [-9; 0].

Table 4.8: Percentage of patients with waist circumference in the high risk category (n=111)

		Regimen 1 (%)	Regimen 2 (%)
(>80cm female) (>94cm male)	High risk	47.54	54.00

The percentage of patients on the 1st line regimen who had waist circumference measurements in the high risk category (>80cm in females and >94cm in males) was 47.54%. In the 2nd line regimen group, 54.00% of patients had a waist circumference that placed them at risk of chronic diseases (table 4.8).

4.4.3. Waist to hip ratio

In table 4.9 the median values for waist to hip ratio of patients on the two HAART regimens are indicated.

Table 4.9: Median waist to hip ratio of patients on regimen 1 and 2 (n=111)

	Minimum value	Median	Maximum value
Regimen 1	0.65	0.87	1.08
Regimen 2	0.66	0.87	1.13

Median waist to hip ratios of patients in the two HAART regimen groups were the same at 0.87 (95% CI for median difference [-0.04; 0.02]).

Table 4.10: Percentage of patients with a high risk waist to hip ratio (n=111)

Cut off values	**Category**	**Regimen 1 (%)**	**Regimen 2 (%)**
>0.8 female >0.9 male	High risk	59.02	66.00

Table 4.10 indicates that 59.02% of patients on the 1st line regimen and 66.00% of the patients on the 2nd line regimen had a waist to hip ratio that exceeded the cut off values (>0.8 for females and >0.9 for males).

4.4.4 Body fat percentage

Table 4.11: Median fat percentage of patients on Regimen 1 and 2 (n=84)

	Minimum value	**Median**	**Maximum value**	**95% CI for med diff**
Regimen 1 (%)	9	26	46	-7.1; 2.0
Regimen 2 (%)	13	30	52	

Body composition analysis to assess body fat percentages were performed on 75.67% (n=84) of the total study population. The median fat percentages of patients on regimen 1 and 2 were 26% and 30% respectively.

Table 4.12: Percentage of patients with body fat percentage values in the different categories (n=84)

		1st line regimen	**2nd line regimen**
	Category	% of (n = 40)	% of (n = 44)
< 20%	Low	10.00	6.82
20 - 25%	Normal	35.00	29.55
>25%	High	55.00	63.64

The majority of patients, 55% on the 1st line regimen and 63.64% on the 2nd line regimen had a body fat percentage above the cut off value for a high fat percentage (greater than 25%). Only 35% of patients on the 1st line regimen and 29.55% of patients on the 2nd line regimen had a normal fat percentage (between 20-25%) and the percentage of patients with a low fat percentage was very low at 10.00% of patients on the 1st line regimen and 6.82% of patients on the 2nd line regimen (table 4.12).

4.5 Biochemical markers

Table 4.13 indicates the median values for biochemical variables of patients on regimen 1 and 2.

Table 4.13: Median values for biochemical variables of patients on regimen 1 and 2 (n=109)

	1st line regimen			2nd line regimen			
	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	95% CI for med diff
Glucose (mmol/L)	4.4	4.8	5.1	4.3	4.9	5.3	-0.3; 0.2
Cholesterol (mmol/L)	4.1	4.8	5.6	3.9	4.4	5.1	0.01; 0.85*
HDL (mmol/L)	1.0	1.2	1.6	0.9	1.1	1.3	0; 0.28
LDL (mmol/L)	2.2	2.8	3.4	1.9	2.6	4.5	-0.03; 0.73
Triglycerides (mmol/L)	1.0	1.3	1.8	1.1	1.4	2.1	-0.41; 0.10
Viral load	25	49	49	25	49	170	-24; 0
CD4 cell count	236	352	464	221	350	455	-68; 66

Patients in the regimen 2 group had significantly lower median cholesterol levels than patients in the regimen 1 group (95% CI for median difference [0.01; 0.85]), and HDL levels were near to significantly lower in patients on the 2nd line of HAART therapy (95% CI for median difference [0; 0.28]). The median viral load of patients in the regimen 2 group was very near to significantly higher than that of patients in the regimen 1 group (95% CI for median difference [-24; 0]).

Table 4.14 shows the percentage of patients with biochemical values above or below the normal ranges in the two regimen groups.

Table 4.14: Percentage of patients with biochemical markers above or below normal ranges (n=109)

		Regimen 1 (%)	Regimen 2 (%)
Glucose	> 6.0 mmol/L	11.48	4.17
Cholesterol	> 5.0 mmol/L	39.34	27.66
HDL	< 1.0 mmol/L	22.95	43.75
LDL	> 2.5 mmol/L	60.66	52.08
Triglycerides	> 1.5 mmol/L	34.43	47.92
Viral load	< 25	0.00	2.00
	equal to 25	37.70	26.00
	> 25	62.30	72.00
CD4 count	< 500	80.33	80.00
	>500	19.67	20.00

Glucose values above 6mmol/L occurred in 11.48% of participants on 1st line HAART regimen and 4.17% of participants in the 2nd line regimen group. Almost forty percent and 27.66% of patients in the 1st and 2nd line regimen groups respectively had cholesterol levels above 5mmol/L. High density lipoproteins (HDL) levels were below the cut off value of less than 1mmol/L in 22.95% (1st line regimen) and 43.75% (2nd line regimen) of the patients in the study. Low density lipoproteins (LDL) levels where high (>2.5mmol/L) in 60.66% of patients in the 1st line regimen and 52.08% in the 2nd line regimen group. Thirty four percent of patients in the 1st line regimen group and 47.92 % in the 2nd line regimen group had elevated triglycerides (above 1.5mmol/L).

Only 2 % of patients on the 2nd line regimen had a low viral load, while no patients in the 1st line regimen group had a low viral load. The majority of patients had a viral load above 25 (62.30% -1st line regimen and 72.00% - 2nd line regimen), and the remaining patients (37.70% -1st line regimen and 26.00% - 2nd line regimen) had viral loads equal to 25.

Eighty percent of patients on both the 1st and 2nd line HAART regimens had CD 4 counts below 500. Only 19.67% and 20.00% of patients on the 1st and 2nd line regimens respectively had CD 4 counts above 500.

4.6 Blood pressure

Table 4.15 indicates the median values for systolic and diastolic blood pressure of patients in the two regimen groups.

Table 4.15: Median blood pressure values of patients on regimen 1 and 2 (n=111)

	1st line regimen			2nd line regimen			
	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	95% CI for med diff
Systolic blood pressure (mm Hg)	110	117	134	113	121	133	-7; 5
Diastolic blood pressure (mm Hg)	72	77	86	67	76	83	-2; 7

No statistically significant differences in median systolic and diastolic blood pressure of patients on regimen 1 and 2 could be found.

Table 4.16 shows the percentage of patients with normal and high blood pressure values.

Table 4.16: Percentage of patients with normal and high blood pressure (n=111)

		Regimen 1 (%)	Regimen 2 (%)
≥135/85	High	27.87	28.00
<135/85	Normal	72.13	72.00

Blood pressure values indicated that 27.87% of patients on the 1st line regimen and 28.00% on the 2nd line regimen had an elevated blood pressure. An elevated blood pressure reading was indicated by a systolic value of more than or equal to 135mmHg and/or diastolic value more than or equal to 85mmHg.

4.7 Lifestyle factors that can impact on HIV / AIDS

4.7.1 Smoking habits

Table 4.17: Smoking habits of patients on HAART (n=111)

	1st line regimen		2nd line regimen	
	N	% of the group	N	% of the group
	61		50	
1. Never smoked	48	78.69	42	84.00
2. Currently smoke	11	18.03	7	14.00
3. Formerly smoked	2	3.28	1	2.00

Most patients, 78.79% (1st line regimen) and 84.00% (2nd line regimen) reported that they had never smoked. In the 1st line regimen group 18.03% of patients were current smokers and 3.28% were former smokers. The 2nd line regimen group indicated that 14.00% of patients in this group currently smoked and 2% formerly smoked (table 4.17).

4.7.2 Alcohol consumption

Table 4.18: Alcohol consumption of patients on HAART (n=111)

	1st line regimen		2nd line regimen	
	N	% of the group	N	% of the group
	61		50	
1. Never used alcohol products	48	72.13	32	64.00
2. Currently use alcohol products	11	21.31	12	24.00
3. Formerly used alcohol products	2	6.55	1	2.00

Reported alcohol consumption indicated that 72.13% and 64.00% of patients on the 1st and 2nd line regimens respectively never used alcohol. Twenty percent of patients in the 1st line regimen group currently used alcohol and 6.56% of patients had formerly used alcohol. Current alcohol users in the 2nd line regimen group accounted for 24.00%, while 12.00% of this group had formerly used alcohol.

4.7.3 Levels of physical activity in patients on HAART

Table 4.19 below indicates the level of physical activity of the patients in the study based on a 24 hour recall of physical activity (during a week day) and frequency of activities not performed every day.

Table 4.19: Median levels of physical activity of patients on 1st and 2nd HAART regimens (n=111)

	1st line regimen			2nd line regimen			
	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	95% CI for med diff
PAL	0.91	1.10	1.28	0.90	0.96	1.19	-0.03; 0.16

Table 4.20: Percentage of patients with physical activity levels in the different categories (n=111)

		1st line regimen	2nd line regimen
PAL	Category	% of (n = 61)	% of (n = 50)
1-1.39	Sedentary	81.96	93.88
1.4-1.59	Low	8.20	4.08
1.6 - 1.89	Active	6.56	0.00
>1.9	Very active	3.28	2.04

Most of the patients on HAART were sedentary (81.96% and 93.88% of patients in the 1st and 2nd line regimen groups respectively). In the 1st line regimen group 8.20% of patients had low activity levels, 6.66% were active and 3.28% were very active. Similar results were seen in the 2nd line regimen group where 4.08% of patients had low activity levels and only 2.04% were very active (table 4.20).

4.8 Self reported medical history and family medical history

4.8.1 Self reported medical history

Table 4.21: Self reported medical history of patients on HAART (n=111)

	1st line regimen		2nd line regimen	
	N	% of the group	N	% of the group
1. Diabetes	61		50	
Yes	3	4.92	1	2.00
No	58	95.08	49	98.00
2. High blood pressure	61		50	
Yes	8	13.11	9	18.00
No	53	86.89	41	82.00
3. Stroke	61		50	
Yes	1	1.64	6	12.00
No	60	98.36	44	88.00
4. Heart disease/ Angina/ Heart attack	61		50	
Yes	3	4.92	1	2.00
No	58	95.08	49	98.00
5. Cancer	61		50	
Yes	1	1.64	2	4.00
No	60	98.36	48	96.00
6. Liver disease/ Hepatitis/ Jaundice	61		50	
Yes	3	4.92	1	2.00
No	58	95.08	49	98.00
7. Lung disease e.g. emphysema or asthma	61		50	
Yes	4	6.56	4	8.00
No	57	93.44	46	92.00
8. Tuberculosis	61		50	
Yes	22	36.07	20	40.00
No	39	63.93	30	60.00

In both groups the reported prevalence of tuberculosis (TB) was the highest, with 36.07 % and 40.00% of patients in the 1st and 2nd line regimen respectively. Hypertension was the most common chronic disease reported in both groups following TB (13.11% in the 1st line regimen group and 18.00% in the 2nd line regimen group).

4.8.2 Family medical history

Table 4.22: Self reported family medical history (n=111)

	1st line regimen		2nd line regimen	
	N	% of the group	N	% of the group
1. Diabetes	61		50	
Yes	19	31.15	13	26.00
No	42	68.85	37	74.00
2. High blood pressure	61		50	
Yes	30	49.18	30	60.00
No	31	50.82	20	40.00
3. Stroke	61		50	
Yes	11	18.03	10	20.00
No	50	81.97	40	80.00
4. Heart disease/ Angina/ Heart attack	61		50	
Yes	8	13.11	4	8.00
No	53	86.89	46	92.00
5. Cancer	61		50	
Yes	8	13.11	4	8.00
No	53	86.89	46	92.00
6. Liver disease/ Hepatitis/ Jaundice	61		50	
Yes	0	0.00	3	6.00
No	61	100.00	47	94.00
7. Lung disease e.g. emphysema or asthma	61		50	
Yes	17	27.87	10	20.00
No	44	72.13	40	80.00
8. Tuberculosis	61		50	
Yes	26	42.62	9	18.00
No	35	57.38	41	82.00
9. HIV / AIDS	61		50	
Yes	25	40.98	21	42.00
No	36	59.02	29	58.00

Family medical history showed that 31.15% of patients in the 1st line regimen had a family history of diabetes and 26% of patients in the 2nd line regimen group. Almost fifty percent and 60.00% of patients in the 1st and second line regimen respectively had a family history of high blood pressure. Eighteen percent (1st line regimen) and 20.00% (2nd line regimen) of patients reported a family history

of strokes and cancer. A family history of liver disease was present in 6.00% of the 2nd line regimen group. A family history of lung disease was present in 27.87% (1st line regimen) and 20.00% (2nd line regimen), while tuberculosis family history was present in 42.62% (1st line regimen) and 18.00% (2nd line regimen). Forty percent of patients on the 1st line regimen and 42.00% of patients on the 2nd line regimen reported that they had a family member who was infected with HIV.

4.9 Associations between variables

Table 4.23 indicates the association between low physical activity levels and body mass index above 25kg/m^2.

Table 4.23: Association between patients with low physical activity levels and high BMI on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	18	29.5%*
Regimen 2 (n=50)	27	54.0%*

Significantly more patients on regimen 2 (54%) had low levels of physical activity combined with high BMI than patients on regimen 1 (29.5%). The 95% confidence interval for the percentage difference was [-40.9; -6.1].

Table 4.24: Association between patients with low physical activity levels and high fat percentage (>25%) on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=40)	19	47.5%
Regimen 2 (n=44)	28	63.6%

Body composition analysis indicated that a higher percentage of patients (63.6%) on regimen 2 had higher fat percentages when compared with patients (47.5%) on regimen 1. The 95% confidence interval for the percentage difference was close to significant [-35.4; 4.9].

Table 4.25: Association between patients with low physical activity levels and high risk waist to hip ratios on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	33	54.1%
Regimen 2 (n=50)	33	66.0%

Trends were very similar in both regimen 1 (54.1%) and 2 (66.0%) when comparing low physical activity level with high waist to hip ratio (>0.8 in females and >0.9 in males). Both groups had a high percentage of patients that had waist to hip ratios that increased their risk for chronic diseases. The 95% confidence interval for the percentage difference was [-28.8; 6.3], indicating that the difference was not significant.

Table 4.26: Association between patients with low physical activity levels and high risk waist circumference on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	26	42.6%
Regimen 2 (n=50)	27	54.0%

Fewer patients on regimen 1 (42.6%) had a high waist circumferences (>80cm in females and >94cm in males) and lower physical activity levels than compares to patients on regimen 2 (54.0%). Although a higher percentage of patients on regimen 2 had an increased risk for chronic disease as indicated by high waist circumference than patients on regimen 1, the difference was not statistically significant. The 95% confidence interval for the percentage difference was [-28.8; 7.1].

Table 4.27: Difference between patients with elevated triglyceride levels on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	21	34.43%
Regimen 2 (n=48)	23	47.92%

The percentage of patients who had high triglyceride levels (>1.5mmol/l) was higher in regimen 2 (47.92%) than in regimen 1 (34.43%). The 95% confidence interval for the percentage difference was not significant [-30.9; 4.9].

Table 4.28: Difference between patients with low HDL levels on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	14	22.95%
Regimen 2 (n=48)	21	43.75%

Significantly more patients on regimen 2 (43.75%) had low high density lipoprotein levels (HDL) when compared with patients on regimen 1 (22.95%). Low HDL was classified as being lower than 1mmol/l. The 95% confidence interval for the percentage difference was close to significant at [-37.3;-3.1].

Table 4.29: Difference between patients with high blood glucose levels on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	7	11.48%
Regimen 2 (n=48)	2	4.17%

A higher percentage of patients on regimen 1 (11.48%) had high blood glucose levels (6.0mmol/l) compared to those on regimen 2 (4.17%). The 95% confidence interval for the percentage difference was [-4.1; 18.1], indicating that the difference was not significant. The small number of patients with high blood glucose levels makes it difficult to draw conclusions from these results.

Table 4.30: Difference between patients with high risk waist circumferences on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	29	47.54%
Regimen 2 (n=50)	27	54.0%

In both regimen 1 (47.54%) and 2(54.0%) a large percentage of patients presented with waist circumference levels above the recommended cut offs (>80cm in females and >94cm in males). The 95% confidence interval for the percentage difference was not significant [-24.2; 11.9].

Table 4.31: Difference between patients with high blood pressure on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	21	34.43%
Regimen 2 (n=50)	14	28.0%

Twenty eight percent of patients on regimen 2 and 34.43% of patients on regimen 1 had high blood pressure (≥ 135/85). The 95% confidence interval for the percentage difference was not significant [-10.9; 22.8].

Table 4.32: Difference between the incidence of insulin resistance syndrome in patients on the regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	3	4.92%
Regimen 2 (n=50)	5	10.0%

Insulin resistance syndrome was described as having a high waist circumference (>80cm in females and >94cm in males) together with three additional factors, namely; elevated blood glucose levels (6.0mmol/l), high blood pressure (≥ 135/85), low HDL (<1.0mmol/l) and/or high triglycerides (>1.5mmol/l). According to this classification only a small percentage of patients presented with insulin resistance syndrome in regimen 1 (4.92%) and 2 (10.0%). However it must be noted that there were more patients that presented with a combination of the above mentioned criteria but failed to have the necessary four out of five requirements. The 95% confidence interval for the percentage difference was [-16.9; 5.2] and is therefore not statistically significant.

Table 4.33: Association between patients who smoke and have high cholesterol on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	3	4.9%
Regimen 2 (n=48)	2	15.4%

When comparing all the smokers in the two group's cholesterol levels, 3 patients (4.9%) in regimen 1 and 2 patients (15.4%) of regimen 2 had high cholesterol. The 95% confidence interval for the percentage difference was not statistically significant [-9.6; 9.8].

Table 4.34: Association between patients with CD4 counts below 500 on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	49	80.33%
Regimen 2 (n=50)	40	80.00%

The amount of patients that had CD4 counts below 500 was very high in both groups, considering that these patients are on HAART. In the patients on regimen 1, 80.33% of patients had a CD4 count below 500, similar results occurred in patients on regimen 2 (80.00%). No significant differences between the two groups were found (95% confidence interval for percentage difference [-14.2; 15.6]).

Table 4.35: Difference between patients with high body fat percentages on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=40)	22	55.00%
Regimen 2 (n=44)	28	63.64%

Similar findings were apparent in both regimen 1 (55.0%) and 2 (63.64%) when comparing high body fat percentage in patients in the different groups. Both groups had a large number of patients who presented with a high fat percentage (>25%). The 95% CI for the percentage difference was not significant at [-28.3; 11.9].

Table 4.36: Association between patients with high body fat percentages and a high risk waist circumference on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=40)	15	37.5%
Regimen 2 (n=44)	22	50.00%

Half of the patients in regimen 2 had a high fat percentage (>25%) and high risk waist circumference (>80cm in females and >94cm in males). Less patients in regimen 1 (37.5%) had both high fat percentages and waist circumferences, but the difference was not significant (95% CI for percentage difference [-31.9; 8.5]).

Table 4.37: Association between patients with low fat intake and low HDL levels on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	13	21.3%
Regimen 2 (n=48)	17	35.4%

More patients on regimen 2 (35.4%) had low HDL levels (<1.0mmol/l) when consuming a diet low in fat (less than 35%), when compared with patients on regimen 1 (21.3%). The 95% confidence interval for the percentage difference was close to significant at [-30.6; 2.7].

Table 4.38: Association between patients with low fruit and vegetable intake and CD4 counts below 500 on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	19	31.1%
Regimen 2 (n=48)	19	39.6%

According to the recommendations of the food guide pyramid fruit and vegetable consumption should be between 5-9 servings per day. Patients who consumed less fruit and vegetables and had a CD4 cell count below 500, accounted for 31.1% and 39.6% in regimen 1 and 2 respectively. The 95% CI for the percentage difference was not significant at [-7.1; 28.8].

Table 4.39: Association between patients with low CD4 counts (below 500) and high viral load (25 or higher) on regimen 1 and 2

	Number	Percentage
Regimen 1 (n=61)	49	80.3%
Regimen 2 (n=48)	39	78.0%

A high percentage of patients on regimen 1 (80.3%) and 2 (78%) had a combination of a low CD4 count (<500) and a high viral load (>25) even though they are on HAART. The 95% confidence interval for the percentage difference was [-12.5; 17.8], which was not statistically significant.

CHAPTER FIVE: DISCUSSION OF RESULTS

5.1 Introduction

The main objective of this study was to obtain a better understanding of the nutritional status of HIV infected adults on different antiretroviral regimens. In this chapter, the results will be discussed according to dietary intake, anthropometric data, biochemical markers, physical activity levels and other lifestyle factors that can impact on HIV / AIDS as well as associations between variables. Although limited data is available on the nutritional status of HIV infected adults on HAART (Arendt *et al*., 2008), the results from this study will be compared to both studies conducted on HIV infected adults on HAART (Duran *et al*., 2008; Jamie *et al*., 2006; Mulligan *et al*., 2005; Barth *et al*., 2008; Almeida *et al*., 2009; Domingo *et al*., 2003; Blass *et al*., 2008) and those not using ARVs (Hendricks *et al*., 2008; Vorster *et al*., 2004; Shah *et al*., 2005; Capili and Anastasi, 2008; Hadigan *et al*., 2001; Arendt *et al*., 2008; Baekken *et al*., 2008; Wonja *et al*., 2007). Finally, a short overview of the limitations experienced during the implementation of the study will be highlighted.

5.2. Dietary intake

5.2.1 24 hour recall and food frequency questionnaire

Optimal nutritional status is critical in the management of HIV / AIDS (WHO, 2003; Duran *et al*., 2008; Fenton and Silverman, 2008, 1010). According to Kim *et al.* (2001), nutrition is often overlooked even though there are well established links between immune function and nutrition. In order to optimize the efficiency of HAART, it is vital that adequate nutrition be achieved to optimize the benefits of antiretroviral drugs (Marcason, 2009) that can significantly prolong the lives of HIV-infected individuals (Tomkins, 2005; Wanke, 2005).

When comparing intakes of foods in the various groups as categorized according to the Food Guide Pyramid (USDA, 1992), it was clear that in most cases patients' intakes were below recommendations. The quality of their diets was poor in variety and available nutrients. Of particular concern, was the low consumption of fruits and vegetables. Only 26.23% and 34.00% of patients on the 1st and 2nd regimen respectively consumed the required servings of fruit per day. According to diet histories, only 1.64 % and 6.00% of patients in the 1st and 2nd regimen respectively ate the required amount of vegetables per day. The low intake of fruits and vegetables correlated with the results found in a study that was carried out on HIV infected persons on HAART in São Paulo, Brazil (Duran *et al*., 2008). According to Duran *et al*. (2008), mean scores for fruit and vegetable intakes in their study were also low. Diets that are rich in fruits and vegetables meet the requirements for micronutrients, fibre and macronutrients, and have also been shown to reduce the risk for cardiovascular disease (Lichtenstein *et al.,* 2006). Many patients attributed the low fruit and vegetable consumption to financial factors, poverty and unemployment. Yet a vast majority of the patients (approximately 70%) reported daily consumption of sweets, chocolates, chips and carbonated beverages. This highlights the lack of knowledge among patients to make better food choices and select foods that will benefit their health and well being rather than promote chronic diseases, which are exacerbated in the presence of HIV infection and HAART. According to Hendricks *et al*. (2008), CD4 counts were higher in patients that consumed more fruits and vegetables in a study undertaken in Boston including patients from the Nutrition for Healthy Living (NFHL) study that were HAART naïve. Educating HIV infected individuals about the importance of consuming at least 5-9 servings of fruits and vegetables daily is vital (WHO, 2003).

The nutrition transition in low-income South Africans, especially those that are urbanized, has resulted in higher intakes of vegetable fats and refined carbohydrates (as seen in this sample) and plays a critical role in the development of chronic diseases in both HIV infected and uninfected individuals (Vorster *et al.,* 2004). A high consumption of refined carbohydrates, specifically

maize meal was evident in this study population, and 96.72% (regimen 1) and 84.00% (regimen 2) reported eating maize meal daily. This practice is a common occurrence in the South African population as maize meal is a staple food (Vorster *et al*., 2004). According to Vorster *et al*. (2004) a high intake of maize meal and samp was apparent in asymptomatic HIV-infected Africans in the North West Province, South Africa included in the Transition in Health and Urbanisation in South Africa (THUSA) study. A diet high in refined carbohydrates and processed foods is regarded by the WHO to be a high risk dietary practice (WHO, 2006).

Fats (both amount and types) play a critical role in the management of dyslipidemia, which is prevalent in HIV infected patients on HAART (specifically PI therapy) (Montessori *et al*., 2004; Stein, 2009; Grinspoon, 2005). Patients should be encouraged to consume a diet rich in monounsaturated fats and limit the use of saturated and trans fats (Lichtenstein *et al*., 2006). Diets low in saturated fats and trans fatty acids are associated with a reduced risk for the development of cardiovascular disease (Lichtenstein *et al*., 2006). Results obtained from the food frequency questionnaires in this study showed that participants consumed more polyunsaturated fats like sunflower oils and margarines (91.8% in regimen 1 and 80.00% in regimen 2) as well as full cream dairy products rather than low fat dairy products, which has the potential to increase their intakes of saturated fats. Health practitioners should encourage the use of monounsaturated fats to improve dyslipidemia and even insulin resistance (Krummel, 2008, 852) as HIV-infected patients often develop both insulin resistance and dyslipidemia (Arendt *et al*., 2008; Salomon *et al*., 2002).

A study conducted in São Paulo, Brazil on HIV infected patients receiving HAART showed that refined carbohydrate and saturated fats in the diet, may affect the development of central obesity regardless of the total energy intake (Jaime *et al*., 2006). This information again highlights the importance for nutrition education in the HIV infected population.

5.2.2 Energy and macronutrient intake

HIV infection alters the metabolism of all macronutrients (Ware *et al*., 2002). Inadequate macronutrient intake and poor nutritional status in turn can affect immune response (Cunningham-Rundles *et al*., 2005; Kim *et al*., 2001). Wasting in HIV-infected adults is a clear indication that macronutrient requirements are not being met (ASSAf, 2007).

In this study, the macronutrient splits according to median percentage of total energy per regimen were as follows; 66 % carbohydrate, 16 % protein and 25 % fat in regimen 1 and 59 % carbohydrate, 18 % protein and 27 % fat in regimen 2. Similar macronutrient splits were apparent in a study conducted on asymptomatic HIV-infected Africans in the THUSA study undertaken in the North West Province (Vorster *et al*., 2004). Median carbohydrate intake as a percentage of total energy was statistically higher in patients on regimen 1 as shown in table 4.3. The median for total energy intake was higher in patients on regimen 1. There were no statistical differences for fat and protein intake as a percentage of total energy between the two groups.

In a study conducted in Toronto, Canada on HIV infected male patients with metabolic abnormalities, it was reported that median energy intakes from fat, protein and carbohydrates where within acceptable ranges (Arendt *et al.,* 2008). However the fat intake was close to the upper limit of normal and the carbohydrate intake was closer to the lower range (Arendt *et al.,* 2008).

The intake of fat by the patients accounted for 25 % and 27% of total energy intake for the 1st and 2nd regimen groups respectively. Although, there was no determination of the types of fat used in this population, most of the patients reported that they use “fish oil” or sunflower oil as the main source of fat in their diets as mentioned in 5.2.1. According to Vorster *et al.* (2004), there were significant correlations between the intake of polyunsaturated fats and *elevated* liver enzymes in the asymptomatic HIV-infected Africans included in the THUSA

study and these authors have recommended that HIV-infected patients should limit the intake of polyunsaturated fats (Vorster *et al*., 2004). Improvements in the types of fat used (emphasizing the use of unsaturated fats, specifically monounsaturated fats), as well as an increase in total fat intake (30%-35%) can aid in reducing triglyceride levels and increasing HDL cholesterol levels in people with insulin resistance (Krummel, 2008, 852; Grundy *et al.,* 2001).

5.3 Anthropometric information

Anthropometric measurements that were recorded in this study included BMI, waist circumference measurements, waist to hip ratio and body fat percentage. The findings regarding the anthropometric data will be discussed in the following section.

5.3.1 Body Mass Index

Excessive weight gain and the incidence of obesity and overweight are increasing in the HIV infected population on HAART (Bhavan *et al*., 2008). HIV infected patients on HAART that are overweight have a higher risk for cardiovascular disease (Kaplan *et al*., 2007). According to Maia *et al*. (2005), BMI is usually higher in patients on HAART than patients who are HAART naïve. A study conducted in São Paulo, Brazil on HIV infected patients on HAART reported that patients who were overweight generally had a poor diet quality (Duran *et al*., 2008).

HIV infected patients that had lipodystropy in a study conducted in Texas, America, reported that mean BMI values indicated that the males in the study were mostly overweight and that the females were obese (Shah *et al*., 2005). A Canadian study on HIV infected patients with metabolic syndrome showed the mean for BMI was 26.05kg/m^2 (Arendt *et al*., 2005). These results are similar to the American data presented by Shah *et al*. (2005). A study conducted in New York on HIV infected patients found that 39.7% and 13.3% of patients were

overweight and obese (Capili and Anastasi, 2008). In the present, study the results indicated that the majority of the patients were within the normal weight range according to BMI. More patients, however, were overweight and obese on regimen 2 than on regimen 1 (table 4.6). Median values for BMI confirmed this, and the differences between the two groups were almost statistically significant (table 4.5). Poverty and lack of household food security might be possible contributing factors to lower BMI values in developing countries like South Africa. A longer duration on HAART could also affect the incidence of overweight and obesity, accounting for the differences in BMI results between this study and others completed in similar population groups.

5.3.2 Waist circumference

In HIV infected patients on HAART, lower levels of peripheral fat were seen in a sub-study of the Women's Interagency HIV study, despite the high level of obesity in this population (Mulligan *et al*., 2005). These authors concluded that central obesity may be influenced by HIV infection and HAART, or both (Justman *et al*., 2008). An American study in Texas, conducted on HIV infected patients with lipodystrophy, indicated the mean waist circumference for females was 107.6cm, while for males it was 91.0cm. Approximately half of the HIV infected patients in the present study had high risk waist circumference measurements. The median value for waist circumference in patients on regimen 1 (80cm) and regimen 2 (86cm) did not indicate significant differences. Patients on regimen 2 had higher BMI's than patients on regimen which could account for the higher median waist circumferences. The cut off for waist circumference in woman is $\geq$ 80cm and $\geq$ 94cm in men and measures above these cut-off points indicate an increased risk for the development of cardiovascular disease (Alberti *et al.*, 2006).

5.3.3 Waist to hip ratio

Values above 0.8 in women and 0.9 in men indicate central fat deposition with a possible increased risk for chronic disease (Barasi, 2003, 12). In a study conducted in Massachusetts, on HIV infected adults the mean value for waist to hip ratio was 0.97 in males and 0.96 in females (Hadigan *et al*., 2001). Similar high risk waist to hip ratios where prevalent in the present study. More than half of patients on regimen 2 (66.00%) and 54% of patients on regimen 1, had waist to hip ratios that exceeded the recommended values. Median values in both groups for waist to hip ratio were the same (0.87). However, the THUSA study conducted in the North West Province on asymptomatic HIV-infected Africans found that waist to hip ratio means for men and woman were within normal ranges (Vorster *et al*., 2004). This was possibly due to the fact that the patients in this study were on HAART and might have had fat redistribution which could cause an increase in abdominal fat, thus affecting the waist to hip ratio.

5.3.4 Body fat percentage

Bioelectrical impedance analysis is an inexpensive, quick and noninvasive technique (Kolter *et al*., 1996; Schwenk *et al*., 1999; Batterham *et al*., 1999; Forrester *et al.,* 2008) that was shown by Aghdassi *et al.* (2007), to have a relatively small margin for error when compared to the dual energy x-ray absorptiometry (DEXA) scan and can therefore be used for routine monitoring in HIV infected patients with normal hydration. A fat percentage higher than 25% is regarded as high (Laquatra, 2004). In this study, body fat percentage was high in more than 50% of patients in both regimen groups, as indicated in table 4.12 and the median value for fat percentage was higher in patients on regimen 2 than regimen 1. Median values for fat percentages were not statistically significant between the two regimen groups. In a study, conducted in Massachusetts, mean fat percentage was 22.7% for HIV infected patients with fat redistribution (Hadigan *et al*., 2001), which was lower than the findings in the current study.

5.4 Biochemical markers

According to Nerad *et al*. (2003), current HAART regimens have the ability to reduce viral load to undetectable levels, consequently increasing CD4 counts. HAART is associated with an increased risk for cardiovascular disease and has a number of other health effects, but the benefits of HAART in HIV infected patients with low CD4 counts clearly outweigh any metabolic effects (Aberg, 2009). A three fold increase in risk for coronary heart disease was noted in the DAD study for patients (that were on protease inhibitor therapy) who had changes in blood glucose, blood pressure and lipid levels (Grover *et al.,* 2005; DAD study group, 2007).

A study, conducted in Mpumalanga, South Africa on HIV infected patients on HAART to establish the effectiveness of HAART, found that patients CD4 cell counts increased by 236 and viral loads in 70% of the HIV infected adults were below 50 (Barth *et al.,* 2008). The findings of this study, however, indicated that a large percentage on patients (80.33% in regimen 1 and 80.00% in regimen 2) had CD4 counts below 500, despite being on HAART for six months or longer. Viral loads below 25 were evident in only 2% of the patients on regimen 2, while 37.70% (regimen 1) and 26.00% (regimen 2) of patients had viral loads equal to 25. The majority of the patients (62.30% {regimen 1} and 72% {regimen 2}) had viral loads above 25. No significant difference according to median values for CD4 counts and viral loads were found between the two groups. These results could be due to patients not taking medications as prescribed, resulting in poor drug adherence. Household food security and nutritional status could possibly also affect viral load and CD4 counts. The quality of patient's diets in this study was not optimal and additional nutrition education is necessary in this population. Even though a similar population group was studied in this study and the Mpumalanga study, the variation in results could be due to the fact that the one group is in a rural setting and the other in an urban setting. Differences in the drug adherence training of patients as well as the monitoring of patients at the different sites can also play a very important role in the adherence of patients.

The impact of HAART on biochemical parameters has been widely published and many studies have shown that HAART has a negative impact on blood lipid levels (Montessori *et al*., 2004; Stein, 2009; Grinspoon, 2005). In the present study, this was confirmed, with lipogram results revealing that 60.66% (regimen 1) and 52.08% (regimen 2) of patients had LDL levels above 2.5mmol/l. LDL median values were similar and did not differ significantly between the two groups. Thirty nine percent of patients on regimen 1 and 27.66% of patients on regimen 2 had high cholesterol levels (>5.0mmol/l). High cholesterol levels were significantly higher in patients on regimen 1 when comparing median values with patients on regimen 2. High triglycerides and low HDL levels are associated with an increased risk for insulin resistance and contribute to an increased risk of cardiovascular disease in HIV infected patients on HAART (Shah *et al*., 2005). In this study, it appeared that high triglyceride levels (>1.5mmol/l) affected almost half of the patients (47.92%) on the second regimen and 34.43% of patients on regimen 1. Similar trends were apparent when comparing the HDL levels in both regimens, with 43.75% of patients on regimen 1 and 22.95% on regimen 2 presenting with low HDL levels (<1.0mmol/l). Significant differences were not found between the two groups for HDL, LDL and triglyceride median values as indicated in table 4.13.

In a study, conducted on HIV positive patients on HAART in Porto Alegre, Southern Brazil, it was noted that HAART significantly affected triglyceride and glucose levels (Almeida *et al*., 2009). In a Canadian study on HIV infected men with metabolic abnormalities, similar findings were reported (Arendt *et al*., 2008). They found that the mean values for triglycerides and LDL levels were above the recommended cut off values (Arendt *et al*., 2008).

Within the HIV infected population, the use of HAART also increases the risk for insulin resistance and other metabolic complications (Almeida *et al*., 2009). One of the risk factors for insulin resistance is an increased glucose level (Grundy *et al*., 2001). Elevated glucose levels affected a small proportion of participants in

the current study; 11.48% in regimen 1 and 4.17% in regimen 2, and no significant differences were apparent when comparing median values. The prevalence of insulin resistance in this study will be discussed in section 5.6.2. If dietary and lifestyle changes are not promoted at CCMT sites, the risk for HIV infected patients developing insulin resistance and diabetes grows and uncontrolled blood glucose levels in this population could increase.

5.5 Blood pressure

Factors that are associated with an increased risk for hypertension include, age, male gender, higher body mass index, high total cholesterol values and clinical lipodystrophy (Thiébaut *et al*., 2005; Baekken *et al*., 2008). In a study, conducted in Oslo, Norway, to compare hypertension incidence among HIV infected individuals and the general population, it was reported that combination antiretroviral therapy was an independent predictor of hypertension (Baekken *et al*., 2008). In the same study (Norway) the incidence of hypertension was 44% among patients receiving HAART (Baekken *et al*., 2008). Cut-off points for high blood pressure in this study were $\geq$135/85mmHg. A significant proportion of patients had hypertension (27.87% of patients on regimen 1 and 28.00% on regimen 2), however no significant differences between the two groups for median blood pressure occurred. In the THUSA study, the mean for blood pressure in HIV infected adults was 127/77mmHg for men and 122/77mmHg for woman (Vorster *et al*., 2004). These patients were however not on HAART, but represent a similar population group.

5.6 Lifestyle factors that can impact on HIV/AIDS

In this section, lifestyle factors, namely smoking habits, alcohol consumption and physical activity levels that can possibly have an impact on HIV, are discussed.

5.6.1 Smoking

Cigarette smoking affects immunity, and in a study conducted in Puerto Rico among HIV infected men and women it was shown that patients who reported current smoking had lower CD4 counts and a worse viral immune profile (Wojna *et al.,* 2007). HIV-related lung cancer is becoming a problem in HIV infected patients on HAART (Bazoes *et al*., 2008) and pneumonia incidence is doubled in HIV infected patients that smoke (Murdoch *et al*., 2008).

The current study found that most patients had never smoked, while 18.03% (regimen 1) and 14.00% (regimen 2) were current smokers. Even though the prevalence of smoking has been reported to be higher amongst HIV infected patients, specifically in low socioeconomic groups (Feldman *et al*., 2006; Duval *et al*., 2008; Murdoch *et al*., 2008), poverty and the additional expense related to smoking could be the reason for these results. In a study, conducted in North Carolina, on HIV-infected patients receiving HAART, 67% reported currently smoking (Murdoch *et al.,* 2008). Thirty one percent of males and 16.7% of females reported that they were current smokers in a study on HIV infected patients with lipodystrophy conducted in Texas, USA (Shah *et al*., 2005). In the Texas study 22.2% (males) and 50% (females) were former smokers (Shah *et al*., 2005).

Adherence to HAART is affected by smoking habits, in a study in the Bronx, New York, it was reported that the 63.5% of prescribed medications where taken by smokers, while 84.8% of prescribed medications were taken by non-smokers (Shuter and Bernstein, 2008).

5.6.2 Alcohol

HIV infected individuals often use alcohol (Cheng *et al*., 2009; Chander *et al*., 2008) even though reduced adherence to HAART is associated with alcohol consumption (Samet *et al*., 2004). In a study in Canada, in HIV infected males

with metabolic abnormalities, alcohol consumption was low and only 3 patients in the sample population consumed more than 20g of alcohol per day (Arendt *et al*., 2008). Most patients in the current study reported that they did not drink alcohol at all, and only 21.31% (regimen 1) and 24.00% (regimen 2) of patients reported currently drinking alcohol. In the Women's Interagency HIV study in America which was conducted in HIV positive women, 14%-24% of woman reported hazardous drinking, which impacted negatively on CD4 counts and increased symptoms of depression (Cook *et al*., 2009). Alcohol intake should be assessed in HIV infected patients and treated, as hazardous drinking is correlated with altered lipid profiles (Miguez-Burbano *et al*., 2009; Cook *et al*., 2009) and an increased risk of developing HIV-associated lipodystrophy (Cheng *et al*., 2009).

5.6.3 Physical activity

Regular exercise reduces very low density lipoproteins (VLDL), increases HDL levels and in certain individuals can reduce LDL levels. Improvements in blood pressure and insulin resistance are possible with regular exercise as well as favourable cardiovascular functioning (Grundy *et al*., 2001). An American study on HIV infected patients with lipodystrophy reported that 67% of males and 50% of females exercised regularly (Shah *et al*., 2005). Physical activity questionnaires indicated that the majority of patients in the current study were sedentary [81.96% (regimen 1) and 93.88% (regimen 2)]. The differences in median values for physical activity levels in regimen 1 (1.10) and regimen 2 (0.96) were almost significant. The lower physical activity levels for patients on regimen 1 could be due to their higher BMI values. A study conducted in Barcelona, Spain on HIV infected adults on HAART indicted that 62.7% of patients that were inactive had increased fat redistribution (Domingo *et al*., 2003). According to the Diet and Lifestyle Recommendations by the American Heart Association (Lichtenstien *et al*., 2006) a sedentary lifestyle is associated with increased risk for developing chronic diseases, such as type 2 diabetes, obesity, osteoporosis, depression and cancer of the colon and breast.

5.7 Self reported medical history and family medical history

Results from the self reported medical history indicated that 36.07% and 40.00% of patients in this study, previously or currently had tuberculosis (TB). Following TB, the prevalence of hypertension was most common (table 4.21). In patients on regimen 1, hypertension was most prevalent, followed by TB and HIV/AIDS. In patients on regimen 2, family medical histories also indicated that hypertension was most prevalent, however HIV/AIDS followed by diabetes was reported in this group.

Daily salt intake was reported by 93.44% (regimen 1) and 94.00% (regimen 2) of patients in this study which could be influencing the high reported prevalence of hypertension in this population. In a study done in Seattle by Crane *et al.* (2006), on patients receiving HAART, positive associations were reported between the use of lopinavir/ritonavir (PI therapies) and elevated blood pressure. The latter could also explain the hypertension prevalence in this population.

"South Africa is in the grip of three concurrent epidemics; malnutrition, HIV/AIDS and TB" (ASSAf, 2007). In light of the previous statement by the Academy of Science of South Africa, it is expected that a large percentage of patients in this study, as well as their family members would at some point be affected by these epidemics. Hence the large number of patients reporting the prevalence of HIV/AIDS and TB in their self reported medical histories and family medical histories.

Abnormal glucose metabolism is exacerbated by a family history of diabetes, combined with HAART and overweight (Blass *et al*., 2008). HIV patients receiving HAART in a study in Bonn, Germany showed that 28% of patients had impaired fasting glucose levels (Blass *et al*., 2008). With increased HIV/AIDS prevalence the risk for altered glucose metabolism rises and this may explain the

prevalence of diabetes reported in self reported medical histories and family medical histories.

5.8 Associations

In this section, the various associations that were investigated between variables are discussed.

5.8.1 Physical activity level associations

According to Johnson *et al*. (2007), a modest amount (30 minutes daily) of exercise significantly improves fat distribution (Florindo *et al*., 2007; Domingo *et al*., 2003), metabolic syndrome and risk for cardiovascular disease (Lakka and Laaksonen, 2007), all of which are associated with HIV infected patients on HAART. Despite the benefits of exercise, the majority of patients in this study were sedentary (section 5.6.3). Both patients in regimen 1 and 2 had a high BMI (>24.9kg/m^2) combined with low levels of physical activity. Significantly more patients' on regimen 2 had this combination of low physical activity levels and high BMI. High BMI and variations in the level of physical activity could occur due to the different drugs and associated side effects that are linked with protease inhibitor therapy interventions. PI associated side effects include; abnormal accumulation (lipodystropy) of intramyocellular fat, leading to insulin resistance (Oh and Hegele, 2007; Shah *et al*., 2005).

Excessive body weight is associated with increased risk for cardiovascular disease (Hill *et al*., 2005). According to Lichtenstein *et al.* (2006), increasing physical activity can help to achieve weight loss (Wing and Phelan, 2005), which will assist with improving insulin resistance and associated metabolic abnormalities. Increased physical activity in HIV infected patients improved life satisfaction scores, emotional and physical well being, and body compositions in a study conducted in Puerto Rico on HIV infected Hispanics (Ramirez-Marrero *et al.,* 2004).

5.8.2 Biochemical associations

According to Shah *et al*. (2005) lipid profiles should be checked regularly in patients on HAART, specifically individuals on PI therapy, as high rates of dyslipidemia occur in this population group. In this study, close to significantly more patients on regimen 2 (PI therapy) presented with dyslipidemia (elevated triglyceride levels and low HDL level) when compared to patients on regimen 1 (tables 4.27-4.28). This is in accordance with the results found by Shah *et al*. (2005), and Wanke *et al.* (2005), amongst HIV infected patients on HAART in Texas and Boston, respectively. Lipid profiles are significantly altered by protease inhibitor therapy (Wanke *et al.,* 2005; Montessori *et al*., 2004; Stein, 2009; Grinspoon, 2005) and dyslipidemia is linked to insulin resistance and fat redistribution syndromes (Grover *et al*., 2005; Oh and Hegele, 2007). In a study on HIV infected patients on HAART conducted in Slovenia, 72% of patients presented with dyslipidemia, thus increasing cardiovascular disease risk (Tomazic *et al*., 2004).

Similar results were reported in the Nutrition for Healthy Living (NFHL) study conducted on HIV-infected adults, where almost a quarter of subjects had metabolic syndrome (Jacobson *et al*., 2006). In the NFHL study 77% of patients that presented with metabolic syndrome had low HDL levels and hypertriglyceridemia. The pathogenesis of dyslipidemia is poorly understood (Montessori *et al*., 2004), however the development of dyslipidemia seems to be a common occurrence in HIV infected patients on HAART. Dyslipideamia occurs more commonly in patients receiving protease inhibitor therapy (Montessori *et al*., 2004; Stein, 2009; Grinspoon, 2005). Protease inhibitor therapy may interfere with LDL receptor regulatory proteins (Montessori *et al*., 2004) and mitochondrial dysfunction in skeletal muscle that can cause insulin resistance, with secondary dyslipidemia (Oh and Hegele, 2007).

No significant differences where found between the two regimens when comparing both blood glucose values and blood pressure measurements (tables 4.23 and 4.25).

Metabolic abnormalities such as insulin resistance are prominent in HIV infected patients, in both HAART and HAART naïve patients (Arendt *et al*., 2008; Salomon *et al*., 2002). In this study, one of the objectives was to determine the prevalence of insulin resistance because of the increased risk associated with the use of HAART. However a very small percentage of patients had insulin resistance.

5.8.3 Anthropometric associations

A large percentage of patients on regimen 1 and 2 had high risk waist circumference measurements (section 5.3.2). There was, however, no significant difference when comparing the waist circumference measurements and body fat percentages of patients on the two different regimens. As expected, significantly more patients with a higher body fat percentage had increased waist circumferences (table 4.36).

Indicators for central obesity, such as waist circumference and waist to hip ratio may be altered by HIV infection and HAART, or both (Justman *et al*., 2008). A study conducted in New York by Justman *et al*. (2008), found that among HIV infected woman, on protease inhibitor (PI) therapy, higher CD4 cell counts and age were all independent predictors associated with larger waist to hip ratios. Waist circumference measurements in the PI group were higher in this study (table 4.7), which is similar to findings of Justman *et al*. (2008). In this population, the prevalence of overweight, obesity and high risk body fat percentages were high. These factors can all contribute to elevated waist circumference measurements.

5.8.4 Dietary intake associations

Thirty one percent of patients on regimen 1 and 39.6% of patients on regimen 2, that had low CD4 counts (<500) also reported low intakes of fruits and vegetables. A small percentage of this study population reached the required daily intake of fruits and vegetables. A study conducted in Boston by Hendricks *et al*. (2008), on HIV infected men reported higher CD4 counts with increased intakes of fruit and vegetables. Adequate intakes of vitamins and minerals are needed to ensure that the immune system functions efficiently (Wintergerst *et al.,* 2007). CD4 cells form a part of the immune system, which will be compromised by inadequate micronutrient levels (Wintergerst *et al*., 2007). The association between low fruit and vegetable consumption and reduced CD4 counts could possibly be due to the reduced quality of the diet, in terms of micronutrient intakes from fruits and vegetables in this study population. Increased fruit and vegetable consumption is associated with a reduced risk for the development of chronic disease (Hung *et al*., 2004), and should therefore be recommended to all HIV infected individuals.

5.9 Limitations of the study

During the course of this study various limitations were encountered and these will be discussed in the following section.

5.9.1 Cost of biochemical analyses

Initially, it was thought that routine blood tests were completed on patients to monitor changes that might occur with the initiation of HAART since there are known risks for lipid irregularities in this population. These tests were, however, not being done routinely at the CCMT site included in this study. Initiation of the study was postponed until additional funding could be sourced by the researcher to cover the cost of biochemical analyses. Funding was eventually obtained from the Department of Chemical Pathology at WITS, who also analyzed all blood

samples and made use of the findings from the study to do specific genetic profiling in the same sample.

5.9.2 Sample size

In the initial protocol, a sample size of 60 participants in regimen 1 and 2 was suggested. Once the study commenced, it was clear that there where a lot more patients on regimen 1 than on regimen 2. To overcome this limitation, the Department of Biostatistics (UFS) was consulted and it was agreed that the sample size would be reduced to 50 patients in the second regimen group.

5.9.3 Body composition results

Bioelectrical impedance was used to determine body composition using the Body-stat machine (Bodystat R 1500 – Bodystat, Isle of Man, Limited). All the results where collected on the machine to be downloaded for analysis at the end of the study. Unknown to the researcher the Bodystat machine has a memory capacity to store 100 results which was not large enough to store all the results collected and therefore some of the results were lost. This limitation was overcome by adjusting the sample size with regards to body composition results.

5.9.4 Recall of dietary intake and physical activity level

Participants may over or under report information pertaining to dietary intake as well as physical activity levels due to various factors such as poor memory, misunderstanding, embarrassment or disinterest. Respondents often tend to underreport binge eating, consumption of alcoholic beverages and consumption of foods perceived as unhealthy. The inability to recall accurately the kinds and the amounts of food eaten, as well as the tendency for persons to over report low intakes and underreport high intakes of foods are all limitations of dietary intake methods (Hammond, 2008, 395; Lee and Nieman, 2003, 76). To overcome this limitation, patients where interviewed individually in a separate room to ensure

privacy. Confidentiality of results was also emphasized so that patients could feel more at ease and answer truthfully.

5.9.5 Language barrier

A few of the patients could not speak English and an interpreter who works for the research centre at the clinic had to be used during interviews. This resulted in certain interviews taking longer to complete.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 Introduction

This chapter aims to provide answers to the objectives that were set when this study was initiated, as well as provide recommendations that can be applied in CCMT sites and improve the outcomes for HIV infected patients on HAART in South Africa.

6.2 Conclusions

Determining the nutritional status of HIV-infected patients on HAART was the main objective of this study. In this chapter, the aim is to highlight the main findings in this study and draw conclusions from those in an effort to guide recommendations for future policy making and nutrition intervention protocols.

6.2.1 Dietary intake

Approximately 70% of patients on HAART included in this study consumed less than the required amount of fruit servings per day. Vegetable consumption was even lower and 98% (regimen 1) and 94 % (regimen 2) of patients did not eat the recommended number of servings of vegetables per day. This low intake of fruits and vegetables could be due to lack of income and gaps in nutrition knowledge about the benefits of fruit and vegetable consumption, especially related to the impact on immunity.

Ninety six percent and 84% of patients on regimen 1 and 2 respectively consumed refined carbohydrates daily. Even though patients in both groups reported high carbohydrate consumption, significantly higher total carbohydrate intakes from total energy were reported in patients on regimen 2. High intakes of carbohydrates are a regular occurrence as maize meal is a staple food that is affordable for the majority of the South African population. This dietary habit

might have adverse effects in HIV-infected patients on HAART in terms of chronic disease risk (Vorster *et al*., 2004). Reducing the intake of refined carbohydrates (maize meal) with whole grain carbohydrates is recommend for patients on HAART. Whole grain carbohydrates are costly, and government interventions would be necessary to reduce the cost through legislation, making it a staple food. Salt was reported to be consumed daily by 93.44% of patients on regimen 1 and 94% of patients on regimen 2. Nutrition transition, intake of fast foods and processed foods as well as the possible lack of nutritional knowledge regarding the impact of salt on hypertension are all factors that could contribute to the prevalence of hypertension.

Polyunsaturated fats like sunflower oils and margarines were used daily by 91.8% of patients on regimen1 and 80.00% of patients on regimen 2. Full cream dairy products were used more frequently than low fat dairy products, due to the cheaper price. Unfortunately the amounts of food items consumed were beyond the scope of this study, the latter practice however could possibly increase saturated fat intake which would have negative outcomes for patients on HAART, considering their risk for cardiovascular disease and other metabolic abnormalities. Peanut butter, which is a source of unsaturated fat, was consumed less frequently (65.57% {regimen1} and 62.00% {regimen2}). Unsaturated fats have beneficial effects when used as part of a dietary intervention for improving dyslipidemia in this population. No significant differences in dietary intake were apparent between patients on regimen 1 and 2.

Dietary intakes of participants in this study showed that nutrient intakes were poor and that the quality of patient's diets was not conducive to optimal nutritional status. Without improvements in dietary intake and attention to nutrition education interventions patients on HAART in this population will not reap the full benefits of antiretrovirals and improved quality of life that they deserve.

6.2.2 Anthropometric information

BMI was above 25kg/m^2 in 32.79% and 56% of patients on regimen 1 and 2 respectively. The median BMI value was higher in patients on regimen 2, and when compared with the median BMI for patients on regimen 1, the difference was close to significant. There was a positive association between a BMI above 25kg/m^2 and low physical activity. This association occurred in more patients on regimen 2 and the difference was statistically significant. Approximately half of all patients in this study had waist circumference measurements above the recommended 80cm for females and 94cm for males. Fifty nine percent (regimen 1) and 66% (regimen 2) of patients also had undesirable waist to hip ratio measurements. No statistical differences were shown when comparing median values for waist circumference and waist to hip ratio between the two groups. Central obesity, increased BMI and high risk anthropometric measurements were reported in this study and the findings can probably be attributed to HAART, as well as low physical activity levels and poor dietary habits. High body fat percentages (more than 25%) were present in more than half of all the patients in this study, however comparisons of median values between the two groups were not significant. No significant difference with regard to anthropometric data was recorded between patients on regimen 1 and 2. A large percentage of patients are at risk of developing chronic disease according to the results of the anthropometric assessments.

6.2.3 Biochemical markers

As expected, the prevalence of dyslipidemia in this population was high. Thirty nine percent of patients on regimen 1 and 27.66% of patients on regimen 2 had high total cholesterol levels. LDL cholesterol levels where elevated in a 60.66% of patients on regimen 1 and in 52.08% on regimen 2. Almost half of patients (47.92%) on the second regimen and 34.43% of patients on regimen 1 also had high triglyceride levels. HDL levels were low in a large percentage of patients (43.75% of patients on regimen 1 and 22.95% of patients on regimen 2).

Dyslipidemia is a common consequence of HAART, however the occurrence of this condition could possibly also be the result of poor dietary habits. Total cholesterol median values were significantly higher in patients on regimen 1.

Elevated glucose levels were apparent in a small proportion of the study population (11.48% in regimen 1 and 4.17% in regimen 2). Despite all patients using HAART, low CD4 counts and high viral loads were prevalent in the majority of participants, indicating reduced effectiveness of medication possibly due to adherence issues as well as poor nutritional status combined with a lack of knowledge.

6.2.4 Lifestyle factors

The majority of the patients in this study had never smoked, with only 18.03% of participants on regimen 1 and 14.00% on regimen 2 reporting currently smoking. Reported alcohol consumption was low, with most patients indicating that they did not drink at all. More than one fifth of patients on regimen one (21.31%) and 24.00% (regimen 2) of patients currently drank alcohol. Smoking habits and alcohol consumption in the current population were generally lower than those reported in other studies (discussed in 5.6.1 and 5.6.2), but physical activity levels were very low. Eighty two percent of patients on regimen 1 and 93.88% of patients on regimen 2 were sedentary.

6.3 Recommendations

Recommendations for dietary intake, anthropometry, biochemical markers and lifestyle factors will be summarized now in the following section of this chapter.

6.3.1 Dietary intake

Optimal nutrition is a necessary component for all patients infected with HIV (Nerad *et al.*, 2003; Hendricks *et al*., 2008), and needs to be accessible by

individuals to enhance their quality of life, improve health and ensure better response to drug regimens (ASSAf, 2007).

Nutrition interventions should encompass multiple, integrated approaches that need to include the public and health practitioners to ensure the best outcomes for HIV infected individuals (ASSAf, 2007; Kennedy and MacIntyre, 2003; Donald, 2000). The nutritional assessment of HIV infected patients' needs to be made a priority (Earthman, 2004; Nerad *et al*., 2003; Spencer *et al*., 2007; Kotler, 2000; Gerrior and Neff, 2005). Dietary intake, such as 24 hour recalls and food frequency questionnaires reflect both economic and lifestyle factors, (Mangili *et al*., 2006) and can provide dietary intake information about an individual's usual food intake, selection and eating pattern (Hammond, 2008, 395).

Currently "optimal" specific nutrient needs of HIV infected individuals are not clear (Coyne-Meyers and Trombley, 2004; Vorster *et al*., 2004), but health practitioners should apply dietary interventions which will optimize nutritional status (Vorster *et al*., 2004). Nutrition interventions should aim to be culturally sensitive and take into account local available resources (ASSAf, 2007).

Improved nutrition-related knowledge and practical solutions to enhance nutritional status in the HIV infected population is a key factor that should be implemented using well-described protocols in all health care systems (ASSAf, 2007)

6.3.2 Anthropometry

Excessive weight gain and the incidence of obesity and overweight are increasing in the HIV infected population, especially in those on HAART (Bhavan *et al*., 2008). Increased visceral and abdominal fat is associated with an increased risk for the development of glucose intolerance (Montessori *et al.*, 2004) and metabolic abnormalities (Marcason, 2008). Clinical nutrition assessments in HIV infected patients should include measurements such as

waist circumference measurements, weight, height and body mass index (Spencer *et al.,* 2007).

HIV infected patients do have higher risks for the development of chronic disease, therefore it is important that validated screening tools be used to assess nutritional risk (Nerad *et al*., 2003). Anthropometric measurements and screening should be carried out at all institutions that treat HIV-infected patients, even in the absence of a registered dietitian (Spencer *et al*., 2007).

6.3.3 Biochemical markers

It is clear from the available literature that there are increased risks for altered lipid profiles and metabolic changes in the HIV population, particularly those who receive HAART (Aberg, 2009). Routine screening for lipid abnormalities for patients on HAART should form part of standardized protocol at CCMT sites to improve the management of these lipid alterations. Lipograms can also be used along with waist circumference measurements, blood pressure and fasting glucose levels to screen for insulin resistance which is increased in this population. Non-drug interventions such as dietary and lifestyle modifications should be included in the management of dyslipidemia and additional focus should be placed on reducing cardiovascular disease risk (Alberti *et al*., 2006) though dietary changes, reduced total caloric intake, attaining ideal body weight and increased physical activity (Oh and Hegele, 2007).

6.3.4 Lifestyle factors

A small number of smokers with HIV seem to be good candidates for normal smoking cessation programmes and unique adapted strategies are necessary for this population (Duval *et al*., 2008). In addition to smoking, alcohol intake should be assessed in HIV infected patients and treated, as hazardous drinking can affect altered lipid profiles (Miguez-Burbano *et al*., 2009; Cook *et al*., 2009) and an increase risk of developing HIV-associated lipodystrophy (Cheng *et al*., 2009).

Excessive body weight increases risk for cardiovascular disease (Hill *et al*., 2005). Increasing physical activity can help to achieve weight loss (Lichtenstein *et al*., 2006; Wing and Phelan, 2005), thus improving insulin resistance and associated metabolic abnormalities. HIV infected patients who are physically active have improved life satisfaction, body compositions, emotional and physical well being (Ramirez-Marrero *et a*l., 2004). Practitioners should therefore encourage patients to increase their daily physical activity levels (Ramirez-Marrero *et a*l., 2004; Capili and Anastasi, 2008) in a culturally sensitive and relevant manner.

6.3.5 Recommendations for further research

According to the Academy of Science in South Africa (ASSAf, 2007) "Well-designed and informative clinical and epidemiological studies are urgently needed to generate and test hypotheses in relation to nutritional support for HIV-infected subjects".

Research to establish nutritional status in HIV-infected patients on HAART on a large scale is necessary in South Africa, and needs to be carried out at various CCMT sites nationwide.

Large studies to establish the incidence of insulin resistance and dyslipidemia in the South African HIV infected populations on HAART are vital. Large studies that include patients on different drug regimens are needed to identify the percentage of patients that are affected by dylipidemia, insulin resistance, and associated metabolic alterations in order to plan relevant interventions to address these problems.

Intervention studies are needed to establish the main causes for non adherence to HAART, so that protocols can be developed and efficacy measured to improve adherence to drug regimens. Improved compliance on regimen 1 is urgently

needed to optimise the effectiveness of the drugs as well as reduce the number of patients changing drug regimens to PI based therapies, since the health risks of being on the 2nd line regimen seem to be higher.

Nutrition intervention studies on HIV infected patients on HAART would be beneficial to establish the effects of dietary changes on disease progression and biochemical markers. Nutrition interventions that would warrant research studies would include interventions to increase the intake of fruits and vegetables and monounsaturated fats, as well as reduce the intake of refined carbohydrate and sugar (Hendricks *et al*., 2008; Krummel, 2008, 852; WHO, 2006). These dietary changes have been listed as areas of importance in current literature and can have an impact on nutritional status and possibly affect disease progression.

Appendix A

Nutritional Status of HIV infected adults on HAART

CONSENT TO PARTICIPATE IN RESEARCH

You have been asked to participate in a research study.

You have been informed about the study by ……..

You may contact Claire Julsing at 083 636 1010 at any time if you have questions about the research or if you are injured as a result of the research.

You may contact the Secretariat of the Ethics Committee of the Faculty of Health Sciences, UFS at the telephone number (051) 405 2812 if you have questions about your rights as a research subject.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to terminate participation.

If you agree to participate, you will be given a signed copy of this document as well as the participant information sheet, which is a written summary of the research.

The research study, including the information above has been verbally described to me. I understand what my involvement in the study means and I voluntarily agree to participate.

_____ _____

Signature of participant Date

Appendix B

Information Document

Study Title: Impact of antiretroviral therapy on the nutritional status of HIV / AIDS infected adults on HAART.

Thank you for being willing to help with this important research project. We are sure that this research project will contribute to improving the nutritional status of HIV / AIDS infected adults in South Africa.
The reason for doing this study is to be able to understand what happens to the nutritional status of HIV / AIDS infected adults when they start HAART.

Invitation to participate: We are asking/inviting you to participate in this research study and give us permission to use the results so that we can understand the impact of HAART on nutritional status in HIV / AIDS infected adults.

What is involved in the study: The aim of the research project is project is to gather information regarding the affects that HAART has on the nutritional status of HIV/ AIDS infected adults who are currently on the treatment plan. The Helen Joseph Clinic has been chosen as the site to gather this information.

For this study we will need HIV / AIDS infected adults who are currently on HAART. The study will be completed during March – May 2008. The study will be carried out during your routine visits to the clinic. You will be asked to complete a questionnaire.

All questions in the questionnaire will be filled out at Helen Joseph Clinic by a registered dietician. Respondents will be asked to complete the following questionnaires during an interview with a registered dietician;

- Dietary intake questionnaires,
- Lifestyle factors questionnaire,
- Physical activity level questionnaire.

We will also take measurements such as weight, height, hip circumference, waist circumference, and a body composition test. Body composition test are done using a bioelectrical impedance, this is non invasive. You are required to fast (not to eat or drink anything) four hours before the test. You can eat breakfast as per normal but do not eat or drink anything once you arrive at the clinic until your body composition test has been completed. Blood tests will be done to determine the following values: glucose, total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL), triglycerides, viral load and CD 4 count. These blood tests are measured routinely at Helen Joseph clinic.

The analysis of the blood tests and information from the questionnaire will help us to determine what the affect of HAART is on the nutritional status of HIV /

AIDS infected patients. Your information and blood results will not be released for other uses without consent, unless required by law.

Risks of being involved in the research study: Medical doctors or registered nurses will be responsible for safely drawing blood samples. In the unlikely event that an adverse event results from the procedure, you will be compensated for any expenses.

Benefits of being involved in the study: By participating in the research project you will help us to understand the affects that HAART has on the nutritional status of HIV / AIDS infected adults which will help with recommendations being made regarding nutrition and HIV / AIDS in the future. You will be given pertinent information on the research project after the results are released. If you are nutritionally at risk you will be referred for nutritional therapy with a registered dietician.

Participation is voluntary and refusal to participate will involve no penalty or loss of benefits to which you are entitled; you may discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law. Organizations that may inspect and /or copy your research records for quality assurance and data analysis include groups such as Ethics Committee for Medical Research. If results are published, this may lead to individual/cohort identification.

Kind regards,

CLAIRE JULSING
Contact details 083 636 1010 / 011 463 4663

Appendix C

Nutritional Status of HIV infected adults on HAART Dietary intake questionnaire 24-hour recall

Regimen: 1

Ouestionnaire number: 2-3

Gender: male (1) female (2) 4-5

Food and fluid intake:

Food/Drinks and amounts	**Milk and milk products**	**Meat and meat alternatives**	**Legumes**	**Fruit ß-carotene**	**Vegetables ß-carotene**	**Fruit Vit C**	**Vegetables Vit C**	**Fruit other**	**Vegetables other**	**Bread and cereals**	**Fats and oils**	**Sweets/Sugar**	**Alcohol**
Breakfast and mid-morning													
Lunch and mid afternoon													
Supper and late night													
Total:													

Evaluation of dietary intake

	Quantity	Energy (kJ)	Protein (g)	CHO (g)	Fat (g)	Below requirement 1	Within requirement 2	Above requirement 3	
Milk and milk products		530	8	12	*5				6
Meat and meat alternatives		315	7		5				7
Legumes		500	7	21	1				8
Soy beans		630	13	8	7				9
Fruit β-carotene		250		15					10
Vegetables β-carotene									11
Fruit vit C		250		15					12
Vegetables vit C									13
Fruit other		250		15					14
Vegetables B		150	2	7					15
Bread and cereal		285	3	15					16
Fats and oils		190			5				17
Sweets/Sugar		170		10					18
Alcohol									19
TOTAL									

* Values may vary depending on the type of milk consumed

(Earl, 2004)

Calculated estimated total values for:

Carbohydrate (g): _____ 20-22

Protein (g): _____ 23-25

Fat (g): _____ 26-28

Energy (kJ): _____ 29-33

Food frequency questionnaire

Number of times per day, per week or per month (only use one option)

Food	/day	/week	/month	
Sweets/ chocolates……..				34-39
Chips (crisp)……..				40-45
Cake/ biscuits……				46-51
Cool drinks……				52-57
Cremora……				58-63
Coffee……..				64-69
Tea……..				70-75
Sugar……..				1-6
Full-cream milk……..				7-12
Low fat/ skim milk……..				13-18
Eggs……				19-24
Peanut butter……				25-30
Soya mince/ legumes (baked beans, dried beans/peas, lentils)…..				31-36
Chicken……..				37-42
Red meat……				43-48
Fish……..				49-54
Bread……..				55-60
Porridge, cooked……..				61-66
Cereal (eg. Morevite/ Pronutro)……..				67-72
Samp/ mielie rice……..				73-78

Margarine/ oil/ fat……..								1-6
Fruit juice……								7-12
Fruit……								13-18
Vegetables……								19-24
Salt/ stock/ Royco……								25-30
Alcohol _____.....								31-36

Appendix D

Approval Letter from Helen Joseph

HEAD / RESEARCH COORDINATOR OF DEPARTMENT / ENTITY IN WHICH STUDY WILL BE CONDUCTED (where applicable)

Name: PROF A. P. MACPHAIL

Signature:

Professor A.P. MacPhail PhD, FCP, FRCP
Department of Medicine
University of the Witwatersrand

Date: 07/03/2008

Entity: CLINICAL HIV RESEARCH UNIT, THEMBA LETHU CLINIC

Tel No: 011 276-8905.

Fax No: 011 276-8885

C:\Documents and Settings\Claire.ATAA\Local Settings\Temporary Internet Files\OLK82\041 Ethics Application - Other Stu 2007.doc

Appendix E

Nutritional Status of HIV infected adults on HAART

LIFESTYLE FACTORS QUESTIONNAIRE
ANTHROPOMETRIC MESAUREMENTS AND BIOCHEMICAL PARAMETERS

(All information in this questionnaire is confidential).

Questionnaire 1-2

Gender: male (1) 3

Age : _____ 4-5

Interview Date: 6-13

LIFESTYLE FACTORS

Which best describes your history of smoking? 14

1. Never smoked
2. Currently smoke
3. Formerly smoked

Which best describes your history of alcohol use? 15

1. Never used alcohol products
2. Currently use alcohol products
3. Formerly used alcohol products

Have YOU ever been diagnosed with the following? 1=yes 2=no

1. Diabetes			16
2. High blood pressure			17
3. Stroke			18
4. Heart disease/ Angina/ Heart attack			19
5. Cancer			20
6. Liver disease/ Hepatitis/ Jaundice			21
7. Lung disease e.g. emphysema or asthma			22
8. Tuberculosis			23

Has a family member (parents, siblings, children) ever been diagnosed with the following?

	1=yes	2=no	
1. Diabetes			24
2. High blood pressure			25
3. Stroke			26
4. Heart disease/ Angina/ Heart attack			27
5. Cancer			28
6. Liver disease/ Hepatitis/ Jaundice			29
7. Lung disease e.g. emphysema or asthma			30
8. Tuberculosis			31
9. HIV / AIDS			32

HAART Medication

List the medication or supplements that you are currently using (including traditional medicine).

_____ 33-34

_____ 35-36

ANTHROPOMETRIC MEASUREMENTS AND BIOCHEMICAL MARKERS

1. Weight (kg)	_____	49-53
2. Height (cm)	_____	54-58
3. Waist circumference (cm)	_____	59-63
4. Hip circumference(cm)	_____	64-68
5. Fat percentage	_____	70-73
6. Fasting glucose concentrations (mmol/L)	_____	74-77
7. Total cholesterol (mmol/L)	_____	1-4
8. LDL cholesterol (mmol/L)	_____	5-8
9. HDL cholesterol (mmol/L)	_____	9-12
10. Triglyceride level (mmol/L)	_____	13-16
11. CD 4 count (mm^3)	_____	17-20
12. Viral load	_____	21-24

13. Blood pressure	_____ systolic	25-27
	_____diastolic	28-30

REFERENCES

Academy of Science in South Africa (ASSAf). 2007. Scientific inquiry into the nutritional influences on human immunity with special reference to HIV infection and active TB in South Africa.

Aghdassi, E., Arendt, B., Salit, I.E. and Allard, J.P. 2007. Estimation of body fat mass using dual energy x-ray absorptiometry, bioelectrical impedance analysis and anthropometry in HIV- positive male subjects receiving highly active antiretroviral therapy. Journal of Parenteral and Enteral Nutrition, vol. 31, no. 2, pp. 135-141.

Alberti, K.G.M.M., Zimmet, P. and Shaw, J. 2006. Metabolic syndrome - a new world-wide definition. A consensus from the International Diabetes Federation. Diabetic Medicine, vol. 23, pp. 469-480.

Almedia, S.E., Borges, M., Fiegenbaum, M., Nunes, C.C. and Rossetti, M.L. 2009. Metabolic changes associated with antiretroviral therapy in HIV-positive patients. Rev Saude Publica, vol. 43, no. 2, pp. 283-290.

Anabwani, G. and Navario, P. 2005. Nutrition and HIV / AIDS in sub-Saharan Africa: an overview. Journal of Nutrition, vol. 21, pp. 96-99.

Andrade, S., Lan, S.J.J., Engelson, E.S., Agin, D., Wang, J., Heymsfield, S.B., and Kotler, D.P. 2002. Use of a Durin-Womersley formula to estimate change in subcutaneous fat content in HIV infected subjects. The American Journal of Clinical Nutrition, vol. 75, no. 3, pp. 587-592.

Appel, L.J., Brands, M.W., Daniels, S.R., Karanha, N., Elmer, P.J. and Sacks, F.M. 2006. Dietary approaches to prevent and treat hypertension: A scientific statement from the American Heart Association. Hypertension, Journal of the American Heart Association, vol. 47, pp. 296-308.

Arendt, B. M., Aghdassi, E., Mohammed, S.S., Fung, L.Y., Jalali, P., Salit, I, E. and Allard, J. P. 2008. Dietary intake and physical activity in a Canadian population sample of male patients with HIV infection and metabolic abnormalities. Current HIV Research, vol. 6, pp. 82-90.

Baekken, M., Os, I., Sandvik, L. and Oektedalen, O. 2008. Hypertension in an urban HIV-positive population compared with the general population: Influence of combination antiretroviral therapy. Journal of Hypertension, vol. 26, no. 11, pp. 2126-2133.

Batterham, M.J., Garcia, R. and Greenop, R. 1999. Measurement of body composition in people with HIV / AIDS: A comparison of bioelectrical impedance and skin fold anthropometry with dual-energy x-ray absorptiometry. Journal of the American Dietetic Association, vol. 99, no. 9, pp. 1109-1111.

Batterham, M.J., Morgan-Jones, J., Greenop, P., Garsia, R., Gold, J. and Caterson, I. 2003. Calculating energy requirements for men with HIV / AIDS in the era of highly active antiretroviral therapy. European Journal of Clinical Nutrition, vol. 57, no. 2, pp. 209-217.

Barasi, M.E. 2003. Human Nutrition: A Health Perspective. 2nd Edition. London: Oxford University Press inc. pp. 12.

Barth, R.E., van der Meer, J.T., Hoepelman, A.T., Schrooders, P.A., van de Vijver, D.A., Geelen, S.P. and Tempelman, H.A. 2008. Effectiveness of highly active antiretroviral therapy administered by general practitioners in rural South Africa. European Journal of Clinical Microbiological Infectious Disease, vol. 27, no. 10, pp. 977-984.

Bazoes, A., Bower, M. and Powles, T. 2008. Smoke and mirrors: HIV-related lung cancer. Current Opinion Oncology, vol. 20, no. 5, pp. 529-533.

Bhavan, K.P., Kampalath, V.N. and Overton, E.T. 2008. The ageing of the HIV epidemic. Current HIV / AIDS Reports, vol. 5, pp. 150-158.

Blass, S.C., Ellinger, S., Vogel, M., Ingiliz, P., Spengler, U., Stehle, P., von Ruecker, A. and Rockstroh, J.K. 2008. Overweight HIV patients with abdominal fat distribution treated with protease inhibitors are at high risk for abnormalities in glucose metabolism – a reason for glycemic control. European Journal of Medical Research, vol. 13, no. 5, pp. 209-214.

Bogden, J.D., Kemp, F.W., Han, S., Li, W., Bruening, K., Denny, T., Oleske, J.M., Lloyd, J., Baker, H., Perez, g., Kloser, P., Skurnick, J. and Louria, D.B. 2000. Status of selected nutrients ans progression of human immunodeficiency virus type 1 infection. American Journal of Clinical Nutrition, vol. 72, pp. 809-815.

Brown, T.T. 2008. Approach to the human immunodeficiency virus-infected patient with lipodystrophy. The Journal of Clinical Endocrinology and Metabolism, vol. 93, no. 8, pp. 2937-2945.

Callaway, C.W., Chumela, W.C., Bouchard, C., Himes, J.H., Lohaman, T.G., Martin, A.D., Mitchell, C.D. Mueller, W.H., Roche, A.F. and Seefeldt, V.D. 1991. Circumference. In Anthropometric Standardization Reference Manual. Edited by Lohman, T.G., Roche, A.F. and Martorell, R. A division of Human Kinetics publishers, Inc. pp. 39-54.

Carpenter, C.C.J., Carpenter, C.C., Cooper, D.A., Fischl, M.A., Gatell, J.M., Gazzard, B.G., Hammer, S.M., Hirsch, M.S., Jacobsen, D.M., Katzenstein, D.A., Montaner, J.S., Richman, D.D., Saag, M.S., Schechter, M., Schooley, R.T., Thompson, M.A., Vella, S., Yeni, P.G. and Volberding, P.A. 2000. Antiretroviral therapy in adults: updated recommendations of the international AIDS society – USA Panel. Journal of the American Medical Association, vol. 283, no. 3 pp. 381 -390.

Centers for Disease Control and Prevention: 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults, MMWR 41:17, 1992, from www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm.

Chander, G., Josephs, J., Fleishman, J.A., Korthuis, P.T., Gaist, P., Hellinger, J., Gebo, K. and the HIV Research Network. 2008. Alcohol use among HIV-infected persons in care: results of a multisite survey. HIV Medicine, vol. 9, no. 4, pp. 196-202.

Cheng, D.M., Libman, H., Bridden, C., Saitz, R. and Samet, J.H. 2009. Alcohol consumption and lipodystrophy in HIV infected adults with alcohol problems. Alcohol, vol. 43, no. 1, pp. 65-71.

Colecraft, E. 2008. HIV / AIDS: Nutritional implications and impact on human development. Proceedings of the Nutrition Society, vol. 67, pp. 109-113.

Cook, R.L., Zhu, F., Belnap, B.H., Weber, K., Cook, J.A., Vlahov, D., Wilson, T.E., Hessol, N.A., Plankey, M., Howard, A.A., Cole, S.R., Sharp, G.B., Ricardson, J.L. and Cohen, M.H. 2009. Longitudinal trends in hazardous alcohol consumption among women with human immunodeficiency virus infection, 1995-2006. American Journal of Epidemioloy, vol. 169, no. 8, pp. 1025-1032.

Coyne-Meyers, K. and Trombley, L.E. 2004. A review of nutrition in human immunodeficiency virus infection in the era of highly active antiretroviral therapy. Nutrition Clinical Practice, vol. 19, no. 4, pp. 340-355.

Crane, H.M., Van Rompaey, S.E. and Kitahata, M.M. 2006. Antiretroviral medications associated with elevated blood pressure among patients receiving highly active antiretroviral therapy. AIDS, vol. 20, no. 7, pp. 1019-1026.

Cunningham-Rundles, S., McNeeley, D.F. and Moon, A. 2005. Mechanisms of nutrient modulation of the immune response. Journal of Allergy Clinical Immunology., vol. 115, no. 6, pp. 1235-1237.

Data collection on adverse events of anti-HIV drugs (DAD) study group. 2007. Class of antiretroviral drugs and the risk of myocardial infarction. The New England Journal of Medicine, vol. 356, no. 17, pp.1723 – 1735.

Dolan, S.E., Frontera, W., Librizzi, J., Ljungquist, K., Juan, S., Dorman, R., Cole, M.E., Kanter, J.R. and Grinspoon, S. 2006. Effects of a supervised home-based aerobic and progressive resistance training regimen in woman infected with human immunodeficiency virus: a randomized trial. Archives of Internal Medicine, vol. 166, no. 11, pp. 1225 -1231.

Domingo, P., Sambeat, M.A., Pérez, A., Ordoñez, J., Rodriguez, J. and Vázquez, G. 2003. Fat distribution and metabolic abnormalities in HIV-infected patients on first combination antiretroviral therapy including stavudine or zidovudine: role of physical activity as a protective factor. Anthropometric Standardization Reference Manual, vol. 8, no. 3, pp. 223-231.

Donald, K. 2001. Nutritional alterations associated with HIV infection. Journal of Acquired Immune Deficiency Syndromes, vol. 25, no. 1, pp. S81-S87.

Drain, P.K., Kupka, R., Mugusi, F. and Fawzi, W.W. 2007. Micronutrients in HIV-positive persons receiving highly active antiretroviral therapy. The American Journal of Clinical Nutrition, vol. 85, pp. 333-345.

Dreyfuss, M.L. and Fawzi, W.W. 2002. Micronutrients and vertical transmission of HIV-1. The American Journal of Clinical Nutrition, vol. 75, no.6, pp.959-970.

Duran, A.C.F.L., Almeida, L.B., Segurado, A.A.C. and Jaime, P.C. 2008. Diet quality of persons living with HIV/AIDS on highly active antiretroviral therapy. Journal of Human Nutrition and Dietetics, vol. 21, no. 4, pp.346-350.

Duval, X., Baron, G., Garelik, D., Villes, V., Dupré, T., Leport, C., Lert, F., Peretti-Watel, P., Ravaud, P. and Spire, B. 2008. Living with HIV, antiretroviral treatment experience and tobacco smoking: results from a multisite cross-sectional study. Antiretroviral Therapy, vol. 13, no. 3, pp. 389-397.

Earl, R. 2004. Guidelines for dietary planning, In Krause's Food, Nutrition and Diet Therapy. Ed. by Mahan, L.K. and Escott-Stump, S. 11th edition. Philadelphia, Pennsylvania: W.B Saunders Company, pp. 376.

Earthman, C.P. 2004. Evaluation of nutrition assessment parameters in the presence of human immunodeficiency virus infection. Journal of Nutrition Clinical Practice, vol. 19, no. 4, pp. 330-339.

Engelson, E.S., Agin, D., Kenya, S., Werber-Zoin, G., Luty, B., Albu, J.B. and Kolter, D.P. 2006. Body composition and metabolic effects of a diet and exercise weight loss regimen on obese, HIV-infected women. Metabolism Clinical and Experimental, vol. 55, pp. 1327-1336.

Faintuch, J., Soeters, P.B., and Osmo, H.G. 2006. Nutritional and metabolic abnormalities in pre-AIDS HIV infection. Nutrition, vol. 22, no. 3, pp.683-690.

Fawzi, W., Msamanga, G., Spriegman, D., and Hunter, D.J. 2005. Studies of vitamins and minerals and HIV transmission and disease progression. The Journal of Nutrition, vol. 135, no. 4, pp. 938-944.

Fee, E. and Brown, T.M. 2006. Michael S Gottlieb and the identification of AIDS. American Journal of Public Health, vol. 96, no. 6, pp. 982.

Feldman, J.G., Minkoff, H., Schneider, M.F., Grange, S.J., Cohen, M., Watts, H., Gandhi, M., Mocharnuk, R.S. and Anastos, K. 2006. Association of cigarette smoking with HIV prognosis among woman in the HAART era: A report from the women's interagency HIV study. American Journal of Public Health, vol. 96, no. 6, pp. 1060-1065.

Fenton, M. and Silverman, E. C. 2008. Medical nutrition therapy for human immunodeficiency virus disease, In Krause's Food and Nutrition Therapy. Ed. by Mahan, L.K. and Escott-Stump, S. 12th edition. Philadelphia, Pennsylvania: W.B Saunders Company, pp. 991-1020.

Fields-Gardener, C., Ferquesson, P., American Dietetic Association and Dietitians of Canada. 2004. Position of the American Dietetic Association and Dietitians of Canada: Nutrition intervention in the care of persons with human immunodeficiency virus infection. Journal of the American Dietetic Association, vol. 104, no. 9, pp. 1425-1441.

Fisher, K. 2001. Wasting and lipodystrophy in patients infected with HIV: a practical approach in clinical practice. The AIDS Reader, vol. 11, no. 3, pp. 132-147

Florindo, A.A., de Oliveira Latorre Mdo, R., Jamie, P.C. and Segurado, A.A. 2007. Leisure time physical activity prevents accumulation of central fat in HIIV/AIDS subjects on highly active antiretroviral therapy. International Journal of STD & AIDS, vol. 18, no. 10, pp. 692-696.

Fomundan, H., Mathews, C. and Malangu N. 2006. ARV regimens, In Prevention and management of side effects and drug interactions (ART). First edition, South Africa: Jacana Media, pp.2.

Forrester, J.E., Sheehan, H.M. and Joffe, T.H. 2008. A validation study of body composition by bioelectrical impedance analysis in human immunodeficiency virus (HIV) positive and HIV negative Hispanic men and women. Journal of the American Dietetic Association, vol. 108, no. 3, pp. 534-538.

Frary, C.D. and Jonson, R.K. 2004. Energy, In Krause's Food, Nutrition and Diet Therapy. Ed. by Mahan, L.K. and Escott-Stump, S. 11th edition. Philadelphia, Pennsylvania: W.B Saunders Company, pp. 21-38.

Gee, M. 2008. Weight management, In Krause's Food and Nutrition Therapy. Ed. by Mahan, L.K. and Escott-Stump, S. 12th edition. Philadelphia, Pennsylvania: W.B Saunders Company, pp. 532-562.

Gerrior, J.L. and Neff, L.M. 2005. Nutrition assessment in HIV infection. Nutrition in Clinical Care, vol. 8, no. 1, pp. 6-15.

Grinspoon, M.D. 2005. Metabolic syndrome and cardiovascular disease in patients with human immunodeficiency virus. The American Journal of Medicine, vol. 118, no. 2, pp. 23S-28S.

Grover, S.A., Coupal, L., Gilmore, N. and Mukherjee, J. 2005. Impact of dyslipidemia associated with highly active antiretroviral therapy on cardiovascular risk and life expectancy. The American Journal of Cardiology, vol. 95, no. 3, pp. 586-591.

Grundy, S.M., Becker, D., Clark, L.T., Cooper, R.S., Denke, M.A., Howard, J., Hunninghake, D.B., Illingworth, R., Luepker, R.V., McBride, P., McKenney, J.M., Pasternak, R.C., Stone, N.J. and Van Horn, L. 2001. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on the detection, evaluation and treatment of high blood cholesterol in adults (adult treatment panel III). Journal of the American Medical Association, vol. 285, no. 19, pp. 2486- 2497.

Hadigan, C., Jeste, S., Anderson, E.J., Tsay, R., Cyr, H and Grinspoon, S. 2001. Modifiable dietary habits and their relation to metabolic abnormalities in men and women with human immunodeficiency virus infection and fat redistribution. HIV/AIDS, vol. 33, pp. 710-717.

Haffner, S.M. and Miettinen, H. 1997. Insulin resistance implications for type II diabetes mellitus and coronary heart disease. American Journal of Medicine, vol. 103, pp. 152-162.

Hammer, S.M., Eron, J.J., Reiss, P., Schooley, R.T., Thompson, M.A., Walmsley, S., Cahn, P., Fischl, M. A., Gatell, J.M., Hirsch, M.S., Jacobson,

D.M., Montaner, J.S.G., Richman, D.D., Yeni, P.G. and Volberding, M.D. 2008. Antiretroviral treatment of adult HIV infection 2008 recommendations of the International AIDS society – USA panel. The Journal of the American Medical Association, vol. 300, no. 5, pp. 555-570.

Hammond, K. 2008. Assessment: Dietary and clinical data, In Krause's Food and Nutrition Therapy. Ed. by Mahan, L.K. and Escott-Stump, S. 12th edition. Philadelphia, Pennsylvania: W.B. Saunders Company, pp. 395.

Hattingh, Z., Walsh, C., Veldman, F.J. and Bester, C.J. 2009. The metabolic profiles of HIV-infected and non-infected women in Mangaung, South Africa. The South African Journal o Clinical Nutrition, vol. 22, no. 1, pp. 23-28.

Hendricks, K.M., Mwamburi, D.M., Newby, P.K. and Wanke, C.A. 2008. Dietary patterns and health and nutrition outcomes in men living with HIV infection. The American Journal of Clinical Nutrition, vol. 88, no. 6, pp. 1584-1592.

Hill, D.J., White, V.M. and Scollo, M.M. 1998. Smoking habits of Australian adults in 1995: trends and concerns. The Medical Journal of Australia, vol. 168, pp. 209-213.

Hill, J.O., Thompson, H. and Wyatt, H. 2005. Weight maintenance: what's missing? Journal of the American Dietetics Association, vol. 105, no. S1, pp. S63-S66.

Hubley, J. 2002. The AIDS handbook. 3rd edition. Malaysia: Macmillan Publishers Limited, pp. 2-37.

Hung, H., Joshipura, K.J., Jiang, R., Hu, F.B., Hunter, D., Smith-Warner, S.A., Colditz, G.A., Rosner, B., Spiegelman, D. and Willett, W.C. 2004. Fruit and vegetable intake and risk of major chronic disease. Journal of National Cancer Institute, vol. 96, no. 21, pp. 1577-1584.

Irlam, J.J.H., Visser, M.M.E., Rollins, N.N. and Siegfried, N. 2005. Micronutrient supplementation in children and adults with HIV infection. Cochrane Database of Systematic Reviews, vol. 19, no. 4, pp. 1-14.

Jacobson, D.L., Tang, A.M., Spiegelman, D., Thomas, A.M., Skinner, S., Gorbach, S.L. and Wanke, C. 2006. Incidence of metabolic syndromes in a cohort of HIV-infected adults and prevalence relative to the US population (National Health and Nutrition Examination Survey). Journal of Acquired Immune Deficiency Syndrome, vol. 43, no. 4, pp. 458-466.

Jain, R.G., Furfine, E.S., Pedneault, L., White, A.J. and Lenhard, J.M. 2001. Metabolic complications associated with antiretroviral therapy. Antiviral Research, vol. 51, no. 3, pp. 151-177.

Johnson, J.L., Slentz, C.A., Houmard, J.A., Samsa, G.P., Duscha, B.D., Aiken, L.B., McCartney, J.S., Tanner, C.J. and Kraus, W.E. 2007. Exercise training amount and intensity effects on metabolic syndrome (from studies of a targeted risk reduction intervention through defined exercise). American Journal of Cardiology, vol. 100, no. 12, pp. 1759-1766.

Justman, J.E., Hoover, D.R., Shi, Q., Tan, T., Anastos, K., Tien, P.C., Cole, S.R., Hyman, C., Karim, R., Weber, K. and Grinspoon, S. 2008. Longitudinal anthropometric patterns among HIV-infected and HIV-uninfected women. Journal of Acquired Immune Deficiency Syndrome, vol. 47, no. , pp. 312-319.

Kaplan, R.C., Kingsley, L.A., Sharrett, A.R., Li, X., Lazar, J., Tien, P.C., Mack, W.J., Cohen, M.H., Jacobson, L. and Gange, S.J. 2007. Ten-year predicted coronary heart disease risk in HIV-infected men and women. Clinical Infectious Disease, vol. 45, no. 8, pp. 1074-1081.

Kennedy, R.D., and MacIntyre, U.E. 2003. Development and testing of the South African National Nutrition Guidelines for people living with HIV/AIDS. South African Journal of Clinical Nutrition, vol. 16, no. 1, pp. 12-16.

Kim, J. H., Spiegelman, D., Rimm, E. and Gorbach, S. L. 2001. The correlates of dietary intake among HIV-positive adults. The American Journal of Clinical Nutrition, vol. 74, no. 6, pp. 852-861.

Kosmiski, L.A., Kuritzkes, D.R., Lichtenstein, K.A., Glueck, D.H., Gourley, P.J., Stamm, E.R., Scherzinger, A.L. and Eckel, R.H. 2001. Fat distribution and metabolic changes are strongly correlated and energy expenditure is increased in the HIV lipodystropy syndrome. AIDS, vol. 19, no. 15, pp.2037-2041.

Kotler, D.P., Burastero, S., Wang, J. and Pierson, R.N. 1996. Prediction of body cell mass, fat-free mass and total body water with bioelectrical impedance analysis: effects of race, sex and disease. American Journal of Clinical Nutrition, vol. 64, no. 3 supplement, pp. 489S-497S.

Kotler, D.P. 2000. Nutritional alterations associated with HIV infection. Journal of Acquired Immune Deficiency Syndromes, vol. 25, pp. S81-S87.

Krummel, D.A. 2008. Medical nutrition therapy for cardiovascular disease, In Krause's Food and Nutrition Therapy. Ed. by Mahan, L.K. and Escott-Stump, S. 12th edition. Philadelphia, Pennsylvania: W.B Saunders Company, pp. 883-864.

Kurtizkes, D.R., Boyle, B.A., Gallant, J.E., Squires, K.E. and Zolopa, A. 2003. Current management challenges in HIV: Antiretroviral resistance. The AIDS Reader, vol. 13, no. 3, pp. 133.

Lakka, T.A. and Laaksonen, D.E. 2007. Physical activity in prevention and treatment of the metabolic syndrome. Applied Physiology, Nutrition and Metabolism, vol. 32, no. 1, pp. 76-88.

Langenhoven M and Wolmarans P. 1997, Assessment of dietary intake, In Epidemiology: a manual for South Africa. Ed by Katzenellenbogen JM, Joubert G, Abdool K. Cape Town:Oxford University press, p. 250.

Laquatra, I. 2004. Nutrition for Weight Management, In Krause's Food, Nutrition and Diet Therapy. Ed. by Mahan, L.K. and Escott-Stump, S. 11th edition. Philadelphia, Pennsylvania: W.B Saunders company, pp. 558- 593.

Lee, R.D and Nieman, D.C. 2003. Nutritional Assessment. Third Edition, Mc Graw Hill Company: New York.

Levy, J.A. 2009. Not an HIV cure, but encouraging new directions. The New England Journal of Medicine, vol. 360, no. 7, pp. 724-725.

Lichtenstein, A.H., Appel, L.J., Brands, M., Carnethon, M., Daniels, S., Franch, H.A., Franklin, B., Kris-Etherton, P., Harris, W.S., Howard, B., Karanja, N., Lefevre, M., Rudel, L., Sacks, F., Van Horn, L., Winston, M. and Wylie-Rosett, J. 2006. Diet and lifestyle recommendations revision 2006, a scienfictic statement from the American Heart Association Nutrition Committee. Circulation, vol. 114, pp. 82-95.

Lindegaard, B., Hansen, T., Hvid, T., van Hall, G., Plomgaard, P., Ditlevsen, S., Gerstoft, J. and Pedersen, B.K. 2008. The effect of strength and endurance training on insulin sensitivity and fat distribution in human immunodeficiency virus-infected patients with lipodystropy. Journal of Clinical Endocrinology and Metabolism, vol. 93, no. 10, pp. 3860-3869.

Long, M.C., King, J.R. and Acosta, E.P. 2009. Pharmacologic aspects of new antiretroviral drugs. Current HIV/AIDS Reports, vol. 6, pp. 43-50.

Macallan, D.C. 1999. Wasting in HIV infection and AIDS. The Journal of Nutrition, vol. 129, no. 1, pp. 238S-242S.

Maia, B.S., Engelson, E.S., Wang, J. and Kotler, D.P. 2005. Antiretroviral therapy affects the composition of weight loss in HIV infection: Implications for clinical nutrition. Clinical Nutrition, vol. 24, no. 6, pp. 971-978.

Mangili, A., Murman, D.H., Zampini, A.M. and Wanke, C.A. 2006. Nutrition and HIV infection: Review of weight loss and wasting in the era of highly active antiretroviral therapy from the nutrition for healthy living cohort. Clinical Infectious Diseases, vol. 42, pp. 836-842.

Malvy, D., Thiébaut, R., Marimoutou, C. and Dabis, F. 2001. Weight loss and body mass index as predictors of HIV disease progression to AIDS in adults. Journal of the American College of Nutrition, vol. 20, no. 6, pp. 609-615.

Marcason, W. 2009. What does the term “HIV-associated lipodystrophy” mean? Journal of the American Dietetic Association, vol. 109, no. 2, pp. 364.

Martinez, E., Mocroft, A., Garcia-Viejo., M.A., Pérez-Cuevas, J.B., Blanco, J.L., Mallolas, J., Bianchi, L., Conget, I., Blanch, J., Phillips, A. and Gatell, J.M. 2001. Risk of lipodystrophy in HIV-1 infected patients treated with protease inhibitors: a prospective cohort study. Lancet, vol. 24, no. 357, pp. 592-598.

McDermott, A.Y., Shevitz, A., Must, A., Harris, S., Roubennoff, R. and Gorbach, S. 2003. Nutrition treatment for HIV wasting: a prescription for food as medicine. Nutrition Clinical Practice, vol. 18, no. 1, pp. 86-94.

McDermott. A.Y., Terrin, N., Wanke, C., Skinner, S., Tchetgen, E. and Shevitz, A.H. 2005. CD4+ cell count, viral load and highly active antiretroviral therapy use are independent predictors of body composition alterations in HIV-infected adults: A longitudinal study. Clinical Infectious Diseases, vol. 41, pp. 1662-1670.

Mechanick, J.I. and AACE Nutrition Guidelines Task Force. 2003. American association of clinical endocrinologists medical guidelines for the clinical use of dietary supplements and nutraceuticals. Endocrine Practice, vol. 9, no. 5, pp. 417-470.

Merson, M.H. 2006. The HIV/AIDS pandemic at the 25-the global response. The New England Journal of Medicine, vol. 354, no. 23, pp. 2414-2417.

Miguez-Burbano, M.J., Lewis, J.E. and Malow, R. 2009. Alcohol and race/ethnicity elicit different changes in lipid profiles in HIV-infected individuals receiving highly active antiretroviral therapy. Journal of the Association of Nurses in AIDS Care, vol. 20, no. 3, pp. 176-183.

Monsen, E.R. 1992. Research. 1st edition. Chicago: The American Dietetic Association.

Montessori, V., Press. N., Harris, M., Akagi L. and Montaner J.S.G. 2004. Adverse effects of antiretroviral therapy for HIV infection. Canadian Medical Association Journal, vol. 170, no. 2, pp. 229-238.

Morris, L. and Cilliers, T. 2008. Viral structure, replication tropism, pathogenesis and natural history, In HIV / AIDS in South Africa. Ed. by Abdool Karim, S.S. and Abdool Karim, Q. 2nd edition. South Africa: Cambridge University Press, pp. 1405-1407.

Murdoch, D.M., Napravnik, S., Eron, J.J. and Van Rie, A. 2008. Smoking and predictors of pneumonia among HIV-infected patients receiving care in the HAART era. The Open Respiratory Medicine Journal, vol. 2, pp. 22-28.

Nerad, J., Romeyn, M., Silverman, E., Allen-Reid, J., Dieterich, D., Merchant, J., Pelletier, V.A., Tinnerello, D. And Fenton, M. 2003. General nutrition management in patients infected with human immunodeficiency virus. Clinical Infectious Diseases, vol. 36, pp. S52-S62.

Nutrition Information Centre of the University of Stellenbosch (NICUS). 2009. Alternative nutritional remedies for people living with HIV / AIDS. [Internet] Available from: http://sun025.sun.ac.za [Accessed on 17 January 2009].

Oguntibeju, O.O., van den Heever, W. M. J. and Van Schalkwyk, F.E. 2007. The interrelationship between nutrition and the immune system in HIV infection: A review. Pakistan Journal of Biological Sciences, vol. 10, no. 24, pp. 4327-4338.

Oh, J. and Hegele, R.A. 2007. HIV-associated Dyslipidemia: pathogenesis and treatment. Lancet Infectious Disease, vol. 7, pp. 787-796.

Perloff, D., Grim, C., Flack, J., Frohlich, E.D., Hill, M., Mc Donald, M. and Morgenstern. 1993. Human blood pressure determination by sphygmomanometry. Circulation, vol. 88, pp. 2464-2465.

Piscitelli, S.C., Burstein, A.H., Welden, N., Gallicano, K.D. and Falloon, J. 2001. The effect of garlic supplements on the pharmacokinetics of saquinavir. Journal of Clinical Infectious Disease, vol. 35, no. 3, pp. 343.

Pratt, R.J. 2003. The evolution of a pandemic, In HIV &AIDS, A foundation for nursing and healthcare practice. 5th Edition. Malta, BookPower, pp. 1-21.

Ramirez-Marrero, F.A., Smith, B.A., Meléndez-Brau, N. and Santana-Bagur, J.L. 2004. Physical and leisure activity, body composition, and life satisfaction in HIV-positive Hispanics in Puerto Rico. Journal of the Association of Nurses in AIDS Care, vol. 15, no. 4, pp. 68-77.

Rosenberg, E.S. and Walker, B.D. 1998. HIV 1-specific helper t cells: A critical host defence. AIDS Research Human Retrovirus, vol. 14, pp. S143-S147.

Russo, A.L., Maconi, G.J., Spinelli, P.J., Feloce, D.I., Eboli, M.J., Ferrari, D.J., Lombardo, C. and Beratario, L. 2001. Effect of lifestyle, smoking and diet on development of intestinal metaplasia in H.pylori positive subjects. The American Journal of Gastroenterology, vol. 96, no. 5, pp. 1402-1408.

Sadovsky, R., Collins, N., Tighe, A.P., Safeer, R.S., Morris, C.M. and Brunton, S.A. 2008. Dispelling the myths about omega-3 fatty acids. Postgraduate Medicine, vol. 120, no. 2, pp. 92-100.

Salomon, J., De, T.P. and Melchior, J.C. 2002. Nutrition and HIV infection. British Journal of Nutrition, vol. 87, pp. S111-S119.

Samet, J.H., Horton, N.J., Meli, S., Freedberg, K.A. and Palepu, A. 2004. Alcohol consumption and antiretroviral adherence among HIV-infected persons with alcohol problems. Alcoholism: Clinical and Experimental Research, vol. 28, pp. 572-577.

Schambelan, M., Benson, C.A., Carr A., Currier, J.S., Dube, M.P., Gerber, J.G., Grinspoon, S.K., Grunfeld, C., Kotler, D.P., Mulligan, K., Powderly, W.G., Saay, M.S., International AIDS- Society USA. 2002. Management of metabolic complications associated with antiretroviral therapy for HIV- 1 infection: recommendations of an International AIDS Society – USA panel. Journal of Acquired Immune Deficiency Syndrome, vol. 131, no. 3, pp. 257-275.

Schreibman, T. and Friedland, G. 2003. Human immunodeficiency virus infection prevention: strategies for clinicians. Clinical Infectious Diseases, vol. 36, no. 9, pp. 1171-1176.

Schwenk, A., Beisenherz, A., Kremer, G., Diehl, V., Salzberger, B. and Fätkenheuer. 1999. Bioelectrical impedance analysis in HIV-infected patients treated with triple antiretroviral treatment. American Journal of Clinical Nutrition, vol. 70, no. 5, pp. 867-873.

Schwenk, A., Breuer, J.P., Kremer, G., Römer, K., Bethe, U., Franzen, C., Fätkenheuer, G. and Salzberger, B. 2000. Risk factors for the HIV-associated lipodystrophy syndrome in a cross-sectional single-centre study. European Journal of Medical Research, vol. 5, no. 10, pp. 443-448.

Semba, R.D. 2006. Nutrition and infection, In Modern nutrition in health and disease. Ed. by Shils, M.E. and Shike, M. 10th edition. Philadelphia, Baltimore: Lippincott Williams & Wilkins, pp. 1405-1407.

Shah, M., Tierney, K., Adams-Huet, B., Boonyavarakul, A., Jacob, K., Quittner, C., Dinges, W., Peterson, D. and Garg, A. 2005. The role of diet, exercise and smoking in dyslipidaemia in HIV-infected patients with lipodystrophy. HIV Medicine, no. 6, pp. 291-298.

Shevitz, A.H., Wilson, I.B., McDermott, A.Y., Spiegelman, D., Skinner, S.C., Antonsson, K., Layne, J.E., Beaston-Blaakman, A., Shepard, D.S. and Gorbach, S.L. 2005. A comparison of the clinical and cost-effectiveness of 3 intervention strategies for AIDS wasting. Journal of AIDS, vol. 38, no. 4, pp. 399-406.

Shuter, J. and Bernstein, S.L. 2008. Cigarette smoking is an independent predictor of non adherence in HIV-infected individuals receiving highly active antiretroviral therapy. Nicotine & Tobacco Research, vol. 10, no. 4, pp. 731-736.

Skipper, A. 2008. Nutrition Care Manual. American Dietetic Association Nutrition Care Manual Website. Chicago, www.nutritioncaremanual.org.

Spencer, D.C. 2005. The clinical practice of HIV medicine, a practical guide to the care of the HIV infected. 1st edition. Johannesburg, South Africa: Goldstream Books, pp. 4-11.

Spencer, D.C., Harman, C., Naicker., Gorhe, S., Rollins, N., Labadarious, D. Visser, M. and the SA HIV Clinician Society Nutrition Focus Group. 2007. Nutritional guidelines for HIV-infected adults and children in Southern Africa: Meeting the needs. The Southern Journal of HIV Medicine, vol. 3, pp. 22-30.

Stambullin, M., Feliu, S. and Slobodianik, H. 2007. Nutritional status in patients with HIV infection and AIDS. British Journal of Nutrition, no. 98, pp. S140-S143.

Standridge, J.B., Zylstra, R.G. and Adams, S. M. 2004. Alcohol consumption: An overview of benefits and risks. Southern Medical Journal, vol. 97, no. 7, pp. 664 – 672.

Stein, J.H. 2009. Cardiovascular risk of antiretroviral therapy. The New England Journal of Medicine, vol. 356, no. 17, pp. 1773-1774.

Steinbrook, R. 2008. The AIDS Epidemic – a progress report from Mexico City. The New England Journal of Medicine, vol. 359, no. 9, pp. 885-887.

South African National Guidelines on nutrition for people living with TB, HIV/AIDS and other chronic debilitating conditions. 2001. Department of Health.

Summerfield LM. 2001. Physical activity for health and weight management. Nutrition, exercise and behaviour. United States of America; Thompson Learning.

Tabi, M. and Vogel, R.L. 2006. Nutritional counseling: an intervention for HIV-positive patients. Journal of Advanced Nutrition, vol. 54, no. 6, pp.676-682.

Testa, M.A. and Lenderking, W.R. 1999. The impact of AIDS-associated wasting on quality of life: Qualitative issues of measurement and evaluation. The Journal of Nutrition, vol. 129, no. 1, pp. 282S-289S.

Thiébaut, R., El-Sadr, W.M., Friis-Moller, N., Rickenbach, M., Reiss, P., Monforte, A.D., Morfeldt, L., Fontas, E., Kirk, O., De Wits, S., Calvo, G., Law, M.G., Dabis, F., Sabin, C.A. and Lundgren, J.D.; Data collection of adverse events of anti-HIV drugs study group. 2005. Antiviral Therapy, vol. 10, no. 7, pp. 811-823.

Tomazic, J., Silic, A., Karner, P., Vidmar, L., Maticic, M., Poljak, M.,Ihan, A. and Janez, A. 2004. Lipodystrophy and metabolic abnormalities in Slovenian HIV-infected patients. Wien Klin Wochenschr, vol. 116, no. 21, pp. 755-759.

Tomkins, A. 2005. Evidence-based nutrition interventions for the control of HIV /AIDS. South African Journal of Clinical Nutrition, vol. 18, no. 2, pp. 187-191.

United Nations Programme on HIV/AIDS (UNAIDS). 2008. Report on the global HIV/AIDS epidemic 2008: executive summary.

Van Heerden, I.V. and Parry, C.D.H. 2001. If you drink alcohol, drink sensibly. South African Journal of Clinical Nutrition, vol. 14, no. 3, pp. S71-S77.

Valcour, V.G., Shikuma, C.M., Shiramizu, B.T., Williams, A.E., Watters, M.R., Poff, P.W., Grove, J.S., Selnes, O.A., and Sacktor, N.C. 2005. Diabetes, insulin resistance, and dementia amoung HIV – 1 infected patients. Journal of Acquired Immune Deficiency Syndrome, vol. 1, no. 38, pp. 31-36.

Venkataramanan, R. 2000. Milk thistle, a herbal supplement, decreases the activity of CYI and uridine diphoshglucuronosyl transferase in human hepatocyte cultures, Drug Metabolism, vol. 28, no. 11, pp. 1270.

Visagie, C.J. 1999. HIV AIDS the complete story of HIV and AIDS, a practical guide for the ordinary sexually active person. 1st edition. Hatfield, Pretoria: J.L. van Schaik Publishers, pp. 9-19.

Vogel, R.L. 2006. Nutritional counseling: an intervention for HIV-positive patients. Issues and Innovations in Nursing Practice, pp. 676-682.

Vorster, H.H., Kruger, A., Margetts, B.M., Venter, C.S., Kruger, H.S., Veldman, F.J. and MacIntyre, U.E. 2004. The nutritional status of asymptomatic HIV-infected Africans: directions for dietary intervention. Public Health Nutrition, vol. 7, no. 8, pp. 1055-1063.

Wanke, C. 2005. Nutrition and HIV in the international setting. Nutrition in Clinical Care, vol. 8, no. 1, pp. 44-48.

Ware, L.J., Wootton, S.A., Morlese, J.M., Gazzard, B.G. and Jackson, A.A. 2002. The paradox of improved antiretroviral therapy in HIV: potential for nutritional modulation? Proceedings of the Nutrition Society, no. 61, pp. 131-136.

Weston, A.T., Pestosa, R. and Pate, R.R. 1997. Validation of instrument for measurement of physical activity in youth. Journal of the American College of Sports Medicine, vol. 29, no. 1, pp. 138-143.

Wheeler, D.A., Gilbert, C.L., Murrahainen, N., Elion, R.A., Abrams, D.I. and Bartsch, G.E. 1998. Weight loss as a predictor of survival and disease progression in HIV infection. Journal of AIDS Human Retroviral, vol. 18, no. 1, pp. 80-85.

Wing, R.R. and Phelan, S. 2005. Long-term weight loss maintenance. The American Journal of Clinical Nutrition, vol. 82, pp. 222S-225S.

Wintergerst, E.S., Maggini, S. and Hornig, D.H. 2007. Contribution of selected vitamins and trace elements to immune function. Annals of Nutrition and Metabolism, vol. 51, pp. 301-323.

Woods, M.N., Spiegelman, D., Knox, T.A., Forrester, J.E., Connors, J.L., Skinner, S.C., Silva, M., Kim, J.H. and Gorbach, S.L. 2002. Nutrient intake and body weight in a large HIV cohort that includes woman and minorities. Journal of the American Dietetic Association, vol. 102, no. 2, pp. 203 -211.

Wojna, V., Robles, L., Skolasky, R.L., Mayo, R., Seines, O., de la Torre, T., Maldonado, E., Nath, A., Meléndez, L.M. and Lasalde-Dominicci, J. 2007. Associations of cigarette smoking with viral immune and cognitive function in human immunodeficiency virus-seropositive women. Journal of Neurovirology, vol. 13, no. 6, pp. 561-568.

World Health Organization (WHO): Global strategy on diet, physical activity and health (DPAS), 2006.

World Health Organization (WHO): Nutrient requirements for people living with HIV / AIDS, Report of a technical consultation WHO, Geneva, May 2003.