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THE EFFECT OF AN AEROBIC EXERCISE PROGRAM ON THE HEALTH-RELATED QUALITY OF LIFE OF HIV-POSITIVE EMPLOYEES

by

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SYNOPSIS

TITLE :	The effect of an aerobic exercise program on the health related quality of life in HIV positive employees**.**
CANDIDATE :	Margaretha Calitz
PROMOTOR :	Prof. P.E. Krűger
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The human immunodeficiency virus (HIV) together with acquired immunodeficiency syndrome (AIDS) is a world wide pandemic. Sub Sahara Africa, of which South Africa forms a part, is host to the highest HIV population in the world. In the light of this, it is significant to conduct a study of the effect that aerobic exercise might have on the management of disease symptoms.

HIV and AIDS seriously affect the quality of life of the infected person. Decreased quality of life leads to decreases in productivity and increase in absenteeism. This has a negative effect on the economy.

Several symptoms of HIV and AIDS cause quality of life to decrease. In this study the following parameters of health related quality of life were investigated: body composition, functional capacity, pain, anxiety and depression and fatigue. Absenteeism was monitored.

The study further investigates how and why each of these parameters affects health related quality of life, and also the effect of aerobic exercise on the above mentioned parameters.

The body composition of HIV positive persons is affected in one of three ways: wasting of muscle mass due to the virus, obesity because of too high energy intake and too little activity in an attempt to stop wasting, or lipodystrophy due to anti retroviral therapy.

HIV patients have a decreased functional capacity. This may lead to fatigue, another common symptom in HIV patients. The prevalence of anxiety and depression is high in the HIV population, and even more so in South Africa.

It is clear from the literature that aerobic exercise for HIV patients is safe. It is also clear that aerobic exercise has a positive effect on the mentioned parameters – not only on the HIV population, but also on other diseases and the healthy population. Thus the assumption was made that aerobic exercise can be used as a tool to increase health related quality of life in HIV positive persons.

Initially, a quantitative pre-post test experimental design was proposed. In an attempt to recruit enough participants, the discovery was made that HIV is still a highly stigmatised disease in both Mpumalanga and Gauteng. After eighteen months of negotiations with AIDS clinics, mine groups and a newspaper advertisement, only three participants were enrolled. It must be kept in mind, however, that an important factor which influenced recruitment of participants was availability of funds. The indication was that HIV patients are willing to participate if there is proper compensation.

In order to continue with the study, the design changed to a case study. It combined two approaches: qualitative and quantitative. This seems to work well in HIV research. The qualitative and quantitative data supported each other and provided the bigger picture.

The results of this study support the expectation that aerobic exercise enhances the quality of life in HIV infected persons. Body composition and functional capacity improved. Feelings of anxiety and depression decreased and there were indications that pain and fatigue decreased as well. Absenteeism from work decreased in one person.

The conclusion was made that aerobic exercise definitely contributes to the enhancement of quality of life in HIV positive employees. Biokineticists, as exercise specialists, are ideally positioned to provide exercise tests and program prescriptions to

this population and should play a bigger role in the management of HIV and AIDS symptoms.

Key words: HIV AIDS, Exercise, Health-related quality of life, Body composition, Immune function, Functional capacity, Fatigue, Pain, Depression, Anxiety, Absenteeism

OPSOMMING

TITEL :	Die invloed van ‘n aerobiese oefenprogram op die gesondheidsverwante lewenskwaliteit in MIV positiewe werknemers
KANDIDAAT :	Margaretha Calitz
PROMOTOR :	Prof. P.E. Krűger
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Die menslike immuniteitsgebreksvirus (MIV) en gevolglike verworwe immuniteitsgebreksindroom (VIGS) is `n wêreldwye pandemie. Sub-Sahara Afrika, waarvan Suid-Afrika deel vorm, huisves die grootste populasie MIV positiewe persone ter wêreld. Daarom is dit sinvol om die bydrae wat aerobiese oefening kan lewer in die bestuur van hierdie siekte, te ondersoek.

MIV en VIGS hou ernstige implikasies in vir die lewenskwaliteit van die pasiënt. Hierdie verlaagde lewenskwaliteit lei tot laer produktiwiteit en groter afwesigheid van werk onder werknemers en raak die ekonomie nadelig.

MIV en VIGS word gekenmerk deur verskeie simptome wat lewenskwaliteit verlaag. In hieirdie studie is na ‘n paar parameters van gesondheidsverwante lewenskwaliteit gekyk, naamlik liggaamsamestelling, funksionele kapasiteit, pyn, angs en depressie en moegheid. Verder is afwesigheid van werk gemonitor.

In die studie word duidelik aangetoon waarom en hoe elkeen van hierdie parameters gesondheidsverwante lewenskwaliteit beïnvloed en ook hoe aerobiese oefening elkeen van hierdie parameters affekteer.

MIV/VIGS pasiënte se liggaamsamestelling word op een van drie wyses geraak: wegkwyn van spiermassa as gevolg van die virus, obesiteit omdat die pasiënt meer eet

en minder aktief is in ‘n poging om wegkwyning teë te werk, of lipodistrofie as gevolg van anti retrovirale terapie.

Die funksionele kapasiteit van MIV pasiënte is ingeperk en kan aanleiding gee tot moegheid, ‘n ander simptoom wat universeel onder MIV pasiënte voorkom. Die voorkoms van angs en depressie onder MIV pasiënte is hoog en nog selfs hoër in Suid-Afrika.

Uit die literatuur is dit duidelik dat aerobiese oefening veilig is vir MIV positiewe persone. Dit is verder duidelik dat aerobiese oefening ‘n heilsame effek het op al die parameters hierbo genoem, nie net in die MIV populasie nie, maar ook op ander siektes en die normale populasie. Die aanname was dus dat oefening as ‘n hulpmiddel ingespan kan word om die lewenskwaliteit van die MIV positiewe persoon te verhoog.

Aanvanklik sou dit ‘n kwantitatiewe studie met ‘n pre- post toets eksperimentele ontwerp wees. In ‘n poging om genoegsame proefpersone vir die studie te werf, is die ontdekking gemaak dat MIV in Mpumalanga en ook in Gauteng (waar ook werwing gedoen is), steeds ‘n hoogs gestigmatiseerde siekte is. In so ‘n mate dat daar na agtien maande se soek en onderhandel met VIGS klinieke en myngroepe en ‘, koerantadvertensie, slegs drie proefpersone ingewillig het om aan die studie deel te neem. Daar moet egter in gedagte gehou word dat indien ‘n groter begroting beskikbaar was vir hierdie navorsing, dit makliker sou wees om meer proefpersone te bekom. Telkens was die aanduiding dat persone sou deelneem indien hulle vergoed sou word.

Ten einde steeds ‘n sinvolle studie te kon doen, is ‘n gevalle studie aangepak. Daar is egter van ‘n gemengde benadering met kwantitatiewe sowel as kwalitatiewe elemente gebruik gemaak. Hierdie model blyk baie goed te werk in MIV navorsing. Die kwalitatiewe en kwantitatiewe data het mekaar aangevul en versterk. ‘n Geheelbeeld van die lewenskwaliteit met objektiewe sowel as subjektiewe waarnemings is op die manier verkry.

Die resultate in hierdie studie het grootliks ooreengestem met die verwagting dat aerobiese oefening lewenskwaliteit in MIV positiewe persone verhoog.

Liggaamsamestelling en funksionele kapasiteit het verbeter. Gevoelens van angs en depressie het afgeneem en daar was ‘n aanduiding dat pyn en moegheid verbeter het. Afwesigheid van werk het verbeter by een proefpersoon.

Die gevolgtrekking is gemaak dat aerobiese oefening beslis ‘n bydrae kan lewer in die verhoging van lewenskwaliteit in MIV positiewe werknemers. Biokinetici, as oefenkundiges, is uitstekend geposisioneer om oefentoetse en programvoorskrifte vir die MIV populasie te doen en behoort ‘n groter rol te speel in die bestuur van die simptome van MIV en VIGS.

Sleutelterme: MIV, VIGS, Oefening. Gesondheidsverwante lewenskwaliteit, Liggaamsamestelling, Imuunfunksie, Funksionele kapasiteit, Moegheid, Pyn, Depressie, Angs, Afwesigheid van werk

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LIST OF ABBREVIATIONS

ACD	Anaemia of Chronic Disease
ACSM	American College of Sports Medicine
AIDS	Acquired Immunodeficiency Syndrome
Antigens	Antibody generators
APC	Antigen Presenting Cell
ART	Anti Retroviral Therapy
ATP	Adenosine Triphosphate
BDI	Back Depression Scale
BMI	Body Mass Index
bpm	Beats per minute
CES-D	Centre of Epidemiologic Studies Depression Scale
CNS	Central Nervous System
DNA	Deoxyribonucleic acid
DOMS	Delayed Onset Muscle Soreness
g	Gram
Gp	Glycoprotein
HAART	Highly Active Anti Retroviral Therapy
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
HIV+	Human Immunodeficiency Virus Positive
HR-QOL	Health Related Quality of Life
HR	Heart Rate
IASP	International Association for the Study of Pain
IgA	Immunoglobin A
IgG	Immunoglobulin G
Kg	kilogram
m	meter
MET	Metabolic Equivalent
MHC	Major Histocompatibility Complex

MHC2	Class 2 Major Histocompatibility Complex
MNCs	Multi-National Corporation
MOS-HIV	Medical Outcomes Study for Human Immunodeficiency Virus
mRNA	Messenger Ribonucleic acid
MS	Multiple sclerosis
NK	Natural Killer Cell
NRTI	Neuclosite Reverse Transcriptase Inhibitor
ODI	Overseas Development Institute
PMN	Polymorphonuclear
PNS	Peripheral Nervous System
POMS	Profile of Mood state
P	Protein
PTSD	Post Traumatic Stress Disorder
QOL	Quality of life
1 RM	One Repetition Maximum
RA	Rheumatoid Arthritis
REE	Resting Energy Expenditure
RNA	Ribonucleic acid
SI	Syncytium Inducing
SLE	Systemic Lupus Erythemotosus
TB	Tuberculosis
TCR:T	Cell Receptor
TEE	Total Daily Energy Expenditure
TENS	Transcutaneous Electrical Nerve Stimulator
TNF	Tumour Necrosis Factor
VCO_2	Expired Carbon Dioxide
VO_2 max	Maximal aerobic power
WBC	White Blood Cell
WHO	World Health Organization
Yr	Year

CHAPTER 1
INTRODUCTION

1.1 HUMAN IMMUNODEFICIENCY VIRUS (HIV) – A PANDEMIC DISEASE

1.2 EPIDEMIOLOGY

The human immunodeficiency virus (HIV) is a worldwide pandemic and few, if any, aspects of life remain untouched by it (Veenstra & Whiteside, 2005). An estimated amount of 38 to 42 million people worldwide suffer from this disease (Behrman, 2004). Seventy percent (29.3 million) of these people live in Sub-Sahara Africa (Meel, 2005, Simbayi *et al.,* 2007), with 4.3 to 6.6 million of them in South Africa, (www.tac.org.za/community/keystatistics). South Africa is not only the country with the largest HIV positive population in the world, but also the country with the highest rate of infection (Batterham *et al*., 1999, Coetzee, 2006). Figure 1.1 below gives a global view on the HIV pandemic (www.who.int/hiv/facts/index/html).

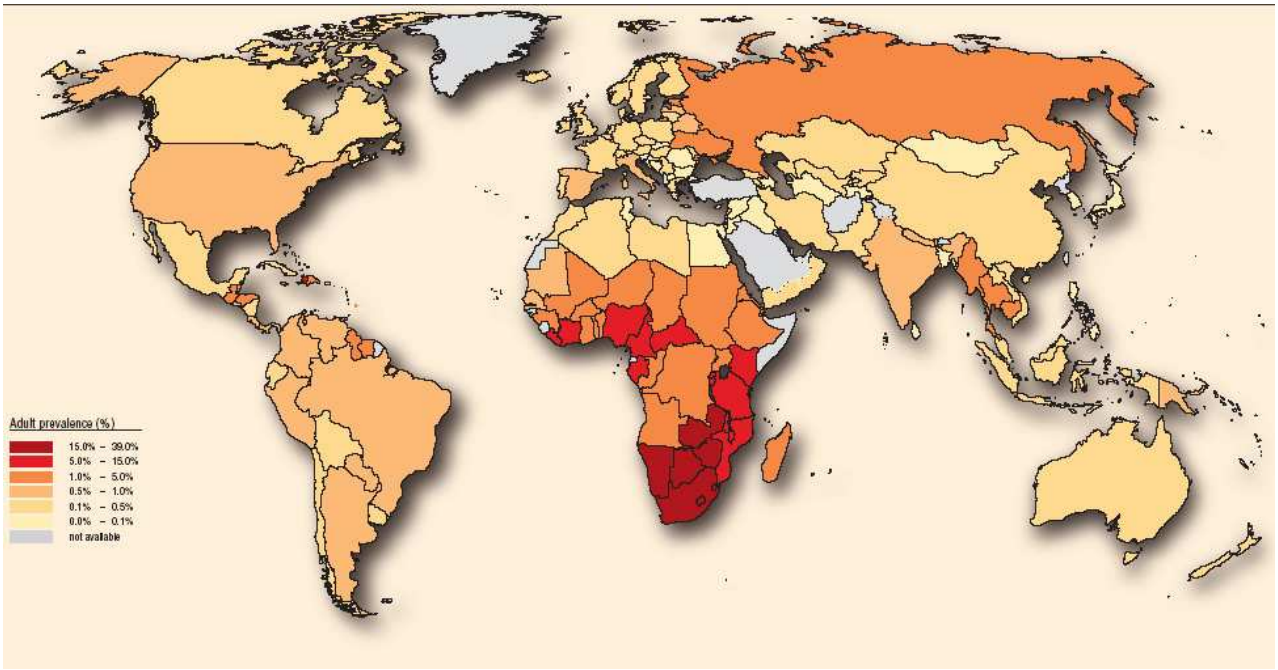

Figure 1.1 A global view of HIV (www.who.int/hiv/facts/index/html)

A report on the demographic impact of HIV/AIDS in South Africa by the Centre for Actuarial Research, reveal just how big and real the HIV/AIDS threat has become in South Africa. The following are some of the key indicators of the HIV/AIDS epidemic in 2006 estimated by the model:

- 38 000 babies will be infected at birth and 26 000 through breast feeding;
- around 1.3% (527 000) of uninfected people will become infected;
- 11% of the population (5.4 million) is infected and of these 11% (600 000) are sick with AIDS;
- in Mpumalanga (where this study was conducted) the total HIV infected population is 446 000;
- of the 5.4 million infected people in South Africa; 1.3 million are under 25 years of age;
- of the 5.4 million infected people, 225 000 are receiving treatment;
- there will be 737 000 total deaths, of which 47% due to HIV and in the age group 15 -49 years, deaths due to HIV will rise to 71%;
- more than 50% of the 15 year olds are not expected to survive to the age of 60. (Dorrington *et al.,* 2006)

In 1997, the Doyle Model predicted that by the year 2000 between 8% and 10% of adults in South Africa would be infected, increasing to 22% in the year 2010 (Williams e*t al.,* 2000). However, in 2001 the national prevalence rate amongst pregnant women was already 24, 8% (Coetzee, 2006).

People are said to be HIV-positive when HIV anti bodies are detected in their blood and are regarded as having AIDS (Acquired Immunodeficiency Syndrome) when their CD4 cell count fall below 200mm^3 (Whiteside & Sunter, 2000).

This disease provides tremendous physical and psychological challenges for those who are infected, as well as for their families and health care providers (Davis, 2004). A reduction in quality of life is a well-reported effect of HIV (Bopp *et al.,* 2004; O'Brien *et*

al., 2004; Meel, 2005) and strategies to improve quality of life for HIV patients will greatly contribute to the management of this disease.

The number of symptoms and associated distress are highly associated with poorer quality of life in HIV. Thus, according to Webb (2004), symptom management is a particularly important area of health related quality of life in HIV. This view is supported by Neidig *et al.* (2003:38) "*Symptom management is an essential but often neglected component of HIV care".*

Nurses in AIDS care targeted the management of symptoms, including fatigue, pain and medication side effects, as the most important research priority in HIV/AIDS (Webb, 2004).
"*The struggle against the epidemic has been hampered by the curse of believing in and promoting single magic bullets. The merits of a holistic approach to tackling the HIV/AIDS epidemic have been acknowledged and this is most likely to be successful in reducing economic impacts in the long term*" (Veenstra & Whiteside, 2004 : 202).

This study hopes to contribute to the team effort of HIV/AIDS management.

1.3 ECONOMIC IMPACT AND ABSENTEEISM

HIV has a huge economic impact which will take years to unfold, but the effect can already be seen on household and sector/firm levels (Veenstra & Whiteside, 2004).

HIV/AIDS affects not only the infected person, but also his family, community and country. It has a devastating impact on development in Africa (Nattrass, 2004). Without treatment, people experience accelerated losses. On household level people have loss of companionship and income. On community and national levels, they experience loss of productivity because of absenteeism from work and death (Phaladze *et al*; 2005).

Since the use of antiretroviral medicines (ART), the treatment for HIV has lead to prolonged survival and lower severity of co-morbid medical illness (Mondy *et al.,* 2007). There was a shift in perspective from an acute end-of life infection to that of a chronic but manageable disease. Health related quality of life has become increasingly important with subsequent implications for the long term care of HIV positive individuals (Elliot *et al.,* 2002). The longer life expectancy of ART users will benefit the economy in the long run. In November 2003, the South African Cabinet announced that government would provide antiretroviral medicines, as part of the Comprehensive HIV and AIDS Care, Management and Treatment Plan for South Africa, to all people in need through government hospitals and clinics (www.tac.org.za/community/arvsites.htm).

Bell *et al.* (2006) describes in three steps how AIDS can severely retard economic growth:

1. AIDS destroys human capital in a selective way, striking primarily young adults. Some years later they become sick and their productivity is reduced and absenteeism increased. When they die in their prime, the human capital formed in them through child-rearing and education, is destroyed.
2. AIDS weakens the mechanisms that create human capital in the next generation. If one or both parents die before their offspring reach adulthood, the transmission of knowledge and potential productive capacity across the two generations will be weakened.
3. Because the children of AIDS victims become adults with little education and limited knowledge received from their parents, they are less able to invest in their own children's education. This vicious cycle may eventually precipitate a collapse of economic productivity (Bell *et al.,* 2006).

Greener (2002) also mentions that high mortality due to HIV in Africa retards the economy.

Recent research by the Overseas Development Institute (ODI) has suggested that the private sector has begun to recognize the impact of HIV/AIDS on the bottom line, both directly and indirectly. It is estimated that a company can generate an average return of

US$3 for every US$1 invested in employee health due to a reduced absenteeism, better productivity and reduction in employee turnover (Goetzel *et al.,* 2005). Indirectly there are also important implications on the supply chain. Many multi-national corporations (MNCs) have therefore become involved in HIV/AIDS initiatives of three main types: a community-based partnerships, supply chain support, and sector-based initiatives (Overseas Development Institute (ODI), 2007).

1.4 EXERCISE AND HIV / AIDS

Exercise is consistently listed among the three most common complementary and alternative therapies utilized by HIV infected persons (Ciccolo *et al*., 2004). Research shows that aerobic exercise benefits pshycological and immunologic functioning of individuals with HIV (Galantino *et al.,* 2005). No reports that cite any negative effects on immune and disease markers were found. According to the literature it can be assumed that both aerobic and resistance exercise for HIV-positive people is safe and can be used to improve functional status and quality of life (Roubenoff & Wilson, 2001; Baigis *et al*., 2002).

Several exercise studies reported an increase in CD4 cell counts, (LaPerriere *et al.,* 1991, LaPerriere *et al.,* 1994, Perna *et al.,* 1999) while other studies found no difference in CD4 cell count due to exercise (Bopp *et al.,* 2004). The two critical exercise variables that determine whether a bout of exercise will cause disturbances in immune function are intensity and duration (Gabriel *et al.,* 1992). In a study by Mitchell *et al*. (2002) healthy persons participated in exercise for 75 minutes at 55% of VO_2 peak. Neither the exercise intensity nor the duration was found to be immunosuppressive. The exercise in this study will be much shorter and only slightly more intensive, thus according to these findings, no decrease in immunity is expected.

On the other hand, high-intensity exercise among HIV negative individuals, has been shown to produce acute immunosuppressive effects that diminish with subsequent training (Smith, 2003). Thus, it is possible that even moderate-intensity exercise, of

sporadic frequency, exerts a temporary immunosuppressive effect among those who are already immunocompromised (Perna *et al.* 1999). It is suggested that single irregular bouts of medium intensity exercise might lead to a drop in CD4 counts, while regular exercise is associated with an improvement in CD4 count.

Perna *et al*. (1999) suggested that it is possible that inconsistent exercise attendance detracted from the noncompliant exercisers' ability to adapt to the physical strain of exercise, which may explain the drop in CD4 cell count in their study.

Stringer (1999) concluded in his study that exercise training resulted in a substantial improvement in aerobic function while immune indices were essentially unchanged. Quality of life markers improved significantly with exercise. Exercise training is safe and effective in this patient group and should be promoted for HIV^+ patients.

1.5 AEROBIC EXERCISE AND QUALITY OF LIFE

There is evidence that aerobic exercise is sufficient to increase positive mood state, vigour, energy and positive well-being (Ciccolo *et al.,* 2004). The positive functional and psychological effects of exercise on the well-being of healthy individuals and older adults with chronic disease have been well researched and documented (Losito *et al.,* 2006). Aerobic overload training also significantly improves a variety of functional capacities related to oxygen transport and use. Because the cardiovascular system and respiratory systems are intimately linked with aerobic processes, related functional changes occur (McArdle *et al.,* 2001). These functional changes have a direct impact on the daily experience of quality of life (QOL) (Galantino *et al.*, 2005).

Diminishing VO_2 max in adults with HIV appears to be one mechanism of fatigue and physical disability. Aerobic insufficiency may result in functional limitations placed on performance of daily activities and on physical disability (Cade *et al*., 2004).

HIV positive persons respond physically to exercise in the same manner than other populations and it can therefore be assumed that their QOL will improve similarly (Ciccolo *et al.,* 2004).

1.6 RESEARCH METHODOLOGY

1.6.1 Research approach

A qualitative and quantitative approach was used in this study.
"Case studies can be based on any mix of quantitative and qualitative evidence."
(Yin, 2003:15)

"*Sometimes the combination of approaches may best answer your research question."* (Broom *et.al., 2004*: 127)

"*Combining qualitative and quantitative research provides an opportunity to analyze complementary datasets, providing a more complete picture than either method can alone.*" (Galantino *et al.,* 2005: 1091)

"It *is increasingly common for qualitative and quantitative approaches to be used in the same study"* (Endacott, 2007: 10).

The general distinction between qualitative and quantitative approaches tends to be based on inductive (qualitative) versus a deductive (quantitative) reasoning (Broom *et al.,* 2004). In inductive approaches, information is gathered from a specific case, and then generalized to theory, whereas in deductive approaches the study starts with theory and individual cases is tested to the theory (Thomas & Nelson, 1996).

This case study is quantitative and deductive where parameters such as VO_2 max, body composition, pain, depression, anxiety, fatigue and absenteeism are measured and the

hypothesis is based on the theory that certain changes will take place in these parameters due to an aerobic exercise program. It has a qualitative and inductive approach when recording the patients' experience of the exercise program and the subjective effect of the program according to the patients. This mixed approach allows for a more comprehensive research and provides an option to explore personal experiences "…*beyond the boundaries of a questionnaire"* (Overcash, 2003:179). In this way, the biokineticist gets more insight into the personal experience of aerobic exercise by HIV patients. This study hopes to contribute to a greater understanding of the HIV patient.

1.6.2 Research design

A research design is the logic that links the data to be collected to the initial question of the study (Yin, 2003:19).

1.6.3 Type of research

The type of research used was a multiple-case study. The nature of this case study is explanatory.

A case study is a systematic inquiry into an event or a set of related events, which aims to describe and explain the phenomenon of interest (Zucker, 2001). According to Tellis (1997), a case study is an ideal methodology when a holistic, in-depth investigation is needed. It is designed to bring out the details from the viewpoint of the participant by using multiple sources of data. It is obvious that the most relevant and valid information about ability to function and quality of life must come from the people themselves (Wu, 1999). The focus is thus on describing and explaining the essence of a phenomenon and its meaning in participants` lives (Sorin-Peters, 2004). This study gives biokineticists information on how HIV positive patients experience and benefit from an aerobic exercise program. This information is not freely available, due to the issues of confidentiality and stigmatism surrounding HIV positive persons.

The case study's unique strength is its ability to deal with a full variety of evidence: artefacts, documents, interviews, observations and specific tests (Yin, 2003). In this study interviews, observation and specific testing were the main tools used to gather evidence. Although case studies consist of a rigorous, detailed examination of a single/multiple case(s), the purpose of a case study is not to make generalizations (Thomas & Nelson, 1996).

Yin (2003) distinguishes between statistical generalization and analytical generalization. Statistical generalization is the most common way of generalizing but is not applicable to case studies, because an inference is made about a population on the basis of empirical data collected about a sample. Case studies are, however, not sampling units and analytical generalization must be used instead. With this method previously developed theory is used as a template with which to compare the empirical results of the case study.

1.6.4 Components of a case study

According to Yin (2003), five components of a case study research design are especially important:

- The study's questions
- Its propositions (if any)
- Its unit(s) of analysis (Chapter 4)
- The logic linking the data to the propositions (Chapter 4)
- The criteria for interpreting the findings (Chapter 4).

1.6.4.1. Study question (research question)

The case study strategy is most likely to be appropriate for "how" and "why" questions. The study question for this study focuses on *how* an exercise program affects the quality of life of HIV positive employees.

1.6.4.2 Propositions

HYPOTHESIS 1

HIV infection leads to a reduction in the quality of life of HIV-positive patients (Eller, 2001). The reduction in quality of life is caused by several symptoms experienced by HIV patients. The most common causes listed in the literature include body composition alterations, fatigue, anxiety, depression and pain (Cunningham *et al.,* 1998, Davis, 2004, Ownby & Dune, 2007). All of these symptoms have been documented to improve from exercise.

Aerobic exercise has been proved to have a positive effect on functional status in HIV-infected patients (Berg & Van Puymbroeck, 2005). Thus, besides being beneficial to the experience of the above mentioned symptoms, exercise leads to improvements in aerobic capacity. This is associated with an improvement in functional status and with a better QOL. Aerobic exercise leads to an improvement in QOL in HIV patients and is proved to be safe for this population (Mars, 2003). Thus, HIV positive employees who participate in an aerobic exercise program are expected to experience a better health related quality of life (HR-QOL). Improvements in body composition, aerobic capacity, anxiety, depression and pain are expected, but no significant changes in CD4 cell counts are expected. Several studies found no influence on CD4 cell count due to exercise (Dudgeon *et al.*, 2004).

HYPOTHESIS 2

Absenteeism from work makes a large contribution to HIV related costs (Coetzee, 2006). It has been reported that HIV leads to a reduced ability to work (Bell *et al.,* 2006). HIV-infected persons who participate in a regular exercise program, are expected to experience a better QOL which might result in a lower tendency towards absenteeism.

1.7 STUDY OBJECTIVES

1. To determine the effect of aerobic exercise on the HR-QOL in HIV positive employees.
2. To determine whether participation in exercise by this population leads to a decrease in absenteeism.
3. To document as many possible data while working with this group – even if it is not in the scope of this study and will not be published in this study.

CHAPTER 2

THE HUMAN IMMUNODEFICIENCY VIRUS (HIV): EFFECTS ON HEALTH-RELATED QUALITY OF LIFE.

2.1. The Human Immunodefiency Virus (HIV)

Human immunodeficiency virus (HIV) is a member of the Retroviridae family of viruses (commonly known as retroviruses), and classified in the subfamily lentiviruses (Lèvy, 1993; Microsoft Encarta Encyclopaedia Standard, 2006). Human infection with HIV results in a complex clinical disease known as acquired immune deficiency syndrome (AIDS), which may take ten years or more to develop. HIV was isolated in 1983 almost simultaneously by three groups of scientists: Luc Montagnier's group at the Pasteur Institute in Paris, Robert Gallo's group at the National Cancer Institute, and a group headed by Jay Levy at the University of California, San Francisco (Whiteside & Sunter, 2000; Lawn, 2004).

Initial infection with HIV may cause a brief flu-like illness, which is typically followed by a long asymptomatic period during which progressive damage to the immune system occurs, resulting eventually in the onset of clinical disease (Smith & Daniel, 2006).

There are two main types of HIV, known as HIV-1 and HIV-2. (Barnett & Whiteside, 2002). HIV-1 is responsible for the majority of infections in the world, while both HIV-1 and HIV-2 are prevalent in Africa. HIV-2 is associated with a less aggressive disease course than HIV-1. HIV 1 is categorised into several different groups. Of these, Group M is the major cause of infection world wide (Modi *et al.,* 2007). This group is further divided into eleven subtypes or clades, named A to K. Clade C predominates in part of sub-Saharan Africa and Asia, while clade B is more common in Europe and North America (Modi *et al*., 2007).

Retroviruses are classified by their unique feature: the need to convert their genomic RNA into DNA (the process of reverse transcription) using an enzyme that they carry

(reverse transcriptase). The outer surface of HIV is a lipid "envelope" derived from the cell membrane of infected cells. Protruding from the surface are the viral transmembrane glycoprotein (gp41) and the envelope glycoprotein (gp120) that allow HIV to bind and fuse with a target cell. Within the envelope, the viral core protein, p17, forms the matrix of the virion particle, and the core protein, p24, forms an inner cylindrically shaped nucleoid. The nucleoid contains two strands of viral genomic RNA (the genetic material of HIV) and the associated reverse transcriptase enzyme (Donegan *et al., 1990;* Microsoft Encarta Encyclopaedia Standard, 2006). The human immunodeficiency virus has to enter the body and attach itself to host cells. After infection, the viraemia (virus particles in the blood stream) attach themselves to the CD4 and macrophages cells (Barnett & Whiteside, 2002).

HIV infects certain human cells by binding its envelope glycoproteins gp120 and gp41 to specific molecules on the surface of the cells. Only cells that carry the appropriate molecules are susceptible to infection by HIV (Whiteside & Sunter, 2000). In the 1980s, scientists quickly recognized that a molecule called CD4, which is found particularly on certain T-lymphocytes (a type of white blood cell), was the primary binding site, but it was only in 1996 that other co-receptors that are also required for infection were identified (Ward, 1998).

There are two main parts, essentially: the inner core (the "pill-shaped" section in Figure 2.1 below), and the viral membrane. The viral membrane encloses the particle, and has about nine or ten gp160 spikes embedded in it which are involved in binding and membrane fusion when the virus particle attaches to a cell. The inner core is the "payload" of the virus, containing the viral RNA and some enzymes (reverse transcriptase, protease, integrase) (www.mcld.co.uk/hiv/?q=viral).

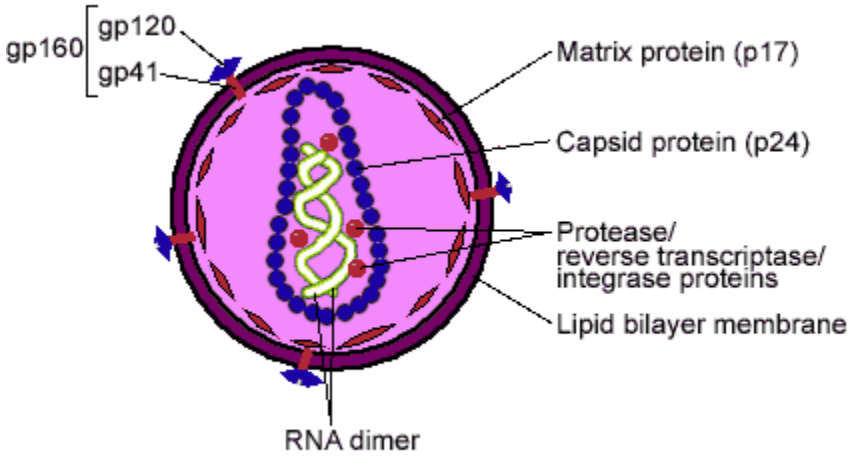

Figure 2.1: HIV particle (http:www.niaid.nih.gov/factsheets/howhiv.htm)

There are two main types of CD4 cells:

1. CD4 positive T cells which organize the body's overall immune response to foreign bodies and infections. These cells are the primary targets of HIV. HIV must enter the body and attach themselves to CD4 cells before a person become infected (Hole, 1987).
2. Macrophages: HIV also attacks immune cells called macrophages. Macrophages engulf foreign invaders and ensure that the body's immune system recognize them in the future (Zen & Parkos, 2003).

HIV infection leads to low levels of $CD4^+$ T cells through three main mechanisms: firstly, direct viral killing of infected cells; secondly, increased rates of apoptosis in infected cells; and thirdly, killing of infected $CD4^+$ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When $CD4^+$ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections (Coffin *et al.,* 1986).

Natural killer (NK), or CD16+ lymphocyte cells, are also affected. They play a role in immune surveillance against tumour cells and viruses in non-specific natural immunity. While NK cells are not greatly affected in AIDS, their cytotoxicity is significantly reduced

early in the disease process (Mars, 2003). Those who progress rapidly to AIDS have lower NK cell numbers than those with slower disease progression (Eller, 2001).

As HIV disease progresses, HIV variants called syncytium-inducing (SI) strains evolve within the individual's body. SI variants can use an additional co-receptor on human cells, called CXCR4. This may allow HIV to infect a wider range of cells and may help to explain why the emergence of SI variants is associated with a worse prognosis (Microsoft Encarta Encyclopaedia Standard, 2006).

Once fusion has taken place, reverse transcription then occurs to convert the viral genomic RNA into double-stranded DNA. The viral DNA is transported to the cell nucleus and is integrated, or inserted, into the normal cellular chromosomal DNA (Whiteside & Sunter, 2000). When the right activation signals are present, the process of making new virions begins. Using the replication machinery of the host cell, the integrated viral DNA is transcribed to make messenger RNA (mRNA) and new strands of viral genomic RNA. The viral mRNA is then translated into a protein string that is cleaved into specific viral proteins. Assembly of new virions then takes place within the cell, and the new HIV particles are released by budding from the cell surface, taking a piece of the cell membrane as their envelope (Ward, 1998).

HIV replication can directly kill CD4+ T-lymphocytes. The loss of these cells paralyses the immune system and is one mechanism by which HIV infection causes AIDS (Coetzee, 2006).

A number of anti-HIV drugs have been developed, each targeting a different stage in this viral life cycle. By 2004, nine reverse transcriptase inhibitors and six protease inhibitors had been developed, with more in development. The widespread use of combinations of these agents in the developed world has resulted in dramatic reductions in rates of HIV-related illness and death. Several members of a new class of drugs, which inhibit the binding or fusion of HIV to host cells, are now in clinical development (Schneider *et al.,* 2005).

After attachment the virus penetrates the wall of the cell and attach to the DNA of the host cell. When the virus is inside the cell, it cannot be traced by the bodies' immune system. Inside the cell the virus transcribes DNA from a RNA template to open the door to the cell nucleus. This copied DNA intergrades easily with the genes of the host. This is converted into more viruses, which break out and destroy the host cell and are released as viraemia to infect other CD4 and macrophages cells. (Whiteside & Sunter, 2000; Barnett & Whiteside, 2002). See figure 2.2 below.

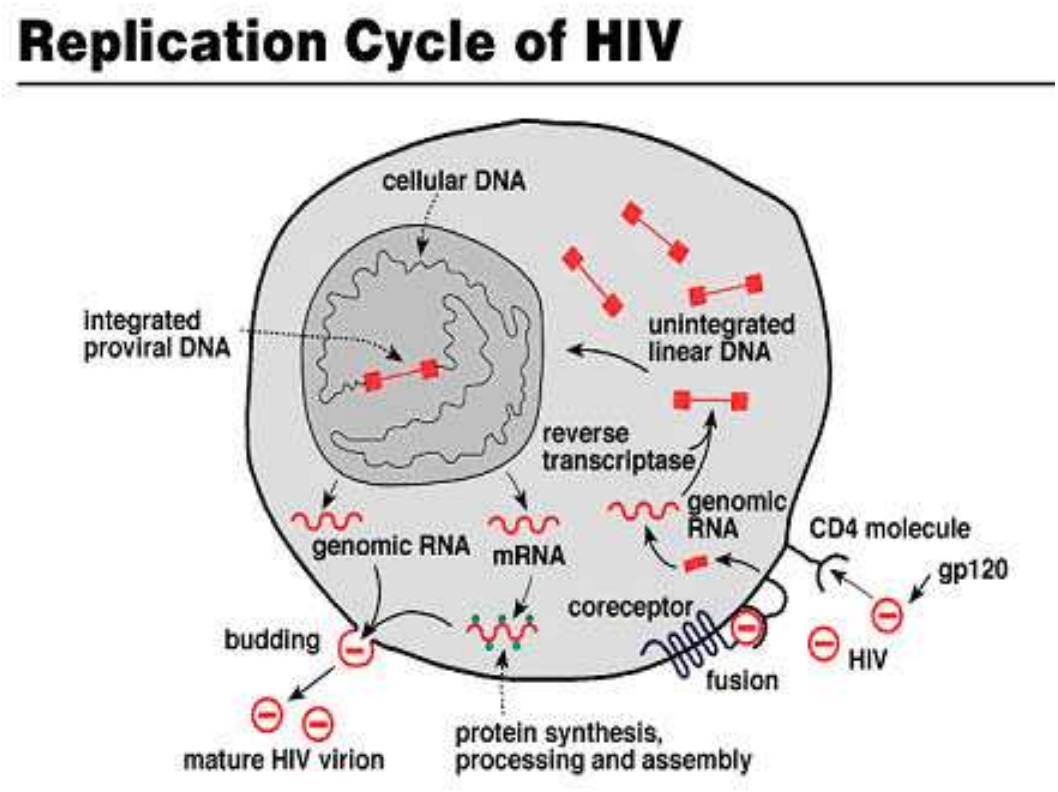

Figure 2.2: Replication cycle of HIV

(www.aegis.com/topics/basics/hivandaids.html)

Once infection has taken place, the battle between the virus and the immune system starts. Initially many cells are infected, but the immune system fights back by manufacturing a vast number of antibodies. Although the viral load is high and the immune system comes under pressure, the HIV status of the patients can still not be detected. This is commonly referred to as the window period. At this stage the person is

highly infectious. At the end of the window period the person might experience an episode of illness, but will not be seen as a marker of HIV because it will resemble the symptoms of flu (Buchbinder *et al.,* 1994). The window period is followed by a long incubation period. During this stage the viruses attack the cells very quickly. According to Barnett and Whiteside (2002), up to 5% of the body's CD4 cells (about 2 million cells) may be destroyed each day by the billions of virus particles.

The virus eventually destroys the immune cells more rapidly than they can reproduce, causing the number of CD4 cells to fall.

2.2 CD4+ count

The number of CD4+ cells in a healthy person is 1200 CD4+ cells per micro litre of blood (Meyer & Meij, 1987). As infection progresses, the number will fall. When the CD4+ cell count falls below 200 mm^3, opportunistic infections begin to occur and a person is said to have acquired immunodeficiency syndrome (AIDS). Infections will increase in frequency, severity and duration until the person dies (McHeyzer-Williams *et al.,* 2006).

2.3 From HIV to AIDS

HIV gradually moves through various stages until the patient has AIDS. The website of the World Health Organization (WHO), divides HIV infection into four stages:

Stage 1: HIV enters the body, duplicating itself rapidly into CD4+ cells. No signs, swollen lymph glands, but usually not a cause of alarm.

Stage 2: Minor skin problems, head or chest colds and weight loss. Herpes zoster may occur.

Stage 3 Amount of HIV in body increase and more CD4+ cells are destroyed. More serious problems occur such as chronic diarrhoea, profound weight loss, fever pneumonia and TB.

Stage 4: Very serious diseases occur such as pneumocytis carinii pneumonia, oesophageal thrust, infection of the brain such as toxoplasmosis, severe diarrhoea and cancers such as Karposi`s sarcoma (www.who.int/facts/index/html).

Two other commonly used classifications are the Walter Reed Classification and the Centre for Disease Control coding for AIDS:

Walter Reed Classification:

WR1	CD4 count ≥ 400/mm³, no signs or symptoms
WR2	CD4 count ≥ 400/mm³, lymphadenopathy present
WR3	CD4 count < 400/mm³, normal delayed hypersensitivity
WR4	CD4 count < 400/mm³, partial cutaneous anergy
WR5	CD4 count<400/mm³, complete cutaneous anergy or oral thrush present
WR6	CD4 count < 400/mm³, opportunistic infection present

This classification is typically used where facilities to test CD4+ cell count are available (Mars, 2003).

Centre for Disease Control coding for AIDS

A	Asymptomatic. Patient able to transmit the disease and immune system compromised.
B	Early symptomatic pre-AIDS. Fever and/or diarrhoea persisting more than 1 month, involuntary weight loss and/or diagnosis of an infectious disease associated with HIV
C	AIDS. CD4 count < 200 cells/mm³ and/or the presence of a major complication such as opportunistic infection or malignancy (Mars, 2003)

This classification model was developed to use in areas where there are no access to testing facilities (Makoane *et al.*, 2005)

2.4 Infection

A person can only get HIV in the following ways:

1. **From unprotected sexual intercourse** with a person who already has HIV.
2. **From mother to child**. The HIV infected mother can pass the virus on to the unborn child. This can happen in the womb, but most commonly happens through childbirth and breast-feeding.
3. **Direct contact with the blood of a HIV infected person**. This is rare, but a freshly open wound that comes in contact with HIV infected blood may lead to infection. When HIV infected blood is transfused, it will cause infection.
4. **By sharing needles or syringes** with a HIV infected person.
5. **By sharing toothbrushes and razor blades** with an infected person.

(HIV and AIDS: Prevention, Care and Treatment)

2.5 Anti-retroviral therapy (ART)

2.5.1 Use of ART in South Africa

"*The magnitude of HIV infection in South Africa and the number of impoverished people who desperately need antiretroviral therapy is overwhelming. Lifetime costs associated with antiretroviral therapy and political intransigence remain the most important obstacles to adequate management of HIV infection in many countries, including South Africa, where the availability of finance determines access to therapy.*" (Antiretroviral therapy in adults, South African HIV clinicians Society Clinical Guidelines, 2002:1)

The national ART programme can be expected to play an important role in the future outcome of the epidemic. It is predicted that by 2010, there will be roughly 388 000

AIDS deaths per annum rather than the 505 500 that would have been expected (Figure 2.3).

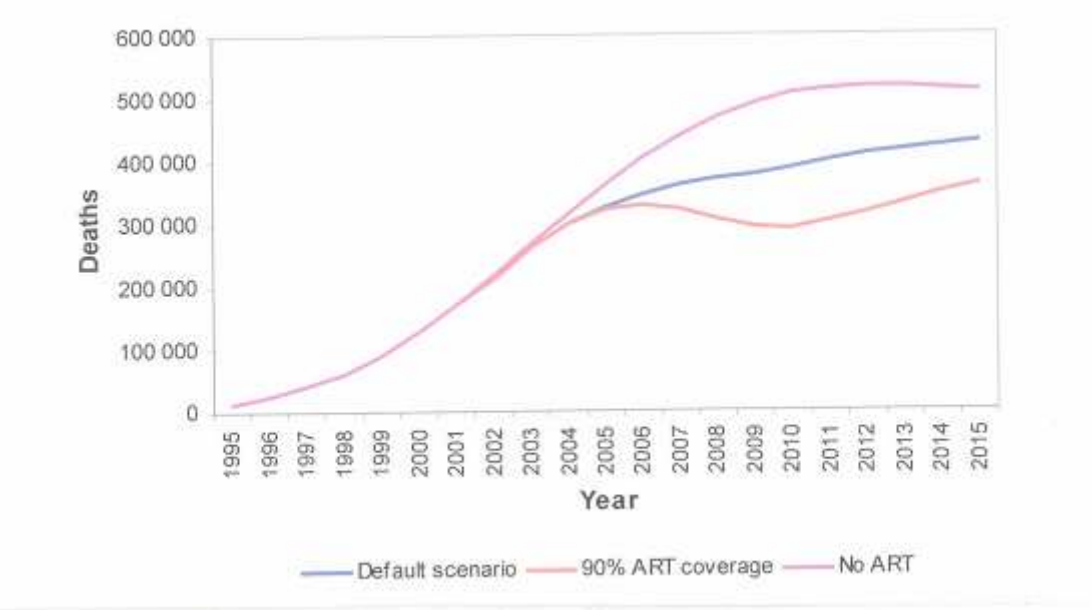

Figure 2.3: Projected number of AIDS deaths by level of coverage of national ART programme (Dorrington *et al*., 2006).

2.5.2 Goals of ART

The primary goals of ART are:

- maximal and durable suppression of viral load;
- restoration and/or preservation of immunological function;
- improvement of quality of life;
- reduction of HIV-related morbidity and mortality.

(Battaglioli-De Nero, 2006)

2.5.3 Standard of care

Single drug regimens (monotherapy) should not be used in the treatment of HIV – infection. Dual drug regimens are better than no therapy, but are unlikely to produce long-term durable benefits in most patients (Charalambous *et al*., 2007). This should

only be applied to patients who have already developed AIDS. However, triple combinations are the standard of care. Triple combination therapy is also called highly active antiretroviral therapy (HAART) (Antiretroviral therapy in adults, South African HIV clinicians Society Clinical Guidelines, 2002).

2.5.4 Classes of antiretroviral agents and their mechanisms of action

Antiretroviral agents inhibit one or two key viral enzymes required by HIV for intracellular viral replication. Reverse transcriptase is an enzyme that is essential for completion of early stages of HIV replication (Microsoft Encarta 2006). Nucleoside reverse trancriptase inhibitors like zidovudine, didanosine, zalcitabine and lamivudine inhibit it by mimicking the normal building blocks of HIV DNA. These were the first the first class of agents developed to fight HIV infection (Sension, 2007). Non-nucleoside reverse transcriptase inhibitors like studavine, efavirenz and nevirapine, also inhibit it by direct involvement on the enzyme (Antiretroviral therapy in adults, South African HIV clinicians Society Clinical Guidelines, 2002).

Protease is another enzyme which is required for the assembly and maturation of fully-infectious viral progeny. By inhibiting late stages of HIV replication, protease inhibitors like efavirenz, ritonavir and indinavir suppress viral load. (Sension, 2007)

Although ART and even more HAART, caused a decline in mortality in HIV infected individuals, it has some serious side effects of which the biokineticist must take notice. This therapy has been successful in reducing viral load, increasing lymphocytes, delaying onset of AIDS and increasing the survival rate of HIV –infected individuals, but it is also related to the development of gastrointestinal disorders, liver problems, lipodystrophy, insulin resistance, hyperglycemia, hypercholesterol and decreased bone density (Ramirez-Marrero *et al.*, 2004).

The South African HIV Clinicians Society's Guidelines for Antiretroviral Therapy in Adults (2002), provides the following table with information on major side effects of ART agents:

Table 2.1: Major side effects of ART agents

Side effect/ Complication	Nucleoside reverse transcriptase inhibitor	Non-nucleoside reverse transcriptase inhibitor	Protease inhibitors
GI tolerance	Yes	No	No
Pancreatitis	Yes	Yes	Yes
Peripheral neuropathy	Yes	No	No
Allergic reaction	Rare	Yes	Rare
Lipoatrophy	Yes	Unknown	Unknown
Lactic acidosis	Yes	No	No
Raisedcholesterol and triclyceride	Unknown	Yes: Efavirenz	Yes
Insulin resistance	No	No	Yes
Neuropsychiatric manifestations	No	Yes: Efavirenz	Yes
Lypodystrophy	Yes	Unknown	Yes

2.5.5 Adherence to anti retroviral therapy

Adherence to treatment regimens is essential to the success of ART in patients infected with HIV. An adherence level of 95% is required in order to maintain virological suppression (Battaglioli-De Nero, 2006). Nonadherence is common to all chronic diseases, but because nonadherence to ART medication does not have immediate adverse consequences, adherence to ART seems to be a special problem. Further more, nonadherence to ART leads to drug resistance in HIV. This can result in new strains of HIV developing (HIV and AIDS: Prevention, Care and Treatment). Depression is consistently mentioned as one of the causes of nonadherence to ART (Valente 2003,

Battaglioli-De Nero, 2006, Simbayi *et al*., 2007). Thus, interventions to relieve depression, like exercise, may help to improve adherence to ART.

2.6 Effect of HIV on health-related quality of life

Clinical research and interest in health-related quality of life (HR QOL) began more than 50 years ago with the World Health Organization's definition of health as not just the absence of disease, but a state of physical, mental and social well-being (Webb, 2004).

There are two broad categories in which QOL can be divided. The first uses a satisfaction model based on generic measures of well-being and life satisfaction in multiple domains, with most of them unrelated to health. The second category includes HR-QOL and is based on measures of sickness impact (Eller, 2001). It refers to how well a person functions to his or her perception of well-being in the physical, mental and social domains of life (Hays *et al.*, 2000). QOL can also be defined as how people perceive their emotional, functional, physical and social status (Ayàn *et al.,* 2007). This study looks at quality of life from a health -related point of view. Webb (2004) mentioned that HR-QOL must be distinguished from the more general term quality of life often used in the literature. Where the general term is used in research articles, the content of the article was used as criteria to determine whether it is relevant to this study or not. HR-QOL focuses on factors as they relate to health, emphasizing patients` symptom status, functional status and general health perception. Major aspects of HR-QOL include the extent of physical and emotional symptoms, as well as physical, emotional, social and cognitive functioning and patient perception of well-being (Webb, 2004).

Although QOL is a multidimensional construct that does not have a universally agreed-upon definition, researchers have agreed on many concepts concerning HR-QOL. The Word Health Organization Quality of Life Group defined QOL as individuals' perceptions of their position in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns (Phaladze *et al.*, 2005).

The QOL of people with HIV/AIDS in Sub Saharan Africa is a complex constellation of disease, poverty, stigma, discrimination and lack of treatment combined with family life, work and social activities (Phaladze *et al.*, 2005).

Assessing HR- QOL in HIV positive patients is important for documenting the burden of chronic disease, tracking changes in health over time, assessing the effects of treatments and gauging return from health-care investments (Hays *et al.*, 2000). HIV infection and its treatment may result in numerous physical and mental changes that affect a patient's QOL (Davis, 2004). HIV-positive patients report lower HR-QOL than the general population does (Webb, 2004). Furthermore, persons with AIDS reported lower HR-QOL than persons with other chronic conditions such as cancer and depression (Webb, 2004).

Antiretroviral therapy (ART) significantly prolongs life and has changed HIV infection from a terminal disease to a chronic disease, but also contributes to losses in QOL (Carrieri *et al.*, 2007). Multiple factors beyond disease stage apparently influence both physical and psychological dimensions of QOL. Early studies of persons with HIV showed a positive relationship between physical functioning and self reported QOL (Eller, 2001). Many of these symptoms can be treated, thus alleviating discomfort or distress and improving QOL and, perhaps, health outcomes (Davis, 2004).

In a study by Eller (2001), the relationship among sociodemographic variables, depression, immunity and fatigue was investigated. Work status, income and education were the sociodemographic variables significantly related to HR-QOL. In this study, better immune status (CD4+ counts) was only moderately linked to better QOL. Strong and significant relationships were observed between QOL and subjective measures of depression and fatigue. In regression analysis, depression and fatigue explained 58% and work status 28% of the variance in QOL.

Hays *et al*. (2000) studied a probability sample of 2,864 HIV infected patients. Participants were interviewed and answered questions on physical functioning, role

functioning, pain, general health perceptions, emotional well-being, social functioning and energy. These factors were evaluated over the previous 4 weeks. The results showed that physical functioning and emotional well-being among patients with symptomatic HIV were worse than for patients with several other chronic diseases. The association between employment status and HR-QOL likely reflects a combination of the loss of employment that is a common consequence of HIV on the one hand, and the role of work-life in promoting well-being on the other hand (Hays *et al*., 2000).

An association between higher income and better physical and mental health was observed. These patients may have better access to high-quality medical care, which may lead to improvements in health-related QOL.

Hays *et al.* (2000) concluded that the need for supportive and mental health services is likely to be greater in HIV patients than in patients with other chronic diseases. Medical and supportive services should be provided to symptomatic patients, either by identifying the course or treating them directly. The biokineticist uses exercise as a modality to treat several of the mentioned symptoms affecting health related QOL, and can play a role in HIV care. In a study by Barroso *et al.* (2002), the most frequently reported symptoms in HIV infected patients were fatigue, sleep disturbances, pain, anxiety, sadness and nausea. Although HIV therapy has evolved since the time of that study, many of the clinical factors affecting QOL in the mid- 1990`s remain key QOL issues today (Davis, 2004).

Makoane *et al.* (2005) studied the symptoms experience of people living with HIV/AIDS in Southern Africa. Demographic and self-reported data were gathered, using a descriptive design. HIV patients from South-Africa, Botswana, Lesotho and Swaziland were targeted. A list of a possible 64 symptoms was used and patients had to indicate the frequency and intensity of the symptoms they experienced.

The patients in their study were extremely ill. Of the 64 possible symptoms, the most frequently experienced symptom was fatigue, followed by weakness, concern over

weight loss, fear/worries and painful joints. Makoane *et al.* (2005) concluded that psychological symptoms such as fear and depression are reported more frequently than physical symptoms. Thus, strategies to manage these psychological symptoms are as important as strategies to manage physiological symptoms. Exercise, as described in Chapter 3, is an ideal way to manage both these kind of symptoms.

In a study by Cunningham *et al.* (1998), constitutional symptoms and health-related quality of life in patients with symptomatic HIV disease was researched in the pre-ART era. They found that the presence, number and severity of constitutional symptoms in HIV disease are strongly related to HR-QOL. Identifying and treating these very common symptoms (like fatigue and depression) has the potential to improve QOL in HIV patients.

Phaladze *et al.* (2005) investigated QOL and the concept of "living well" in Sub Saharan Africa among 743 HIV+ patients. According to their findings, daily functioning was the most significant predictor of life satisfaction. As fatigue prevents a person to function properly on a daily basis, this research supports the work done by Mokaone *et al.* (2005) that found fatigue to be the biggest threat to QOL. Phaladze *et al.* (2005) concluded that health care providers could teach and support strategies, such as nutrition and exercise, to reduce functional disability.

2.6.1 Effect of HIV on body composition

Body composition abnormalities are common in people with HIV and AIDS. (Foster,1996, Batterham *et al.,*1999, Corless *et al.,* 2004) These abnormalities are often disfiguring and diminish the quality of life of the affected individual substantially. A study by Corless *et al*. (2004) indicated that when a person's weight is closer to their ideal, HIV-positive individuals exhibit better quality of life. In an early study Parisien *et al.* (1993) urge that anthropometric measures be included as routine in clinical practice for patients with HIV to assess changes in body weight and body mass. In a study by Wilson *et al. (2002)*, it was found, however, that clinicians do not have to measure body

composition to understand the impact of changes in weight on physical functioning. Contrary to their expectations, it is sufficient enough to follow total body weight (Wilson *et al.,* 2002). Their study included few wasted subjects (11,2% of the group), thus the question can be asked if this will also be true for a bigger sample of wasted subjects.

Changes in body composition threaten the sense of self and body image. HIV patients with morphological changes expressed anxiety, fear, frustrations and uncertainty about their changing bodies (Reynolds *et al.*, 2006). According to Wohl (2005), the most distressing long-term complication associated with HIV therapy have been those in which body shape and physical appearance has been altered.

As persons with HIV/AIDS live with this chronic illness, focusing on weight change and body image must be addressed if enhanced QOL is to be achieved. An interesting finding was that there is a clear difference in the relationship between QOL and body image of women and men. It appears that the QOL of males is more closely linked to body weight status. (Corless *et al.,* 2004).

2.6.1.1 Wasting

Wasting of muscle in HIV positive people has been well documented (Batterham *et al*., 1999). Concern about weight loss was listed the third most experienced complaint by HIV patients in Southern Africa (Makoane *et al.,* 2005).

Wasting is defined as unintentional weight loss of 10% or more of usual body weight. Wasting is one of only three serious sequalae of HIV infection that has not rapidly declined since antiretroviral therapy has become widely available. Data now shows that even a 5% weight loss or a drop of two points on the body mass index (BMI), is associated with worse prognosis and increased mortality in HIV infection (Roubenoff & Wilson, 2001).

Neutron activation studies showed that both potassium and nitrogen were depleted in HIV positive subjects, where as cross-sectional imaging documented depletion in skeletal mass (Kotler, 2000). Some reports noted a lack of weight gain and elevated resting energy expenditure (REE) (hypermetabolism) among patients receiving ART (Kosmiski *et al.,* 2007) Thus, wasting remains a serious problem. When a HIV infected person's weight is higher and closer to their ideal, these individuals exhibit better quality of life (Corless *et al*., 2004).

Besides being life threatening, wasting is also associated with poor physical functioning. It is presumed that the association between physical function and weight loss is driven by the decline in lean body mass, especially muscle mass, which occurs with wasting (Roubenoff & Wilson, 2001).

2.6.1.2 Lipodystrophy

At the 5th Conference on Retroviruses and Opportunistic Infections held in Chicago in 1998, physicians from all over the world described cases of patients infected by HIV with body fat redistributions and metabolic abnormalities (Martinez *et al.*, 2001).

These body changes included an increase in truncal fat and a decrease in subcutaneous fat (Figure 2.4). It frequently manifested with peripheral wasting in arms, legs and face (Figure2.6A) and buffalo hump (Figure 2.5A & B) (Batterham *et al.*, 1999). It may also involve localized abdominal fat gain and breast enlargement in both sexes (Reynolds *et al.,* 2006).

Metabolic abnormalities included hypertriglyceridaemia and insulin resistance, as well as bone metabolic abnormalities. These symptoms manifested in patients using ART, especially protease inhibitors. These problems were commonly named lipodystrophy, but there is limited knowledge on the pathogenesis and epidemiology of it (Kosmiski *et al.,* 2007).

Since the use of antiretroviral therapy, HIV has been treated as a chronic illness, despite the fact that it remains a life threatening disease (Cade *et al.,* 2004; Ciccolo *et al.,* 2004; O'Brien *et al.*, 2004; Ronald & Sandel, 2005). Although ART allows for a reduction in HIV-related mortality, the extension in a patient's length of life is associated with a reduction in quality of life. The use of ART brings along several new treatment challenges (Reynolds *et al.*, 2006). In contrast with the pre-ART era, few patients using ART experience opportunistic infections (Sension, 2007).

In developed countries, HIV infection is accepted more readily in the society than it used to be. Good communication, laws to protect HIV patients and supportive non-governmental organizations help patients to cope better and live normal lives in society. Unfortunately these advances are not applicable to developing countries. The success in communicating with the general population about the risks of HIV and the ways it can be managed, seems not to reach the people. It is still a taboo for the majority of patients to report HIV (Martinez *et al.,* 2001).

While doing this study, this view was confirmed. The most difficult part was to find HIV positive persons who were willing to enrol into the study. Although South Africa (and Mpumalanga) has high HIV infection rates, it was not reflected in the number of available HIV patients.

Patients with HIV lipodystrophy had significantly greater resting energy expenditure (REE) and total daily energy expenditure (TEE). This suggests that hypermetabolism may be another feature of lipodystrophy syndrome. This increase in REE may be a chronic and adaptive response to an inability to store tryglyceride fuel in a normal matter. Subcutaneous adipose tissue makes up 85% of total body fat in lean individuals and it acts as an important metabolic buffer. If this buffering capacity is compromised, fat accumulation in nonadipose tissues such as the liver and skeletal muscle occurs with detrimental metabolic consequences (Kosmiski *et al*., 2007).

Although lipodystrophy are characterized by fat redistribution and metabolic abnormalities, body fat changes have the main impact on the quality of life of patients (Wohl, 2005). Most patients with lipodystrophy syndrome experience mild to moderate changes in body fat, while severe changes are described in approximately 20% of patients (Sension, 2007).

Body changes are normally noticed suddenly. The main negative impact of lipodystrophy can be attributed to stigmatisation. Facial lipodystrophy in particular that can be readily seen by others, and may identify AIDS in a way that is similar to wasting. Lipodystrophy reduces the QOL of HIV patients by limiting physical activity, lowering self-esteem and bringing fear, despondency, loneliness and isolation (Dudgeon *et al*., 2004).

Reynolds *et al.* (2006) conducted a qualitative study to improve understanding of the psychosocial effects and components of lipodystrophy. They found that the morphological changes associated with lipodystrophy are highly stigmatising and may have adverse psychological and social functioning effects. This may in turn impair quality of life, reduce treatment effectiveness and hasten disease progression (Reynolds *et al.*, 2006).

Metabolic abnormalities do not have a direct impact on QOL, but their consequences and their treatment may do. The risk for cardiovascular disease is higher due to hyperlipidaemia and insulin resistance, although epidemiology studies so far have not demonstrated a major impact on the incidence of cardiovascular disease (Wohl, 2005).

Makoane *et al.* (2005) studied the symptoms experienced by people living with HIV in Southern Africa. They argue that even after antiretroviral therapy does become available, symptom management will continue as a key component of HIV management because of its relationship to the side effects of medication, medication adherence and quality of life. Lipodystrophy syndrome reduces HR-QOL in HIV/AIDS patients by

limiting social activities, affecting body image and lowering self-esteem, often leading to depression (Webb, 2004).

Figure 2.4 : Lipodystrophy: Typical trunkal fat accumalation and wasting of arms.
(www.virusmyth.com/aids/news/bodydeform.htm)

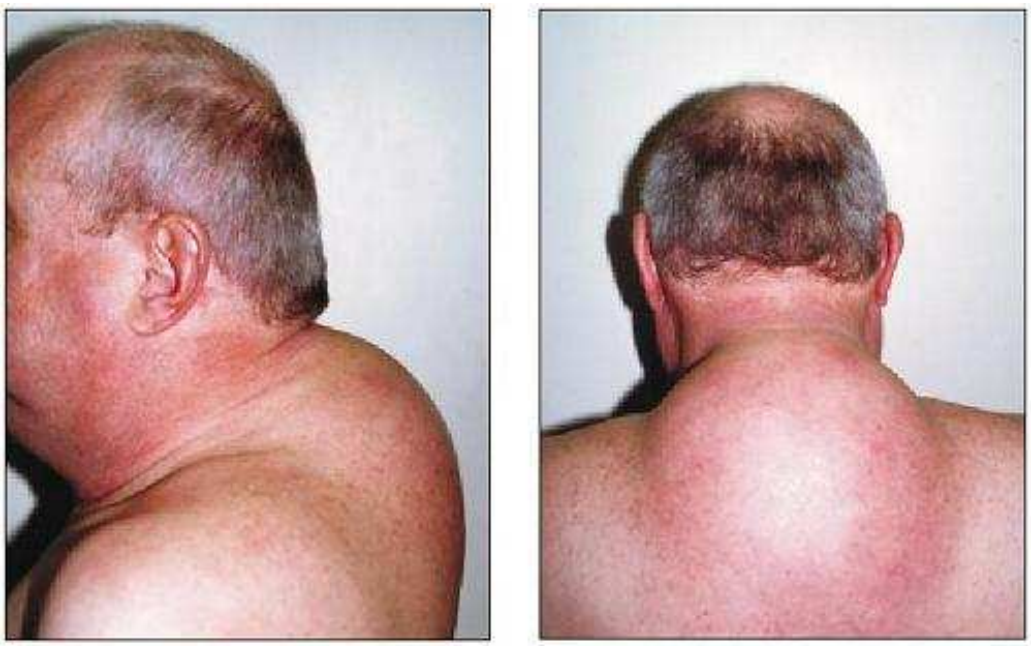

Figure 1) Left and right *A 52-year-old human immunodeficiency virus (HIV)-1-infected man presented with a football-sized mass in the dorsal cervical area ('buffalo hump'). It had existed as a minor area of fullness for several years, but had dramatically increased in size over the preceding year, after the protease inhibitor indinavir was added to his antiviral regimen*

Figure 2.5 A & B : Typical buffalo hump associated with lipodystrophy
(www.virusmyth.com/aids/news/bodydeform.htm)

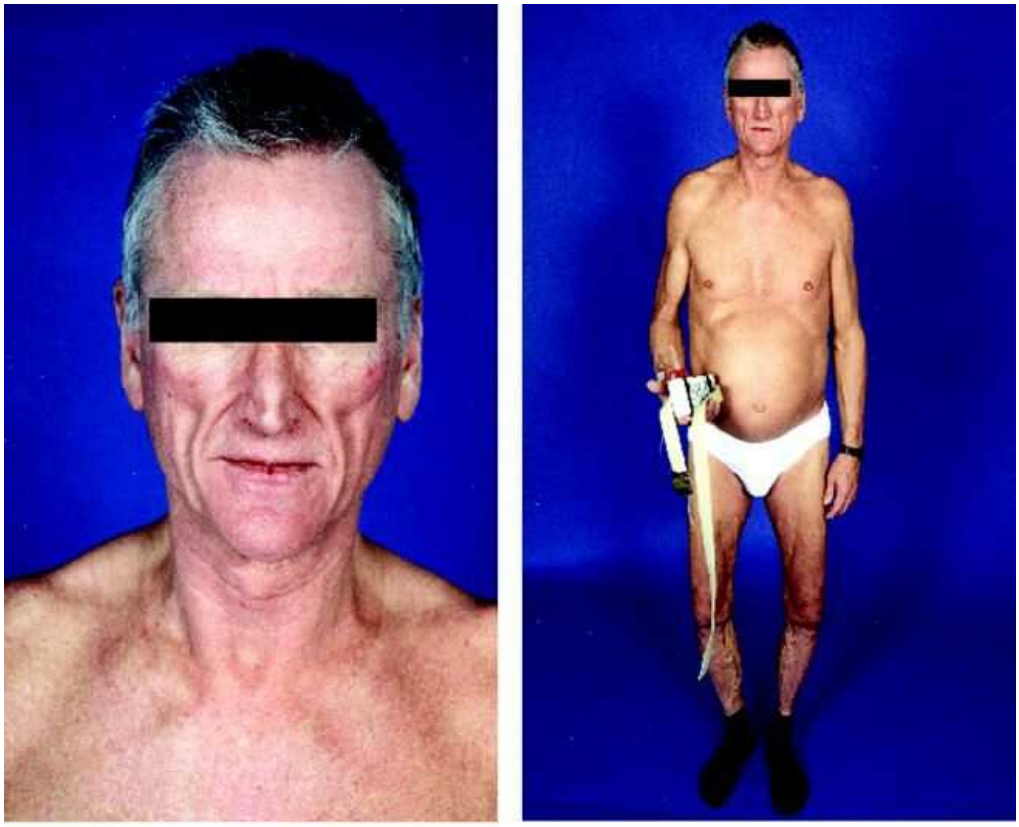

Fig. 1. Perifer fedtatrofi og central fedtakkumulation hos en hiv-patient i højaktiv antiretroviral terapi.

Figure 2.6 A : Lipoatrophy of the face associated with lipodysytrophy
B : Peripheral wasting with a redistribution of fat at the stomach.
(www.virusmyth.com/aids/news/bodydeform.htm)

2.6.1.3 Obesity

Although classically a wasting disease, obesity is increasingly common among HIV infected individuals receiving ART in the USA. Mokaone *et al.* (2005) listed concern about weight gain, however, only as item number 57 from a possible 64 most experienced symptoms in HIV + patients in Southern Africa. It should be mentioned that the patients in their survey did not use ART.

An interview (13/10/2005) with a nursing sister at the local government hospitals' HIV clinic revealed interesting information. According to her, all patients visiting the clinic receive ART. Despite the use of ART there are still some patients with significant

wasting. This might be due to malnutrition. In the local community there is still a huge stigma connected to being diagnosed with HIV, which often results in loss of jobs and support from family and friends. Poverty is a further reason for malnutrition and wasting. On the other hand, she sees several HIV patients (mainly women) who are obese. This observation correlates with findings by Engelson *et al*. (2006). They described obesity as an: "…*unexpected health problem in HIV-infected women*" (Engelson *et al.,* 2006:1333).

Reasons for obesity might be physical inactivity and overconsumption of high-energy supplements. The central reason for obesity is an excess of energy intake relative to energy expenditure (Sarsan *et al.,* 2006).

Some women stop using illicit drugs when diagnosed with HIV, which promotes weight gain. Some patients have a fear for wasting and take active measures to increase body weight (Engelson *et al.,* 2006).

Rasoolinejad *et al*. (2004) studied the prevalence of thyroid dysfunction among HIV and AIDS patients. According to their findings hypothyroidism is prevalent in HIV/AIDS patients. Hypothyroidism is associated with lower basal metabolism rate and higher body weight (Meyer, 1988), which might be a reason for obesity in HIV patients.

2.6.2 Depression and Anxiety

2.6.2.1 Anxiety

Anxiety is a universal symptom in people living with HIV/AIDS (Kemppainen *et al.,* 2003). Makoane *et al.* (2005) found that people living with HIV in South Africa reported more psychological symptoms such as anxiety, than physical symptoms. This is often due to stress caused by lost of income or inadequate income.

Corless *et al*. (2002) asked 422 HIV infected (non AIDS and AIDS) persons to list their most common symptoms. Anxiety was found to be the most prevalent symptom. Several studies reported that HIV infected persons with these symptoms may benefit from exercise (O'Brien *et al*., 2004).

Although there is limited evidence supporting a direct relationship between stress and AIDS progression, there are a few studies suggesting that stress influences the coarse of HIV disease (Remor *et al.,* 2007). Stress can cause anxiety and depression in HIV patients (Makoane *et al.;* 2005). In a study by Remor *et al.* (2007) it was assessed whether perceived stress as measured by the Perceived Stress Scale was associated with a decline in CD4 cell counts in 100 HIV+ patients in Spain. The findings suggest perceived psychological stress is associated with CD4 cell decline, independent of sociodemographic factors and disease status (Remor *et al.,* 2007).

2.6.2.2 Depression

Depression as a result of extreme psychological stress was reported as a common symptom associated with HIV infection (Sukati *et al*., 2005). In the general South African population, 29% reported feeling depressed, compared to the 42% of people living with HIV (Simbayi *et al.,* 2007). It is a common experience in people living with HIV and is underdiagnosed and -treated (Eller *et al.,* 2005). In a study among adults with HIV infection, it was found that those with symptoms of depression or other probable mood disorders had significantly lower HR-QOL scores than did those without depression (Neidig *et al.*, 2003).

Untreated depression along with other co morbid conditions may increase costly clinic visits, hospitalisation and may reduce adherence to treatment and quality of life (Valente, 2003). It was strongly associated with psychosocial QOL in HIV-positive samples (Eller, 2001).

One third to one half of people living with HIV experience symptoms of depression (Eller *et al.,* 2005). The distress associated with being diagnosed with HIV infection can result in anxiety and depression about a range of issues, including mortality, stigma, treatment and change in daily lifestyle (Davis, 2004). When compared to matched groups with other chronic medical conditions, quality of life in persons living with HIV is significantly lower (Eller, 2001).

Some antiretroviral medication directly increases depressive moods and anxiety, but it can also be due to reactions to the adverse effects of ART (Ciccolo *et al*., 2004). On the other hand, protease inhibitor antiretroviral medications may decrease depression, although rates of depressive symptoms continue among 46% to 52% of those in treatment (Valente, 2003).

The incidence of depression in persons with HIV appears to vary by gender and risk group. Depression occurred in 30% of women, 21% to 58% of homosexual men and 30% of men, as reported by Eller (2001). Simbayi *et al.* (2007) reported that HIV positive women in South Africa experience more depressive symptoms than men, who have a higher tendency towards alcohol and drug abuse (Simbayi *et al.,* 2007). Depression results in productivity losses via increased rates of absenteeism and short-term disability as well as impaired work performance (Valente, 2003).

There is some evidence that depression may influence the trajectory of HIV disease. Eller *et al*. (2005) reported two studies to support this. Firstly a study in North Carolina reported that depressive symptoms were associated with faster progression in AIDS over a five and a half year period. Secondly, a study in 2001 also reported faster HIV disease progression in women with depressive symptoms, which was independent of sociodemographics and clinical factors or substance abuse. Depressive symptoms are reported to be a significant predictor of non-adherence to HIV in HIV+ samples. (Eller *et al.,* 2005).

Furthermore, an association between depression and reduced lymphocyte populations and natural killer cell activity was supported by a meta-analysis and review. Some studies also reported lower CD4+ lymphocyte counts and rapid declines in this marker in depressed HIV patients. (Eller, 2001).

Some researchers investigated the difference in depression among patients in different stages of the disease. The three stages that were used are: early or asymptomatic stage, midstage or symptomatic disease and late stage or AIDS. In some studies, those in the early-stage scored higher on overall quality of life with a decrease as the disease progressed. A few other studies reported higher levels of depression in patients in the midstage of HIV disease (Eller, 2001). On the other hand, Valente (2003) reported depression to be the second and third most important debilitating symptom HIV+ patients experienced, regardless of the severity of HIV disease.

There is also a clear relationship between depression and pain. Pain is associated with interference in mood and enjoyment in life, which increases with the intensity of the pain (Evans *et al.,* 1998). Rosenfeld *et al.* (1996) reported in an earlier study that HIV patients with pain had significantly more depressive symptoms, psychological distress and felt more hopeless than those without pain.

In a study by Eller (2001) a sample of 81 HIV-positive adults was recruited over 6 months. The relationships between sociodemographic variables, depression, immunity and fatigue were explored. Of the group of 81 patients, 27 were at early stage, 27 at midstage and 27 had AIDS. The group at midstage had the lowest quality of life, thus reported amongst other things, the highest scores of depression. This suggests that factors other than clinical status influence depression in HIV patients. These may include feelings of greater uncertainty and hopelessness and less control at this stage of the disease. Unemployed persons who were not working and those with lower incomes or education reported poorer quality of life (Eller, 2001).

2.6.3 Fatigue

Fatigue has been described as tiredness that is unrelieved by a full night of sleep, (Ancoli-Israel *et al*., 2001) and has a profound adverse impact on HIV-positive patients' quality of life. It restricts their daily activities and compromises their subjective sense of well-being, and potentially even compromises treatment by leading to missed appointments (Davis, 2004). It has been found that many people had to cease or decrease work commitments, which led to social isolation compounded by difficulties maintaining contact with activity and family (Barroso *et al.,* 2002).

AIDS patients with fatigue spend more of their time sleeping than patients without fatigue and reported significantly greater interference with work, daily activities, self-care and social interactions (Breitbart *et al.*, 1998).

Among people living with HIV/AIDS, fatigue is a common, although frequently under-recognized and undertreated symptom (Siegel *et al.,* 2004). Jenkins *et al.* (2006) also mention that research, exploring the experience of HIV-associated fatigue, has not been extensively reported and as a consequence, may not be well understood.

In HIV positive people, 20% to 80% of patients reported fatigue, whereas up to 85% of AIDS patients reported fatigue (Eller, 2001). According to Breitbart *et al.* (1998), 10% to 30% individuals with early asymptomatic HIV and 40% to 50% of people with AIDS, suffer from fatigue and it is associated with impaired physical functioning and poor quality of life.

Typically, as HIV disease progresses, fatigue becomes more prevalent. Fatigue can be due to depression and anxiety or to physical disorders (Cade *et a*l., 2002). Fatigue is the symptom most frequently listed by HIV patients in Southern Africa, according to a study by Makoane *et al.* (2005).

The etiology of fatigue is multi factorial. Risk factors for fatigue are clinical AIDS, depression and haemoglobin (Hb) levels less than 12g/dL (Davis, 2004). Anaemia occurs in 95% of HIV-patients and commonly coexists with fatigue, according to Webb (2004). Breibart *et al*. (1998) found a small but significant association between hemoglobin levels and the presence of fatigue. Jenkins *et al*. (2006) support this view. According to their study many physical ailments related to HIV disease complicate the assessment and management of fatigue. Hormonal deficiencies, liver dysfunction and hypothyroidism are suggested to contribute to fatigue in HIV (Barroso, 1999)

Fatigue is often associated with HIV treatment. Some HIV therapies (anti retroviral medication such as zidovudine, lamivudine, didanosine and stavudine) suppress bone marrow production of the red blood cells and that leads to anaemia. Also, living with a chronic disease can cause anaemia of chronic disease (ACD), which is quite common in HIV infected patients (Davis, 2004).

Fatigue in patients with HIV/AIDS may also be related to lack of rest, poor diet, depression, anxiety, infection and pain (Webb, 2004). In an early study, Breibart *et al.* (1998) documented fatigue in 438 ambulatory AIDS patients over a period of 28 months. They found that fatigue was more prevalent in woman and patients with advanced disease and associated with high levels of overall psychological distress and a lower level of QOL. Although fatigue is one of the symptoms of depression, this study showed that depression and fatigue each made unique contributions to the prediction of psychological stress and QOL.

There is, however, contradictory evidence regarding the association between HIV-related fatigue and stage of disease. In the above mentioned study a relationship was found, but Darko *et al.* (1992) found no relationship in their study on fatigue, sleep disturbance, disability and indices of progression of HIV disease.

One of the first studies to examine the prevalence of fatigue and the relative importance of psychological, biological and treatment factors, solely in the HAART era, was

conducted by Henderson *et al.* (2005). In this study, 65% HIV patients reported significant fatigue. They did not demonstrate an association between the presence of fatigue and more advanced HIV disease as measured by CD4 cell count. Fatigued HIV patients were significantly more disabled than their nonfatigued counterparts.

According to Millikin *et al.* (2003) individuals with asymptomatic HIV-infection and those with good immunological status reported levels of fatigue similar to that by HIV-negative controls, indicating an association between disease stage and fatigue.

A study by Eller (2001), described earlier, investigated the relationship among sociodemographic variables, depression, immunity and fatigue and the degree to which they predicted quality of life in persons living with HIV. Strong and significant relationships were observed between QOL and subjective measures of depression and fatigue.

Cade *et al.* (2004) reported a study where 31% of women and 53% of men with asymptomatic HIV reported at least one limitation to physical activity due to fatigue. In the same study, almost half of the respondents who reported fatigue also reported a chronic inability to participate in other life activities, such as working at a job (Cade *et al.*, 2004).

Barroso and Lynn`s (2002) descriptive HIV study revealed that 68% of participants were depressed while 48% believed there was a link between fatigue and depression. The site of fatigue in the human body may be classified as central (Figure 2.7), that is, in the brain or spinal cord of the central nervous system, or it may be peripheral, located in the muscles tissue itself or at the junction of the muscle and nerve fibre (Williams, 1995).

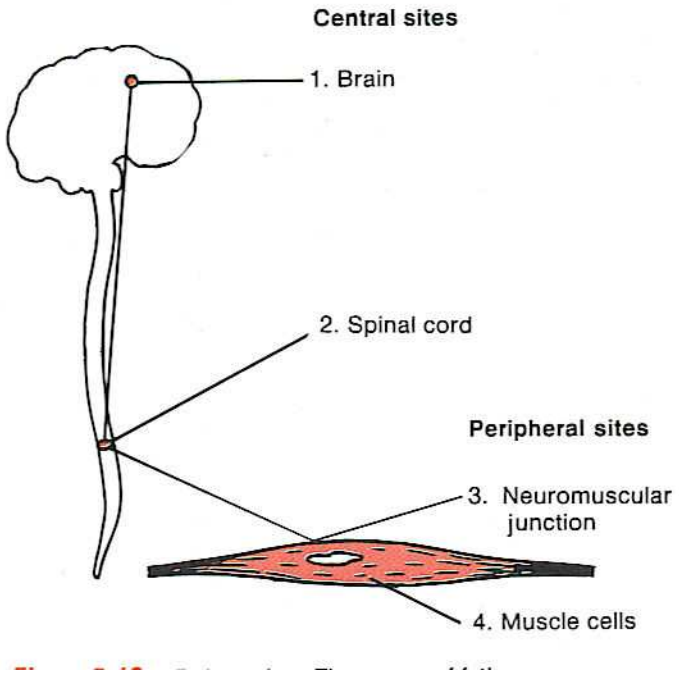

Figure 2.7 : Fatigue sites in the human body. (Williams, 1995:79)

"*The causes of fatigue are complex and may involve central sites such as the brain and spinal cord or peripheral muscle sites. Hypoglycemia, or low blood sugar, could adversely affect the functioning of the brain, while acidity associated with the production of lactic acid could possibly interfere with optimal energy production in the muscle cells"* (Williams, 1995:79)

2.6.3.1 Peripheral fatigue

When work or exercise is done, the oxidative system (Figure 2.8) provides energy (adenosine triphosphate [ATP]) to the working muscles through the oxidation of glucose, fatty acids and amino acids in the mitochondria. The oxygen system, like the lactic system, cannot be used directly as a source of energy for muscle contraction, but it does produce ATP in rather large quantities from other energy sources in the body (Williams, 1995).

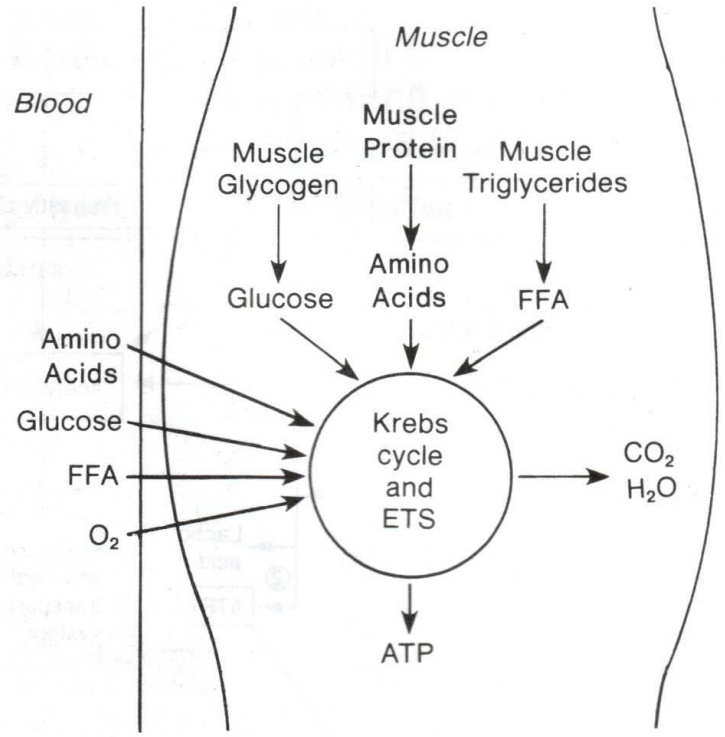

Figure 2.8 : The oxygen energy system (Williams, 1995: 63)

Disruption of any part of the pathway – from pulmonary extraction of atmospheric oxygen to mitochondrial uptake and utilization, including inhaling into the lung capillaries, blood transport by the heart and circulatory system to the working muscle cell, and movement across the cell and into the mitochondria – would impair oxidative metabolism (Cade *et al.,* 2004). Ordinary daily activities such as housework, shopping and light garden work have an energy requirement of 3 to 5 metabolic equivalents (METs). One MET equals the average resting metabolic rate in the general population: 3,5mL of oxygen consumed per kilogram of body weight per minute. (Williams, 1995).

A physical activity that lasts over a minute requires the presence and use of oxygen to liberate energy. The glycolytic pathway comes into action when activity is sustained at a high oxygen demand and the slow responsiveness of the oxidative system requires that the source of energy must be supplemented by another pathway. The non-oxidative pathway provides small amounts of energy rapidly, but amongst its by-products are

hydrogen ions and lactic acid. These acids tend to lower the intracellular pH and high concentrations of these are associated with fatigue. Thus, in order for an individual to do a certain physical activity without becoming fatigued, the oxidative metabolic pathway must be effective enough to meet the energy demand with the minimal non-oxidative supplementation. When the aerobic capacity is insufficient to meet the energy demands, it is called aerobic insufficiency. This may lead to functional limitations placed on performance of daily activities (Baechle & Earle, 2000).

One of the mechanisms of fatigue in HIV patients appears to be diminished aerobic capacity. Diminished VO_2 max has been identified among adults with HIV and ranges approximately 15% to 40% below that predicted for sedentary age-matched controls without HIV (Cade *et al*., 2002). Further more, functional aerobic impairment (VO_2 max ≥ 27% of predicted values for age and sex) was found in both adolescents and adults who had asymptomatic to mildly symptomatic HIV infection (Cade *et al*., 2004).

Ventilatory threshold occurs at a point during progressive physical activity load where carbon dioxide expired and minute ventilation begins to increase more rapidly than inspired oxygen. Pothoff *et al.* (1994) reported that ventilatory threshold occurs earlier during maximal exercise tests in people with HIV than in people without HIV. This increase in expired carbon dioxide (VCO_2) has been associated with increases in blood lactate and hydrogen ions.

It was also reported that in persons with HIV, ventilatory threshold already occurs during the energy requirements associated with light instrumental activities of daily living (3-4 METs) (Cade *et al*., 2004). Thus, aerobic impairment and oxidative metabolic dysfunction might count for fatigue related disability in HIV positive adolescents and adults.

A qualitative study on ART using HIV patients by Reynolds *et al.* (2006) revealed that a decrease in energy levels due to morphological changes, were a predominant complaint amongst participants. A number of participants described feeling fatigued, sluggish and

short of breath due to extra body weight. Some also described how extra abdominal fat constrained their mobility and how they had less body strength due to loss of muscle mass (Reynolds *et al.,* 2006).

Neucleosite reverse transcriptase inhibitors (NRTIs) play a central role on antiretroviral therapy. The major side effects of NRTs are described earlier on in Table 2.1. One of the side effects is lactic asidosis. Duong *et al.* (2007) investigated the limitations of exercise capacity in NRTI-treated HIV patients with hyperlactataemia. According to them, NRTIs can cause mitochondrial dysfunction and cellular toxicity that leads to fatigue. Fatigue adds an additional burden to the already overwhelming task of coping with HIV and AIDS and may result in greater levels of depression and feelings of hopelessness (Breitbart *et al.*, 1998).

2.6.3.2 Central fatigue

The human immunodeficiency virus affects all systems of the body (Valente, 2003). Tesio *et al.* (2006) presented a model for fatigue generation in multiple sclerosis, where lesions to the central nervous system occur (Figure 2.9). Because HIV has a direct effect on the central nervous system (Smith *et al.,* 2002) central fatigue due to lesions of the central nervous system, may contribute to fatigue in HIV:

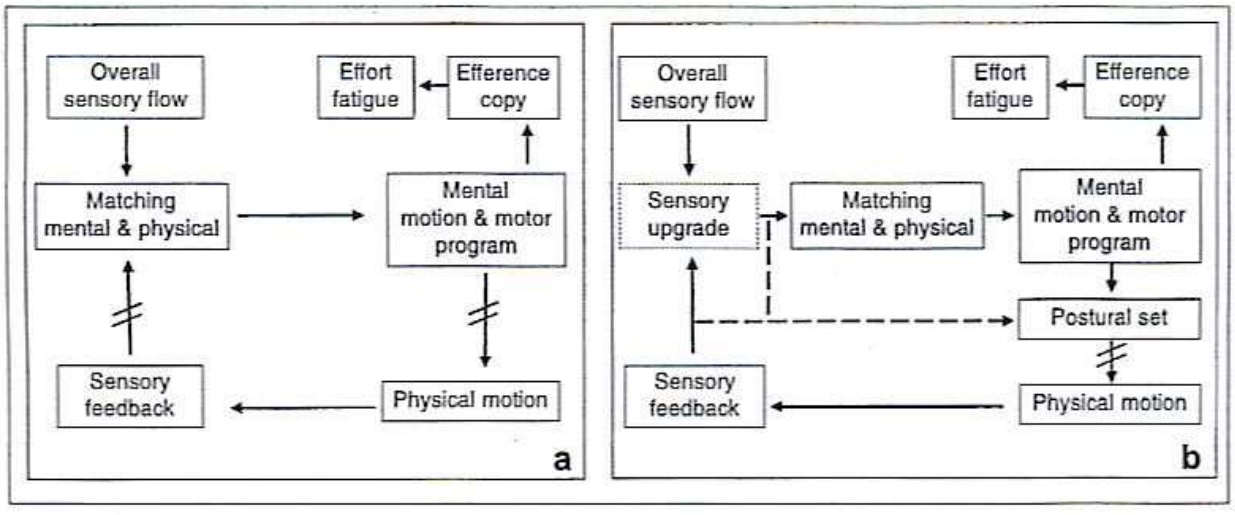

Figure 2.9: Model for generation of central fatigue (Tesio *et al.,* 2006).

a) Fatigue reflects the need for an excessive motor command, generating an excessive efferent copy of itself. The excess command strives to compensate for the mismatch between intended and perceived movement. Reduced perception may arise from either a decreased movement, or a decreased sensory feedback.
b) The model is refined through the inclusion of the involuntary postural movements always accompanying voluntary movements. A decreased voluntary motion may also stem from alteration of the background postural activity. A decreased sensory feedback may also act by preventing the timely upgrade of proper postural program (Tesio *et al*., 2006).

2.6.4 Pain

Pain was found to be a major contributor to the lower QOL experienced by HIV-infected individuals in the pre-ART era (Holzemer *et al*., 1998). It is a common and pervasive symptom for persons infected with HIV (Smith *et al.*; 2002). Chronic pain, defined as a pain that passed the span of three months (Merksey & Bogduk, 1994), is common in HIV patients (Frich & Borgbjerg, 2000)

Newshan *et al*. (2002) studied the occurrence of pain in patients in the post-ART era and found that pain is still one of the commonly experienced symptoms. Pain impairs functional ability and limit physical activity, affecting HR-QOL in HIV patients (Webb, 2004). Larue *et al. (*1997) looked at HIV patients at different stages of disease and found that those patients with significant pain reported lower quality of life than those with no pain. Significant pain had an independent negative impact on the HIV patient's quality of life after adjustment to treatment setting, stage of disease, fatigue, sadness and depression (Larue *et al*., 1997). McCormack *et al.* (1993), however, found that there did not appear to be a correlation between pain and severity of disease in HIV patients, suggesting that pain in this population is non-specific to the time course of the disease.

Although the etiology varies, pain most commonly stems from the direct effect of HIV on the central or peripheral nervous systems, opportunistic infections or ART use (Smith *et al*., 2002). The nervous system consists of afferent (sensory) and efferent (motor) pathways with association pathways to connect and co-ordinate the two. The functional unit of the nervous system is a nerve cell with its processes. Together they form what is known as a neuron (Meyer & Meij, 1987).

Nerve cells conduct impulses in only one direction. The dendrites carry the impulses to the nerve cell and the axons carry the impulse away from the nerve cell. A neuron can be divided into three portions (Figure 2.10):

1. Receptor portion: cell body and dendrites which receive the impulse
2. Conductile portion: axon which carries the impulse. A myelin sheath on this portion increases the conduction velocity.
3. Effector portion: end of the axon which produces an effect on other neurones and muscles. (Electro Therapist training manual: 12)

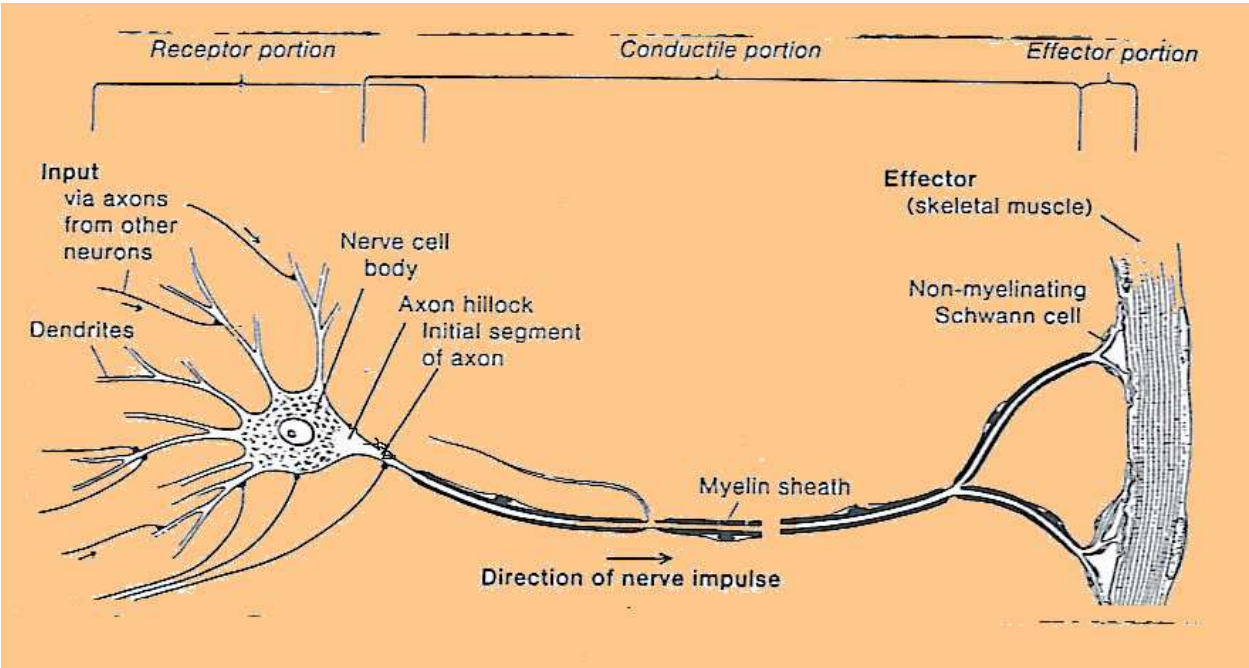

Figure 2.10: Diagram illustrating the receptor, conductile and effector portions of a typical neuron (Electro therapist Training Manual: 12)

Nerves carry impulses to and from the central nervous system (CNS), which is composed of the brain and spinal cord. The peripheral nervous system (PNS) sends impulses to and receives impulses from the CNS. (Hole, 1987).

Pain receptors are found in nearly all types of body tissue and they are stimulated by different impulses, electric, mechanical, chemical, or cold or heat (Meyer & Meij, 1987). Pain is felt when a coded message travels from the injured area to the brain where it is decoded, analysed and reacted to. This pain message travels from the injured area along the peripheral nerves to the spinal cord. Here the message is switched to the central nerves that travel up the spinal cord to the brain. The pain message is then interpreted and referred back to the injured area where pain is then felt (Hole, 1987).

This route involves a number of synapses (Figure 2.11). A synapse is the site of contact between neurons at which one neuron is excited or inhibited by another neuron.

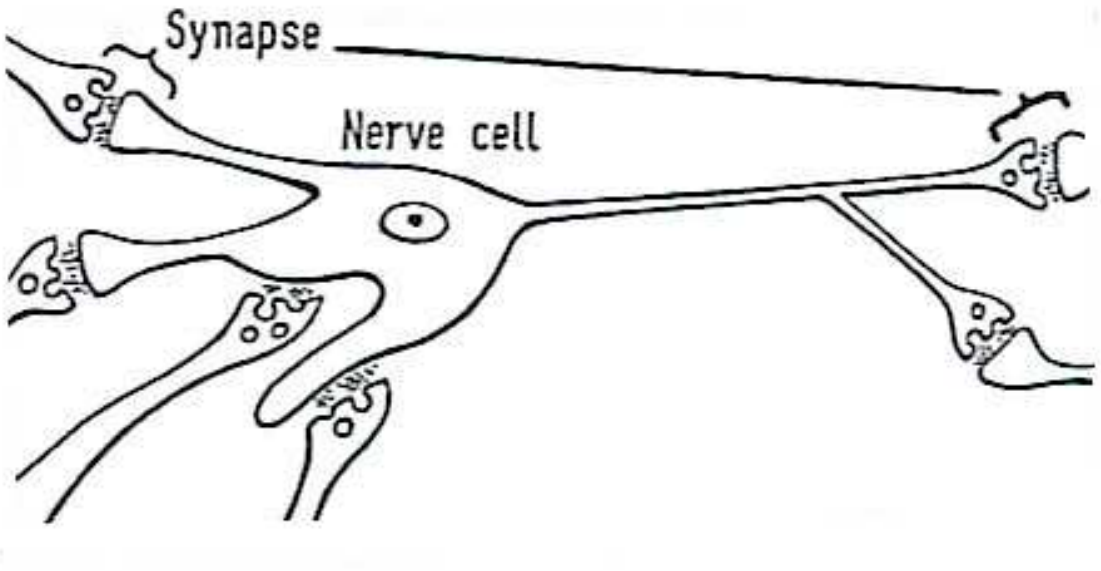

Figure 2.11: A nerve synapse (Electro therapist manual: 13)

The International Association for the Study of Pain (IASP) adopted a definition for pain, which declares that pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (IASP,

1986). The two most widely accepted theoretical conceptualisations of pain are the parallel processing model of pain distress and the gate control theory (Kolt & Snyder-Mackler, 2003):

2.6.4.1 Parallel processing model of pain

According to this model pain can be processed along two pathways, namely informal and emotional. The informal pathway focuses on issues such as location of pain, cause of pain and sensory characteristics of pain. The emotional pathway in the model produces a particular emotional response to pain. Research shows that when focus is on informational elements of pain, significant less pain is experienced, than when focus is on its emotional aspects (Kolt & Snyder-Mackler, 2003). Given the high emotional stress experienced by the HIV patients, the health care provider can lead the patient to focus on the informational elements rather than the emotional aspects. Several studies suggested that pain in HIV is associated with perceived disease progression which in turn increases emotional stress (Webb, 2004, Evans *et al.,* 1998). Questions focusing on the location of the pain and sensory characteristics and explaining the possible cause of the pain to the patient might be helpful in focusing on the informational pathway.

2.6.4.2 Gate control theory of pain

In this theory the assumption is that the dorsal horns of the spinal cord contain a neural mechanism that acts as a pain gate, controlling pain impulses. This gate between the peripheral and central nervous system can control the flow of impulses to the central nervous system by increasing or decreasing them. An open gate will result in an increase in pain experience while a closed gate results in less pain experienced. How the gates behave is determined by a complex interaction of distal afferent stimulation and descending influences from the brain. When the amount of information passing through the gate exceeds a critical level, the neural mechanism responsible for pain

experience and control is activated and the gate is opened (McCulloch & Transfeldt, 1997; Kolt & Snyder-Mackler, 2003).

Peripheral neuropathy is the most common neurological complication in HIV disease (Nicholas *et al.,* 2002). Modi *et al.* (2007) documented neurological diseases in 75% of the hospital-based HIV positive patients in their South African study (Modi *et al.,* 2007). It is also the most common cause of pain in AIDS patients (Frich & Borgbjerg, 2000). It is often associated with the use of neurotoxic antiretroviral medication such as didanosine, studavine and pyridoxine (Newshan *et al*., 2002, Nicholas *et al*., 2002), although no connotation between antiretroviral therapy and the occurrence of pain was observed by Frich and Borgbjerg (2000) in their study.

Regardless of the underlying etiology of neuropathy, persons with neuropathy experience decreases in physical activity and mobility, fatigue, poor sleep, depression, anxiety, interference in daily activity and a lower QOL (Ownby & Dune, *2007*).

Frich and Borgbjerg (2000) conducted a study to determine the prevalence, incidence and characteristics of pain connected to AIDS. HIV+ patients (n=95) were enrolled in a prospective longitudinal study and interviewed every six months during a two-year period, or until death. The overall incidence of pain was 88% and 69% of the patients suffered constant pain interfering with daily living to a degree described moderate to severe. The most common pain locations were: extremities (32%), head (24%), upper gastrointestinal tract (23%) and lower gastro intestinal tract (22%). Pain conditions were connected to various opportunistic infections, Karposi`s sarcoma or lymphoma. Pain in the extremities was predominantly of neuropathic origin (21%). The survival rate for patients without pain at entry was significantly higher than the survival rate of patients in pain. Patients reported that they feel that physicians did not take pain seriously (Frich & Borgbjerg, 2000).

In a qualitative study by Ownby and Dune (2007), the processes by which HIV patients manage peripheral neuropathy were investigated. This study revealed that most HIV patients are unaware of the effect that the virus and ART have on the peripheral

nervous system. At first they find the pain different to the pain they were used to and often do not link it to HIV. Some see it as a punishment. Peripheral pain were described as "…*like someone shocking me*", "*nagging pain*", "*pain deep to the bone*", "*unbearable*" and "*stepping on glass*" (Ownby & Dune, 2007:52). This study further revealed that over time, the naturopathic pain becomes more of a secondary problem and the participants felt more frustration over physical limitations than the pain itself. The value of the acceptance of pain can help predict well-being in patients suffering from chronic pain. It seems that coping strategies, like exercise, play a more significant role when the patient accepted pain as being part of the disease. The biokineticist prescribing exercise programs to HIV patients must take the patients' acceptance of his pain in consideration, as this might predict adherence to and success of the program.

Individuals with persistent pain are known to be at heightened risk for posttraumatic stress disorder (PTSD). This is an anxiety disorder that manifests itself following exposure to a traumatic event (Smith *et al*., 2002). PTSD predicted increased pain intensity and interference ratings in a study by Smith *et al*. (2002) on the impact of PTSD on pain experience in persons with HIV/AIDS. They suggested that treatment of PTSD might lower the severity and impact of pain in HIV patients.

A rather unexpected source of pain amongst HIV patients with lipodystrophy was reported by Reynolds *et al.* (2006). Peripheral wasting resulted in focal fat loss and caused pain with prolonged sitting. Some HIV patients interviewed in this study carry along a cushion to sit on to prevent pain (Reynolds *et al*., 2006).

2.7 HIV and absenteeism

Absenteeism makes the largest contribution to HIV related costs (Figure 2.12) (Whiteside & Sunter, 2000)

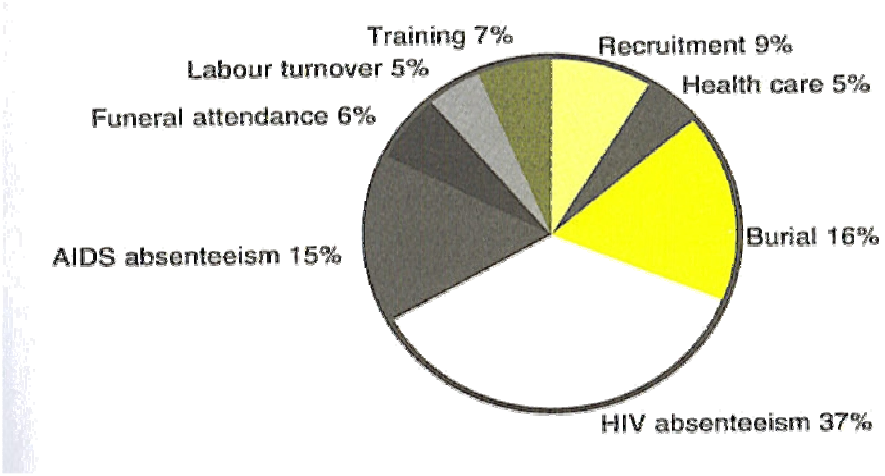

Figure 2.12 : Distribution of increased labour costs due to HIV/AIDS (Whiteside & Sunter, 2000: 13)

In an early study by Leigh *et al.* (1997) AIDS patients reported 3 to 4 times more absence than the HIV-negative group, while HIV positive employees without AIDS, had absence rates within the range for the national average. The HIV positive group with AIDS will be forced to leave their jobs earlier than persons without HIV infection (Leigh *et al.,* 1997). In a more recent study by Coetzee (2006) it is confirmed that absenteeism increased as a result of HIV/AIDS.

HIV may lead to a reduced ability to work in infected patients, which is an additional cost to society beyond that of health care resources (Sendri *et al*., 2004). Symptomatic HIV patients are less likely to be employed, according to a study by Cunningham *et al*. (1998). Simbayi *et al.* (2007) reported that one in five persons in their study on internalised stigma and discrimination among HIV positive persons in Cape Town had lost a place to stay or a job because of their HIV status.

Pelletier *et al.* (2004) researched changes in health risk and work productivity over time. They concluded that individuals, who reduced one health risk, improved their presenteeism by 9%. It can be assumed that if a HIV positive employee follow an exercise program and reduces his health risks, absenteeism might decrease.

International research on the impact of AIDS on firms tends to draw a distinction between direct and indirect costs. Absenteeism, sick-leave, funerals and in-firm medical costs count as direct costs, while broader economic underdevelopment due to AIDS contributes to indirect costs (Nattrass, 2004).

The most obvious impact of HIV/AIDS on the business environment is its effect on the labour force (Deloitte & Touche, 2002). A particularly pertinent aspect is that infection levels are very high among young, economically active persons (Aids Epidemic Update World Health Organization UNAIDS, 2008).

CHAPTER 3

EXERCISE: EFFECTS ON HEALTH-RELATED QUALITY OF LIFE

3.1 Exercise and health-related quality of life

Unfortunately, the natural desire and compulsion for movement waste away with many adults (Barteck, 1999). Exercise and physical activity are two interrelated and synonymously used terms, but they are also terms with particular characteristics. Physical activity is defined as body movements caused by the activation of skeletal muscles with the resulting increase in energy expenditure. Exercise is defined as physical activity that is planned, structured and repetitive (Ramirez-Marrero *et al.,* 2004).

Both physical activity and exercise have been positively related to physical fitness. Good levels of physical fitness contribute to health and well-being by improving the ability to perform daily activities with vigour, reducing levels of fatigue and providing extra energy (Czerny, 2005).

The minimum daily recommendation for a healthy lifestyle is 30 minutes of at least moderate intensity physical activity daily, as suggested by the U.S Department of Health and Human Services (Aldana *et al.,* 2005).

HIV is associated with lower quality of life. Factors contributing to decrease QOL include activity limitations due to fatigue, changes in body composition, pain, depression, anxiety and nausea. Exercise is one possible management strategy for addressing these issues (O`Brien *et al.,* 2004).

The positive effects of exercise on health related QOL have been well described in the literature, as mentioned in the previous paragraphs. Glass *et al.* (2004) took a different approach when they investigated the effect of brief exercise cessation on several QOL parameters in healthy individuals.

They hypothesized that exposure to “stressors” such as infections and trauma, may lead to symptom expression (pain, fatigue and other somatic symptoms) in healthy individuals who are genetically predisposed to chronic multi symptom illness. Their findings supported the hypothesis that some individuals would develop symptoms following one week of exercise cessation. This study further stresses the importance of exercise to improve health related QOL by preventing symptom expression (Glass *et al.,* 2004).

3.2 Immune system explained

Because the human immunodeficiency virus attacks the immune system of the infected person, this study gives a thorough overview on how the immune system works. The effect of exercise on the immune system will also be discussed.

An infection is a condition caused by the presence of some kind of disease-causing agent. Such agents are termed pathogens, and they include viruses and micro-organisms such as bacteria, fungi and protozoans as well as other parasitic forms of life. The human body is equipped with a variety of defense mechanisms that help to prevent the entrance of pathogens or act to destroy them if they enter the tissues (Hole, 1987).

An immune system is a collection of mechanisms within an organism that protects against disease by identifying and killing pathogens and tumor cells. It detects a wide variety of agents, from viruses to parasitic worms, and needs to distinguish them from the organism's own healthy cells and tissues in order to function properly. Detection is complicated as pathogens adapt and evolve new ways to successfully infect the host organism (Beck & Habicht, 1996). To survive this challenge, several mechanisms evolved that recognize and neutralize pathogens. Even simple unicellular organisms such as bacteria possess enzyme systems that protect against viral infections. The

basic immune mechanisms include antimicrobial peptides called defensins, phagocytosis, and the complement system.

The immune systems of vertebrates such as humans consist of many types of proteins, cells, organs, and tissues, which interact in an elaborate and dynamic network. As part of this more complex immune response, the vertebrate system adapts over time to recognize particular pathogens more efficiently. The adaptation process creates immunological memories and allows even more effective protection during future encounters with these pathogens. This process of acquired immunity is the basis of vaccination (www.niaid.nih.gov/publications/immune).

Disorders in the immune system can cause disease. Immunodeficiency diseases occur when the immune system is less active than normal, resulting in recurring and life-threatening infections. Immunodeficiency can either be the result of a genetic disease, such as severe combined immunodeficiency, or be produced by pharmaceuticals or an infection, such as the acquired immune deficiency syndrome (AIDS) that is caused by the retrovirus HIV. In contrast, autoimmune diseases result from a hyperactive immune system attacking normal tissues as if they were foreign organisms. Common autoimmune diseases include rheumatoid arthritis, diabetes mellitus type 1 and lupus erythematosus. These critical roles of immunology in health and disease are areas of intense scientific study (Rosen *et al.,* 1995).

3.2.1 Layered defense in immunity

The immune system protects organisms from infection with layered defenses of increasing specificity. Most simply, physical barriers prevent pathogens such as bacteria and viruses from entering the organism. If a pathogen breaches these barriers, the innate immune system provides an immediate, but non-specific response. Innate immune systems are found in all plants and animals (Litman *et al.,* 2005).

However, if pathogens successfully evade the innate response, vertebrates possess a third layer of protection, the adaptive immune system, which is activated by the innate response. Here, the immune system adapts its response during an infection to improve its recognition of the pathogen. This improved response is then retained after the pathogen has been eliminated, in the form of an immunological memory, and allows the adaptive immune system to mount faster and stronger attacks each time this pathogen is encountered (Mayer, 2006)

Table 3.1 : Components of the immune system (www.immuno.path.cam.ac.uk)**.**

Components of the immune system	
Innate immune system	**Adaptive immune system**
Response is non-specific	Pathogen and antigen specific response
Exposure leads to immediate maximal response	Lag time between exposure and maximal response
Cell-mediated and humoral components	Cell-mediated and humoral components
No immunological memory	Exposure leads to immunological memory
Found in nearly all forms of life	Found only in jawed vertebrates

Both innate and adaptive immunity depend on the ability of the immune system to distinguish between self and non-self molecules. In immunology, self molecules are those components of an organism's body that can be distinguished from foreign

substances by the immune system (Smith, 1997). Conversely, non-self molecules are those recognized as foreign molecules. One class of non-self molecules is called antigens and is defined as substances that bind to specific immune receptors and elicit an immune response (Alberts *et al.,* 2002).

3.2.2 Surface barriers

Several barriers protect organisms from infection, including mechanical, chemical and biological barriers. The waxy cuticle of many leaves, the exoskeleton of insects, the shells and membranes of externally deposited eggs, and skin are examples of the mechanical barriers that are the first line of defense against infection (Smith, 1997).

However, as organisms cannot be completely sealed against their environments, other systems act to protect body openings such as the lungs, intestines, and the genitourinary tract. In the lungs, coughing and sneezing mechanically eject pathogens and other irritants from the respiratory tract. The flushing action of tears and urine also mechanically expels pathogens, while mucus secreted by the respiratory and gastrointestinal tract serves to trap and entangle microorganisms (Boyton & Openshaw, 1997).

Chemical barriers also protect against infection. The skin and respiratory tract secrete antimicrobial peptides such as the β-defensins (Agerberth & Gudmundsson, 2006). Enzymes such as lysozyme and phospholipase A2 in saliva, tears, and breast milk are also antibacterials (Hankiewicz & Swierczek 1974; Moreau *et al.*, 2001). Vaginal secretions serve as a chemical barrier following menarche, when they become slightly acidic, while semen contains defensins and zinc to kill pathogens (Fair *et al.*, 1976; Yenugu *et al.,* 2003). In the stomach, gastric acid and proteases serve as powerful chemical defenses against ingested pathogens.

Within the genitourinary and gastrointestinal tracts, commensal flora serve as biological barriers by competing with pathogenic bacteria for food and space and, in some cases,

by changing the conditions in their environment, such as pH or available iron (Gorbach, 1990). This reduces the probability that pathogens will be able to reach sufficient numbers to cause illness. However, since most antibiotics non-specifically target bacteria and do not affect fungi, oral antibiotics can lead to an "overgrowth" of fungi and cause conditions such as a vaginal candidiasis (yeast infection) (Hill & Embil, 1986). There is good evidence that re-introduction of probiotic flora, such as pure cultures of the lactobacilli normally found in yoghurt, helps restore a healthy balance of microbial populations in intestinal infections in children and encouraging preliminary data in studies on bacterial gastroenteritis, inflammatory bowel diseases, urinary tract infection and post-surgical infections (Reid *et al.*, 2003; Salimen *et al.,* 2005).

3.2.3 Innate immunity

Microorganisms that successfully enter an organism will encounter the cells and mechanisms of the innate immune system. The innate response is usually triggered when microbes are identified by pattern recognition receptors, which recognize components that are conserved among broad groups of microorganisms (Medzhitov, 2007). Innate immune defenses are non-specific, meaning these systems respond to pathogens in a generic way (Alberts *et al.,* 2002). This system does not confer long-lasting immunity against a pathogen. The innate immune system is the dominant system of host defense in most organisms (Litman et *al.,* 2005).

3.2.4 Humoral and chemical barriers

3.2.4.1 Inflammation

Inflammation is one of the first responses of the immune system to infection (Kawai & Akira, 2006). The symptoms of inflammation are redness and swelling, which are caused by increased blood flow into a tissue. Inflammation is produced by eicosanoids and cytokines, which are released by injured or infected cells. Eicosanoids include prostaglandins that produce fever and the dilation of blood vessels associated with

inflammation, and leukotrienes that attract leukocytes (Miller, 2006; Ogawa & Calhoun, 2006). Common cytokines include interleukins that are responsible for communication between white blood cells; chemokines that promote chemotaxis; and interferons that have anti-viral effects, such as shutting down protein synthesis in the host cell (Le *et al.,* 2004). Growth factors and cytotoxic factors may also be released. These cytokines and other chemicals recruit immune cells to the site of infection and promote healing of any damaged tissue following the removal of pathogens (Martin & Leibovich, 2005).

3.2.4.2 Complement system

The complement system is a biochemical cascade that attacks the surfaces of foreign cells. It contains over 20 different proteins and is named for its ability to “complement” the killing of pathogens by antibodies. Complement is the major humoral component of the innate immune response (Rus *et al*., 2005).

In humans, this response is activated by complement binding to antibodies that have attached to these microbes or the binding of complement proteins to carbohydrates on the surfaces of microbes. This recognition signal triggers a rapid killing response (Liszweski *et al*., 1996). The speed of the response is a result of signal amplification that occurs following sequential proteolytic activation of complement molecules, which are also proteases. After complement proteins initially bind to the microbe, they activate their protease activity, which in turn activates other complement proteases, and so on. This produces a catalytic cascade that amplifies the initial signal by controlled positive feedback (Sim & Tsifstoglou, 2004).The cascade results in the production of peptides that attract immune cells, increase vascular permeability, and opsonize (coat) the surface of a pathogen, marking it for destruction. This deposition of complement can also kill cells directly by disrupting their plasma membrane (Rus, *et al*, 2005).

3.2.4.3 Cellular barriers of the innate system

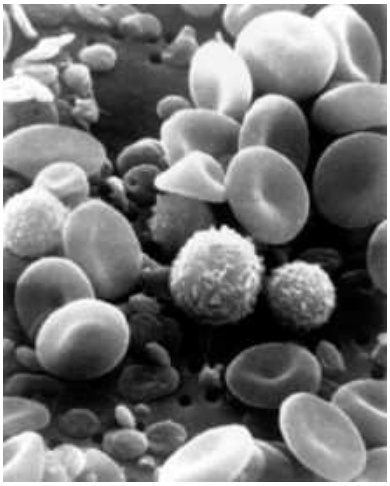

Figure 3.1: ***A scanning electron microscope image of normal circulating human blood. One can see red blood cells, several knobby white blood cells including lymphocytes, a monocyte, a neutrophil, and many small disc-shaped platelets*** *(*Hole, 1987: 623*).*

Leukocytes (white blood cells) act like independent, single-celled organisms and are the second arm of the innate immune system (Alberts *et al.,* 2002). The innate leukocytes include the phagocytes (macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells. These cells identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms. Innate cells are also important mediators in the activation of the adaptive immune system (Pancer & Cooper, 2006).

Phagocytosis is an important feature of cellular innate immunity performed by cells called 'phagocytes' that engulf pathogens or particles. Phagocytes generally patrol the body searching for pathogens, but can be called to specific locations by cytokines (Alberts *et al*., 2002). Once a pathogen has been engulfed by a phagocyte, it becomes trapped in an intracellular vesicle called a phagosome, which subsequently fuses with another vesicle called a lysosome to form a phagolysosome. The pathogen is killed by

the activity of digestive enzymes or following a respiratory burst that releases free radicals into the phagolysosome (Ryter, 1985; Langermans *et al.,* 1994*).* Phagocytosis evolved as a means of acquiring nutrients, but this role was extended in phagocytes to include engulfment of pathogens as a defense mechanism (May & Machesky, 2001).

Neutrophils and macrophages are phagocytes that travel throughout the body in pursuit of invading pathogens (Zen & Parkos, 2003). Neutrophils are normally found in the bloodstream and are the most abundant type of phagocyte, normally representing 50% to 60% of the total circulating leukocytes. During the acute phase of inflammation, particularly as a result of bacterial infection, neutrophils migrate toward the site of inflammation in a process called chemotaxis, and are usually the first cells to arrive at the scene of infection. Macrophages are versatile cells that reside within tissues and produce a wide array of chemicals including enzymes, complement proteins, and regulatory factors such as interleukin 1 (Hole, 1987). Macrophages also act as scavengers, ridding the body of worn-out cells and other debris, and as antigen-presenting cells that activate the adaptive immune system (Mayer, 2006).

Dendritic cells are phagocytes in tissues that are in contact with the external environment; therefore, they are located mainly in the skin, nose, lungs, stomach, and intestines. They are named for their resemblance to neuronal dendrites, as both have many spine-like projections, but dendritic cells are in no way connected to the nervous system. Dendritic cells serve as a link between the innate and adaptive immune systems, as they present antigen to T cells, one of the key cell types of the adaptive immune system (Guermonprez *et al*., 2002).

Mast cells reside in connective tissues and mucous membranes, and regulate the inflammatory response (Krishnaswamy *et al.,* 2006). They are most often associated with allergy and anaphylaxis. Basophils and eosinophils are related to neutrophils. They secrete chemical mediators that are involved in defending against parasites and play a role in allergic reactions, such as asthma (Kariyawasam & Robinson, 2006). Natural

killer (NK cells) cells are leukocytes that attack and destroy tumor cells, or cells that have been infected by viruses (Middelton *et al.,* 2002).

3.2.4.4 Lymphocytes

The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are the major types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow (Liszweski *et al.,* 1996). B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response. The CD4 cells (T cells) are the prime target of HIV.

Both B cells and T cells carry receptor molecules that recognize specific targets. T cells recognize a “non-self” target, such as a pathogen, only after antigens (small fragments of the pathogen) have been processed and presented in combination with a “self” receptor called a major histocompatibility complex (MHC) molecule. There are two major subtypes of T cells: the killer T cell and the helper T cell. Killer T cells only recognize antigens coupled to Class I MHC molecules, while helper T cells only recognize antigens coupled to Class II MHC molecules. These two mechanisms of antigen presentation reflect the different roles of the two types of T cell. A third, minor subtype is the γδ (gamma/delta) T cells that recognize intact antigens that are not bound to MHC receptors (Holtmeier & Kabelitz, 2005).

In contrast, the B cell antigen-specific receptor is an antibody molecule on the B cell surface, and recognizes whole pathogens without any need for antigen processing. Each lineage of B cell expresses a different antibody, so the complete set of B cell antigen receptors represent all the antibodies that the body can manufacture (Hole, 1987).

3.2.4.5 Killer T cells

Killer T cells directly attack other cells carrying foreign or abnormal antigens on their surfaces (NAIAD). Killer T cell are a sub-group of T cells that kill cells infected with viruses (and other pathogens), or are otherwise damaged or dysfunctional. As with B cells, each type of T cell recognizes a different antigen. Killer T cells are activated when their T cell receptor (TCR) binds to this specific antigen in a complex with the MHC Class I receptor of another cell. Recognition of this MHC: antigen complex is aided by a co-receptor on the T cell, called CD8. The T cell then travels throughout the body in search of cells where the MHC I receptors bear this antigen. When an activated T cell contacts such cells, it releases cytotoxins, such as perforin, which form pores in the target cell's plasma membrane, allowing ions, water and toxins to enter. The entry of another toxin called granulysin (a protease) induces the target cell to undergo apoptosis (Radoja *et al.,* 2006). T cell killing of host cells is particularly important in preventing the replication of viruses. T cell activation is tightly controlled and generally requires a very strong MHC/antigen activation signal, or additional activation signals provided by "helper" T cells (Radoja *et al.,* 2006).

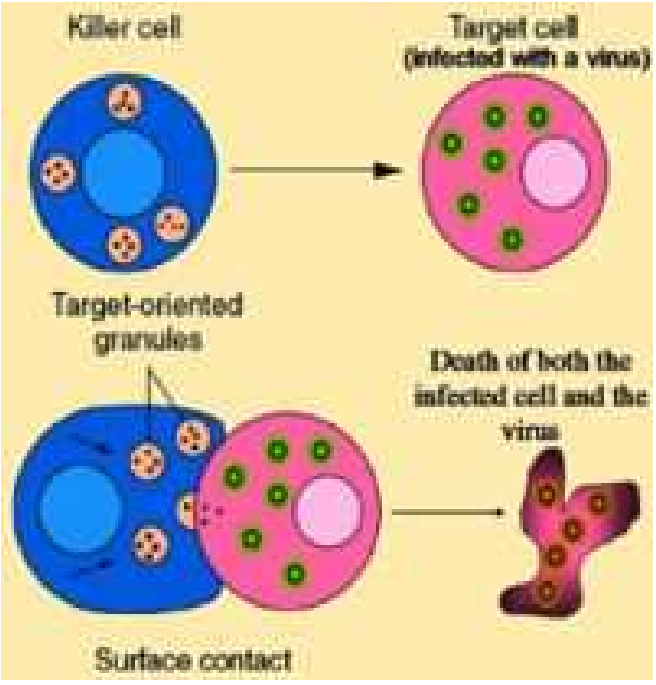

Figure 3.2 : Killer T cells attacking other cells (Harty *et al.,* 2000).

3.2.4.6 Helper T cells

Function of T helper cells: Antigen presenting cells (APCs) present antigen on their Class II MHC molecules (MHC2). Helper T cells recognize these, with the help of their expression of CD4 co-receptor (CD4+). The activation of a resting helper T cell causes it to release cytokines and other stimulatory signals that stimulate the activity of macrophages, killer T cells and B cells, the latter producing antibodies. The stimulation of B cells and macrophages succeeds a proliferation of T helper cells (Abbas *et al.,* 1996).

Helper T cells regulate both the innate and adaptive immune responses and help determine which types of immune responses the body will make to a particular pathogen. These cells have no cytotoxic activity and do not kill infected cells or clear pathogens directly. They instead control the immune response by directing other cells to perform these tasks (McHeyzer-Williams *et al.,* 2006).

Helper T cells express T cell receptors (TCR) that recognize antigen bound to Class II MHC molecules. The MHC: antigen complex is also recognized by the helper cell's CD4 co-receptor, which recruits molecules inside the T cell that are responsible for T cell's activation. Helper T cells have a weaker association with the MHC:antigen complex than observed for killer T cells, meaning many receptors (around 200–300) on the helper T cell must be bound by an MHC:antigen in order to activate the helper cell, while killer T cells can be activated by engagement of a single MHC:antigen molecule. Helper T cell activation also requires longer duration of engagement with an antigen-presenting cell (Kovacs *et al.,* 2002).

The activation of a resting helper T cell causes it to release cytokines that influence the activity of many cell types. Cytokine signals produced by helper T cells enhance the microbicidal function of macrophages and the activity of killer T cells. In addition, helper T cell activation causes an upregulation of molecules expressed on the T cell's surface,

such as CD40 ligand (also called CD154), which provide extra stimulatory signals typically required to activate antibody-producing B cells (Grewal & Flavell, 1998).

3.2.4.7 T cells

γδ T cells possess an alternative T cell receptor (TCR) as opposed to CD4+ and CD8+ (αβ) T cells and share the characteristics of helper T cells, cytotoxic T cells and NK cells. The conditions that produce responses from γδ T cells are not fully understood. Like other 'unconventional' T cell subsets bearing invariant TCRs, such as CD1d-restricted Natural Killer T cells, γδ T cells straddle the border between innate and adaptive immunity (Grewal & Flavell, 1998). On one hand, γδ T cells are a component of adaptive immunity as they rearrange TCR genes to produce receptor diversity and can also develop a memory phenotype. On the other hand, the various subsets are also part of the innate immune system, as restricted TCR or NK receptors may be used as pattern recognition receptors. For example, large numbers of human Vγ9/Vδ2 T cells respond within hours to common molecules produced by microbes, and highly restricted Vδ1+ T cells in epithelia will respond to stressed epithelial cells (Holtmeier & Kabelitz, 2005).

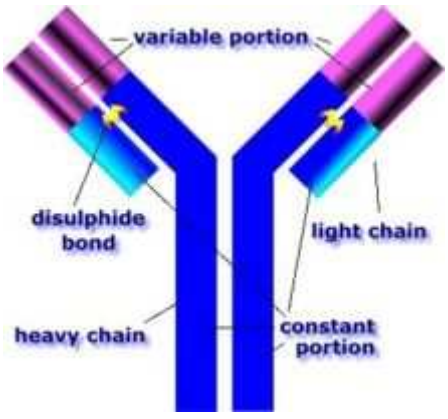

Figure 3.3: An antibody is made up of two heavy chains and two light chains. The unique variable region allows an antibody to recognize its matching antigen (www.niaid.nih.gov/factsheets/howhiv.htm).

3.2.4.8 Immunological memory

When B cells and T cells are activated and begin to replicate, some of their offspring will become long-lived memory cells. Throughout the lifetime of an animal, these memory cells will remember each specific pathogen encountered and can mount a strong response if the pathogen is detected again. This is "adaptive" because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen and prepares the immune system for future challenges. Immunological memory can either be in the form of passive short-term memory or active long-term memory (Keller & Stiehm, 2000).

3.2.4.9 Passive memory

Newborn infants have no prior exposure to microbes and are particularly vulnerable to infection. Several layers of passive protection are provided by the mother. During pregnancy, a particular type of antibody, called IgG, is transported from mother to baby directly across the placenta, so human babies have high levels of antibodies even at birth, with the same range of antigen specificities as their mother (Saji *et al.,* 1999). This is passive immunity because the fetus does not actually make any memory cells or antibodies, it only borrows them. This passive immunity is usually short-term, lasting from a few days up to several months. In medicine, protective passive immunity can also be transferred artificially from one individual to another via antibody-rich serum (Keller & Stiehm, 2000).

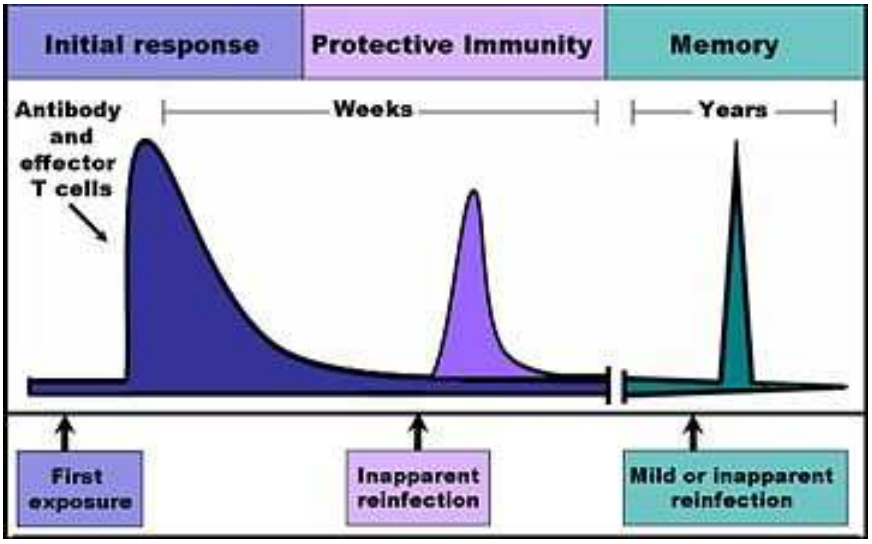

Figure 3.4: The time-course of an immune response begins with the initial pathogen encounter, (or initial vaccination) and leads to the formation and maintenance of active immunological memory (www.niaid.nih.gov/factsheets/howhiv.htm).

3.2.5 Disorders of human immunity

The immune system is a remarkably effective structure that incorporates specificity, inducibility and adaptation. Failures of host defense do occur, however, and fall into three broad categories: immunodeficiencies, autoimmunity, and hypersensitivities.

3.2.5.1 Immunodeficiencies

Immunodeficiencies occur when one or more of the components of the immune system are inactive. The ability of the immune system to respond to pathogens is diminished in both the young and the elderly, with immune responses beginning to decline at around 50 years of age due to immunosenescence (Aw *et al.,* 2007). In developed countries, obesity, alcoholism, and drug use are common causes of poor immune function. However, malnutrition is the most common cause of immunodeficiency in developing countries (Chandra, 1997).

Diets lacking sufficient protein are associated with impaired cell-mediated immunity, complement activity, phagocyte function, IgA antibody concentrations, and cytokine production. Deficiency of single nutrients such as iron; copper; zinc; selenium; vitamins A, C, E, and B_6; and folic acid (vitamin B_9) also reduces immune responses (Chandra, 1997). Additionally, the loss of the thymus at an early age through genetic mutation or surgical removal results in severe immunodeficiency and a high susceptibility to infection (Chandra, 1997).

Immunodeficiencies can also be inherited or 'acquired' (Alberts *et al.,* 2002). Chronic granulomatous disease, where phagocytes have a reduced ability to destroy pathogens, is an example of an inherited, or congenital, immunodeficiency. AIDS and some types of cancer cause acquired immunodeficiency (Copeland & Heeney, 1996).

3.2.5.2 Autoimmunity

Autoimmunity is the failure of an organism to recognize its own constituent parts (down to the sub-molecular levels) as *self*, which results in an immune response against its own cells and tissues. Any disease that results from such an aberrant immune response is termed an autoimmune disease. Prominent examples include Coeliac disease, diabetes mellitus type 1 , systemic lupus erythematosus (SLE), Sjögren's syndrome, Churg-Strauss Syndrome, multiple sclerosis (MS), Hashimoto's thyroiditis, Graves' disease, idiopathic thrombocytopenic purpura, and rheumatoid arthritis (RA) (Stefano, *et.al., 2002).* The human immunodeficiency virus is not an autoimmune disease.

3.2.5.3 Hypersensitivities

The term hypersensitivity is used to describe immune responses which are damaging rather than helpful to the host. Nearly 40 years ago Gell and Coombs proposed a classification scheme which defined 4 types of hypersensitivity reactions. The first 3 are mediated by antibody, the fourth by T cells (www.immuno.path.cam.ac.uk). HIV is not described as a hypersensitivity disease.

3.3 The effect of exercise on the immune system

The following three markers of immune status are often measured in HIV studies: CD4+, CD16+ (also called natural killer cells) and CD4+/CD8+ ratio (Schneiderman, *et al.,* 1999; Eller, 2001).

Physical activity has been shown to cause disturbances in circulating white blood cell number and function that appear to be dependant on the intensity and duration of the exercise and associated release of stress hormones (Mitchell *et al.*, 2002). The circulating numbers and functional capacities of leukocytes may be decreased by repeated bouts of intense prolonged exercise (Gleeson, 2003). Although there are few empirical studies on overtraining and immune function, it has been postulated that excessive exercise is associated with suppressed immune function (Smith, 2003).

According to Moreira de Araújo and Facio (1997) exercise increases the white blood cell (WBC) count in proportion to the effort. During exercise there is a rise in granolocytes, monocytes, and lymphocytes. Among the lymphocytes subset, NK cells usually increase most during exercise. This increase in WBC is, no doubt, mediated by mechanical effects of increased cardiac output (WBC enter the blood from reserve pools in lung, liver, and especially the spleen) and a surge in blood adrenaline concentration (Moreira de Araujo & Facia, 1997).

However, exercising lymphocytosis is brief and it decreases 5 minutes of ending the exercise and 1 hour late may be below the pre-exercise baseline. It could be correlated with the level of cortisol. Usually after 4 to 6 hours the lymphocyte count is back to the baseline (Lawless *et al.,* 1995).

The function of lymphocytes and NK cells seems to increase during exercise, even when it is a light exercise. It is mediated by releasing of adrenaline and cytokines. However, lymphocyte mitogenesis is blunted in the late stages of exercise, which is influenced by cortisol. The temporary enhancement of NK activity by exercise occurs regardless of the exerciser's sex, age, fitness, or training. Once habituated, the NK

enhancement falls off in response to stress, not to the exercise per se (Eichner & Calabrese, 1994).

Little research was done about the changes in blood levels of immunoglobulins. There are some studies suggesting little increase with moderated exercises and decrease with endurance exercises (Moreira de Araújo & Facio 1997).

Exercising also increase the blood level of PMN cells. There is an increase during exercise and 2 to 4 hours later. The delayed rise in PMN is probably mediated by cortisol, which spurs release from bone marrow and hinders regress from the blood stream. Cytokines released from damaged muscles also contributes to leukocytosis after exercise. Although increased in number, the PMN activity decreases, with a resultant decline in phagocytic defence against infections. Another interesting fact is that strenuous exercising may lead to enough tissue damage to evoke acute phase response. This response can modulate immune response activating complement , releasing TNF , interferons , interleukins, and others cytokines (Eichner & Calabrese, 1994; Lawless *et al.,* 1995).

3.4 HIV and Exercise

In apparently healthy individuals free of HIV infection, moderate-intensity exercise will cause neutrophil proliferation, epinephrine and cortisol secretion, a temporary decline in lymphocite levels and an elevated number of natural killer cells and increased cytokine levels (Bopp *et al*., 2003).

During and immediately after exercise the total number of leukocytes in circulation increases roughly in proportion to the intensity of duration of the exercise performed (Nieman, 1994).

During the post exercise period there is a decline in numbers of circulating lymphocytes and monocytes to below resting levels. If the exercise is particularly heavy or has a long

duration, the fall in lymphocytes may even become evident before the end of the session and may not regain homeostasis for several hours (Plowman & Smith, 1997).

The circulating numbers of neutrophils continue to increase, peaking 2 hours post exercise. This decrease in lymphocytes and monocytes and increase in neutrophils is known as the biphasic response. The lymphocyte count remains low for 3 to 6 hours. Eosinophils also vacate the blood, while basophils are affected only minimally (Nieman, 1994).

Moderate activity increases the number, percentage and activity of NK cells, and the increased activity may persist for 24 hours. Exhaustive exercise on the other hand, causes a reduction in NK cell activity that may continue for several days (Hoffman-Goetz, 1998). This period after severe exercise when a NK cell activity decrease is known as the Open Window Period (Mars, 2003). During this period, microbial agents can establish infection. The open window hypothesis, if true, might mean that it could be dangerous for persons in immunocompromised states to do intense exercise, since there is a risk for opportunistic micro-organisms to establish themselves during this period (Smith, 2003).

Although severe stress is generally thought to be immunosuppressive (Nieman, 1994, Plowman & Smith, 1997; Shore *et al.,* 1999), a study by Mitchell *et al*. (2002) on the effect of exercise, heat and hydration on immune function in a healthy population did not support this hypothesis. In their study ten healthy, moderately trained men participated in a 75-minute bicycle ride at an intensity of 55% of VO_2 max. They were exposed to heat stress as well as dehydration. The numerous responses assessed in this investigation indicated that the combination of exercise and heat exposure produced an additive effect that was indicative of enhanced immune function (Mitchell *et al.,* 2002).

Exercise prescription for the HIV+ population must take into account the possible negative effects on immune system by high intensity aerobic exercise. Higher intensity exercise sessions decrease the effectiveness of the immune system, leading to more

opportunistic infections among HIV-free individuals (Bopp *et al*., 2003). For this reason high-intensity exercise prescription has been avoided in the HIV positive population, and moderate intensity exercise has been most often recommended. Perna *et al.* (1999) found no decline in immunity in HIV patients due to moderate exercise.

O`Brien *et al.* (2004) did a systematic review to examine the effectiveness and safety of aerobic exercise interventions on immunological/virological outcomes in adults living with HIV/AIDS. They concluded that performing constant or interval aerobic exercise, or a combination of constant aerobic and progressive resistive exercise, for at least 20 minutes, at least 4 times per week for 4 weeks, may be beneficial and appears to be safe for adults living with HIV/AIDS (O'Brien *et al.,* 2004).

3.5 Benefits of exercise for HIV+ persons

> "An *intriguing, nonpharmacological treatment for preventing and managing complications of HIV infection is moderate intensity exercise training"* (Dudgeon *et al.,* 2004: 81).

3.5.1 Aerobic exercise

According to Stringer (1999), the desired goals of a regular aerobic exercise program in HIV + patients, include the following:

- Improved aerobic capacity and functional status;
- Improved immune function/indices;
- Maintenance of or improvement of lean body mass; and
- Improvement of quality of life.

Research studies support that exercise and physical activity are not only safe for HIV-positive persons, but also beneficial to their health by improving the body's ability to fight the infection (Mars, 2003). It can benefit HIV-positive individuals by reducing

centralized obesity and peripheral wasting associated with HAART (Ramirez-Marrero *et al.,* 2004).

Exercise also holds several other benefits for HIV patients. Bopp *et al.* (2003) summarised the changes in exercise parameters with varying stages of HIV infection (Table 3.1).The benefits from exercise are clear from the bottom row of the table.

Sedentary lifestyle and physical inactivity has been determined to be a risk factor in the development of a variety of diseases, such as diabetes, coronary heart disease, depression and various types of cancer (Aldana *et al.,* 2005). It can be expected that these diseases also occur in HIV+ patients. Exercise may enhance the immune status by reducing negative affective states and by modulation of levels of endogenous opiates and stress hormones (Ramirez-Marrero *et al*., 2004). Several studies proved that aerobic exercise reduces the risk of these diseases in HIV negative individuals (Dudgeon *et al*., 2004) and presumably HIV positive persons can derive the same benefits (Stringer, 1999).

Table 3.2 : Changes in Exercise Parameters with varying stages of HIV infection (Bopp *et al*., 2003).

Parameter	**Asymptomatic**	**Early Symptomatic**	**AIDS**
Exercise capacity	Decreased	Very decreased	Extremely decreased
Oxygen consumption	Increased in sub maximal workloads	►Very increased - sub maximal workloads. ►Decreased at maximal exercise. ►Decreased at ventilatory threshold.	More severe dysfunction than Stage ll

Effects of exercise training	►CD4 cell count very increased. ►Delayed symptom onset. ►Increased muscle size and strength. ►Decreased symptom severity. ►Decreased % body fat.	►CD4 cell count increased. ►decreased symptom severity. ►Delayed onset of AIDS. ►Improved QOL. ►Decreased viral load. ►Improved mental health.	►Further research needed.

Although the use of ART increases the risk to develop metabolic disease, Mondy *et al.* (2007) concluded in their study on metabolic syndrome in urban HIV infected patients, that traditional risk factors like unhealthy lifestyle play a more significant role in the development of metabolic syndrome than do the use of ART. This finding stresses the role that biokineticists has to play in promoting healthy lifestyle in all population, including the HIV population.

It is well known that in addition to the use of prescribed medications, positive thoughts and emotions can influence immune status and overall health (Van Jaarsveld, 2003). Several traits have been identified in HIV long-term survivors, including (a) having a commitment, meaning or purpose in life; (b) having a sense of social and communal responsibility; and (c) engaging in exercise and physical activities (Ramirez-Marrero *et al.,* 2004). This again emphasise the potential role that exercise can play in the management of HIV.

There is evidence that aerobic exercise is sufficient to increase positive mood state, vigour, energy and positive well-being (Ciccolo *et al.,* 2004). Aerobic overload training also significantly improves a variety of functional capacities related to oxygen transport and use. Because the cardiovascular system and respiratory systems are intimately linked with aerobic processes, related functional changes occurs (McArdle *et al.,* 2001). These functional changes have a direct impact on the daily experience of QOL.

Diminishing VO_2 max in adults with HIV appears to be one mechanism of fatigue and physical disability. Aerobic insufficiency may result in functional limitations placed on performance of daily activities and in physical disability (Cade *et al*., 2004).

Therapeutic exercise has been found to increase functional capacity (and thus VO_2 max) in HIV infected individuals (Bopp *et al.,* 2003). If this relationship exists in an HIV-infected population, increased functional capacity may decrease HIV-related disability and allow for longer independent living.

HIV-positive persons respond physically in the same manner to exercise than other populations (Mars, 2003) and it can therefore be assumed that their QOL will improve similarly.

Several exercise studies reported an increase in CD4 cell counts (LaPerriere *et al.*, 1991; LaPerreire 1994; Perna *et al.,* 1999) while other studies found no difference in CD4 cell count due to exercise (Schneiderman *et al.,* 1999, Terry *et al.* 1999, Dudgeon *et al.,* 2004). The critical exercise variables that determine whether a bout of exercise will cause disturbances in immune function are intensity and duration (Gabriel *et al.,* 1992). In a study by Mitchell *et al*. (2002) healthy persons participated in exercise for 75 minutes at 55% of VO_2 peak. The exercise intensity and duration was found not to be immunosuppressive.

On the other hand, among HIV negative individuals, high-intensity exercise has been shown to produce acute immunosuppressive effects that diminish with subsequent training. Thus, it is possible that even moderate-intensity exercise, of sporadic frequency, exerts a temporary immunosuppressive effect among those who are already immunocompromised (Perna *et al.,* 1999).

It is suggested that single irregular bouts of medium intensity exercise might lead to a drop in CD4 counts, while regular exercise is associated with an improvement in CD4 count (Perna *et al.,* 1999).

Stringer *et al*. (1999) concluded in their study that exercise training resulted in a substantial improvement in aerobic function while immune indices were essentially unchanged. Quality of life markers improved significantly with exercise. Exercise training is safe and effective in this patient group and should be promoted for HIV^+ patients (Stringer, 1999).

Ramirez-Marrero *et al*. (2004) conducted a descriptive study to examine the psychological, behavioural and biophysical characteristics in a group of 68 HIV positive men and women. They also evaluated the differences by gender and level of physical activity on selected psychological and biophysical parameters.

Physical- and leisure time activities, life satisfaction, depression, CD4 counts and body composition characteristics of HIV patients were described in this study. Their findings showed that physical activity is beneficial and not harmful to HIV-positive patients. Further more, they concluded that a sedentary lifestyle in HIV-positive individuals could lead to obesity and its associated health problems. It seemed that this group preferred leisure activities that require little or no physical effort. Without the inclusion of leisure-time physical activities of moderate intensity, the potential cardiovascular, metabolic and physical health benefits of leisure activities are limited (Ramirez- Marrero *et al.,* 2004).

In the literature, HIV is often compared to other chronic and life threatening diseases such as cancer (Cade *et al.,* 2004). The World Health Organization's approach to pain in HIV is based on the assumption of no difference between the care of patients with AIDS and the care of patients with advanced cancer (Frich & Borgbjerg, 2000). Thus, it would be acceptable to borrow from the literature on exercise for cancer patients and apply to HIV patients.

Kirshbaum (2005) mentioned in an article on physical activity for breast cancer patients, that it is important to recognize that some people will be more likely to adhere to an exercise program than others. An individualised approach based on the patients` beliefs

is particularly important. She also mentioned that positive reinforcement of behaviour is most beneficial if given during and after exercise sessions. This can be accomplished by offering encouragement, setting goals that can be attained over a period of time or by incorporating outcome measures that record changes in weight or mood. Patients can also be advised to keep an exercise diary and share their experiences when they come for follow up treatment.

Some commonly identified barriers to exercise for cancer patients are:

- Economic constraints.
- Absence of an exercise partner can hamper long-term adherence.
- Lack of transport.
- Lack of childcare.
- Lack of safe surroundings (Kirshbaum, 2005).

Critical components for intervening with adults based on previous theoretical contributions have been summarised by Marcus *et al*. (1996). These include:

- enhancing the perceived benefits of physical activity;
- enhancing self-efficiency – the degree to which an individual believes he or she can successfully execute a particular behaviour, including promoting confidence;
- increasing intentions to exercise and identifying of barriers;
- increasing enjoyment of physical activity so that it fits in with a person's lifestyle and interests;
- enhancing social support from other patients and family; and
- promoting moderate intensity activity.

3.5.2 Resistance exercise

Progressive resistance exercise and strength training have helped to increase lean body mass and strength in HIV-positive patients (Roubenhof & Wilson, 2001).

3.6 Safety of exercise for the HIV+ population

Exercise is consistently listed among the three most common complementary and alternative therapies utilized by HIV infected persons (Ciccolo *et al*., 2004). No reports that cite any negative effects on immune and disease markers were found. In fact, a growing amount of literature suggest that regular exercise for HIV infected persons is safe and does not significantly change CD4+ cell counts or HIV-RNA copies (Neidig *et al*., 2003).

It appears that the first bout of exercise will not detrimentally affect the immune status of the HIV patients (Mars, 2003). According to the literature it can be assumed that both aerobic and resistance exercise for HIV-positive people is safe and can be used to improve functional status and quality of life (Roubenoff & Wilson, 2001; Ciccolo *et al*., 2004, Engelson *et al.,* 2006).

3.7 Exercise as complementary therapy in the management of HIV disease

3.7.1 Exercise and body composition (see 2.6.1 – already discussed)

3.7.2 Exercise and wasting (see 2.6.6.1 – already discussed)

Although this study looks at the effect of aerobic exercises on QOL in HIV-positive employees, a brief look at resistance exercise will serve to help biokineticists when prescribing exercise programs for this population.

The fundamental unit of muscular performance in humans is the motor unit. A muscle is made up out of numerous motor units, which are composed of muscle fibres (Baechle & Earle, 2000). Increases in force output are achieved by recruiting additional motor units. When exercised regularly, the muscle fibres adapts to the exercise stimulus. Adaptations to resistance training are specific to the type of exercise performed. In order to improve wasting, muscle hypertrophy will be the goal of a resistance exercise

program. The exercise prescription for muscle hypertrophy are three to six sets of 6 to 12 repetitions with 67% -85% of a persons 1 RM (Baechle & Earle, 2000).

Formal exercise programs involving resistance training provide benefits to individuals with HIV/AIDS, such as preservation of muscle mass and muscle strength (Bopp *et al.,* 2004). According to this, it seems that hypertrophy-training prescription will suit HIV patients' need of preserving muscle mass. Muscle strength will still be preserved and even developed by a hypertrophy prescription (Barteck, 1999). Exercise is closely linked to body image (O`Brien *et al.*, 2004).

Roubenhoff and Wilson (2001) found a significant improvement in function in wasted subjects. In their study, 6 men with wasting and 19 men and women with HIV, but no wasting, were recruited. Both groups followed a progressive resistance-training program for 8 weeks, 3 times per week. They focused on the large muscle groups and included the following machines: double leg press, leg extension, seated chest press and seated row. Participants trained at 50% of their 1 repetition maximum (1-RM) for the first session, at 60% for the second session and at 75%-80% of their 1-RM for the remainder of the sessions. Three sets of eight repetitions were done. After this 8-week period, participants went back to their usual activity phase and were invited to be evaluated after another 8 weeks. The results showed a significant improvement in function in the wasted group. This functional improvement was linked to an improvement in strength, and not with an improvement in lean body mass. According to Roubenhoff & Wilson (2001), the goal of treatment in wasting has traditionally been to normalize lean body mass, with the assumption that normalization of structure will lead to normalization of function. Experience with strength training, however, has shown that strength gains are far greater than increases in lean body mass.

Exercise was the most frequently used strategy to attempt body change, as reported by Reynolds *et al*. (2006). Patients reported doing sit ups as an attempt to flatten stomachs and resistance exercises to counter act peripheral muscle wasting. It is not clear from this study if exercise actually made a difference to disfigured bodies. Participants also

described frustrating attempts to get their medical providers to listen and respond to their body-change symptoms (Reynolds *et al.*, 2006). Biokineticists, as members of the medical provider chain, are in a good position to address fears, pain and frustration regarding changing body composition, as they are familiar with anthropometry. They can play a role in prescribing exercise programs and monitor body changes.

It is important to keep in mind that physical functioning is not the only indicator of QOL in HIV patients. As mentioned earlier, Corless *et al.* (2004) found a relationship between body image and QOL, especially in men. A wasted body leads to a lower body image and to lower QOL.

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While there are no negative reports on the effect of resistance training for HIV patients (Mars, 2003), progressive resistance exercise programs can safely be prescribed to HIV patients as a means to improve lean body mass and improve physical functioning. Biokineticists are well equipped to prescribe these programs in a safe manner.

3.7.3 Exercise, obesity and lipodystrophy

The goals of weight loss in obese persons include maintaining skeletal muscle and other lean tissues, while losing mainly fat mass. This is accomplished by restricting energy intake and increasing energy expenditure, because the central reason for obesity is an excess of energy intake relative to energy expenditure (Sarsan *et al.,* 2006).

Many of the health risks of obesity are related to fat distribution rather than fat content (Engelson *et al.,* 2006) Further more, weight loss has been effective in promoting both improved lipid profile and increased insulin sensitivity. By following an exercise program including resistance exercise for the main muscle groups, muscle mass is preserved, which has a positive effect on metabolism (Williams, 1995).

Engelson *et al.* (2006) hypothesized that in obese HIV-positive women, significant weight loss could be achieved and that proportion of visceral fat to subcutaneous fat loss would be related to the baseline as well as the quantity of total weight loss. They evaluated the effects of diet and exercise on glucose metabolism by frequently sampled intravenous glucose tolerance tests, and hypothesized that irrespective of ART, the decrease in fat mass and fat distribution would correlate with improvements in insulin resistance and fasting lipids (Engelson *et al.,* 2006). Participants in their study exercised for 90 minutes under supervision, three times per week. Aerobic exercise consisted of treadmill walking at an intensity of 70% to 80% of estimated maximal heart rate, for thirty minutes. Resistance training was done on a multigym apparatus and focused on seven major muscle groups. Three sets of 8 to 10 repetitions each were done.

The findings in the above mentioned study partly supported the hypothesis. Significant changes in body composition, weight, strength and fitness through diet and exercise have been achieved. However, there was a lack of improved insulin sensitivity and other surrogate markers for cardiovascular risk (lipids) in HIV infected women, despite fat loss. This means that the effect of lifestyle changes in HIV positive persons may be reduced if compared with non-HIV conditions. Driscoll *et al.* (2004) reported that combination therapy, consisting of exercise and a pharmacological agent (metformin) was more effective in increasing insulin sensitivity than metformin alone.

In a more recent study, Robinson *et al.* (2007) reported similar findings. After a sixteen week exercise intervention programme that consisted of aerobic and resistance training, the participants had an improvement in aerobic capacity and strength and a decrease in trunk fat mass, but no significant decreases in triglycerides and insulin sensitivity.

Desired body weight and fat loss can be promoted safely through restricting energy intake and an exercise program in HIV infected women. It holds significant positive effects on self-reported fitness and quality of life, especially a reduction in perceived limitation in ability to work, improved vitality and life satisfaction (Engelson *et al.,* 2006).

From a biokinetic perspective, it is important to bear in mind that HIV positive patients may also be obese. The same basic principals of weight loss that will be applied to non-HIV populations can safely be applied to obese HIV patients. Patients must be informed that they might not experience the same metabolic benefits from exercise as their healthy counterparts and regular visits to their physician or clinic, as well as pharmacological treatment must be promoted.

According to Kosmiski *et al*. (2007) there is evidence that resting metabolic expenditure (REE) is increased in many if not most patients with HIV lipodystrophy. This is supported by Mars (2003), who mentioned that REE is increased by about 10% in weight stable HIV positive men without active opportunistic disease and may be further raised by illness or treatment. This leads to hypometabolism.

In Kosmiski`s study short-term energy restriction caused a rapid and significant fall in REE. Energy restriction was accomplished by limited dietary intake. This study supports the notion that energy expenditure and REE may be uniquely coupled in lipodystrophy syndrome (Kosmiski *et al.,* 2007). When exercising, the metabolic rate increases. This is also known as the thermic effect of exercise (TEE) (Williams, 1995). This may lead to the question if exercise may be a disadvantage to the HIV patient with lipodystrophy who already has a raised REE. No studies exploring this question were found. However, Mars (2003) mentioned that the maintenance of adequate nutrition should be taken into account when considering adding exercise to the treatment regimen. In cases where the patient suffers from nausea, anorexia or oral infection, it may be a problem to maintain adequate energy intake (Mars, 2003).

Although it can be expected that exercise will improve metabolism in HIV patients and thus might lead to greater losses in fat mass , the broader spectrum of benefits derived from exercise will most properly outshine the possible negative impact of increased metabolic rate.

There is no proof that lipodystrophy is completely reversible (Kosmiski *et al*., 2007). Physical training has been reported to improve central obesity, but exercise will not help for lipoatrophy of the face. Physicians are exploring the possibility of facial implants (Martinez *et al*., 2001), but in South Africa, as a developing country, this will not be an option for to the broader population.

3.7.4 Exercise, depression and anxiety

Exercise has been shown to be a useful treatment for anxiety and depression for a wide range of chronic disease populations (Elliot *et al.,* 2002). Already in 1976, Thaddeus Kostrubala documented the improvements that occurred with patients suffering from depression when they exercised for a significant period of time (McPhail, 2006).

The effect of exercise as a treatment for depression was compared to the use of medication in a study by Blumenthal *et al.* (1999). The conclusion was that the patients that used exercise as treatment did as well as those who used medication during an intervention of four months. Furthermore, the exercise group had better long-term reductions in depression symptoms than those who used medication. As depression is one of the most common symptoms reported by HIV patients, these findings may be useful in the treatment of depression in the HIV population, and support the involvement of biokineticists in HIV care.

The study by McPhail (2006) is consistent with the findings of a study by Christmas and Anderson (2000) that concluded that aerobic exercise is superior to placebo or to no treatment in depressive patients. According to Brenes *et al.* (2007), both psychological mechanisms (increased self-efficacy, reduced negative patterns) and biological mechanisms (alterations in central norepinephrine activity, reduced activity of HPA axis, increased secretion of beta endorphins) may be responsible for the favourable effect of exercise on mood.

HIV infected individuals respond physically to exercise in a similar manner as those from other populations and it can be accepted that they will experience the same benefits from exercise (Ciccolo *et al*., 2004). Aerobic exercise is one of the most frequently reported alternative and complementary activities utilized by HIV-infected individuals (Neidig *et al.,* 2003).

Neidig *et al*. (2003) studied the efficacy of aerobic exercise training for the management of depressive symptoms experienced by adults living with HIV infection. They enrolled 60 HIV infected adults into a 12-week study. Participants were required to attend three supervised 1-hour training sessions per week. Trained exercise leaders coached them to exercise for a minimum of 30 minutes at an intensity of 60%-80% of maximum oxygen uptake (VO_2 max) Participants chose an aerobic exercise modality from among treadmill, stationary bicycle and walking. VO_2 max was determined on a treadmill according to the guidelines of the American College of Sports Medicine (2000) standards.

At study entry 20% to 35% of participants reported depressive symptoms. Participants who completed the 12-week aerobic exercise program reported improvements in depressive symptoms and depressed mood as compared to a control group who only maintained usual activities. This provides evidence that a program of moderately intense aerobic exercise might be an effective approach to preventing or reducing prevalent symptoms of depression in HIV infected persons (Neidig *et al.*, 2003).

Neidig *et al*. (2003) reported that their study did not yield racially balanced treatment groups. Despite significant retention efforts, few black men and no black women completed the exercise intervention. Individuals who were lost from the study were often among the working poor and reported abrupt changes in employment, unreliable transport and increased family responsibilities as reasons for premature discontinuation. The researchers suggest that future researchers should budget for personnel and services that support participant retention in future exercise studies. Although this study was conducted in the USA, this will be especially true for HIV exercise studies in South

Africa, where the majority of HIV infected people are poor. In a randomised controlled trail, 60 HIV+ patients participated in a 12 weeks aerobic exercise program. A significant reduction in depressive mood was reported (Eller *et al*., 2005).

In an early study by LaPerriere in 1990 (LaPerriere *et al.*, 1991) a sample of 50 gay males took part in 5 weeks of exercise training. They reported attenuated increases in depressive-dejection and tension-anxiety in non-exercisers following notification of positive serostatus. Men on testosterone therapy who engaged in exercise during 12 weeks of therapy had significant improvement in depression symptoms compared to non-exercisers.

At this point in time, exercise is not often formally prescribed as a part of the management of HIV symptoms. However, exercise as a self-care strategy to manage depressive symptoms, were reported in more than one study. Eller *et al.* (2005) reported that engaging in physical activity comprised 11% of the self-care strategies for depression reported to them.

Together with the use of pharmacological agents and psychotherapy, health-promoting activities such as exercise seem to have a positive effect in the treatment of depression (Valente 2003). Aerobic exercise may help prevent or reduce depressive symptoms experienced by persons living with HIV infection (Neidig *et al.*, 2003).

"*Physical activity seems to stimulate the brain to produce neurotransmitters and other chemicals that bring about a reduction of depression as well as an improvement on positive emotions"* (McPhail, 2006 :10).

Despite the recent progress in the treatment of HIV, anxiety remains a pervasive aspect of living with HIV disease (Kemppainen *et al.;* 2006). In addition to the impact on QOL, HIV-related anxiety can also play a role in determining health outcomes.

3.7.5 Exercise and fatigue

HIV appears to be amenable to behavioural-based interventions designed to delay its progression and enhance health status and QOL. One such intervention is exercise training (Rojas *et al.,* 2003; O'Brien *et al.*, 2004).

There is a distinction between the types of fatigue that occurs after physical exertion (acute fatigue) versus fatigue that is associated with a disease (chronic fatigue). Acute fatigue quickly responds to rest or sleep, whereas disease-induced chronic fatigue was found to be responsive to activity or regular exercise, even if it is of a low intensity (Lee *et al., 2006)*

Exercise is one of the self-care strategies most commonly adopted by adults with HIV infection to manage fatigue, although some patients reported that they rather spare their energy by not doing exercise (Siegel *et al*., 2004). Rest has been the primary intervention for the treatment of fatigue in cancer patients, but evidence clearly illustrates that further inactivity can exacerbate the symptom (Losito *et al.,* 2006). An aerobic training program can break the vicious circle of lack of exercise, impaired performance and easy fatigability (Carlson *et al.,* 2006).

Evidence for an achievable aerobic training effect has been documented in the literature, (LaPerriere, 1991; LaPerriere, 1994; Rojas *et al.,* 2003), suggesting a potential role for exercise therapy in the management of HIV. Several studies reported an increase in VO_2 max and ventilatory threshold for exercising HIV patients (Cade *et al.,* 2004). These physiological adaptations to aerobic exercise training may improve fatigue, decrease functional limitations and reduce physical disability resulting from HIV infection. According to Cade *et al.* (2004) physical therapists can play an important role in diagnosis and management of aerobic insufficiency and the related physical dysfunction in people with HIV.

Siegel *et al*. (2004) reported on strategies for coping with fatigue among HIV-positive individuals fifty years and older. One hundred HIV-infected older adults were enrolled in

this study and interviewed at two occasions. A nondirective focused interview technique was used. They found that nearly all participants tried multiple strategies to alleviate their fatigue and that they are receptive to further suggestions from health care providers. Self-care strategies adopted included use of supplements, exercise, sleep and rest and modifying mental outlook.

One participant in the above mentioned study, a 50-year old Hispanic, gave more details on how exercise helps him. On a question of what he does to eliminate the fatigue, he answered that he does moderate exercise like climbing stairs and walking. Later he joined a gymnasium where he walked on the treadmill and did isometric and stretching exercises. He spoke to a recreationist who explained to him the benefits of exercise and he took the advice. He found that exercise was indeed helpful for his fatigue (Siegel *et al.,* 2004). This highlights the role that the biokineticist has to play, not only in prescribing exercise programs, but also in educating patients on the benefits of exercise. For this patient, knowledge motivated him to continue with his exercise program.

Fatigue in HIV is often compared to that in other chronic diseases such as cancer, multiple sclerosis and fibromialgia (Frich & Borgbjerg, 2000). Yates (2006) reported that women who engage in mild aerobic exercise during chemo therapy treatment for breast cancer, experience less fatigue. According to Yates (2006), it was almost counterintuitive for women receiving chemo therapy to exercise. Chemotherapy patients tend to rest because they feel unwell and tired. This seems to set up a vicious cycle: the less active you are the less energy you have for daily life. It can be assumed that this will also be true for the HIV patient. On the one hand, studies reported an urge to rest and the importance to adhere thereto (Jenkins *et al.* 2006), and on the other hand too much rest has a negative effect on energy levels (Yates, 2006).

Losito *et al.* (2006) presented a conceptual framework to explain the effects of group exercise on fatigue and quality of life during cancer treatment. This framework can be

customised to serve as a conceptual framework to explain the effect of aerobic exercise on QOL and fatigue (Figure 3.5) .

3.7.6 Exercise and pain

The World Health Organization's approach to pain in HIV is based on the assumption of no difference between the care of patients with AIDS and the care of patients with advanced cancer (Frich & Borgbjerg, 2000).

Exercise has been cited as a potential analgesic for different types of pain. HIV-infected persons experience similar chronic musculoskeletal pain (aching and cramping) than fibromyalgia patients. Long-term exercise training was shown to be an effective pain reducer in fibromyalgia patients (Ciccolo *et al*., 2004).

Thus, this type of pain management may be effective for HIV-infected individuals as well. Maquet *et al*. (2007) give a review on the benefits of physical training in fibromyalgia. According to their literature study, there is evidence that aerobic exercise increases pain threshold. The release of endorphins resulting from stimulation of the optioid system normally occurs when exercise exceeds the aerobic threshold, or last more than 60 minutes or when exercising at low levels of intensity when performed by subjects strongly deconditioned (Maquet *et al*., 2007).

HIV patients will normally fall into the latter category, which might mean that the deconditioned HIV patient can experience a pain relief effect from exercise although the duration of the training session is shorter than in healthy population.

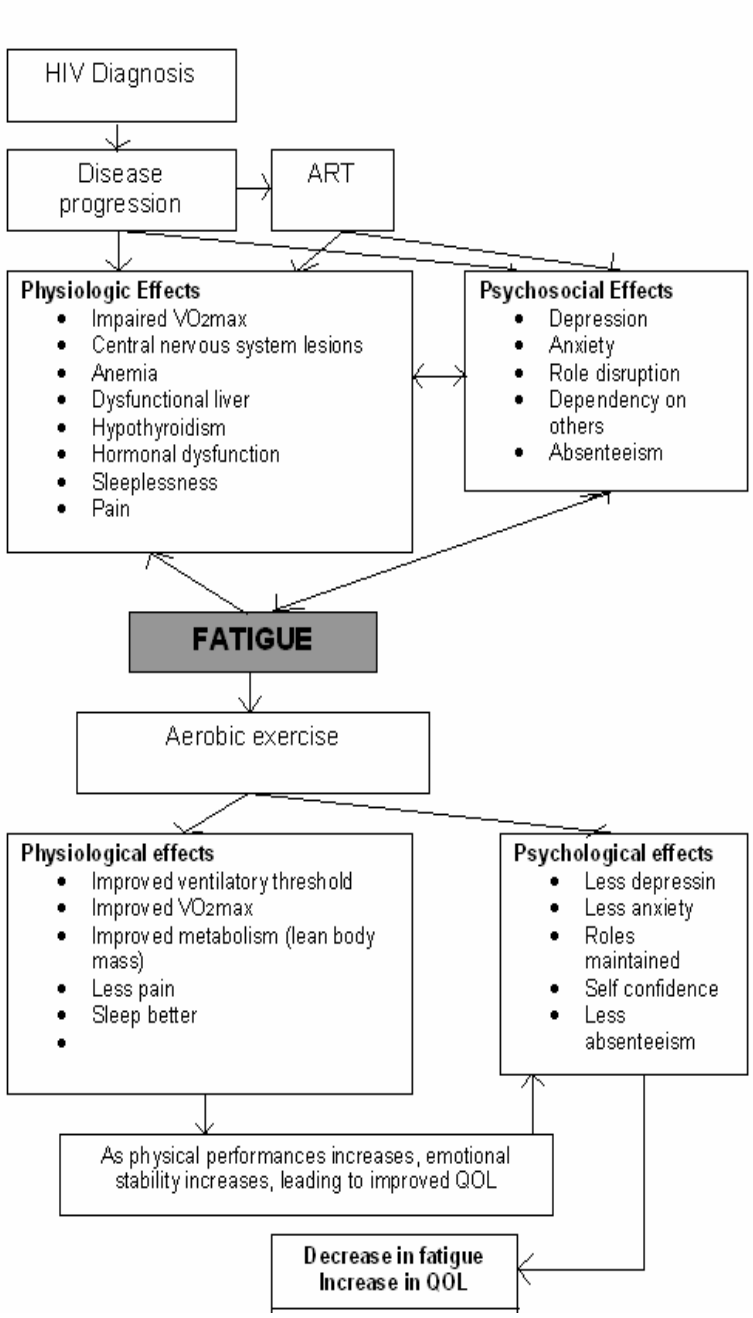

Figure 3.5 : Conceptual framework to explain the effects of aerobic exercise on fatigue and QOL in HIV patients. Adapted from Losito *et al.* (2006)

Serum cortisol concentrations rise progressively during exercise, and a workload of 60% of VO_2 max seems to be the critical level above which a rise in cortisol

concentrations occurs. Cortisol, a glucocorticoid, has been linked to increased thresholds to dental and other pain (Kiefel *et al.,* 1989).

No studies investigating the cortisol levels of HIV positive patients were found. Chatzitheodorou *et al.* (2007), hypothesised in their study on the effect of high intensity exercise in chronic lower back pain that high intensity aerobic exercise will result in higher serum cortisol levels. However, although their study proved that aerobic exercise alleviated pain, disability and psychological strain, it did not influence cortisol concentrations (Chatzitheodorou *et al.,* 2007).

Some exercise-associated analgesia is a result of direct activation of pain-inhibiting brain substrates by type II and type IV afferent nerves. There is evidence that exercise leads to increased secretion of ß-endorphin by the pituitary gland and by the leucocytes and macrophages in injured tissues, that contributes to exercise-induced analgesia (Paulev *et al.,* 1989).

Hoffman *et al.* (2005) also report on evidence that aerobic exercise causes an acute analgesic effect in healthy subjects, because it reduces stress due to the secretion of certain endorphins and therefore it might help to decrease pain (Hoffmann *et al.,* 2005). They further suggested that such reductions in pain perception can last for nearly 30 minutes after subjects have exercised at intensities of more than 50 percent of maximal oxygen uptake for more than 10 minutes.

Other possible mechanisms of pain relief by aerobic exercise that were reported in a longitudinal study in arthritis patients, include exercise protection against secondary fibromyalgia, increased resistance to musculoskeletal micro-injury, psychologically based increase in pain threshold, innately high pain threshold influencing decision to exercise vigorously, or other psychological mechanisms (Bruce *et al*., 2005)
Only 8% of the participants in a study by Frich and Borgbjerg (2000) (described in Chapter 2) tried alternative treatments for pain, such as acupuncture, visualization and

exercise. Some of the participants reported increased well-being as a result of alternative treatment, but whether it included exercise, was not stated.

In a recent study on strategies by HIV patients to cope with neuropathic pain, the following strategies were listed: personal changes, rest, massage, heat and cold modalities, exercise, herbals, humour, TENS, prayer and meditation. However, it was not mentioned what kind of exercise was done by the participants (Ownby & Dune, 2007).

Nicholas *et al. (*2002) reported that 8% of the participants in their study on self care management for neuropathy in HIV patients, used exercise as self-care behaviour for pain, although with limited resolution.

> "*These strategies* (exercise and rest/elevation of extremities) *are not known to be effective for reduction in neuropathy and should be considered as adjuncts to other strategies." (*Nicholas *et al.,* 2002:770)

Although the kind of exercise was not described in this study, it seems from the above mentioned quote and the context of the text that the exercises done by participants refer more likely to resistance or stretch exercises of the extremities, and not to aerobic exercise.

3.8 Exercise and absenteeism

Many corporations use health promotion programs as a reactionary effort to curtail ever increasing employee-related expenses, mainly health care costs and lost productivity (Aldana *et al.,* 2005).

The results from programs that measured the impact of exercise on absenteeism show mostly favourable effects (Aldana, 2001). Corporate fitness and wellness programmes have lead to a decrease in absenteeism amongst employees in several studies:

The travellers Corporation in the USA reported that its health promotion yielded a 19% reduction in sick leave use over a four year period, while DuPont reduced absenteeism by 47.5% over 6 years for the participants in their wellness program (Turner, 2005).

Aldana *et al.* (2005) reported a significant difference in absenteeism among those who participate in voluntary wellness programs. In their two year study they compared health care costs and absenteeism between participants and non-participants in a wellness program. Non-participants had higher rates of illness-related absenteeism.

Employee absence levels at Prudential in the United Kingdom have fallen dramatically during trails of a health and well-being scheme in two of the company's sites. According to Alison Meale, people policy manager of Prudential, daily absence decreased from 6.5 days to 2 days per person (Czerny, 2005).

According to Altchiler and Motta (1994), worksite exercise programs have the potential of alleviating anxiety, improving health and fostering greater psychological as well as physical well-being for employees.

HIV positive persons (employees) experience lower quality of life than their healthy colleagues (Eller, 2001). The above mentioned studies included HIV negative populations. If a HIV negative population had reduced absenteeism due to corporate fitness programs, it can be assumed that a HIV positive employee population will respond in the same positive way. A HIV infected person will experience the same training effect than a healthy person (Mars, 2003), and thus an improvement in quality of life and a decrease in absenteeism can be expected.

However, due to confidentiality, it will not be possible to refer HIV patients to a corporate gymnasium. The biokineticist who works in a corporate wellness environment, will only know his patients` HIV status if the patient discloses it to him. Proper exercise testing will provide the information to prescribe a safe exercise program, even if the HIV status

is unknown. The benefits and importance of exercise for HIV positive persons should be promoted among all employees. *"Despite positive results in limited research studying the effects of physical activity in under-presented groups, certain groups have often been overlooked regarding the promotion of physical activity. Groups such as multiple sclerosis and HIV…."* (Berg & Van Puymbroeck, 2005: 26). Corporate HIV programs should include the promotion of exercise.

CHAPTER 4
METHODOLOGY

4.1 Introduction

This study makes use of the case study procedures as described by Robert Yin in his book *Case Study Research: Design and Methods* (2003). When proper procedures are followed, the case study researcher will be following methods as well developed and tested as any in the scientific field (Tellis, 1997).

The initial design for this study was experimental. For this design, two groups of at least fifty participants were needed. The Middelburg Provincial Hospital agreed that patients from their HIV clinic may participate, if the Mpumalanga Health Department gave its approval. Unfortunately, after almost one year of correspondence, there was still no answer to this request. A request was then sent to the HIV clinic at a local mine, with no positive outcome. A power station also turned the request down, stating that HIV is a sensitive issue and they only get involved in wellness days with HIV testing and counselling. After that, a request was sent to Love Life, a non government organisation that supports HIV victims. A group of patients at Orange Farm near Vanderbijlpark agreed to participate, but only if they would receive significant remuneration, which the budget for this study did not allow.

An advertisement in a local newspaper yielded two participants, and one other participant was referred from a private HIV support group in Witbank, Mpumalanga, after a conversation with the group leader. The design was changed from experimental to a case study. Three participants were not enough to do an experimental study, but they suit the case study model very well.

The approach also shifted from quantitative to a mixed approached of quantitative and qualitative data which resulted in a more in depth study. The new design and approach answered the research question in a more comprehensive way.

4.2 The unit of analysis

According to Yin (2003) the unit of analysis is related to the fundamental problem of defining what the "case" is. It can vary from an individual to a corporation (Zucker, 2001).

Various contemporary reports in psychology, sociology and education have studied the individual as the unit of analysis and have used the case study method to develop rich and comprehensive understanding of people (Zucker, 2001).

In this study, there are three units of analysis: Person A, B and C. They all completed an informed consent (Appendix A) before participation in the study. Confidentiality about their identity is of the utmost importance to them. Their rights are protected by the informed consent.

4.3 Profile of the participants (units of analysis)

A. **Person A** was enrolled into the study on 22-03-2007. His intervention ended on 17-07- 2007. He is a 41 year old full time employed artisan on a mine in the Middelburg (Mpumalanga) area. He responded on an advertisement for participants in this study in a local newspaper on 2 February 2007.

In June 2003 he took part in a voluntary HIV screening at a wellness day at the mine. His results were positive. Before and after the test he received counselling from the sister at the medical centre. He does not use anti retroviral medication because his CD4 cell count is too high to qualify. Every six months his CD4 cell count is tested. He lives with a woman and has four children of, the youngest which is 16 years.

Person A is a friendly extrovert. He takes responsibility for his illness. The fact that he responded to the advertisement provides proof for this observation.

B. **Person B** is a 36 year old female and was diagnosed as HIV positive in 2002. She works full time as a cleaner/tea girl at an engineering company in the Middelburg (Mpumalanga) area. She is a single parent and has two children, aged 13 and 9 years.

She attends a support group for HIV positive persons in Witbank, a city located 30km from Middelburg. The leader of the group was telephonically informed about the study on 03-03-2007. He then encouraged her to participate in this study. Her intervention started on 14-05-2007 and ended on 13-09-2007. She is on antiretroviral therapy and her CD4 cell count is tested every six months.

Although physically she looked healthy, her behaviour was more like an ill person when compared to person A and C, and she needed more motivation to complete her exercise sessions.

C. **Person C** is 31 years old and work full time as an attendant at a petrol station, also in Middelburg (Mpumalanga). He was diagnosed with HIV at a local clinic in 2000 when he had a flu that lasted for several weeks. He is a friend of Person A, who encouraged him to participate in the study. His intervention started on 12-06- 2007 and ended on 09-10-2007.

Person C has the lowest CD4 cell count of the three participants. His CD4 cell count is tested every six months. He is on antiretroviral therapy. He is single and does not have children. Although his CD4 cell count is low, he enjoyed the exercise program and was able to attend all the sessions. He was more motivated than Person B. His biggest complaint was fatigue.

Because only three persons participated in the case study, it was possible for the researcher to schedule the training sessions to accommodate the participants. In this manner Person A and C completed all the sessions, and Person B lost one session on 31-07-2007 due to fatigue and fever. If there were more participants, it would have been more difficult to achieve a zero drop out rate.

4.4 Linking data to propositions: analysis of case study evidence

According to Yin (2003:109) data analysis consist of "…*examining, categorizing, tabulating, testing or otherwise recombining both quantitative and qualitative evidence to address the initial propositions of the study".*

Unlike statistical analysis, there are few fixed formulas to guide the researcher with analysis of case study evidence (Endacott, 2007). Much depends on an investigator's own style of rigorous thinking, along with the sufficient presentation of evidence and careful consideration of alternative interpretations (Yin, 2003).

4.5 Analytic Strategy

Yin (2003) mentions three general analytical strategies, namely:

- Relying on theoretical propositions: The propositions help to focus on certain data and ignore other data. It also helps to organise the entire case study.
- Thinking about rival explanations: This study did not have a rival hypothesis, but in analysing the data rival explanations were addressed. The more rivals that the study addresses and rejects the more confidence can be placed on the findings.
- Develop a case description. This is a less preferable strategy, but serves as an alternative when applying the other approaches is difficult.

The analysis of this study mainly relied on theoretical propositions, but also kept rival explanations in mind (e.g. reasons for absenteeism, fatigue, obesity). Yin (2003) proposes the use of a set of analytic manipulations as described by Miles and Huberman (1994).

Table 4.1: Analytic manipulations described by Miles and Huberman (1994) and mentioned by Yin (2003), used in this study.

Analytic manipulation	Used in this study
Putting information into different arrays	Yes
Making a matrix of categories and placing the evidence in such categories	Yes
Creating data display-flowchart and other graphics-for examining the data	Yes
Tabulating the frequency of different events	Yes
Putting information in chronological order or using some temporal scheme	Yes

This is supported by Endacott (2007) when she mentions that common to all approaches in analysing case study data, is the process of developing codes and categories. General categories (or themes) may be developed from the data, which are then broken into more explicit codes. Overcash (2003) also identifies thematic analysis as a commonly used method of analysing data in narrative research.

4.6 Criteria for interpreting the study's findings

The goal of the case study is to describe as accurately as possible the fullest, most complete description of the case (Zucker, 2001).

4.7 Criteria for judging the quality of research

In order for a research design to represent a logical set of statements, the quality of a given design can be judged according to certain logical tests (Yin, 2003). Four tests have been commonly used to establish quality of research, namely construct validity, internal validity, external validity and reliability. Yin (2003) proposes tactics on how to deal with these tests when doing case studies.

Table 4.2: Case study tactics for four design tests as used in this study, adapted from Yin (2003)

Test	Case study Tactic	Used in this study
Construct validity:	1. Use multiple sources of evidence	Yes
	2. Establish a chain of evidence	Yes
	3. Have key informants review draft case study report	Yes (Only narrative reports)
Internal validity:	1. Do pattern-matching	Yes
	2. Do explanation building.	Yes
	3. Use logic models	Yes
	4. Instrumentation: same person uses same equipment and protocol for tests	Yes
External validity:	1. Use theory (single-case study)	No
	2.Use replication logic (multiple-case study)	Yes

Reliability	1. Use case study protocol. 2. Develop case study data base.	Yes Yes

Endacott (2007) gives three criteria for validity and reliability in qualitative research:

1. Credibility – return data to the subjects for verification. This will be done with the narrative reports. This correlates with Yin`s strategy for construct validity as described in Table 4.2 above.
2. Transferability – of the theory rather than "sample to the population.' This refers to analytical generalization as explained by Yin (2003) and mentioned earlier in this study.
3. Dependability – auditability. Researchers often use a narrative diary to record theoretical, methodological and analytic choices.

4.8 Narrative research methodology

Narrative is used to describe a variety of ways humans perform the telling of events. Narrative data can be seen as the result of a communication exchange. It is not only the stories contributed by the participants, but also the evaluating and analysing of those stories (Overcash, 2003).

Participants in this study gave a monthly narrative report on their experiences of the exercise program. This was done by an informal interview where the patients were not guided with a set of questions. Only one question was asked: How do you experience the exercise program at this stage?

The interviews were recorded and then typed. The typed version was given to the participants to review. In this way the construct validity of the study was enhanced (Yin, 2003). None of the participants changed the reports. Analysis was done as the reports

were typed. According to Endacott (2007), a central tenet of qualitative research is early data analysis whilst collecting the data. All interviews are included in Chapter 5.

4.9 Intervention

A sixteen-week aerobic exercise program with a frequency of 3 times per week.

4.9.1 Duration (of the study)

A shortcoming of several other HIV-studies (O'Brien *et al*; 2004) might be that the period of the exercise program (8 to 12 weeks) was too short to establish a training effect. The participants in this study were highly unconditioned and the initial intensity would have been too low to see results.

4.9.2 Overload

In order to obtain a training adaptation, a physiological system must be exercised at a level beyond that to which it is presently accustomed. This is called the principle of overload. Duration, frequency and intensity are the variables most often manipulated to provide overload to systems of the body (Mars, 2003).

4.9.3 Duration (of the training sessions)

The duration of a training session is often influenced by the exercise intensity (Baechle & Earle, 2000:499). Ciccolo *et al*. (2004) recommend a duration of 20 minutes to 60 minutes per session for HIV patients.

The sessions for this study were scheduled to last for 30 minutes each. This is in line with the recommendation of the U.S. Department of Health and Human Services: "*The minimum daily recommendation for a healthy lifestyle is 30 minutes of at least moderate intensity physical activity daily, as suggested by the U.S Department of Health and Human Services* "(Ramirez-Marerro *et al.;* 2004:74).

Another practical reason why sessions were limited to 30 minutes was because the participants are employed and their time for exercising was limited.

4.9.4 Frequency

The training status of the athlete is one of three factors that will determine the frequency of exercise sessions (McArdle *et al*, 2001). The other two factors mentioned by them are interaction between exercise intensity and duration and the specific sport season. The latter is not applicable to the participants in this study. Ciccolo *et al.* (2004) recommended 3 to 5 training session per week for HIV patients. According to Stringer (1999) and Dudgeon *et al*. (2004), the typical frequency prescription for HIV patients is 3 times per week (Stringer; 1999; Dudgeon *et al.,* 2004).

The frequency of the training sessions was three times per week, which allowed for proper rest periods between sessions, as the training status of the participant was below average. "*Recovery from individual sessions is essential if the athlete is to derive maximum benefits from the subsequent training session* "(Baechle & Earle, 2000: 499).

4.9.5 Intensity

Training intensity and training duration usually have a reversed linear relationship, with higher intensity being associated with lower duration (Baechle & Earle, 2002:498).

According to Stringer (1999) both moderate (40%-60% of VO_2 max) and heavy aerobic exercise (60% - 80% of VO_2 max) may be used as the exercise training paradigm for HIV+ persons (Stringer, 1999). Cicollo *et al.* (2004) supported this intensity prescription when they recommended an intensity of 50% -85% of VO_2 max for HIV patients. Dudgeon *et al*. (2004) did a review into the research that has been performed using exercise as an intervention for HIV-infected persons. According to them, typical

prescription has included work at 50% to 85% of VO_2 max, or 60%-85% of maximum heart rate (Dudgeon *et al.,* 2004).

Because there is a close relationship between heart rate and oxygen consumption, heart rate is likely the most frequently used method for prescribing aerobic exercise intensity (Baechle & Earle, 2000).

The subjects in this study trained at 50% of their maximum heart rate during the first few sessions, and the intensity increased with 10% every 4 weeks to 80% during the last sessions. The Karvonen method (Appendix C) was used to determine maximal heart rate. This method was previously used in other HIV studies to determine aerobic intensity (O'Brien *et al.;* 2004)

Exercise was done on a stationary bicycle, which was equipped with a heart rate monitor.

4.10 Measurements

The subjects underwent a pre-test before the intervention started.

The pre-test contained the following measurements:

1. **Anthropometric equations** to determine changes in body composition. The Drinkwater and Ross (1980) equation was used.
2. **VO_2 max** was determined indirectly by using the Fox sub maximal ergonometry test with the Fox equation (VO_2 max = 6.3 – 0.0193 x HR subm).
3. **CD4 cell count**: The subjects test their CD4 cell count every 6 months. Measurements closest before and closest after the intervention will be used to determine if the intervention had an effect on the immune system.

4. **Anxiety and depression** were measured by the MOS-HIV (Medical Outcomes Study – HIV). The MOS-HIV was developed to evaluate aspects of well-being and functional status in HIV patients (Webb; 2004)
5. **Pain** was measured by the MOS-HIV.
6. **Fatigue** was measured by the MOS-HIV.
7. **Absenteeism**: Absenteeism was measured by record keeping. The subjects kept record of every day during the 16-week period that he was absent from work due to HIV related symptoms.
8. **Narrative report**: Subjects were interviewed monthly and shared their subjective experience of the exercise intervention. This is in the form of a narrative report.
9. **Diet**: According to Dudgeon *et al.* (2004) all HIV studies must take nutrition in consideration to rule out changes in the patients due to their diet. Subjects in this study were asked to continue eating as they did before entry into the study.

4.10.1 The MOS-HIV

The MOS-HIV Health Survey is available internationally for the measuring of health related quality of life in HIV positive persons (Rojas *et al.,* 2003). It has been widely used in clinical trails and in observational studies (Wu, 1997). It has proved to be useful in demonstrating the impact of medical interventions for HIV disease and AIDS on patient functioning and well-being in clinical trials and cohort studies (Schifano *et al.,* 2003).

The MOS-HIV traces its genealogy back to several well-tested questionnaires, particularly those developed in the late 1970`s for the RAND Health Insurance Experiment and the mid 1980`s for the Medical Outcomes Study (Wu, 1999).

The MOS-HIV has had relatively limited use in drug injection users. The overwhelming effects of drug injection use and the chaotic lifestyle that accompanies it may reduce

responsiveness (Wu, 1997). Participants in this study were not drug users. It consists of 35 questions, which assess 10 dimensions of HR-QOL (Wu, 1999).

4.10.1.1 Internal reliability of MOS-HIV

Data from numerous studies supports the internal reliability of the multi-item scales in the MOS-HIV (Wu, 1999). In most cases Cronbach`s Alpha exceeded 0.70 suggesting adequate reliability for group comparisons.

Table 4.3: Internal consistency (Cronbach`s Alpha) of MOS-HIV Subscales (Wu, 1999).

Population	Asx and early ARC	All stages	AIDS/MAC	CD4 100-300	CD4 100-300	AIDS CD4<100	All stages	CD4 50-300
Sudscale (N)	117	99	68	290	205	1231	162	1022
General health perceptions	S	S	0.79	0.87	0.83	0.81	0.83	0.83
Physical functioning	0.86	0.84	0.86	0.83	0.83	0.85	0.89	0.83
Role functioning	0.50	0,87	NA	0.89	0.77	0.77	0.82	0.76
Mental health	0.86	0.80	0.87	0.83	0.86	0.83	0.83	0.85
Energy/ fatigue	0.78	0.87	0.82	0.87	0.82	0.87	0.87	0.88
Health distress	0.91	0.92	NA	0.92	0,92	0.90	0.92	0.89
Cognitive functioning	0.84	0.87	0.9	0.89	0.86	0.89	0.91	0.91
Pain	S	S	S	S	S	0.83	0.63	0.70

4.10.1.2 Construct validity

Multitrait analysis supports the convergent and discriminant construct validity of the scales and suggests that they measure distinct aspects of health across different stages of illness (Wu, 1997; Wu, 1999).

Table 4.4: Construct validity for the MOS-HIV (Wu, 1999).

Concurrent measures
Karnofsky Performance Status scores
Sickness Impact Profile
Quality of well-being scale
HOPES
Standard Gamble Utility
Fanning QOL Scale
EuroQol
Depression Scale scores
Frequency and severity of physical and mental symptoms
6 minute walk test performance
Cognitive function tests
Visual acuity
Campbell's Quality of Americas Life
Severity of illness(Rabaneck Severity Score)

4.10.1.3 Responsiveness

Preliminary findings from three completed clinical trails support the responsiveness of the scales (Wu, 1999).

4.10.1.4 Contents of the MOS- HIV

The measure evaluates general health perceptions, pain, physical and cognitive functioning, role and social functioning, mental health, energy/fatigue, and health distress QOL and health transition. The MOS-HIV takes less than 5 minutes to complete, is easy to administer, is well accepted by patients and can be self or interview administered. Sub scales are scored from 0-100, with physical and mental health summary scores also calculated. The MOS-HIV has demonstrated reliability and validity in patients with HIV/AIDS and is responsive to changes in patients' clinical status (Webb, 2004). It has been used extensively in clinical trails, is available in 14 languages and in preliminary analysis, has proven validity in various populations, such as women and African Americans. The tool does, however omit several clinical parameters pertinent to HIV such as sleep, somatic symptoms, sexual dysfunction, eating behaviour and body image (Webb, 2004). The symptoms that are excluded by the MOS-HIV are not relevant to this study. The MOS-HIV questionnaire is included in Appendix D.

4.10.1.5 Analysis of the MOS-HIV:

- General health (5 items)
- Pain (2 items)
- Physical function (6 items)
- Role function (2 items)
- Social function (1 item)
- Mental health (5 items)
- Vitality (4 items)
- Health distress (4 items)
- Cognitive function (4 items)

- QOL (1 item)
- Health transition (1 item)

The raw count of each scale is calculated and then converted into a 0-100 scale. This makes it possible to compare different categories with each other. A higher score indicates a higher quality of life

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CHAPTER 5:

RESULTS

5.1 Anthropometry

5.1.1 PERSON A:

Age: 41

Sex: Male

Height: 1,76m

Table 5.1: Anthropometry Person A

	22-03-2007	17-07-2007
Weight	85.1kg	83.8kg
Fat mass%	19.13%	18.11%
Bone mass %	19.69%	19.62%
Muscle mass %	36.89%	36.92%
Residual mass %	32.98%	33.52%

5.1.2 PERSON B

Ag: 36

Sex: Female

Height: 1, 65

Table 5.2 Anthropometry Person B

	14-05-2007	13-09-2007
Weight	79.3kg	77.2kg
Fat mass%	31.24%	30.15%
Bone mass %	17.49%	17.51%
Muscle mass %	31.16%	32.45%
Residual mass %	21.33%	21.46%

5.1.3 PERSON C

Age: 31

Sex: Male

Height: 1,72m

Table 5.3: Anthropometry Person C

	12-06-2006	09-10-2007
Weight	66.7kg	66.5kg
Fat mass%	11.25%	11.14%
Bone mass %	20.13kg%	20.64%
Muscle mass %	32.81%	33.32%
Residual mass %	31.42%	31.31%

5.2 VO_2 max

Table 5.4: VO_2 max Person A

Person A	22-03-2007	17-07-2007
VO_2 max (ml/kg/min)	38	39.8

Table 5.5: VO_2 max Person B

Person B	14-05-2007	13-09-2007
VO_2 max (ml/kg/min)	26.2	29.8

Table 5.6: VO_2 max Person C

Person C	12-06-2007	09-10-2007
VO_2 max (ml/kg/min)	36.8	38.5

5.3 MOS HIV scores

5.3.1 Pre-test

Table 5.7 MOS-HIV Pre tests

	Person A	Person B	Person C
General health perceptions	43.26	37.78	39.46
Physical functioning	71.90	65.24	62.76
Role functioning	51.00	49.89	50.00
Social functioning	65.98	54.71	58.57
Cognitive functioning	64.72	66.18	63.53
Pain	62.55	54.12	58.70
Mental health	67.34	54.50	60.65
Vitality	55.23	43.24	48.86
Health distress	59.31	51.70	53.18
Quality of life	64.25	53.26	61.76
Health transition	60.84	58.98	59.23
Total MOS-HIV score	**60.58**	**53.60**	**56.06**

5.3.2 Post-test

Table 5.8: MOS-HIV Post tests

	Person A	Person B	Person C
General health perceptions	50.89	39.52	44.77
Physical functioning	74.62	67.35	67.51
Role functioning	63.68	56.87	59.79
Social functioning	65.88	65.34	63.96
Cognitive functioning	68.51	67.15	63.80
Pain	63.35	56.38	62.42
Mental health	70.84	57.41	64.89
Vitality	59.78	45.09	50.47
Health distress	61.41	54.57	59.76
Quality of life	67.55	56.05	66.15
Health transition	65.87	59.12	64.98
Total MOS-HIV score	**64.76**	**56.80**	**60.77**

5.4 CD4 Cell count

Table 5.9: CD4 cell counts of Person A

Person A	18-01-2007	16-07-2007
CD4+ cell count (per millilitre)	725	731

Table 5.10: CD4 cell counts of Person B

Person B	13-02-2007	23-09-2007
CD4+ cell count (per millilitre)	552	536

Table 5.11 CD4 cell counts of Person C

Person C	07-04-2007	15-10-2007
CD4+ cell count (per millilitre)	328	329

5.5 Absenteeism

5.5.1 Person A

Days not able to work due to HIV related symptoms: 0

5.5.2 Person B

Days not able to work due to HIV related symptoms: 2

She complained about fatigue and fever on 30-07-2007 and 31-07-2007

5.5.3 Person C

Days not able to word due to HIV related symptoms: 0

5.6 Narrative reports

After every second week of the 16 week intervention period, every participant had to answer the following question after the training session: How do you experience the exercise program at present? The answers were recorded and then typed.

5.6.1 Person A

Date: 20-04-2007

Eish! Hmm…Hmm… (laugh). It was tough...those first two weeks. I didn,t realise that I was so bad. Hmm… my legs were sore in the beginning. Now it is better. I was out of breath shortly after I started to cycle. I felt very tired. I think I am getting fitter now. (laugh). Maybe, I don't know. But I will come next week. You know, actually I like it!

Date:22-05-2007

I am much fitter now, serious! (laugh). Even at work, I feel better. Climb the stairs easier…hmm…not so tired. Eish, that first two weeks! (laugh) But now I feel good. You know, I thought I was not going to last! You told me not to quit, now I won`t (quit). I like the bicycle. Hie…it is a good thing to exercise!

Date: 21-06-2007

No, I like this exercises. I will not stop, you know… eh…eh… it makes me feel happy. When your HIV status is positive, you know, you…you…eh..worry a lot. So many things you worry about. But the exercises, it is good. It makes me feel good. It makes me tired, but not for long.

Date: 17-07-2007

I want to keep on exercising. Eh…eh…every HIV person must exercise, you know? Sometimes you think, eish(!) I am sick, I cannot exercise. That is very wrong..eh…eh… it makes you fit. At work you feel stronger. You feel healthy.You know, there is a man, I am going to send him to you. Yes. He has the slims (word used for AIDS).He must come and exercise too. I am very happy to be fit (laugh)!.

5.6.2 Person B

Date: 15-06-2007

I…I...it is not too bad. I am not fit yet. Sometimes I don`t want to come. Then I am too tired. But I come. I promised to come. Only the transport. Hie… It is a problem. Some

days the taxis are already gone when I am finished here. But, the exercises, it is not too bad. Yes.

Date: 16-07-2007

Oooo… (laugh). I think I am getting fitter and fitter. My breath…it is better. I can walk for longer…eh…at the work I don`t get tired so much. But some days…hie!.... then I am very tired. This HIV, it makes you tired. But I think the exercises help. My pain is less at night.

Date: 15-08-2007

No, I was ill this month….had fever and was too tired. I missed two days at work…yes…I was very ill. May be it is the medication. I feel nausea, some days. The exercises…I think it is a good thing. I like to come and train here with you…I…I will not train on my own. Eh… I feel good when I train here.

Date:13-09-2007

I am definitely much more fit than the first day. (laugh!) I am stronger…eh…I feel stronger. It was not too difficult. But when you are tired, very very tired, you cannot exercise. Then I must stay in bed. But I liked the exercises. My pain is better and I am not so tired when cleaning at work.

5.6.3 Person C

Date: 12-07-2007

I used to play soccer before I was ill. I like sport! Eh…eh… now that is why I like the exercises. I like sport. If I cycle too fast, I get tired, so now I cycle slow like you told me.

Date:13-08-2007

People say you have "slims", you cannot work…you cannot do exercise. No, I can work and I can exercise. I feel fit. My medication sometimes makes me feel ill, but when I exercise I feel better. I must keep on exercising.

Date:12-09-2007

Sometimes I am very tired when I exercise, but then I slow down, then I feel better. See …. my legs… (show me his legs) see,… all this muscles. It is from the bicycle. I am a strong man like I used to be before I was ill. I like it! (laugh) Training is a good thing.

Date: 09-10-2007

Now I can cycle faster and keep it there all the time. Eish, I like the exercises! And my legs are stronger….eh…I feel good. I am sick but I feel good.

CHAPTER 6
DISCUSSION

6.1 VO_2 max

The age normative values for peak aerobic capacity, by indirect calorimetry during exercise testing, for sedentary men and women with no known pathology or impairments in the 50th percentile ranges, are as follows:

Table 6.1: VO_2 max norms

	20-29yr	30-39yr	40-49yr	50-59yr
VO_2 max ♂	45.0	41.0	38.0	35.0
VO_2 max ♀	43.0	34.0	31.0	28.0

(American College of Sports Medicine, 2000)

All three participants showed an improvement in VO_2 max. This is in accordance with several previous HIV studies (Rojas *et al.*, 2003, O`Brien et *al.,* 2004) and was expected in the hypothesis.

Person A`s initial VO_2 max was 38ml/kg/min, which is the value that was expected according to the American College for Sports Medicine's norms for sedentary healthy adults. After 16 weeks of aerobic exercise his VO_2 max increased to 39.8ml/kg/min, which is still in the range for his age according to the norms. Low VO_2 max values in HIV positive persons might be one of the reasons for fatigue in this population (Cade *et al.,* 2004). Person A did not complain a lot about fatigue, which might be due to the fact that his VO_2 max was not lower than healthy sedentary adults and the intensity of the exercise was moderate. Of the three participants, his CD4 cell count was the highest, which might also be a reason for less fatigue. According to Bopp *et al*. (2004), lower CD4 cell count is associated with higher levels of fatigue.

Person B had a VO_2 max of 26.4ml/kg/min before the exercise intervention. This is 22% lower than the norm for healthy sedentary women. This is not surprising, as Rojas *et al.*

(2003) and Dudgeon *et al.* (2004) found VO_2 max in HIV seropositive adults to be well below average. After the intervention her VO_2 max increased to 29.7 ml/kg/min. Although this represents an increase, it is still well below the norm for her age (34ml/kg/min). Person B reported fatigue throughout the study, but more in the beginning. Her below-average VO_2 max may be one of the reasons for her fatigue. She believes that HIV makes a person feel tired. Even though that was her belief, she reported less fatigue during the last month of the intervention. This is reflected in the MOS-HIV scores.

Person C showed an increase in VO_2 max from 36.8ml/kg/min to 38.5ml/kg/min. The norm for his age, however, is 41ml/kg/min. This means that his VO_2 max is 11% below the average norm, which was expected, as mentioned in the previous paragraph. Of the three participants, his disease progress was the most advanced, with a CD4 cell count below 350mm³. He also reported diarrhoea which was not documented for the purpose of this study. Despite his advanced state of illness, it was still possible to improve his VO_2 max and thus his general level of fitness.

6.2 Body composition

All three participants showed an increase in muscle mass and a decrease in fat mass.

Person A did not have any visible body composition alterations due to HIV or its treatment. His fat percentage dropped with 1.02 percentile points. The norms for men (age 40 to 49) are 12% - 17%, according to the Drinkwater and Ross method (Drinkwater & Ross, 1980) used in this study. (Krüger & Van Vuuren, 2005).

This means that Person A has, after the 16 week training intervention, still a fat percentage above the average norms. He appeared to be a healthy, slightly overweight person. This is in contrast with the findings by Foster, (1996), Batterham *et al*. (1999) and Corless *et al.* (2004), who mentioned that body composition abnormalities are

common in people with HIV and AIDS. As previously mentioned he does not use antiretroviral medication, a fact that excludes possible body alterations due to ART.

His muscle mass slightly increased from 36.89% to 36.93%. This increase is not significant. It must be kept in mind that an aerobic exercise program and not a resistance program was followed. Thus, the aim of the prescribed program was not to increase muscle mass, but to improve aerobic capacity.

Person B is on antiretroviral treatment. According to her, she used to be an obese person prior to her diagnosis. She has dropped two clothes sizes since she was diagnosed with HIV five years ago and before she started with ART. However, she is still overweight and does not want to lose more body fat, as it makes her feel like the disease is progressing. Before the intervention her fat percentage was 31.24%, and it decreased to 30.15% after 16 weeks of aerobic exercise.

Engelson *et al.* (2006), reported obesity amongst HIV positive women as an unexpected health problem. Although person B was obese before she was diagnosed with HIV, her BMI was 29.13 kg/ m^2 before the intervention and 28,36kg/m^2 after the intervention. This falls in the overweight category (Williams, 1995). Smith *et al.* (2001) recruited HIV positive adults in an aerobic exercise study and reported that the majority of participants had a BMI higher than the accepted norms.

It can be assumed that one of the reasons for her overweight was physical inactivity. According to Sarsan *et al.* (2006), inactivity is one of the reasons for obesity and overweight. When she started to become more active and participated in the study, her fat mass decreased. Another reason for her overweight is periods of overconsumption of food with high kilojoule values. Although this study did not investigate diet as a parameter of QOL, one of the study objectives was to document as many as possible data while working with HIV positive persons. Person B disclosed that sometimes she overeats in an attempt to prevent wasting. This happened especially when signs of lipoatrophy in the arms, legs and face were noticed for the first time. Indeed, Person B

has a moderate amount of peripheral wasting and an accumulation of fat in the abdomen and trunk. It is important that HIV patients receive the right information about healthy weight and energy intake and expenditure.

Person B was uninformed and believed several myths about HIV. Before the study she believed that she had to be as inactive as possible to save energy and prevent fatigue. She also believed that she had to eat food "…*that make her fat*" like oily and starchy food. This, however, actually decreased her energy levels. It is clear that the biokineticist, as an exercise therapist, has a role to educate and inform the HIV patient about fact concerning general health and well-being. In the case of Person B, this knowledge helped to enhance her QOL, as is reflected in her MOS-HIV scores.

Person B`s muscle mass increased from 31.16% to 32.45%. This increase is most likely due to her participation in an exercise program after several years of inactivity. Although the resistance of the bicycle was not very high, it was enough to overload the muscles of the deconditioned legs. The circumference of her thighs increased after 16 weeks of aerobic exercise on a bicycle, which correlates with the slight increase in muscle mass. According to Baechle & Earle (2000) overload of muscle tissue leads to hypertrophy of the muscle. It can be expected that if the study continued for a longer period of time, the increase in muscle mass would not be significant. The reason would be that in her initial deconditioned state, the resistance of the bicycle was enough to overload the leg muscles, but as she became more conditioned, the resistance would not be enough to cause muscle hypertrophy.

Person C had a fat percentage of 11.25% before the intervention started and it decreased to 11.14% after the intervention. This is not a significant decrease. His fat percentage falls in the acceptable range of 9% to 15% (Krüger & Van Vuuren, 2005). He clearly has the classical bodily alterations described in lipodystrophy. The skin folds on his arms and legs were very thin in comparison with the subscapula, supra iliac and para umbilicus measurements. He also has lipoatrophy in the face. Parisien *et al.* (1993) suggested in an early HIV study, that body composition measures must be

included as routine in clinical practice for HIV patients. This might be a useful practice in cases of wasting, but in a lipodystrophy case like Person C, the kind of anthropometric measurements deserve attention. Body fat percentage gives an indication of total body fat, but no indication of the location of the fat. In lipodystrophy a redistribution of fat occurs, which means that total fat percentage might be unchanged as fat losses on the arms and legs counteracts fat gain on the abdominal and trunk areas. Future studies may find circumferences to give a better indication of lipodystrophy progression.

A comparison between the thicknesses of specific skin folds, or waist circumference, may also be a practical manner to monitor lipodystrophy in HIV positive patients. Indeed, a study by Smith *et al.* (2001) used waist circumference as a measure to determine the effect of aerobic exercise on body composition in HIV–infected adults. They found that a 12 week aerobic exercise program resulted in decreased waist circumferences in 52 patients. Although fat mass of the participants in the current study decreased, a significant decrease in waist circumference could not be established. Roubenhoff *et al.* (1999) also reported in an earlier study that strength training in combination with aerobic exercise, were successful in reducing trunk fat in HIV patients with lipodystrophy. The reason why significant changes in trunkal fat were not observed in the current study might be that only one participant (Person C) showed classical body alterations due to lipodystrophy, but even so, his waist circumference was not extremely big and his BMI was not too high. In the other studies mentioned, either BMI was higher or lipodystrophy symptoms more advanced.

Person C gained 400g muscle mass. The important thing about his muscle gain was that it was visible on his upper legs. His quadriceps appeared to be more hypertrophied (to him) than before the study. The self image of this person was enhanced by this increase in muscle mass. He repeatedly mentioned how big and strong his leg muscles became since he exercised. This correlates with the finding by Corless *et al.* (2004) that there is a relationship between body image and quality of life, especially in men. According to their study a wasted body leads to a lower body image and to lower quality

of life. It can be assumed that the opposite will also be true: a more muscular body leads to a better body image and to a higher QOL.

6.3 CD4 cell count

The CD 4 cell counts of all three participants showed little difference before and after the intervention. This is in accordance with the hypothesis that no significant change was expected. In early studies aerobic exercise was found to significantly increase CD4 cell count (LaPerriere *et al.*, 1991, Perna *et al.,* 1999). However, these results were unique. The inconsistency in the effect of exercise on CD4 cell count may stem from the different populations being examined. The group studied by LaPerriere *et al*. (1991) were from a lower socioeconomic status with greater life stress than the other groups. The authors suggested that their study used exercise as a form of stress management and the rise in CD4 cell counts represents normalization of stress-induced CD4 cell depletion. The studies by LaPerriere *et al*. (1991) were well controlled and had an experimental design (LaPerriere *et al*., 1991).

Of the three participants, two (Person B and Person C) were from a lower socio-economic status. However, their CD4 cell counts did not increase due to a decrease in life stress by means of exercise. Although causal relationships cannot be determined using an explanatory multiple case study design, the researcher worked very intimately with the participants and is not aware of any external factors that could have increased or decreased stress levels.

The results in this study support the findings in several studies that exercise is safe for HIV positive persons. The possibility that too intense exercise may further suppress the already immunosupressed immune system of the HIV patient, was mentioned before the intervention started (Bopp e*t al.,* 2003). According to Dudgeon *et al*. (2004) higher intensity physical activity and overtraining have been showed to decrease effectiveness of the immune system in both humans and animals. However, Mars (2003:8) stated that "i*t appears that the first bout of exercise will not detrimentally affect their (HIV+ patients)*

immune status". The results of the current study imply that longer duration, lower intensity aerobic exercise may provide health benefits while preventing deleterious effects seen in high intensity training.

These results further indicate that the Karvonen method is useful in unconditioned HIV persons. All three participants` exercise intensity was established by this method. The intensity for each individual was 50% of maximum heart rate, and it was increased every four weeks with 10 % to establish an overload effect (Baechle & Earle, 2000).

6.4 Fatigue

In the MOS-HIV, the four-item vitality scale gives an indication of energy and fatigue. As discussed earlier, all three participants mentioned fatigue in their narrative reports. Their fatigue was reflected in their MOS-HIV scores.

Person A scored 55.23 on the Vitality scale. This is his third lowest score out of 11 scores. His vitality score increased with 4.55 points to 59.78 after the intervention.

For person B, her vitality score of 43.24 was her second lowest score. This score means that she experienced fatigue most of the time. After the intervention her score increased to 45.09. This represents an increase of only 1.85 points. For this participant fatigue is a real threat to her QOL. She mentioned in her last narrative report that moderate fatigue can be handled, but when she experiences severe fatigue, she has to lie down and rest." *But when you are tired, very very tired, you cannot exercise. Then I must stay in bed".* This is in accordance with a study by Jenkins *et al.* (2006), who reported that if rest was required, there was nothing to gain from ignoring the urge, "…*otherwise my body sort of collapses and it is painful to keep on going*" (Jenkins *et al.,* 2006:1127).

Person C reported fatigue, but only during exercise sessions. In the first session he exercised at a too high intensity which led to exhaustion. According to Lee *et al.* (2006),

this type of fatigue can be described as acute fatigue and responds rapidly on rest. After his level of intensity was again explained to him, he trained at the appropriate level and was able to complete the sessions. His vitality score increased from 48.6 to 50.47 after the intervention.

Although person C was in the most advanced stage of HIV disease of the three participants, he did not have the lowest fatigue score, neither did he report fatigue in his narrative reports. According to the literature (Breibart *et al.*, 1998; Millikin *et al.,* 2003) there is an association between disease stage and fatigue. The results of person C does not correlate with these findings. The reason may be that he has a more positive attitude than Person B and appeared to be less depressed. He indeed had a higher depression score than Person B. Milliken *et al.* (2003) found an association between depression and fatigue. This finding correlated with the literature that found no association between fatigue and disease stage (Darko *et al.,* 1992, Henderson *et al.,* 2005).

Lee *et al.* (2006) concluded in their study on the effects of regular exercise on pain, fatigue and disability in patients with rheumatoid arthritis (RA), that female participants with a lower education level are more likely to have perceived more pain. Person B is the only female who participated in the study, thus, gender may be a contributing factor to her higher fatigue end pain scores.

Their study further found that regular exercise had significant benefits for RA patients, and that exercise had a more profound effect on fatigue than on pain. In the current study, the total increase in fatigue (8.27 points) exceeded the total increase in pain (7.07 points). This finding supports the finding by Lee *et al*. (2006).

However, at an individual level, for Person B exercise had a greater effect on pain than on fatigue. According to her MOS-HIV scores, she experienced higher levels of fatigue compared to pain. One of the reasons that may explain this is the fact that she is overweight. Overweight is associated with greater levels of fatigue (Hills *et al.,* 2005).

Although the participants were full time employed, they were deconditioned at the beginning of the intervention, especially Persons B and C. Person A had a VO_2 max of a normal value if compared to healthy sedentary adults. However, it is doubtful if a sedentary adult can be described as conditioned.

Deconditioning is a complex physiological process in which the lack of use of the body's cardiovascular, neuromuscular, biomechanical and musculoskeletal systems leads to a decrease in their functional capacity and the body's efficiency (Clark & White, 2005). When functional capacity decreases, fatigue increases (Breitbart *et al.,* 1998). One of the reasons for this deconditioning is inactivity. Person B believed that she had to be inactive in order to prevent fatigue. Person C terminated his participation in sport when he was diagnosed HIV positive and became more inactive. Person A did not participate in any form of exercise. His HIV status was not mentioned as the reason for this. This inactivity leads to fatigue, which in turn, leads to greater inactivity. This vicious cycle needs to be reversed in order for the HIV patient to experience greater vitality and higher energy levels. Supervised exercise sessions proved to help these patients to become more active and experience less fatigue.

Another reason for fatigue in HIV positive persons is depression (Siegel *et al.,* 2004). All three participants had an increase in their mental health and health distress scores, an indication that their feelings of depression decreased. Because of this linear relationship between depression and fatigue, this must also be considered as one of the reasons for improved vitality.

Furthermore Siegel e*t al.* (2004) mentioned that HIV patients perceived fatigue as an indirect indication of their overall health status. The general health perceptions scores of all three participants increased after the intervention.

As discussed earlier, there is a relationship between functional capacity (VO_2 max) and fatigue (Cade *et al*., 2004). The increase in the participant's functional capacity is reflected by the decrease in fatigue.

The decreases in fatigue experienced by all three participants are consistent with the findings by Neuberger *et al.* (1997) and Lee *et al.* (2006), namely that disease-induced chronic fatigue is reduced by exercise. Another study supporting this finding was conducted by Smith *et al.* (2001). They concluded that a 12 week supervised aerobic exercise program resulted in a decrease in fatigue. The 52 HIV positive participants in their study trained three times per week at an intensity of 60% -80% of their VO_2 max. Fatigue levels decreased, regardless of CD4 cell count levels.

According to Henderson *et al.* (2005), there is growing evidence that nonpharmacological treatments, such as graded exercise therapy, are effective in the treatment of fatigue occurring in chronic fatigue syndrome. The results of this study add to this growing pool of evidence.

6.5 Anxiety and depression

The mental health scales and health distress scales of the MOS-HIV measure depression and anxiety. A low score on the mental health scale means the patient feels nervous and depressed all of the time, while a high score means he feels happy, peaceful and calm. A low score on the health distress scale indicates feelings of despair, discouragement and fear, while a high score indicates that these feelings are not present (Wu, 1999).

Person A had an initial mental health score of 67.34. After the intervention it increased to 70.84. His health distress scores, an indication of anxiety, also showed an increase from 59.31 to 61.4. This represents relative high scores and indicates that he does not feel nervous, depressed, despairing or fearful most of the time.

According to his narrative report, however, he did experience negative thoughts *("when your HIV status is positive, you worry a lot"),* but he mentioned that the exercises made him feel "good". This is the subjective view of a HIV positive person on the effect that aerobic exercise has on his feelings of depression and anxiety. McPhail (2006) supports this in his paper on the therapeutic benefits of physical activity, where he states that exercise is an effective modality to the treatment of depression. In this paper he quotes Joan Baez, who said "…*action is the antidote to despair*" (McPhail, 2006:9).

Person B had the lowest mental health scores and health distress scores of the three participants. Her scores both increased after the intervention. Her mental health score increased with 2.91 points and her health distress score increased with 2.87 points. Although this represents an increase, it is below the average increase of 3.55 and 3.85 respectively, for the three participants. Even for this person who had lower scores, feelings of depression and anxiety decreased after the 16 week intervention period.

In experimental designs, a threat to external validity is the Hawthrone effect (Thomas & Nelson, 1996). In this scenario a person may tend to perform better due to the special attention from the researcher or associates. Person B mentioned in her narrative report that she would not exercise if she had to do it on her own and unsupervised. Thus, part of the reason for her adherence and achievements are directly related to the influence and motivation by the researcher. This was not experimental research and external validity was controlled by the use of replication logic (Yin, 2003). However, it can be assumed that she would have dropped out if the personal contact with the researcher was less intimate. Biokineticists may play a bigger role in the motivation of depressed HIV patients in order to achieve better outcomes. A participant in a HIV study by Galantino *et al.* (2005) further supports the value of supervised training when he said: *"Being in a group and doing the exercises together with our leader is the only way I would exercise. I`d never stick to it alone at home"* (Galantino *et al.,* 2005:1089)

Person C had the most significant increases in both mental health and health distress scores. His mental health score increased with 4.24 points and his health distress score with 6.58 points. This is well above the average increase in this study.

HIV/AIDS is perhaps the most stigmatized medical condition in the world. Internalized stigma has been related to the development of depressive symptoms (Simbayi *et al*., 2007). Person C revealed in his narrative report something about this stigma "*People say you have slims, you cannot work, you cannot exercise*". And then he realized that he could work and he could do exercise. *"No, I can work and I can exercise".* This knowledge might have reversed the internalized stigma and this may be one of the reasons why his depression and anxiety scores increased above the average. By successfully participating in an exercise program, it seemed that he gained self confidence and self respect. Reduction in depression leads to a significant improvement in health related QOL (Elliot *et al.,* 2002). For this person exercise enhanced his QOL significantly by reducing his feelings of depression.

The findings in the current study that aerobic exercise has a positive effect on depression, are consistent with several studies in the literature and add to the overall body of research linking aerobic exercise and improved mood.

Brenes *et al.* (2007) concluded that aerobic exercise is an effective treatment for depression in older people. They mentioned that besides biological mechanisms, psychological mechanisms such as increased self-efficacy and reduced negative patterns, may contribute to improvement in mood state. None of the three participants in the current study exercised since their HIV diagnosis, which may be one of the reasons why they might have experienced increases in self-efficacy and feelings of achievement during and after the intervention.

McPhail (2006) reported similar outcomes in a study that compared exercise as treatment for depression to the use of medication. The conclusion was that the patients who used exercise as treatment did as well as those who used medication during an

intervention of four months. Furthermore, the exercise group had better long-term reductions in depression symptoms than those who used medication. The current study did not take the use of anti-depressive medication into account, but the findings support the view that exercise is effective as treatment modality for depressive symptoms.

Neidig *et al.* (2003) published the first report on the effects of aerobic exercise training for depressive symptom management in HIV-infected adults. Participants in their study completed a 12 week aerobic exercise program and reported improvements in depressive symptoms and depressed mood as compared to a control group that maintained usual activities. Although their study used the Profile of Mood State (POMS), Centre for Epidemiological Studies-Depression Scale (CES-D) and the Beck Depression Inventory (BDI) to measure depressive symptoms, and the current study used the MOS-HIV scale, all these scales are widely used in HIV research (Neidig *et al.*, 2003, Rojas *et al.,* 2003) and the current study supports the findings by Neidig *et al.* (2003).

6.6 Pain

The MOS HIV has two questions related to pain. Bodily pain is one of the areas not accessible to physiological measurement and may only be evaluated using patients` assessments (Wu, 1999). A low score is an indication of severe and limiting pain, while a high score indicates no limitations due to pain.

Pain is one of the most common symptoms in HIV (Frich & Borgbjerg, 2000). The main cause of pain in HIV patients is peripheral neuropathy (Ownby & Dune, 2007). The MOS-HIV, however, only measures pain, and not the nature or location of the pain. Exercise proved to decrease the intensity of pain in HIV patients (Nicholas *et al.*, 2002). Indeed, all three participants experienced decreased pain after the intervention period, according to their MOS-HIV pain scores.

Person A had an initial pain score of 62.55. It increased to 63.35 after the intervention. His pain is not limiting. Besides complaining about delayed onset muscle soreness (DOMS), he did not report pain again in the narrative reports. According to Sznymanski (2001) muscle pain and stiffness may occur when the intensity of the exercise is more than the body is accustomed to.

Person B reported that her pain was less at night and also less at work. These narrative pain reports are confirmed by her pain score in the MOS HIV. She had the lowest pain score of the three participants, but it increased with 2.26 points – an indication that her pain decreased. Pain is a subjective sensation and experience (Modi *et al.,* 2007), and Person B experienced more pain than the other two participants, although she appeared to be less ill than Person C. For her, participation in aerobic exercise decreased her subjective experience of pain.

Person C had the most significant decrease in pain. His pain scale increased from 58.7 to 60.73.Although he did not mention pain in his narrative reports, his experience of pain decreased with 4.01 points after the intervention period. Person C was diagnosed seropositive in 2000. Of the three participants, he has lived with HIV/AIDS the longest.

According to Ownby and Dune (2007), living with pain is a process of learning. Initially pain is the focal point of the patient's existence, yet, with time, the pain became more of a secondary concern in their lives. This might explain why Person C did not mention his pain in his narrative reports. A significant decrease of pain after the interventions indicates that he does experience pain, although he does not mention it often. This decrease in pain contributes to his overall increase in quality of life.

The findings of this study support the results from an early study by McCormack *et al.* (1993) that pain is non-specific to time course of the disease and not that of Larue *et al*. (1997) and Evans *et al.* (1998) who found that there was a correlation between stage of disease and severity of pain.

The decrease in pain experienced by the participants correlates with the findings by Glass *et al.* (2004). In their study the effect of brief exercise cessation on pain in healthy individuals was investigated. Eight of the 17 subjects in their study went on to develop somatic symptoms (including pain) following 1 week of exercise cessation. Person B, who experienced exercise cessation practically since she was diagnosed with HIV in 2002, and person C since his diagnosis in 2000, reported a decrease in pain after 16 weeks of aerobic exercise. Especially in the case of Person C, who used to exercise before his diagnosis, it can be argued that the exercise cessation added to his experience of pain.

In a study by Lee *et al.* (2006), the effect of regular exercise on pain, fatigue and disability in patients with rheumatoid arthritis, was investigated. Pain in rheumatoid arthritis is caused by inflammation of the joints and tissues. Pain in HIV is caused by several factors discussed earlier, but inflammation is one of the causes (Larue *et al.,* 1997).

Lee *et al.* (2006) found that regular exercise did not decrease pain experience, which differ from the results of the current study. A possible explanation for the difference in finding may be the type of exercise investigated. Lee *et al.* (2006) studied regular exercise done by individuals at home. Participants in their study completed a questionnaire. Persons who indicated that they exercise more than three times per week for at least 20 minutes in duration and for more than 6 consecutive months, were regarded as exercisers. The intensity and type of exercise were not determined. According to the literature, aerobic exercise at a certain level results in a decrease in pain (Hoffmann *et al.,* 2005). This may be the reason why no decreases in pain were reported.

Another explanation may be that in the study by Lee *et al.* (2006), an exercise program was not prescribed to previously inactive patients, as in the current study. The immediate effect of exercise on pain reduction in previously inactive persons may be more noticeable than in persons who have exercised for 6 months or more.

6.7 Absenteeism

Persons A and C have not been absent from work for one day due to HIV, during the intervention period. According to them they did not have a tendency towards absenteeism before the intervention started.

Neither Person A or C has AIDS, although person C has a low CD4 cell count (328-229 /mm). According to Leigh *et al.* (1997) absenteeism is not higher in the HIV positive population when compared to the healthy population, but only in the AIDS population. This may explain why these two participants did not report HIV related absenteeism.

Person B reported two days absent from work during the four month intervention period. This was due to fatigue and fever, which are HIV related. According to her, her absenteeism rate was approximately two days per month before the intervention started. Person B does not have AIDS. She had all over lower scores in the MOS-HIV, and her total quality of life score was the lowest of the three participants. After the intervention her QOL score increased with 3.4 points. Higher QOL is associated with lower absenteeism rates (Czerny, 2005). It might be that the increase in Person B`s QOL, had lead to a reduced rate of absenteeism. However, because of confidentiality, it was not possible to verify the days absent from work with the employers without exposing any of the participants.

If it is true that Person B was more absent from work before the intervention (as she indicated), it is contrary to a study by Altchiller and Motta (1994). They found in their 8 week exercise study that employees participating in aerobic exercise reported decreases in anxiety, but that the exercise had no effect on absenteeism. Their study did not include HIV positive employees and measured only state of anxiety and absenteeism. It might be that other parameters of QOL, such as fatigue, have a greater effect on absenteeism than anxiety. According to Person B the reason for her absenteeism was fatigue. This may explain why her absenteeism rate decreased (according to her) after 16 weeks of aerobic exercise.

6. 8 Narrative reports

A lot can be learned from the subjective narrative reports by participants in a study (Overcash, 2003). The short narrative reports in this study were analysed by explanation building, logical reasoning (Yin, 2003) and identifying themes and categories (Endacott, 2007).

Several themes were analysed from the narrative reports by Person A, B and C.

6.8.1 Enjoyment

From the beginning to the end Person A and C mentioned that they enjoyed the training sessions. During the last interview Person B also mentioned that she likes the exercises. Participation in joyful activities leads to a better quality of life (Aldana *et al.,* 2005).

6.8.2 Knowledge

During the first narrative report Person A mentioned that he did not realised how restricted his physical condition had became. Both his muscular fitness ("*sore leg muscles*") and cardiovascular fitness ("*out of breath*") were restricted. By participating in exercise the participant gained insight into his physical status, something that he would not know if he did not participate. Now he was able to do something about his fitness levels. The same awareness of physical status was observed with Person B (...*I am not fit yet*…).

6.8.3 Responsibility

The observation that Person A takes responsibility for his health was further strengthened through his narrative reports. Not only does he want to keep on

exercising, he also sent a friend to participate and benefit from the exercises. Person C announced that he *must* continue exercising, an announcement that demonstrates responsibility towards himself. The same responsibility was not observed in Person B. She also had a lower quality of life according to her MOS-HIV. Future studies may investigate the relationship between taking responsibility for ones health, QOL and disease progression.

6.8.4 Fatigue

A central theme in all three participants' narrative reports was fatigue. Fatigue is one of the most frequently reported symptoms in HIV patients (Siegel *et al.,* 2004). The intensity of the exercise for HIV positive persons is of great importance. Corless *et al.* (2004) recommended an intensity of 50% to 80% of VO_2 max. This is supported by Mars (2003). The biokineticist working with HIV patients must be sensitive for the intensity of the prescribed program. The feedback from the patient is important. A HIV patient may force himself to train harder in order to prove to himself that he is not that ill, or because he used to be an athletic person, as in the case of Person C. However, as mentioned earlier, the Karvonen method has proved to be an effective method to determine intensity. The patient must simply adhere to the prescribed intensity level.

Although his prescription was at an intensity of 50 % of maximum heart rate, Person C forced himself to train harder during the first exercise session. It led to extreme fatigue during the training session. The intensity was decreased to the prescribed norm ("…*I get tired, so now I cycle slow like you told me*") and he was able to complete all 16 weeks of training, with progression in intensity ("*I can cycle faster and keep it there all the time*") (Chapter 5.6.3)

On the positive side, all three participants reported that overall fatigue decreased as the sixteen week period progressed.

6.8.5 Improved performance at work

All three participants reported better performance at work (subjective). This might be due to improved fitness levels. Persons with a higher degree of fitness, have a better performance at work (Addley *et al.,* 2001). The overall improvement in quality of life might also be one of the reasons for better performance at work.

6.8.6 Progression and achievement

The objective measurements of physical functioning (VO_2 max) showed improvement. The subjective experience by all three participants correlates with this measured improvement. All three mentioned that they feel more fit than before. This feeling of progression and achievement may serve to lessen feelings of hopelessness and depression (Remor *et al.,* 2007) due to HIV infection. It my also give the patient a sense of control over his disease. According to McPhail (2006) many patients respond poorly to serious illness or injury because they feel they have lost control of their lives. They then become depressed and passive victims to their health conditions. A therapeutic program that includes exercise helps the patient re-establish a sense of control over his life again.

6.8.7 Intrinsic believe in the value of exercise

Another theme from the narrative reports is expressed belief of all three participants that exercise is good for them and helps to improve their QOL. Initially Person B believed the opposite, but after education she mentioned in her narrative report that exercise helped her. If a person believes that exercise is good and compulsory, it makes the task of the biokineticist easier, because there will be a greater adherence to the exercise program and thus better results.

6.8.8 Transport

Although not a central theme, the issue of transport deserves attention. Person B mentioned that unreliable transport was an obstacle to her. In a study by Neidig *et al*. (2003), transport problems were also mentioned by low socio economic patients as one of the reasons for non compliance in their study. Future researchers must keep the issue of transport in mind when planning a HIV study. In a big sample it would have been more difficult to arrange for transport.

6.9 Drop out rate

Several HIV studies reported high drop out rates (Neidig *et al*., 2003). These high rates were due to a mixture of circumstances like death, poor transport and lack of motivation. This study reported a zero drop out rate, which is in contrary with findings in other HIV studies. The reason for this may be the small size of the participating group. Because the group consisted out of only three persons, every member received adequate attention and worked closely and personally with the researcher. The small size of the group made it possible for the researcher to arrange for transport when difficulties arose. If the group was bigger, this would not have been possible without proper funding for the study. Another reason may be because exercise was done in a group (Carlson *et al.* 2006; Losito, *et al.* 2006) and at a training facility and not on their own at home (Carlson *et al.,* 2006).

CHAPTER 7
CONCLUSION

Aerobic exercise has a positive effect on the HR-QOL in employees living with HIV. The quantitative and qualitative data provided confirmation that a 16 week aerobic exercise program enhanced the HR-QOL among the three participants. It seems that aerobic exercise is a safe complimentary method to manage HIV symptoms, and in this manner enhances QOL.

The results in this study showed that regular, moderate intensity aerobic exercise improved VO_2 max in HIV patients. All three participants had an increased functional capacity, which resulted in a decrease in fatigue. Fatigue, one of the most common symptoms experienced by HIV patients, can be improved by participation in aerobic exercise.

The CD4 cell counts of all three participants did not show any significant changes after 16 weeks of exercise. This is in accordance with most research on HIV and exercise. The conclusion can be made that, although aerobic exercise do not slow down the progression of the disease, it is safe for HIV patients. Bearing in mind all the benefits derived from aerobic exercise, this safe modality should be highly recommended for the management of HIV symptoms.

The body composition of all three participants improved, with higher lean mass and decreased fat mass, although not significantly in Person C. Changes in body composition due to HIV and ART, have a negative effect on body image. Wasting is also associated with disease progression by the patient. For Person C, with the typical body composition caused by lipodystrophy, hypertrophy of the leg muscles lead to a better body image.

Obesity and overweight amongst HIV patients is not uncommon. Person B, an overweight person, managed to decrease her BMI after 16 weeks of aerobic exercise,

without changing her diet. The conclusion can be made that for overweight as well as wasted HIV patients, aerobic exercise has a positive effect on body composition and body image.

Mental health and health distress scores for all three participants indicated fewer feelings of depression and anxiety after 16 weeks of exercise. Because of the high prevalence of depression amongst HIV patients, exercise therapy should be promoted. Decreases in depression and anxiety may lead to better adherence to ART therapy and visits to the clinic. In South Africa, where depression amongst HIV patients is higher than in developed countries, aerobic exercise can play an even bigger role. Aerobic exercise does not have to be expensive. Walking, jogging or cycling is within the reach of every HIV patient. Another conclusion is that decreases in depression will result in decreased absenteeism in HIV positive employees.

In this study it is concluded that pain is not specific to time course of the disease. Person C, who had the most advanced disease progression, did not report the highest experience of pain. It is further concluded that aerobic exercise effectively reduced the subjective experience of pain by all three participants, and therefore should be promoted amongst HIV patients.

Absenteeism did not affect two of the participants, but one reported a decrease in absenteeism rate from 2 days per month to 0.5 days per month. However, this could not be confirmed with the employer, due to confidentiality.

This study further revealed that HIV is still a highly stigmatized illness in Mpumalanga. After repeated unsuccessful efforts over an 18 month period, only three HIV positive volunteers were enrolled into the study.

It further seems that exercise is not often prescribed or proposed to HIV patients by health care professionals in the Middelburg area. None of these three participants received any advice or information about exercise and HIV at their clinics or at the work

place. One of the participants believed that exercise will adversely affect her illness. Another stopped exercising when he was diagnosed HIV positive.

A mixed research approach, combining qualitative and quantitative data seems to be an effective method to use in biokinetic research. The quantitative data provided unbiased evidence of QOL improvement, while the qualitative data revealed the personal experience of the participants in a way that is not possible by using quantitative measures. Especially in the case of HIV, where patients do not often disclose their status, the qualitative data may be useful for the biokineticist to understand the patient better. Furthermore, the limitations in quantitative analysis due to the small sample size may be compensated for by qualitative data interpretation.

The purpose of a case study is not to make generalizations, because case studies are not sampling units. Rather, analytical generalization was used. Previously developed theory was used as template to compare the results of this study.

7.1 RECOMMENDATIONS

1. Living in a country that is host to the largest HIV population in the world (Simbayi *et al.,* 2007), biokineticists should be aware of the role that they can play in the management of this disease.
2. Biokineticists should be part of the multi- disciplinary team approach towards HIV management and should claim their rightful place in the team of health care providers.
3. Exercise as a complementary therapy for HIV must be promoted among HIV patients.
4. Biokineticists should educate HIV patients on healthy lifestyle habits.
5. Myths about HIV and exercise must be revealed.
6. HIV workshops held in the workplace should also include information on HIV and exercise.

7. Supervised exercise sessions for HIV patients are recommended, because the interpersonal contact with the supervisor (biokineticist) seems to have a positive effect on the outcomes.
8. General wellness and fitness programs in the workplace are recommended. In this way HIV positive employees who did not disclose their HIV status, will automatically benefit from it.
9. The good practice of proper exercise testing is important when prescribing exercise programs, because often the biokineticist will not know that his patient is HIV positive. The results of the exercise tests will guide the prescription of intensity, duration and frequency of the exercise program.

Aerobic exercise must be promoted amongst HIV positive employees. Although it is no cure for HIV, nor proven to stop the progression of this bizarre disease, it leads to an enhancement in the health related quality of life of the HIV patient. It is a way in which a sick stigmatized person can regain self respect and take some control over a situation that sometimes seems to be out of control.

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Person C, an enthusiastic and cooperative participant, died 7 months after the intervention was completed. Maybe the last words in his last narrative report summarise the effect of aerobic exercise on HIV positive patients the best:

"I am sick, but I feel good".

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INTERVIEW

Sr. Agnes Mabena. Middelburg Aids Clinic, 13/10/2005.

APPENDIX A

INFORMED CONSENT

I _____
(Full name of prospective participant)

have been informed of the procedures and requirements to participate in a research project dealing with the effect of aerobic exercise on the health related quality of life in HIV positive employees, to be conducted in Middelburg, Mpumalanga.

I am willing to participate in the said project at my own risk.

I declare hereby that no information has been withheld that could exclude me from participating in an exercise programme, and am aware that I am entitled to withdraw from the study at nay time should I wish.

I hereby also grant the researcher permission to use my results for publication and/or presentation purposes, with my anonymity being ensured.

_____ _____
Signature of prospective participant Date

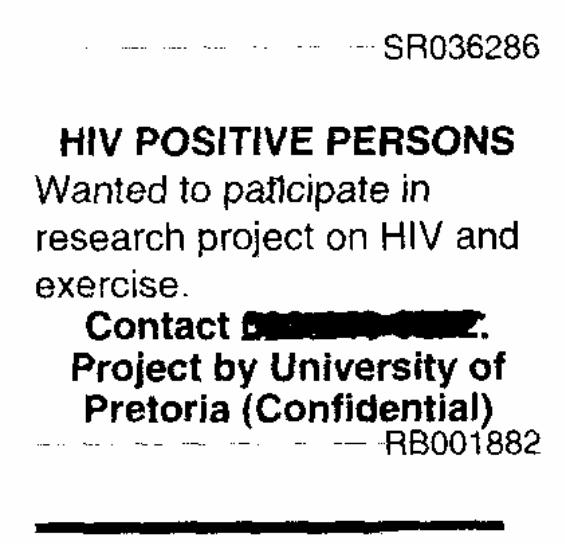
Tel: _____ (h) _____(w)

Witness

1. _____
2. _____

APPENDIX B

NEWSPAPER ADVERTISEMENT



SR036286

HIV POSITIVE PERSONS

Wanted to participate in research project on HIV and exercise.

Contact [redacted].

Project by University of Pretoria (Confidential)

RB001882

[redacted]

Middelburg Observer 2 February 2007

APPENDIX C: Karvonen method for calculation of target heart rate
(Baechle & Earle, 2000:500)

Target Heart Rate Calculations

Karvonen Method

Formula:

Age-predicted maximum heart rate (APMHR) = 220 – age

Heart rate reserve (HRR) = APMHR – resting heart rate (RHR)

Target heart rate (THR) = (HRR × exercise intensity) + RHR

Do this calculation twice to determine the target heart rate range (THRR).

Example:

A 30-year-old athlete with an RHR of 60 bpm is assigned an exercise intensity of 60-70% of functional capacity:

APMHR = 220 – 30 = 190 bpm

RHR = 60 bpm

HRR = 190 – 60 = 130 bpm

Lowest number of the athlete's THRR = (130 × 0.60) + 60 = 78 + 60 = 138 bpm

Highest number of the athlete's THRR = (130 × 0.70) + 60 = 91 + 60 = 151 bpm

When monitoring heart rate during exercise, divide the THRR by 6 to yield the athlete's THRR in number of beats for a 10-s interval:

138 ÷ 6 = 23 151 ÷ 6 = 25

The athlete's THRR is 23-25 beats per 10 s.

APPENDIX D: Exercise Program

Week 1: Cycle 30 minutes at 50% of functional capacity. Keep resistance low enough to maintain target heart rate (HR) 3 x per week

Person A
Resting HR: 78 bpm
Age: 41
Target HR = **128 bpm** or 21 beats per 10 seconds
Cycle at 128 bpm or 21 beats per 10 seconds

Person B
Resting HR: 83 bpm
Age: 36
Target HR: **134 bpm** or 22 beats per 10 seconds

Person C
Resting HR: 80 bpm
Age: 31
Target HR: **135 bpm** or 22 beats per minute

Week 2: Cycle 30 minutes at 60% of functional capacity. Keep resistance low enough to maintain target heart rate (HR) 3 x per week

Person A
Resting HR: 78 bpm
Age: 41
Target HR: **139 bpm** or 23 beats per 10 seconds

Person B
Resting HR: 81 bpm
Age: 36
Target HR: **142 bpm or** 24 beats per 10 seconds

Person C
Resting HR: 79 bpm
Age: 31
Target HR: **145 bpm** or 24 beats per 10 seconds

Week 3: Cycle 30 minutes at 70% of functional capacity. Keep resistance and speed high enough to maintain target heart rate (HR) 3 x per week

Person A
Resting HR: 75 bpm
Age: 41

Target HR: **148 bpm** or 25 beats per 10 seconds

Person B
Resting HR: 81 bpm
Age: 36
Target HR: **153 bpm** or 26 beats per 10 seconds
Person C
Resting HR: 79 bpm
Age: 31
Target HR: 156 bpm or 26 beats per 10 seconds

Week 4 and on 30 minutes at 80% of functional capacity. Keep resistance and speed high enough to maintain target heart rate (HR) 3 x per week.

Person A
Resting HR: 73 bpm
Age: 41
Target HR: **158 bpm** or 26 beats per 10 seconds

Person B:
Resting HR: 79bpm
Age: 36
Target HR: **163 bpm** or 27 beats per 10 seconds

Person C:
Resting HR: 78 bpm
Age: 31
Target HR: **167 bpm** ore 28 beats per second

Note: Start slow for 5 minutes to warm up, only then cycle to reach your target. End the training session with a cool down period (cycle slow) of 5 minutes.

APPENDIX E: MOS-HIV

HIV HEALTH SURVEY

INSTRUCTIONS TO THE STUDY COORDINATOR:

The following questionnaire asks the patient about many aspects of his/her health and health care. It should be given to the patient prior to the clinical exam and preferably in a quiet secluded area (e.g., exam room or other office).

It is important to be familiar with the content and format of the questionnaire before giving it to study participants. At the first visit, please begin by telling the participant: "We would like you to answer some questions about how you are feeling and the kinds of things you are able to do. Your answers will help us understand the effects of the medication you are taking. We appreciate your filling out this questionnaire"

You should then briefly go over the format of the questions and how to complete them. Have the participant complete the questionnaire before vital signs, history and physical are completed.

The questionnaire is very brief and should take no more than 10 minutes to complete. Before giving the patient the questionnaire, please fill out the header(s) and DETACH THIS PAGE.

Each question is in the same general format. Note that the patient is always asked to check one box for
each question. All questions refer to the PAST 4 WEEKS.

Collect the completed questionnaire before the clinical exam. Before going on, review the questionnaire for omissions. If the participant missed any of the questions, point this out and have him/her complete
the omissions.

PLEASE COMPLETE THE FOLLOWING ITEMS AFTER PATIENT COMPLETES THE QUESTIONNAIREOR AFTER YOU ASCERTAIN THAT THIS IS NOT POSSIBLE:

1. How was the questionnaire completed?

1 - Self administered by the study participant

2 - Face-to-face interview that you conducted

3 - Phone interview

4 - Not completed

5 - Other

If other, specify:

2. If you answered 2 or 4, please indicate the reason(s) why:

(1-Yes, 2-No)

Patient refused initially: .....

Patient's reading level not adequate: .....

There was not enough time: .....

Patient forgot reading glasses: .....

Other reason: .....

If other, specify:

MOS-HIVHEALTH SURVEY

INSTRUCTIONS TO PATIENT:
Please answer the following questions by circle the appropriate number.

1. In general, would you say your health is:
(Check One)

Excellent	1
Very Good	2
Good	3
Fair	4
Poor	5

2. How much **bodily** pain have you generally had during **the past 4 weeks?**
(Check One)

None	1
Very Mild	2
Mild	3
Moderate	4
Severe	5
Very Severe	6

3. During **the past 4 weeks**, how much did pain interfere with your normal work (or your normal activities, including work outside the home and housework)?
(Check One)

Not at all	1

A little bit 2
Moderately 3
Quite a bit 4
Extremely 5

4. The following questions are about activities you might do during a typical day. Does your **health now limit you** in these activities? If so, how much?
(Check **one** box on **each** line.)

YES, limited a lot	**1**
YES, limited a little	**2**
NO, not limited	**3**

a. The kinds or amounts of **vigorous** activities you can do, like lifting heavy objects, running or participating in strenuous sports.

1 2 3

b. The kinds or amounts of **moderate** activities you can do, like moving a table, carrying groceries or bowling.

1 2 3

c. Walking uphill or climbing (a few flights of stairs).

1 2 3

d. Bending, lifting or stooping.

1 2 3

e. Walking one block.

1 2 3

f. Eating, dressing, bathing or using the toilet.

1 2 3

5. Does **your health** keep you from working at a job, doing work around the house or going to school?
(Check One)

Yes 1
No 2

6. Have you been unable to do **certain kinds or amounts** of work, housework, or schoolwork because of your health?
(Check One)

Yes 1
No 2

For each of the following questions, please check the box for the one answer that comes closest to the way you have been feeling during the past 4 weeks.

All of the time	**1**
Most of the time	**2**
A Good Bit of the time	**3**
Some of the time	**4**
A Little of the Time	**5**
None of the Time	**6**

7. How much of the time, during the past 4 weeks, has your **health limited your social activities** (like visiting with friends or close relatives)?

8. How much of the time, during the past 4 weeks:
a. Have you been a **very nervous person?** 1 2 3 4 5 6
b. Have you felt **calm and peaceful**? 1 2 3 4 5 6
c. Have you felt **downhearted and blue**? 1 2 3 4 5 6
d. Have you been a **happy person**? 1 2 3 4 5 6
e. Have you felt so **down in the dumps that nothing could cheer you up**? 1 2 3 4 5 6

For each of the following questions, please check the box for the one answer that comes closest to the way you have been feeling during the past 4 weeks.

All of the time	**1**
Most of the time	**2**
A Good Bit of the time	**3**
Some of the time	**4**
A Little of the Time	**5**
None of the Time	**6**

9. How often during the **past four weeks:**

a. Did you feel full of pep?	1 2 3 4 5 6
b. Did you feel worn out?	1 2 3 4 5 6
c. Did you feel tired?	1 2 3 4 5 6
d. Did you have enough energy to do the things you wanted to do?	1 2 3 4 5 6
e. Did you feel weighed down by your health problems?	1 2 3 4 5 6
f. Were you discouraged by your health problems?	1 2 3 4 5 6
g. Did you feel despair over your health problems?	1 2 3 4 5 6
h. Were you afraid because of your health?	1 2 3 4 5 6

10. How much of the time, during the **past 4 weeks:**

a. Did you have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things?
b. Did you forget things that happened recently, for example, where you put things and when you had appointments?
c. Did you have trouble keeping your attention on any activity for long?
d. Did you have difficulty doing activities involving concentration and thinking?

11. Please check the box that best describes whether each of of the following statements is true or false for you.

(Check **one** box on **each** line.)

Definitely True	**1**
Mostly True	**2**
Not Sure	**3**
Mostly False	**4**
Definitely False	**5**

a. I am somewhat ill.	1 2 3 4 5 6
b. I am as healthy as anybody I know.	1 2 3 4 5 6
c. My health is excellent.	1 2 3 4 5 6
d. I have been feeling bad lately.	1 2 3 4 5 6

12. How has the quality of your life been during the **past 4 weeks**? That is, how have things been going for you?

(Check One)

Very well; could hardly be better	1
Pretty good	2
Good and bad parts about equal	3
Pretty bad	4
Very bad; could hardly be worse	5

13. How would you rate your physical health and emotional condition now compared to **4 weeks ago**?
(Check One)

Much better	1
A little better	2
About the same	3
A little worse	4
Much worse	5

THANK YOU VERY MUCH