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THE RELATIONSHIP BETWEEN LOWER LIMB MUSCLE STRENGTH AND LOWER LIMB FUNCTION IN HIV POSITIVE PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

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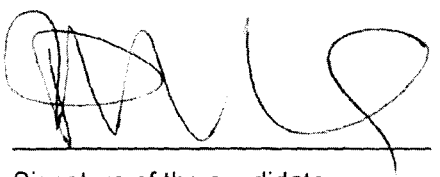
A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Science in Physiotherapy.

Johannesburg, 2015

DECLARATION

I, Peter Clever Mhariwa, declare that this research report is my own work. It is being submitted for the Degree of Master of Science in Physiotherapy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.



Signature of the candidate

Date: 29th day of JULY. 2015

DEDICATION

Surely, goodness and mercy followed me while completing this report. I shall dwell in the house of the Lord forever and ever.

God helped me such that no weapon formed against me during the report writing prospered.

Every tongue which rose against me in judgment, I condemned in Jesus' name, Amen.

To my wife, Lorraine, my children, Theresa, Simbarashe and Tinotenda-Joel,for their prayers and support during my study period.

ABSTRACT

The Human Immunodeficiency Virus (HIV) has been found to cause muscle weakness, wasting and peripheral neuropathies. The specific relationship between lower limb muscle strength and lower limb function in HIV positive patients on Highly Active Antiretroviral Therapy (HAART) has not been examined. The aims of the current study were to establish lower limb muscle strength in HIV positive patients on HAART, establish lower limb muscle strength in HIV negative people, compare lower limb muscle strength between patients who are HIV positive on HAART and HIV negative people, establish lower limb function in patients who are HIV positive on HAART and to establish the relationship between lower limb muscle strength and lower limb function in patients who are HIV positive on HAART.

A cross-sectional, descriptive study design was used. Dynamometry was used to measure lower limb muscle strength. The lower Extremity Functional Scale (LEFS) was used to determine lower limb function. A pilot study was done to establish the feasibility and proficiency required to perform hand held dynamometry. Intra and inter-rater reliability were also determined during the pilot phase.

Intra and inter-rater reliability were high for the raters' measurement of lower limb muscle strength using a dynamometer with 'r' values of 0.97. For HIV positive patients on HAART, 19% (n=22) were in the age band 45-49years, whereas 33% (n=10) of HIV negative subjects were in age interval 25-29 years. Those over 45 years who were HIV positive on HAART constituted 57% (n=64) of the sample.

The mean muscle strength obtained ranged from 9.30kg/m^2 in ankle dorsiflexors to 15.80kg/m^2 in hip extensors in HIV positive people on HAART for an average of 4 years while knee flexors generated 11.81kg/m^2 and knee extensors generated 15.36kg/m^2 in this cohort. In the HIV negative matched group, the mean muscle strength ranged from 11.20 kg/m^2 in ankle dorsiflexors to 17.70 kg/m^2 in hip extensors while knee flexors generated 12.65kg/m^2 and knee extensors generated 17.07kg/m^2.

The majority 78% (n=88) of HIV positive patients on HAART had no difficulty with lower limb function while 22% (n=17) had difficulty. Only 2% (n=2) of HIV positive patients on HAART had quite a bit of difficulty with lower limb functional activities after measurements using the Lower Extremity Functional scale (LEFS).

A multiple linear regression showed that there was a positive correlation coefficient of r=0.71 (p-value=0.00) between lower limb muscle strength and lower limb function. The coefficient of determination 0.50 means that 50% of the changes in lower limb function are attributable to lower limb muscle strength. Gender, employment status and mode of transport also positively affected lower limb function.

A detailed regression model showed that lower limb ankle plantar flexors contributed the most to lower limb function in this cohort. This is contrary to International literature which states that hip and trunk muscles are the most active in HIV negative people during lower limb functional activities. That plantar flexors contribute the most in lower limb functional activities instead of hip and trunk muscles confirms the existence of proximal weakness in this cohort which was established by other researchers.

This study highlighted that 50% of lower limb function is a result of lower limb muscle strength in HIV positive people on HAART attending an outpatient clinic in Mutare, Zimbabwe. Ankle plantar flexors instead of hip flexors were the most active muscle group in lower limb functional activities in this cohort. It therefore means exercise prescription to activate/strengthen hip flexors and other proximal muscles will improve this population's lower limb functional activities since progressive resisted aerobic exercises have been proved to strengthen muscles.

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LIST OF ABBREVIATIONS

ADL	- Activities of Daily living
AIDS	- Acquired Immunodeficiency Syndrome
ANC	- Ante-natal Clinic
ANRS	- Agency Nationale de Recherché sur le Sida
CD4	- Cluster Difference 4
DNA	- Deoxyribonucleic Acid.
HAART	- Highly Active Antiretroviral Therapy
HIV	- Human Immunodeficiency Virus
HRQOL	- Health Related Quality Of Life
ICF	- International Classification of Function
Kg/m^2	- Kilogram's per square meter
LEFS	- Lower Extremity Functional Score
NAC	- National Aids Council
p-value	- Probability value
RNA	- Ribonucleic Acid.
RT	- Reverse Transcriptase
UNAIDS	- United Nations program on HIV and AIDS
UNGASS	- United Nations General Assembly
WHO	- World Health Organization

CHAPTER 1

1. INTRODUCTION

This study is to determine if there is a relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART in Manicaland, a province in eastern Zimbabwe. Studies have shown that HIV generally cause muscle weakness (Myezwa et al., 2009).This is possibly due to effects of HIV disease or HAART on tissue oxygen extraction and utilisation (Carnethon et al., 2005).The use of HAART in HIV treatment has been related to lipodysthophic alterations like lipoatrophy, mitochondrial toxicity and reduction of the activity of oxidative enzymes (Cade et al., 2003). Thus, HIV and HAART negatively influence oxygen kinetics, limiting the extraction/ use of oxygen in lower limb musculature (Cade et al., 2003). Lower oxygen use capacity directly affects physical fitness and consequently, the individual's motivation to perform routine activities (Mendes et al., 2013). The acute phase of HIV/AIDS is thus frequently marked by a substantial loss of physical fitness (Raso et al., 2013).

HIV infected populations have impairments, activity limitations, and participation restrictions (WHO, 2001). Limitations in functional abilities are known to exist in HIV positive patients in Manicaland (Lopman et al., 2007), however the specific effect of HIV on lower limb function is not known.

Human Immunodeficiency Virus (HIV) disease is now described as an episodic condition that is chronic in nature (O'Brien et al., 2009). As with other chronic conditions, rehabilitation has become an important part of the management of HIV impairments (Myezwa et al., 2009). Understanding the impairment's functional limitations, and participation restrictions associated with HIV should be a pre-requisite to rehabilitation intervention (Myezwa et al., 2009).

Activities of Daily Living (ADL) capacity is preserved in more than 90% of the HIV infected patients on treatment with anti-retroviral medication or HAART_but these patients remain limited in rigorous activities such as heavy work ,walking uphill and exercises(Oursler et al., 2009). Kressy et al (2009) established that all HIV positive patients including those on antiretroviral therapy can develop wasting. In patients with HIV infection, wasting, particularly loss of metabolic active lean tissue has been associated with increased mortality, accelerated disease progression, loss of muscle protein mass and impairment of strength and functional state (Grinspoon et al., 2003).Kinsey (2007) however found no

significant difference in lower limb muscle strength between HIV positive females on HAART for seven months and their HIV negative counterparts.

Muscles maintain their mass and function because of a balance between protein synthesis and protein degradation associated with equal rates of anabolic and catabolic processes respectively (Lynch et al., 2007). Muscles grow when protein synthesis exceeds protein degradation (Lynch et al., 2007). HIV induces muscle fibers to differentiate between self and non-self cells, triggering cell mediated muscle fiber injury leading to wasting (Goletz et al., 1997).

Apoptosis is key in cell production and tissue homeostasis; it purges unnecessary, aged or damaged cells (Miro et al., 2005). Abnormal resistance to apoptotic cell death is the basis of developmental malformations, autoimmune disease and many cancers whereas enhanced susceptibility of cells to apoptotic signals participates in tissue damage secondary to acute infections (Miro et al., 2005). Apoptosis is thus linked to the pathogenesis of HIV in that, increased apoptosis of CD4 T cells result in there depletion by HIV's use of CD4 as a primary receptor (Cloyd et al., 2001).

The causes of weight loss and tissue wasting in HIV patients/individuals are multiple and include hypogonadism, malnutrition, anorexia, infection and perhaps an HIV induced hyper metabolic state (Grinspoon et al., 2010). Wasting has been found to result in decreased lower limb muscle strength or compromised balance in 30% of HIV positive individuals causing low muscle mass in legs and gluteal muscles (Carter et al., 2011). Each year of infection with HIV was also found to increase the risk of poor lower limb performance by 8% (Carter et al., 2011). Therefore HIV has the potential to decrease the physical activity levels and functional independence of infected individuals (Kinsey, 2007).

HIV has distinct multifaceted physiological, emotional and societal features at any stage of the disease with the possibility of losing functional capacity and affecting Health Related Quality Of Life (HRQOL) (Van As et al., 2008). Studies on quality of life in HIV positive Sub-Saharan patients are however limited (Mutimura et al., 2007). Sterne et al (2005) found that HAART is becoming more accessible to HIV-infected people in resource limited regions of the world and their quality of life is also improving. HIV affects function in general and more specifically one study has shown that proximal weakness is a common feature when HIV patients were tested using dynamometry (Myezwa et al., 2009). In another study one of two adults with undetectable viral load, which is HIV RNA of less than 50copies/ml (controlled HIV) had poor lower limb muscle performance, which put this population at risk of falls and

fracture (Richert et al., 2011) hence assessment of lower limb strength should be carried out as part of routine HIV care (Carter et al., 2011). Aerobic and progressive strengthening exercises can then be prescribed since these exercises have been associated with improvements in muscle strength, activities of daily living, cardiovascular function and psychological status in general populations (O'Brien et al., 2009). Exercises may also be used to address unwanted changes in weight and body composition in people living with HIV infection (O'Brien et al., 2009).

1.1 PROBLEM STATEMENT

There is not much research done on the relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART in Manicaland, Zimbabwe.HIV has been found to cause muscle weakness, wasting and peripheral neuropathies (Van As et al., 2008). The specific relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART has however not been pursued in Manicaland, Zimbabwe. Establishing lower limb muscle strength in HIV positive patients on HAART provide empirical data that is currently limited. Furthermore, there is need to establish whether there is a relationship between lower limb muscle strength and lower limb function in order to design interventions that can counteract a decrease in lower limb function as well as the impact on specific related function such as core stability. It might also influence policy changes and plans to support provisions of rehabilitation services.

1.2 RESEARCH QUESTION

What is the relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART?

1.3 OVERALL AIM OF THE STUDY

The aim of this study is to establish the relationship between lower limb muscle strength and lower limb function in patients who are HIV positive on HAART.

1.4 STUDY OBJECTIVES

1. To establish lower limb muscle strength in patients who are HIV positive on HAART.
2. To establish lower limb muscle strength in HIV negative patients.
3. To compare lower limb muscle strength between patients who are HIV positive on HAART and HIV negative people
4. To establish lower limb function in patients who are HIV positive on HAART
5. To establish the relationship between lower limb muscle strength and lower limb function in patients who are HIV positive on HAART.

1.5 SIGNIFICANCE OF THE STUDY

This study may contribute to understanding the extent and level of muscle strength and its relationship to lower limb function in adults with HIV infection on HAART. The effect of muscle weakness on specific functions such as sit to stand and balance in standing will help with designing interventions for countering reduction in lower limb function as well as the impact on specific related functions such as core stability where common muscles that have dual function in the lower limbs such as psoas, transverse abdominis and rectus abdominis maybe indirectly affected.

CHAPTER 2

2. LITERATURE REVIEW

2.1 INTRODUCTION

Before looking on the effect of HIV on lower limb function and lower limb muscles, a brief review of what HIV is and how big the problem is in Zimbabwe is undertaken. The disease history in Zimbabwe, that is the prevalence, behavior, how bad was the problem, when did it peak and where it is now will be discussed. The study will also discuss the infection and effects of HIV and HAART on the human body and its specific effects on lower limb muscle strength, together with the impact of HIV on people as they age. A review of the literature on how HIV and HAART affects lower limb function focusing on its effects related to the skeletal system and Health Related Quality of Life (HRQOL) will be done. Interventions to reduce the HIV effects on lower limb muscle strength, lower limb function and HRQOL will also be examined. Methods to establish lower limb muscle strength and lower limb function will be reviewed, highlighting the reasons why these methods were chosen for use in this study.

2.2 METHODOLOGY OF LITERATURE REVIEW

Specific research portals were accessed to search for articles related to the topic of interest e.g. publications, Pub med, Cochrane reviews and Google Scholar. Specific websites were accessed for further explanatory information e.g. Google, World Health Organization (WHO), United Nations program on HIV/AIDs (UNAIDS), United Nations General Assembly (UNGASS) and the National Aids Council (NAC) of Zimbabwe. In addition, the following processes were conducted to gather information relevant to the project: specific research publications, articles, texts and congress presentations were reviewed.

2.3 HISTORY OF HIV IN ZIMBABABWE

HIV prevalence in Zimbabwe in the adult population (15-49 years) was 20% in 2005 down from 22% in 2003 (Lopman et al., 2007). It further dropped to 14% in 2009 (UNAIDS, 2009) then rose to 15% in 2013 (NAC, 2013).

The emergence of HIV-1 resulted from the cross-species transmission of simian immunodeficiency virus from Chimpanzees to humans in West-Central Africa at the beginning of the 20thcentury (Worobey et al., 2008). Group M, responsible for the vast majority of HIV infections worldwide, initially spread throughout Africa. In response to actions of several genetic forces, the HI virus has diversified into different subtypes (Sharp

et al., 2010).The spread of these variants in the human population was not noticed for nearly eight decades (Jungueira et al., 2011). The first records of infection date back to1981 in American patients infected with subtype B virus. These patients presented with clinical symptoms which is known today as AIDS (Gallo et al., 1983, Barre-Sinoussi et al., 1983).

In Zimbabwe, the first cases of HIV/AIDS were identified in the mid-1980s (UNAIDS, 2008). By 1990 (the first year of Antenatal Clinic (ANC) based surveillance) HIV prevalence exceeded 10% (Gregson et al., 2010). According to the United Nations General Assembly (UNGASS) report in December 2007 on HIV and AIDS in Zimbabwe, HIV prevalence was at its peak in 2001 with an estimated prevalence of 27%.The prevalence declined to 23% in 2003, further declining to19% in 2005 and 15% in 2007 (UNGASS,2007).

The National Aids Council (NAC) of Zimbabwe (2013) reported an HIV prevalence of 14% in 2012 in Zimbabwe. The prevalence rose to 15% in 2013. In the June 2013 NAC report, Zimbabwe's three Southern provinces of Bulawayo, Matabeleland North and South recorded the highest HIV figures. Bulawayo had 19% while Matabeleland North and South had 21% each. Harare province reported a prevalence of 13%. Other provinces; Mashonaland central, Masvingo, and Manicaland had 14% each. NAC attributed the high Matabeleland figures to spousal separation. The spousal separation was as a result of people crossing the border to neighbouring countries such as Botswana and South Africa in search of jobs. Gregson et al (2001) however observed that the HIV epidemic in Zimbabwe initially affected more mobile and more educated men. This was because of the men's ability to attract sexual partners irrespective of their geographical location. As early as 1998 risk was similar or perhaps slightly lower for those with secondary education (Gregson et al., 2001).Mbizvo et al (1997) and Machekano et al (1998) found that in Zimbabwe, most incidence estimates were not from population based studies. It therefore means that the June 2013 NAC finding could have been biased. Lopman et al(2008) noted that in virtually all settings where there is a generalized HIV epidemic in Zimbabwe, there is no reliable surveillance systems to monitor new AIDS cases. This poor surveillance is prevalent in most Southern African countries, vital registration systems are unreliable because of substantial underreporting (Feeney, 2001). Hospital records can also be biased, especially in rural areas, since many people die at home and AIDS deaths could be underreported to protect surviving kin from stigma (WHO, 2004).Therefore the June 2013 NAC report might be inaccurate (Feeney, 2001).

2.4 HIV INFECTION AND EFFECTS ON HUMAN BODY

HIV carries its genetic information in the form of RNA (Brenchley et al., 2008). When the virus enters the cell, the RNA is reverse transcribed to DNA. An enzyme called Reverse Transcriptase (RT) reverses the normal transcription process so that a DNA copy is made of the viral RNA genome. This new copy called a provirus is then integrated into the cell genome of the original DNA (Anderson, 2006). After a period of latency, the replicated virons bud out of this lymphocyte and infect other lymphocytes. Many virons are released per day. They continually infect and destroy additional T-lymphocytes leading to immunosupression (Anderson, 2006).

Immunosuppression leaves the individual susceptible to a wide variety of conditions and malignancies which are collectively called opportunistic conditions (Anderson 2006). Among the opportunistic conditions are musculoskeletal effects. They are as a result of muscle derangements due to HIV infection (Otis et al., 2008). Musculoskeletal effects may include polymyositis, rhabdomyolysis, tumor infiltrations, wasting syndromes, severe lower limb weakness and a general feeling of tiredness that does not really go away even after resting (Otis et al., 2008).In the general population, osteoporosis and fractures are common in people infected with HIV (Cotter et al., 2013). The risk of fractures is almost two fold in people living with HIV on HAART compared to the general population (Carter, 2011). HIV positive people experience mobility challenges and a decreased quality of life as a result of frailty secondary to muscle weakness (Cotter et al., 2013).

2.5 HIV SPECIFIC EFFECTS ON MUSCLE

Lower limb muscle weakness is a common complaint among HIV positive patients presenting to family physicians (Sagui, 2005). Although the cause of weakness is occasionally apparent, there are many cases where it is unclear. Therefore comprehensive evaluation of HIV positive patients is necessary. A thorough examination should be coordinated with appropriate laboratory, radiological, electro - diagnostic and pathological studies to identify the exact cause of muscle weakness (Sagui, 2005).

Mascolini (2011) suggested that weakness occurred as a result of the HIV virus' interference with oxygen extraction or use. Cade et al (2003) noted that muscle oxygen extraction and utilisation limitation is a mediator of diminished aerobic capacity in individuals who are infected with HIV on HAART. HAART medication disrupts normal mitochondrial function. This limits muscle oxygen extraction-utilisation in most individuals treated for HIV infection (Cade et al., 2003). These alterations in mitochondrial function

deplete oxygen utilisation in lower limb muscles causing lower limb muscle weakness even when oxygen delivery is unaffected (Cade et al., 2004).

Apart from mitochondrial toxicity in lower limb muscles, HIV is also associated with metabolic disorders causing morphological alterations. Morphological alterations include loss of peripheral subcutaneous fat (lipoatrophy), accumulation of central visceral (intra-abdominal) fat and fat in the dorsal cervical thoracic region (lipohypertorophy) (Garg, 2011). Furthermore morphological alterations together with pain often slow an individual's activity levels resulting in reduced functional activity tolerance and quality of life (Kietrys et al., 2014).

HIV-associated lipodystrophy is associated with HAART regimes that include nucleoside reverse transcriptase inhibitors although other mechanisms maybe involved (Kietrys et al., 2014).Secondary to co-morbidities associated with HIV disease, HAART in some individuals, offer benefits at the cost of debilitating side effects (Bopp et al., 2003). There is loss of lean body mass (LBM) with relative maintenance of total body mass (Mendes et al., 2013).These alterations are associated with reduction in capacity to generate lower limb muscle strength and limitation of functional status (Mendes et al., 2013). The mechanism as reviewed above is related to lipodystophic alterations like lipoatrophy (Dellisola et al., 2004), mitochondrial toxicity (Kohler et al., 2007) and the activity of oxidative enzymes (Cade et al., 2003).

Therefore HIV and HAART negatively influence oxygen usage, limiting the extraction/use of oxygen in the lower limb musculature (Mendes et al., 2013). Lower oxygen use capacity directly affects physical fitness, and consequently, the individual's motivation to perform routine activities (Mendes et al., 2013).

HIV can deprive an individual of his or her physical resources such as mobility, lower limb muscular strength, joint flexibility, endurance and energy (Clingerman, 2003). There is a high prevalence of fatigue and lack of endurance in HIV positive patients, many of whom face challenges with daily functional activities (Rusch et al., 2004). This is exacerbated by a compromised pulmonary function with resultant lower limb muscle weakness and compromised lower limb function (Pothott et al., 1994).

2.6 HIV AND HAART'S EFFECTS ON FUNCTION AND HEALTH RELATED QUALITY OF LIFE (HRQOL)

HI virus has complex effects on the body and can impact the functioning of individuals in everyday life (Myezwa et al., 2011). The disease complexity and potential side effects of HAART make successful disease management a challenge for many individuals (Kietrys et al., 2014). People living with HIV/AIDS on HAART are concerned with the quality of life they are able to lead over and above a treatment's ability to extend life (Gale, 2003). South Africans living with HIV/AIDS' quality of life and elsewhere has been found to be severely compromised (Myezwa et al., 2011).

Increased longevity in HAART era has been mirrored by an increase in co-morbidities and episodic disability experienced by some individuals (Cade et al., 2010). Disability associated with HIV disease can be worsened or relieved by extrinsic factors such as coping strategies and lifestyle choices (O'Brien et al., 2009). Performance–based measures aimed at the upper end of the functional spectrum among middle-aged and older adults with HIV infection identified greater than expected impairments in walking speed, balance, peak exercise capacity, and ability to rise from a chair (Erlandson et al., 2013).

Evidence is there that HIV can replicate in compartments different from plasma (Kashuba et al.,1999) such as the brain thereby establishing viral sanctuaries. Antiretrovirals have limited penetration into these viral sanctuaries where viral replication continues during treatment leading to resistant HIV strains (Saksena et al., 2003). There is resultant brain damage in HIV-positive patients on HAART even though there viral load was suppressed by anti-retroviral therapy. The brain damage decreased lower limb function. This means anti-viral medications might not stop brain damage even among those who are virally suppressed (Perper et al., 2006).

Symptoms of HIV brain damage include depression, memory loss, a slowing of mental response time and sluggishness in lower limb movements. These symptoms can progress to HIV dementia. HIV dementia is a neurological damage that used to affect 20% of HIV patients prior to the advent of antiretroviral therapy (Perper et al., 2006).

Research conducted in 2002 showed that 30% of HIV-positive individuals had problems with lower limb muscle strength or balance (Carter, 2011). Investigators from the French Agency of AIDS and Hepatitis Research (ANRS) CO3 Aquitaine cohort wished to gain a better understanding of Locomotor performance in HIV positive patients in the modern

treatment era of HAART. Locomotor function was assessed using validated tests which include 1- overall balance, 2- distance walked in six minutes at an accelerated speed, 3- time to stand up from an armchair, walk three meters, turn around, walk back to chair and sit down, 4- five times sit-to-stand test and 5- time needed to stand up from a sitting position five times. (Carter, 2011).These patients had been living with HIV for a long time with 83% of them on HAART. Results showed the majority of the patients had poor lower limb function (Carter, 2011).

More than half of HIV positive people in a French Aquitaine cohort had poor leg muscle strength with compromised lower limb function when compared to the general population (Mascolini, 2011). Poor lower limb muscle performance put this population at risk of falls and fractures" (Mascolini, 2011).In a cross-sectional survey done in 2002, data suggested that up to 30% of HIV infected patients had complaints with Locomotor function and balance (Rusch et al., 2004). Antiretroviral drugs, (didanosine, stavudine, zalcitabine and zidovidine) decreased locomotor performance in the early HAART era through a pathway of peripheral neurotoxicity (Scruggs et al., 2008) and adverse effects on the muscle by mitochondrial toxicity which disrupt lower limb muscle structure and function (Bauer et al., 2011). In addition, HAART treatment has been associated with distal sensory neuropathies that affect proprioception and coordination of movement in the lower limbs (Bauer et al., 2011).

HAART treatment though associated with distal sensory neuropathies is now easily accessible, leading to a shift in HAART experiences in hyper-endemic countries. The international classification of Function (ICF) offers a framework for considering the experience of HIV in the era of enhanced access to HAART in South Africa (Hanass-Hancock et al., 2013). The ICF classifies impairments, activity limitations, participation restrictions and the environment as components that all play a role in disability. The ICF is regarded as the most comprehensive model available for describing and understanding disability and function; it is a complex instrument intended to cover all aspects of human functioning (Myezwa et al., 2011).

2.7 IMPACT OF HIV ON MUSCLE STRENGTH AS PEOPLE AGE

HIV is now a chronic disease associated with longevity accompanied by a diverse range of health related challenges like lower limb muscle weakness (Hanass-Hancock et al., 2003).Age associated skeletal muscle sarcopenia is generally characterized by reduced muscle mass and strength. It is manifested by preferential type 11 myofibre atrophy, myofibre necrosis and increased intramuscular content of non-muscle (i.e. adipose and

connective) tissues (Hunter et al., 2004). Preferential type 11b myofibre atrophy partly accounts for loss of lower limb muscle strength with age. The decreased muscle strength is a result of impaired excitation–contraction coupling as calcium release decline with age (Cade et al., 2003)

As people get older, myofibres will change from 1, 11a and 11bfiber types. This is because a different axon type from the heterogeneous fiber distribution pattern normally found in younger muscle now enervates older muscle thereby changing the fibre type(Hunter et al., 2004). Changes in muscle fibre type lead to a decrease in muscle strength because of muscle shrinkage and loss of muscle fibers. Under normal conditions, muscle strength in women and men reaches its peak between the ages of twenty and thirty years. Muscle strength then remains virtually unchanged for another twenty years, if there is no disease or injury (Humphries, 2008). Muscular performance after this point deteriorates at a rate of five percent per decade. This amounts to a loss of thirty to forty percent of muscle strength over the adult life span. Variations in the rate of loss reflect the diversity of occupations, physical activity backgrounds, muscles used and type of muscle contractions (Humphries, 2008).

Decline in skeletal muscle size and alterations in neural function, such as loss of motor neurons, decreased maximal motor unit firing rates and impaired neuromuscular activation (Clark et al.,2012) contributes to reduced lower limb muscle strength in older adults (Doherty, 2003). As a result of these changes, there is selective atrophy and loss of type 11a fibers which have the ability to generate 4-6 times more power than type 1 fibers, compromising successful development of dynamic muscle strength during lower limb functional activities (Reid et al., 2013).Also higher accumulation of intramuscular adipose tissue has been linked with an inability to fully activate muscles during dynamic contractions in lower limb functional activities (Yoshida et al., 2012).

Elderly people when sedentary for a long time experience decrease in muscle strength, compromising their quality of life. HIV/AIDS worsen this situation since HIV decrease muscle strength and function (Souza et al., 2011).Medications, infections (such as HIV infection) and neurological disorders commonly cause lower limb muscle weakness (Roos, 2003). Lower limb muscle power is a determinant of falls, which accelerates disability and mortality (Moreland et al., 2004).

Lower limb muscle strength decrease with age faster in HIV infected individuals compared to HIV negative people, resulting in impairment of Locomotor function, deterioration of functional ability and limitations in activities of daily living (Richert et al., 2011). These muscular impairments are also associated with daily activity limitations and participation

restriction (Rusch et al., 2004). The most common motor impairments in AIDS patients on HAART are slowed movements, gait abnormality, limb inco-ordination, hyper-reflexia, hypertonia and muscular weakness (Bernard et al., 2013).

Loss of skeletal muscle mass has a significant impact on functional performance, independent function and associated quality of life in HIV patients. HAART became the standard of care for HIV intervention in 1995 and the incidence of wasting (involuntary weight loss more than 10% ideal body weight) has declined although it is common (Scott et al., 2007). In the era of HAART, recent work indicates that HIV associated weight loss is primarily due to fat atrophy, which accounts for approximately two-thirds of the weight loss while loss of lean body mass accounts for the other third (Grinspoon et al., 2003). Given the wide ranging physiological consequences of HIV infection and HAART, mechanisms beyond reduction in muscle mass are likely contributors to impaired function (Estanislao et al., 2004).

Half of American adults with controlled HIV infection had poor lower limb muscle strength as assessed through the five-sit-to-stand test (5-STS) (Bernard et al., 2013). HIV patients on HAART present with white matter alterations (Chen et al., 2009), psychomotor slowing and postural instability (Sullivan et al., 2011). Chronic infection with HIV has been associated with skeletal muscle impairment which is related to deterioration of functional ability in activities of daily living (Scott et al., 2007). Lower limb muscle weakness is known in the disease process, but its relationship to central motor command integrity has not been investigated to date (Bernard et al., 2013).

Poor lower limb muscle performance and balance disorders predict the risk of falls and disability in HIV positive people on HAART and elderly community dwelling individuals of the general population (Bliuc et al., 2009). Furthermore, low quadriceps strength is an independent risk factor for hip fracture and a predictor for mortality and fragility fracture (Bliuc et al., 2009). The association between reduced lower extremity strength, poor mobility and functional dependence in HIV positive people on HAART and frail elders are well known (Wang et al., 2009). Fortunately, muscle does not lose its ability to respond to training even in older persons or HIV positive people on HAART (Wang et al., 2009). Older persons and HIV positive people on HAART's functional mobility performance and independence can be improved by enhancing lower limb muscle function (Wang et al., 2009).

2.8 INTERVENTIONS TO REDUCE HIV/HAART EFFECTS ON LOWER LIMB FUNCTION AND HRQOL

Physiotherapy has been shown to improve lower limb functional activities and quality of life in HIV patients on HAART(Javier et al., 2011; Lopez-Sendin et al.,2012).Current literature however lacks well designed studies regarding the specific role of the physiotherapist in the treatment of this population (Pullen et al.,2014). The limited research available is mainly focused on exercise and does not examine the effectiveness of the full spectrum of skilled physiotherapy for treating HIV-related symptoms (Pullen et al.,2014). Given this gap in the literature, it is necessary to develop comprehensive physiotherapy interventions for HIV positive patients on HAART and to understand the comorbidities experienced by this population (Pullen et al., 2014).

World Confederation of Physical Therapy (WCPT) define physical therapy as; "providing services to people and populations to develop, maintain and restore maximum movement and functional ability throughout their life-span; therefore physiotherapists are best placed to design rehabilitation strategies to improve lower limb muscle strength and function(Kumar et al., 2010). Physiotherapy includes the provision of services in circumstances where movement and function are threatened by the process of ageing or that of injury or disease as in HIV infection. Full and functional movement is at the heart of what it means to be healthy (Kumar et al., 2010).

As noted before, HAART has drastically improved the functional movement, prognosis and quality of life of patients infected with HIV on HAART. Some individuals on HAART however still experience neuromuscular problems due to lower limb muscle weakness (Bernard et al., 2013).Identifying the factors beyond the reduction of muscle mass that contribute to impaired function is required for optimizing the design of rehabilitation strategies to improve lower limb muscle strength and functional capacity in this chronically ill patient population (Scott et al., 2007).

Factors to survive for long with AIDS, include a positive attitude towards the illness. (Kendall,1992) Health promoting behaviors (Lutgendart et al.,1994), spiritual activities (Nunes et al., 1995; Kendal et al., 1994) and socializing in groups pertaining to AIDS is also helpful (Kendall, 1992; Lutgendart et al., 1994;Nunes et al., 1995).Aerobic exercises have beneficial psychological and immunological effects on individuals with HIV on HAART (Antoni et al., 1990; LaParriere et al., 1991 and 1994, MacArthur et al.,1993).Effects of exercises on the immune system in chronic illness like HIV however remain largely unexplored (Smith et al., 2007).

Progressive resistance exercise improves strength, power and endurance (Rigbsy et al., 1992, Spence et al., 1990) hence better lower limb function. Additional evidence shows that combined aerobic and progressive resistance exercise enhances strength and endurance for HIV patients on HAART (Rigsby et al., 1992; O'Brien et al., 2004) leading to better lower limb functional status. Most studies which examined effects of aerobic exercises however used fatigue measurement scales to determine adverse effects rather than explore positive effects (Petajan et al., 1996; Mostert et al., 2002).

Tai Chi is a form of light resistance exercise that can be performed by patients who are unable to participate in rigorous programmes (Galantino et al., 2005). Tai Chi improves balance consequently helping prevent falls in the elderly and HIV positive people on HAART (Wolf et al., 1993 and 1996). Social support is also a well-known explanation for high level lower limb functioning in the face of adversity (Gore, 1978; Holahan et al., 1982).

Individual exercises result in psychological and functional enhancement. Group exercises further improved such opportunities (Galantino et al., 2005). Group exercises however require time tables therefore time tabled classes may exclude those who cannot travel or whose work or family commitments prevent attendance (Smith at al., 2007). The interdependence of positive physical changes and enhanced psychological coping due to exercises improves HRQOL (Galantino et al., 2005).

There is evidence that nutritional counseling and support, appetite stimulants, progressive resistance training, and anabolic hormones can reverse weight loss and increase lean body mass thereby improving lower limb muscle strength and lower limb function in HIV infected patients (Grinspoon et al., 2003). Body composition and metabolic changes can also be improved through resistance and aerobic exercise training programs. These exercises are as effective as other non-pharmacological treatments used for managing HIV-related complications and for improving HRQOL (Yarasheski et al., 2001).

Body composition and metabolic abnormalities associated with body fat redistribution, such as glucose, lipid abnormalities and hypertension have been reported in approximately 20-60% of HIV positive patients receiving HAART (Carr et al., 1999). In developing countries, body fat redistribution and metabolic abnormalities have been reported in HAART-treated HIV patients and in HIV infected Africans receiving first line WHO recommended HAART (Stewart, 2002). Cardio respiratory exercise training is an established, cost-effective exercise regime that improved cardiovascular, lower limb function and diabetic risk profile in

HIV positive individuals from Western countries (Stewart, 2002). Regular cardio respiratory exercise training has been recommended in the guidelines for management of HIV-related dyslipidemia and functional loss due to lower limb muscle weakness (Dube et al., 2003).

Furthermore in Sub-Saharan Africa, cardio respiratory exercise training can be an important treatment for body fat redistribution, lower limb functional loss and metabolic disorders in HIV positive individuals taking HAART (Mutimura et al., 2008). Mutimura et al (2008) established that cardio-respiratory training exercises improve lower limb functional loss and body composition. In addition; there is a decrease in waist circumference, waist-to-hip ratio and percentage body fat mass in WHO - recommended HAART – treated HIV positive African subjects with body fat redistribution in Rwanda. Exercise training also reduces total serum cholesterol, glucose and improves cardio respiratory fitness (Mutimura et al., 2008). Characteristics of body fat redistribution however are considerably disfiguring i.e. an individual develops a buffalo hump and loss of fat to the abdomen, breasts and face (Reynolds et al., 2006). Body fat redistribution therefore compromises HIV serostatus privacy, producing social isolation and distress, resulting in psychological repercussions (Blanch et al., 2004). HIV positive patients with body fat redistribution experienced social isolation and stigma because of their body image which forced disclosure of their HIV status (Mutimura et al., 2008).These patients were therefore more likely not to participate in group cardio respiratory exercise training thereby compromising their lower limb functional status. Body fat redistribution also adversely influence patient's attitude towards benefits of HAART leading to decreased adherence to the drugs with subsequent adverse impact on patients' HRQOL (Ammassari et al., 2002).

A positive attitude towards HIV infection (Kendal, 1992), health promoting behaviors (Lutgendart et al., 1994), and spiritual activities (Nunes et al., 1995; Kendal et al., 1994), combined aerobic and progressive resistive exercises enhances lower limb strength, lower limb function and endurance in HIV positive patients on HAART (Rigsby et al.,1992; O'brien et al., 2004).

Current literature promotes moderate exercises as safe and beneficial for HIV positive people on HAART during any stage of their illness, but exhaustive exercises (exercises lasting more than 90 minutes) should be avoided(Anderson, 2006).Exhaustive exercises weakens nonspecific immunity, neutrophil activity decreases with a resultant decline in phagocytic defense against infection (Lawless et al., 1995).

2.9 INSTRUMENTS TO ESTABLISH LOWER LIMB MUSCLE STRENGTH AND LOWER LIMB FUNCTION

Lower limb muscle strength which influences lower limb function is the ability for the muscle to generate maximal force (Reid et al., 2013). Muscle strength in this study refers to characteristics such as muscle force, rate of force development and muscle power (Suominen et al., 2008).

Muscle produces force by sliding filaments crossing each other, which is called a muscle contraction (Suominen et al.,2008). A muscle contraction maybe static (involving no movement) or dynamic (involving movement) (Suominen et al., 2008). In static or isometric muscle contraction, the total length of the muscle does not change and the joint angle remains constant. Maximal isometric muscle force is defined as the maximum voluntary contraction performed at a specific joint angle against an unyielding resistance usually tested with a dynamometer (Suominen et al., 2006).

Several studies have been conducted using dynamometry. The degree to which a patient's lower limb muscles are impaired is established if the clinician has objective normal values against which to compare the patient's lower limb strength (Rothstein et al., 1993). Manual muscle testing such as the oxford scale does not provide such quantitative values (Bohannon,1997). Dynamometry provides quantitative values, to which a patient's performance can be compared (Bohannon, 1997). In a study by Bohannon (1986) involving 30 patients with a mean age of 51.9years (range 17-82 years), three dynamometer strength scores were taken and recorded for each muscle group tested. This was done to calculate test-retest reliability. The correlations calculated for the pairs of strength scores ranged from 0.84 to 0.99 (p-value= 0.01). This demonstrated good reliability. Hand held dynamometer is therefore a reliable procedure (Bohannon, 1986).In this study we used the Wagner Force Dial PD440 dynamometer. The correlations calculated for the three measurement scores ranged from 0.76 to 0.97 (p-value= 0.01). This also demonstrated good reliability of this particular dynamometer.

In the hands of a tester with adequate strength and skill, a hand held dynamometer can be used to measure the strength of ten or more actions on both sides of a patient's body (Bohannon, 1997). The hand held dynamometer incorporates a load cell and has a digital display and is set to read force in Newton's or Kg/m^2 (Bohannon,1997). Lower limb muscle strength testing is done by isolating a particular muscle or muscle group, and then an external force is applied (Dutton, 2009) Resistance applied at the end of the tester range is

termed a "break test" while resistance applied throughout the range is termed a "make test" and the results of the strength testing differ depending on the method used (Dutton, 2009). The isometric hold (break test) shows the muscle to have a higher test grade than the resistance given throughout the range (make test) and the handheld devices used in dynamometry can help quantify the "breaking force" necessary to depress a limb held in a specific position by the patient (Dutton, 2009).Myezwa et al (2009) used dynamometry in HIV populations with good results.

The Lower Extremity Functional Scale (LEFS) is used to evaluate the functional impairment of a patient with disorder of one or both lower extremities (Binkley et al.,1999).It can be used to monitor the patient over time, evaluate the effectiveness of intervention (since it has capacity to detect change in lower limb function), easy to administer and score. LEFS however only measures lower limb function not overall health (Binkley et al., 1999). It is more interpretable with respect to understanding error associated measurement, determining minimally clinically important score changes. It has a sufficient measure of reliability, validity and sensitivity to change at a level that is commensurate with utilization on individual patient level (Binkley et al., 1999). The error associated with a given measure on the LEFS is about ±5 scale points (r=94) indicating excellent reliability (Watson et al., 2004). The construct validity and responsiveness were supported by high correlations with prognostic scores meaning LEFS is reliable, valid and responsive for use in patients with lower limb musculoskeletal dysfunction (Binkley et al.,1999).

The instruments (hand-held dynamometer and Lower Extremity Functional Scale) were valid with good reliability for measuring lower limb muscle strength and lower limb function in HIV positive patients HAART (Bohannon, 1986; Binkley et al.,1999)

CHAPTER 3

3. METHODOLOGY

3.1 INTRODUCTION

In this chapter the research design, instruments, procedure and statistical analysis of the study will be presented and explained.

3.2 STUDY DESIGN

This is a descriptive and cross sectional study.

3.3 STUDY SETTING

This study was conducted at Mutare Provincial Hospital, Manicaland, Zimbabwe.

3.4 ETHICAL CLEARANCE

Prior to commencement of data collection, ethical clearance was obtained from University of the Witwatersrand Human Ethical Research Committee (Clearance Certificate Number M120715 – Appendix A). Ethical clearance was also obtained from the Medical Research Council of Zimbabwe (Approval number MRCZ/B/514 – Appendix B).Permission to conduct the study was sought and granted from Health study office, Medical research council of Zimbabwe and Mutare Provincial Hospital Medical Superintend. We sought this permission through an application form for Medical research council (Appendix E) and application letter for Mutare Provincial Hospital (Appendix F).Written informed consent (Appendix C) from the participants was obtained before they participated in the study. Anonymity and confidentiality of data was ensured by coding the results ensuring no patient identification was given and maintained (Appendix D). Participants were informed of their results.

3.5 PILOT STUDY

The pilot study was done on 30 HIV negative individuals who were 18 to 70 years old in Mutare district to establish lower limb muscle strength in HIV negative people. We randomly sampled 30 HIV negative individuals who were blood donors on the National Blood Transfusion register who would have undergone an HIV test (this is a requirement for blood donors to remain on the donor list). To ascertain if the lower limb muscle strength using dynamometry can be judged as "strong" or "weak", reference values are required. No literature could be found where reference values for lower limb muscle strength in a typical African healthy population were presented.

The pilot study was done to test the feasibility and proficiency of using hand-held dynamometry for the main study.Inter and intra-rater reliability was also established during the pilot phase.

3.6 STUDY POPULATION

HIV+ people in Manicaland aged between 18 and 70 years old on HAART who were already enrolled in the opportunistic infection clinic, attending appointments for monthly check-ups on how they were coping on HAART with doctors and primary health care sisters. Patients attending this clinic came from urban and rural areas.

3.7 INCLUSION CRITERIA FOR MAIN STUDY

Male and female adult HIV positive patients, who were on HAART, 18 to 70 years old and were ambulant.

3.8 EXCLUSION CRITERIA

i. Patients who were non-ambulatory.
ii. Pregnant at time of assessment.
iii. Stroke patients(CVA).
iv. Those with known muscle weakness like Chronic Inflammatory Polyneuropathy Disease and Gullain-Barre syndrome.
v. Diabetic patients.
vi. Patients suffering from alcoholism.
vii. Patients without capacity to follow instructions and give informed consent.

3.9 SAMPLE

3.9.1 Sampling Frame

Our sampling frame was the register for HIV patients on HAART kept at Mutare Provincial hospital. Participants were approached for permission to take part in the study as they came into the clinic.

3.9.2 Sample Size

Using statistical calculation (epi info 3.5.4), using a population size of 3500 HIV positive patients registered at Mutare Provincial Hospital, expected number of patients with Lower limb weakness being 10% (Oursler et al, 2009) of the registered patients (3500) and worst

acceptable being 15% of registered patients at 95% confidence interval, a sample size of 113 participants was calculated .

3.9.3 Sampling

Systematic random sampling was used where we picked every third patient who met the inclusion criteria as they came into the clinic (Castillo, 2009). An equal number of males and females were targeted. Four to six patients were taken per day until we got the sample size. This was done in two months to get the total sample.

3.10 OUTCOME MEASURES

Outcome measures (Table 3.1) was kg/m^2 for lower limb muscle and a functional lower limb score measured using Lower Extremity Functional Scale (LEFS).

Table 3.1: Outcome Measures

Objective	Outcome Measure	Reliability and Validity	Procedure
Muscle strength	kg/m^2	Bohannon (1986)	Dynamometry
Lower limb function	Lower limb function	Binkley et al (1999)	Lower extremity functional scale

3.11 PROCEDURE

Dynamometer was used to measure lower limb muscle strength. The dynamometer tests consisted of isometric "make contractions" in which the patients was to use each tested muscle group to push maximally against the plate and the piston of the hand-held dynamometer for four to five seconds. A commercially available hand-held dynamometer was used for testing. The tester would manually stabilize the body parts proximal to the tested limb segment during testing. Before testing each muscle group, the tester demonstrated to the patient the muscle contraction to be performed. Retests of specific muscle groups were performed 10 to 15 minutes after the initial test. During testing, the tester would keep the dynamometer scale turned from view to remain blind to the score. The participant would then hold the maximal contraction for four to six seconds, and then relax. The scale was read, and the score recorded to the nearest kilogram. The piston of the dynamometer was always held perpendicular to the limb segment towards which it was directed, and the plate of the dynamometer was always placed in the same position on the tested limb (Table 3.2)(Appendix H).

Table 3.2: Specific Patient Limb Positions (Bohannon 1986)

Muscle Group	Patient Position	Limb Positions	Manually Stabilized Part	Dynamometer Placement
Ankle plantar flexors	Supine	Hip and knee extended	Lower limb proximal to ankle	Just proximal to the metatarsophalangeal joints on plantar surface of foot
Ankle dorsiflexors	Supine	Hip and knee extended	Lower limb proximal to ankle	Just proximal to metatarsophalangeal joints on dorsal surface of foot
Knee flexors	Sitting on high chair	Knee and hip flexed at 90 degrees	Thigh	Just proximal to ankle on posterior surface of leg
Knee extensors	Sitting	Knee and hip flexed at 90 degrees	Thigh	Just proximal to ankle on anterior surface of leg
Hip flexors	Supine	Hip flexed to 90 degrees, knee relaxed	Trunk	Just proximal to knee on extensor surface of thigh
Hip extensors	Supine	Hip flexed to 90 degrees, knee relaxed	Trunk	Just proximal to knee on flexor surface of thigh
Hip abductors	Supine	Knee extended, hip in neutral abduction	Contra lateral lower extremity	Just proximal to knee on lateral surface of thigh
Hip abductors	Supine	Knee extended, hip in neutral abduction	Contra lateral lower extremity	Just proximal to knee on medial surface of thigh

1. The Lower Extremity Functional Scale – (Appendix I) was used to determine lower limb function. The Lower Extremity Functional Scale was researcher administered, that is, researcher would ask each participant the questions in the LEFS. Questions were explained to the participants until they understood what was expected for the study. The following is a sample question from the questionnaire.

   "We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your lower limb function(s). Please provide an answer for each activity. Today, do you or would you have any difficulty with:

   (Circle one number on each line that corresponds to your appropriate answer)."

3.12 STATISTICAL ANALYSIS

Muscle strength data was reduced using frequencies and percentages to draw proportional bar graphs. The strength of muscles of patients who were HIV positive on HAART was compared with HIV negative people using an independent t test. Univariate logistic regression was used to analyze demographic data. The relationship between lower limb muscle strength and lower limb function in HIV positive patients was analyzed using multiple regression (testing for association or independence). The p value was set at <0.05 for significance. For each objective the type of analysis is shown in Table 3.3

Table 3.3: Statistical Analysis

Objective	**Statistical tests**
4.1 To establish lower limb muscle strength in patients who are HIV positive on HAART	Mean muscle strength and standard deviation.
4.2 To establish lower limb muscle strength in HIV negative people	Mean muscle strength and standard deviation.
4.3 To compare lower muscle strength between patients who are HIV positive on HAART and HIV negative people.	t-test for two independent samples.
4.4 To establish lower limb function in patients who are HIV positive on HAART	Frequencies and bar graphs. Chi-square
4.5 To establish the relationship between lower limb muscle strength and lower limb function in patients who are HIV positive on HAART	Multiple regression Spearman's rho correlation.

CHAPTER 4

4. RESULTS

4.1 INTRODUCTION

In this chapter the results of the data collected will be presented and analyzed according to the study objectives. The aim of the study was to establish the relationship between lower limb muscle strength and lower limb function in HIV positive patients on Highly Active Antiretroviral Therapy (HAART).The first objective in the study sought to establish lower limb muscle strength in patients who are HIV positive on HAART. The second objective was to determine lower limb muscle strength in HIV negative patients. The third objective was to compare lower limb muscle strength between patients who are HIV positive on HAART and HIV negative people. The fourth objective was to establish lower limb function in patients who are HIV positive on HAART. Objective five was to establish the relationship between lower limb muscle strength and lower limb function in patients who are HIV positive and on HAART.

4.2 PILOT STUDY RESULTS

The purpose of the pilot study was to establish the feasibility of using the hand held dynamometer and techniques for the main study.We used a total of thirteen patients which represents 10% of our study population to determine intra-rater reliability (Tables 4.1a, 4.1b and 4.1c).

Intra-rater reliability was determined by taking the same measurement three times on the same person on hip flexors, knee extensors and ankle dorsiflexors. Inter-rater reliability was ensured by getting the same reading between raters.

Tables 4.1a, 4.1b and 4.1c show the results of reliability measurements with correlation coefficient results using Pearson's 2 tailed t-test for hip flexors, knee extensors and ankle dorsiflexors for 13 of the 30 pilot study subjects.

Table4.1a: Hip Flexor Measurements at 3 Points and Correlation between Measurements

	Hip Flexors			
Participant	**M*1**	**M*2**	**M*3**	**r-value**
1	18	18	17	**0.94(M1&M)**
2	20	21	20	
3	17	17	17	
4	20	21	21	**0.95(M1& M3)**
5	14	14	15	
6	19	19	19	
7	18	16	17	**0.97(M2 &M3)**
8	22	22	21	
9	15	15	15	
10	16	15	16	
11	17	17	17	
12	21	20	20	
13	16	17	17	

M*= measurements.

Correlation is significant at the 0.01 level (2-tailed).

Table4.1b: Knee Extensor Measurements at 3 Points and Correlation between Measurements

	Hip Flexors			
Participant	**M*1**	**M*2**	**M*3**	**r-value**
1	13	14	13	**0.83(M1 & M2)**
2	14	14	14	
3	15	17	16	
4	12	12	12	
5	13	12	12	
6	14	13	13	
7	12	12	13	**0.90(M1 & M3)**
8	16	17	15	
9	14	13	13	
10	13	13	13	
11	12	13	12	
12	17	16	17	**0.86(M2 & M3)**
13	14	13	14	0.86

Correlation is significant at the 0.01 level (2-tailed).

Table4.1c: Ankle Dorsiflexors Measurements at 3 Points and Correlation between Measurements

	Hip Flexors			
Participant	**M*1**	**M*2**	**M*3**	**r-value**
1	11	10	9	**0.89(M1 & M2)**
2	14	14	12	
3	12	11	11	
4	13	12	12	
5	12	12	12	
6	11	11	11	
7	9	10	10	**0.76(M1 & M3)**
8	14	14	14	
9	9	9	10	
10	12	11	13	
11	13	13	12	
12	14	14	14	**0.82(M2 & M3)**
13	9	11	11	

Correlation is significant at the 0.01 level (2-tailed).

A high correlation coefficient (p-value= 0.01) using Pearson's test was established indicating good reliability.

This therefore indicates that the main study measurements were going to be reliable.

4.3 MAIN STUDY RESULTS

4.3.1 Introduction

The main study was conducted during the period June to September 2013.Systematic random sampling was used where every third patient who met our inclusion criteria was measured their lower limb muscle strength and functional status as they came into the clinic. The study sought to recruit both genders, Males (n=57) and females (n=56) were measured.

The results will be presented under the following headings:

Description of the study participants.

i. Lower limb muscle strength in HIV positive subjects on HAART.
ii. Lower limb muscle strength in HIV negative subjects.
iii. Comparison of lower limb muscle strength between HIV positive subjects on HAART and HIV negative subjects.
iv. Lower limb function in subjects who are HIV positive on HAART.
v. Relationship between lower limb muscle strength and lower limb function in patients who are HIV positive on HAART.

4.3.2 Description of the Study Participants

Demographic information of study participants

Table 4.2a and 42b describes demographic characteristic of our study participants.

Table 4.2a: Participants' Demographic Characteristics (n=143)

Demographic Characteristic	HIV Negative Group (n = 30)		HIV Positive Group (n = 113)	
	N	%	n	%
Gender				
Females	13	43.33	56	49.56
Males	17	56.65	57	50.44
Age (Years)				
15-39	24	80.00	34	30.09
40-69	6	20.00	79	69.91
Total	**30**	**100.00**	**113**	**100.00**

The above results show 70% (n=79) of HIV positive patients on HAART in the age band 40-69 years, whereas 80% of HIV negative subjects were below 40 years.

Table4.2b: Participants' Demographic Characteristics (n=143) *(continued)*

Demographic Characteristic	HIV Negative Group (n = 30)		HIV Positive Group (n = 113)	
	N	%	n	%
Employment Status				
Employed	24.00	80.00	73.00	64.60
Unemployed	6.00	20.00	29.00	25.66
Retired	0.00	0.00	11.00	9.73
Gross Monthly Income				

<R500	6.00	20.00	36.00	31.86
R501-R1000	1.00	3.33	14.00	12.39
R1001-R2000	3.00	10.00	28.00	24.78
R2001-R5001	17.00	56.67	33.00	29.20
>R5000	3.00	10.00	2.00	1.77
Housing Environment				
Share a Space/Shack	0.00	0.00	24.00	21.24
RDP				
House/Hostel/Flat	11.00	36.67	20.00	17.70
Town/Residential	18.00	60.00	34.00	30.09
Rural	1.00	3.33	35.00	30.97
Transport Means				
Walking	18.00	60.00	89.00	78.76
Wheeled Transport	12.00	40.00	24.00	21.24

HIV positive subjects on HAART 51% (n=73) are employed earning a salary of R2001-R5000.

The relationship between demographic factors within their categories and functional status in HIV positive people on HAART was tested using univariate logistic regression analysis (Table 4.2c)

Table 4.2c: Relationship of Demographic Factor Category to Functional Status (n=113)

Demographic Factor	Category	Mean Functional Score	Odds Ratio	95% Confidence Interval	R-Value	P-Value
Gender	Males	75.39	1.05	(1.01-1.09)	0.24	0.01
	Females	69.68	0.95	(0.92-0.99)	0.24	0.01
Age	All Ages (18-70 yrs)	72.56	N/A	(63.40-81.37	0.00	0.97
Employment Status	Employed	75.53	1.09	(1.04-1.14)	N/A	0.00
	Retired	74.25	1.07	(0.99-1.15)	N/A	0.00
	Unemployed	62.57	0.07	0.72-1.05	N/A	0.00
	Students	71.00	1.04	(096-1.12)	N/A	0.00
Gross Monthly Income	<R500	52.17	N/A	0.92-1.03	N/A	1.89
	R501-R1000	77.06	N/A	0.94-1.06	N/A	1.72
	R1001-R2000	74.10	N/A	0.98-1.08	N/A	1.69
	R2001-R5001	16.19	N/A	0.92-1.04	N/A	1.78
	>R5000	80.00	N/A	1.05-1.12	N/A	1.36
	Students	71.00	N/A	0.97-1.03	N/A	1.58
Housing Environment	Rural	53.43	0.92	0.95-1.02	N/A	0.23
	Share a Space/Shack	72.67	1.00	0.96-1.04	N/A	0.23
	Town/Residential	73.11	1.02	0.97-1.06	N/A	0.23
	Hostel	80.00	1.01	1.05-1.15	N/A	0.23
Transportation	Walking	66.86	0.92	(0.88-0.97)	0.12	0.07
	Wheeled Transport	76.19	1.09	1.04-1.14)	0.12	0.00

Male participants were found to be functionally better than females. Employed people were functionally better than the unemployed. Gross monthly incomes had no effect on function. Participants who walked as a means of transport had a better functional score than those who used wheeled transport. Participants who had town/residential housing environment had better functional score than the other housing environments.

4.3.3 Lower Limb Muscle Strength in HIV Positive Participants on HAART

The lower limb muscle strength in participants who are HIV positive on HAART are presented in Table 4.3

Table 4.3: Lower Limb Muscle Strength in HIV Positive Participants on HAART (n=113)

Muscle Group	Muscle Strength kg/m^2					
	Whole Group		HIV Positive Males		HIV Positive Females	
	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	12.46	2.79	13.7	2.64	11.21	2.37
Ankle Dorsiflexors	9.33	2.51	10.07	2.38	8.62	2.55
Knee Flexors	11.81	3.63	13.2	3.62	10.27	3.02
Knee Extensors	15.36	5.4	17.64	5.3	12.64	4.04
Hip Flexors	11.24	3.58	13.09	3.04	9.38	3.3
Hip Extensors	15.79	5.07	18.39	4.56	13.11	4.16
Hip Abductors	11.51	3.12	12.88	2.77	10.11	2.85
Hip Adductors	11.09	3.64	13.54	8.8	9.43	2.99

Hip extensors are the strongest muscle group in HIV positive subjects on HAART, while ankle dorsiflexors are the weakest group. This phenomenon is also true in males who are HIV positive on HAART.

Tables 4.4a and 4.4b outline age specific muscle strength in HIV positive males (n=57).

Table 4.4a: Age Specific HIV Positive Males' Muscle Strength (n=57)

Muscle Group	AGE BAND									
	15-19		20-24		25-29		30-34		35-39	
	Muscle Strength kg/m^2									
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	13.80	1.13	13.82	1.39	13/15	0.49	13.22	3.27	12.91	1.27
Ankle Dorsiflexors	9.85	0.49	10.85	0.79	10.30	0.00	9.38	2.36	9.57	2.26
Knee Flexors	15.10	1.27	13.20	2.73	16.30	0.71	12.71	3.83	12.37	3.40
Knee Extensors	20.00	0.00	16.95	1.99	21.00	0.00	17.34	4.91	15.45	3.10
Hip Flexors	12.65	1.06	13.85	2.18	13.40	1.13	12.07	2.67	12.95	3.32
Hip Extensors	13.90	0.42	16.97	2.80	18.00	0.85	18.88	4.55	14.40	2.60
Hip Abductors	13.30	1.27	13.30	2.08	13.70	1.27	13.14	1.74	11.30	3.21
Hip Adductors	13.20	1.98	13.38	0.91	12.40	0.85	14.34	3.03	10.78	1.73

Table 4.4b: Age Specific HIV Positive Males' Muscle Strength (n=57) *(Continued)*

Muscle Group	AGE BAND											
	40-44		45-49		50-54		55-59		60-64		65-69	
	Muscle Strength kg/m^2											
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	12.80	4.54	13.89	2.60	14.13	2.03	13.85	1.58	14.84	2.63	12.87	2.40
Ankle Dorsiflexors	9.77	3.96	9.72	1.69	10.76	1.94	10.54	2.48	9.97	2.59	9.53	1.73
Knee Flexors	11.84	4.13	11.69	3.28	15.08	4.03	16.14	3.04	12.22	2,77	13.24	3.37
Knee Extensors	16.71	7.16	16.34	6.09	19.74	4.42	17.95	7.08	19.81	5.59	16.53	3.99
Hip Flexors	9.80	3.48	13.56	2.85	14.74	2.67	13.29	2.93	14.16	2.95	12.14	2.22
Hip Extensors	16.86	5.40	16.89	3.19	18.64	2.67	21.83	7.14	21.78	4.85	17.08	2.44
Hip Abductors	10.59	3.65	12.80	2.62	13.12	2.15	13.66	2.07	14.72	3.67	11.90	1.69
Hip Adductors	10.02	3.95	13.12	3.42	12.73	2.37	12.07	2.35	15.59	5.30	11.30	1.59

The age band 20-25 years has the lowest mean muscle strength.

Tables 4.5a and 4.5b outline age specific muscle strength in HIV positive females (n=56). Because of the number of the age bands, the tables are split into two.

Table 4.5a: Age (Group 15-39 Years) Specific HIV Positive Females' Muscle Strength (n=56)

Muscle Group	AGE BAND									
	15-19		20-24		25-29		30-34		35-39	
	Muscle Strength kg/m^2									
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	8.50	0.71	12.04	2.26	10.92	3.66	11.53	2.15	12.13	1.97
Ankle Dorsiflexors	7.25	1.77	8.80	1.56	8.10	1.69	8.56	2.81	9.02	3.34
Knee Flexors	8.00	2.21	10.63	2.82	9.10	3.51	10.88	3.20	11.14	2.98
Knee Extensors	13.50	1.41	13.68	4.47	9.40	1.65	13.00	4.17	13.50	3.52
Hip Flexors	3.75	0.35	9.98	3.11	9.40	2.57	8.96	2.78	9.99	3.01
Hip Extensors	20.00	5.66	12.95	4.13	9.82	2.34	13.81	5.77	14.65	4.07
Hip Abductors	12.75	3.18	9.92	4.01	8.05	1.33	10.97	5.55	11.06	2.41
Hip Adductors	7.75	0.35	10.84	3.77	7.70	1.81	9.66	2.99	9.76	2.82

Table 4.5b: Age (Group 40-64 Years) Specific HIV Positive Females' Muscle Strength (n=56) (*Continued*)

Muscle Group	AGE BAND									
	40-44		45-49		50-54		55-59		60-64	
	Muscle Strength kg/m^2									
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	11.15	1.95	11.92	0.80	9.79	2.67	9.00	3.56	9.52	2.48
Ankle Dorsiflexors	9.20	2.03	9.17	2.14	9.34	2.35	7.30	3.07	4.00	2.12
Knee Flexors	10.70	2.18	10.08	3.07	9.84	2.88	7.00	1.14	2.78	0.04
Knee Extensors	13.32	3.60	12.25	5.97	12.80	3.24	6.63	2.50	6.75	0.35
Hip Flexors	10.37	2.28	11.25	6.81	8.57	3.08	6.50	2.97	3.75	0.35
Hip Extensors	13.49	1.93	12.75	4.02	11.54	3.11	9.38	3.35	8.25	0.25
Hip Abductors	10.37	1.90	9.08	1.59	9.22	1.88	8.12	3.61	4.50	0.71
Hip Adductors	10.17	2.11	9.67	3.34	9.79	3.03	6.13	2.66	3.75	0.35

Muscle strength is strongest in the 20-24 years age band.

4.3.4 Lower Limb Muscle Strength in HIV Negative Participants

The study had 30 HIV negative participants, 17 males and 13 females. Lower limb muscle strength (Table 4.6) in HIV negative males (n=17) was compared to HIV negative females (n=13).

Table 4.6: Lower Limb Muscle Strength of HIV Negative Participants (n=30)

Muscle Group	Muscle Strength kg/m^2					
	Whole Group		HIV Positive Males		HIV Positive Females	
	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	15.10	3.29	16.58	3.68	13.77	2.77
Ankle Dorsiflexors	11.17	2.42	11.88	2.20	10.37	2.64
Knee Flexors	12.65	2.24	13.79	3.76	11.35	2.17
Knee Extensors	17.07	4.46	18.87	3.55	14.75	4.36
Hip Flexors	13.05	3.88	15.34	3.57	10.07	2.62
Hip Extensors	17.68	4.65	19.81	3.30	15.06	4.16
Hip Abductors	16.32	4.72	18.19	4.58	14.35	4.72
Hip Adductors	14.13	4.36	16.00	3.47	11.64	4.79

Results in HIV negative subjects (whole group) show very strong hip muscles inclusive (hip flexors, extensors, abductors and adductors). In males, ankle dorsiflexors are the weakest while the hip extensors are the strongest. Hip muscles are overly the strongest muscle

group. In females ankle dorsiflexors and hip flexors are of equal strength but are the weakest muscle groups in the lower limb.

Age specific muscle strength in HIV negative males (n=17) is shown in Table 4.7below.

Table 4.7: Age Specific HIV Negative Males (n=17) Muscle Strength

Muscle Group	AGE BAND													
	15.29		20-24		25-29		30-34		35-29		40-44		45-49	
	Muscle Strength kg/m^2													
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	13.50	0.71	15.00	1.41	15.42	3.99	16.48	3.29	18.25	1.71	21.00	1.41	21.00	5.60
Ankle Dorsiflexors	12.50	0.71	1.00	0.00	10.58	2.23	12.60	2.42	12.75	1.50	14.50	0.71	12.00	0.00
Knee Flexors	12.00	0.00	9.00	1.41	13.83	2.52	13.70	13.12	17.25	7.09	17.50	0.71	10.00	0.00
Knee Extensors	20.50	0.71	13.50	0.71	18.17	2.86	21.15	3.65	20.25	1.26	18.00	2.83	13.50	2.10
Hip Flexors	14.50	0.71	11.00	1.41	14.50	3.29	16.55	2.50	18.50	1.00	20.00	0.00	8.50	0.70
Hip Extensors	20.00	0.00	16.50	0.71	18.65	2.74	20.75	4.13	20.75	0.96	25.00	1.41	18.00	0.70
Hip Abductors	17.50	0.71	14.50	0.71	17.92	3.92	18.45	3.58	17.00	2.16	3.50	0.71	13.00	0.00
Hip Adductors	17.50	0.71	9.00	0.00	16.25	2.34	16.90	3.38	18.00	1.41	18.00	2.83	9.50	0.70

There were no male HIV negative subjects in the 50-54 Age band upwards.Most, 58% (n=9) subjects were in the 30-34 years and 35-39 year age bands with their mean muscle strength varying from 9.00 kg /m^{2}to 30.50 kg/m^2.

Age specific muscle strength in HIV negative females (n=13) is depicted in Table 4.8 below.

Table 4.8: HIV Negative Females (n=13) Age Specific Muscle Strength

Muscle Group	AGE BAND													
	15.19		20-24		25-29		30-34		35-39		40-44		45-49	
	Muscle Strength kg/m^2													
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ankle Plantar Flexors	16.00	1.14	16.17	2.56	12.08	3.14	13.50	1.29	14.00	2.83	11.50	1.68	14.25	1.70
Ankle Dorsiflexors	12.00	0.00	13.67	2.16	10.83	1.17	9.00	0.82	9.50	0.71	7.50	0.58	6.75	1.00
Knee Flexors	9.00	1.14	13.83	1.72	9.83	0.75	10.63	0.48	12.00	0.00	10.60	10.87	13.00	0.00
Knee Extensors	15.00	0.00	20.83	5.04	11.17	1.17	13.25	0.50	13.50	2.12	12.88	1.93	15.00	0.00
Hip Flexors	11.00	1.14	13.67	3.01	9.17	1.92	9.50	0.50	12.50	2.12	8.88	1.95	10.50	0.70
Hip Extensors	17.00	1.14	19.33	4.76	13.42	2.50	9.75	0,96	15.00	1.41	14.75	1.44	16.50	4.95
Hip Abductors	14.50	0.71	20.00	4.73	10.83	3.31	11.50	1.29	17.00	1.41	13.12	4.95	13.25	0.35
Hip Adductors	9.00	0.00	18.67	4.84	8.25	1.08	9.25	0.96	12.90	0.71	8.75	1.90	13.00	0.00

Females over the age of 25 were 69% (n=9) and thus in the majority. Lower limb muscle strength for the females ranged from 6.50kgs/m^2 to 19.30kgs/m^2

4.3.5 Results of Lower Limb Muscle Strength for HIV Positive Subjects on HAART Compared with HIV Negative Subjects

Lower limb muscle strength of 30 HIV negative subjects were compared to those of 30 matched for age and gender HIV positive subjects on HAART (Table 4.9).

Table 4.9: Comparison of 30 HIV Negative and 30 HIV Positive Participants on HAART (matched groups) Lower Limb Muscle Strength

Muscle Group	HIV Positive Mean Muscle Strength (kg/m2)	HIV Negative Mean Muscle Strength (kg/m2)	P-Value
Ankle plantar flexors	12.76	15.36	0.0001
Ankle dorsiflexors	9.66	11.23	0.0001
Knee Flexors	12.30	12.73	0.46
Knee extensors	15.72	17.08	0.08
Hip flexors	11.67	13.33	0.0001
Hip extensors	15.75	17.75	0.0001
Hip abductors	11.98	16.53	0.0001
Hip adductors	11.71	14.11	0.0001

Lower limb muscle strength is significantly different in all muscle groups of the matched groups except knee flexors and extensors with p-values of 0.46 and 0.08 respectively.

Lower limb muscle strength of 17 HIV negative male subjects were compared to those of 17 HIV positive male subjects on HAART.The subjects were matched for age and gender (Table 4.10).

Table 4.10: Comparison of Matched Lower Limb Muscle Strength for HIV Negative and HIV Positive Male Participants on HAART (n=34)

Muscle Group	HIV Positive Mean Muscle Strength (kg/m2)	HIV Negative Mean Muscle Strength (kg/m2)	P-Value
Ankle plantar flexors	13.31	16.58	0.001
Ankle dorsiflexors	10.07	11.88	0.0001
Knee Flexors	13.18	13.79	0.47
Knee extensors	16.78	18.87	0.02
Hip flexors	12.84	15.34	0.0001
Hip extensors	17.22	19.81	0.0001
Hip abductors	12.70	18.19	0.0001
Hip adductors	12.57	16.00	0.0001

All lower limb muscle strength in 17 HIV male negative subjects were higher than the matched 17 male HIV positive subjects on HAART, except knee flexors. Knee flexors are showing a p-value of 0.47.

4.3.6 Results of Compared Lower Limb Muscle Strength between 17 HIV Positive Male Subjects on HAART and 17 HIV Negative Male Subjects by Age Bands

Lower limb muscle strength of 17 HIV negative male subjects were compared to those of 17 HIV positive male subjects on HAART by age bands. The subjects were of the same ages (Table 4.11a-c).

Tables 4.11a-c. Mean lower limb muscle strength for HIV negative and HIV positive male subjects on HAART. (n=34)

Table 4.11a: Comparison of Male Mean Lower Limb Muscle Strength

Muscle group (25-29)	HIV Positive Mean Muscle Strength (kg/m2)	HIV Negative Mean Muscle Strength (kg/m2)	P-Value
Ankle plantar flexors	13.69	15.42	0.17
Ankle dorsiflexors	10.07	10.58	0.53
Knee Flexors	13.06	13.83	0.51
Knee extensors	17.46	18.17	0.63
Hip flexors	13.16	14.5	0.28
Hip extensors	16.16	18.67	0.05
Hip abductors	12.57	17.92	0.01
Hip adductors	12.93	16.25	0.01

Table 4.11b: Comparison of Male Mean Lower Limb Muscle Strength *(Continued)*

Muscle group (30-34)	HIV Positive Mean Muscle Strength (kg/m2)	HIV Negative Mean Muscle Strength (kg/m2)	P-Value
Ankle plantar flexors	12.86	16.48	0.03
Ankle dorsiflexors	9.40	12.60	0.01
Knee Flexors	12.30	13.70	0.40
Knee extensors	16.11	21.15	0.01
Hip flexors	11.68	16.55	0.01
Hip extensors	18.66	20.75	0.32
Hip abductors	12.86	18.45	0.01
Hip adductors	12.56	16.90	0.01

Table 4.11c: Comparison of male Mean Lower Limb Muscle Strength *(Continued)*

Muscle group (35-39)	HIV Positive Mean Muscle Strength (kg/m2)	HIV Negative Mean Muscle Strength (kg/m2)	P-Value
Ankle plantar flexors	13.38	18.25	0.01
Ankle dorsiflexors	10.85	12.75	0.11
Knee Flexors	14.42	17.25	0.46
Knee extensors	16.18	20.25	0.08
Hip flexors	15.05	18.5	0.01
Hip extensors	15.73	20.75	0.01
Hip abductors	13.20	17.00	0.02
Hip adductors	11.80	18.00	0.01

A difference is noted in hip abductors and hip adductors in age band 25-29years.In the age band 30-34 years all other muscle groups are showing significant difference except knee flexors and hip extensors. In the age band 35-39 years there is significant difference in ankle plantar flexors and all hip muscle groups. There is no significant difference in ankle dorsiflexors, knee flexors and knee extensors.

Compared Lower Limb Muscle Strength between 13 HIV Positive Female Subjects on HAART and 13 HIV Negative Female Subjects

Lower limb muscle strength of 13 HIV negative female subjects was compared to those of 13 HIV positive female subjects on HAART (Table 4.12).

Table 4.12: Mean Lower Limb Muscle Strength for HIV Negative and HIV Positive Female Subjects on HAART (n=26)

Muscle Group	HIV Positive Muscle Strength (kg/m^2) (n=13)	HIV Negative Muscle Strength (kg/m^2) (n=13)	P-Value
Ankle plantar flexors	12.04	13.77	0.03
Ankle dorsiflexors	9.13	10.37	0.05
Knee Flexors	11.13	11.35	0.75
Knee extensors	14.34	14.75	0.72
Hip flexors	10.13	10.71	0.45
Hip extensors	13.83	15.06	0.28
Hip abductors	11.04	14.35	0.01
Hip adductors	10.58	11.63	0.35

There is significant difference in muscle strength between ankle plantar flexors, ankle dorsiflexors, hip flexors and hip abductors. There is no significant difference in knee flexors, knee extensors, hip extensors and hip adductors.

Results of compared lower limb muscle strength between 13 HIV positive female subjects on HAART and 13 HIV negative female subjects by age bands

The Lower limb muscle strength of 13 HIV negative female subjects were compared to those of 13 HIV positive female subjects on HAART by age bands (Table 4.13 a-d).

4.13 a-d Shows the mean lower limb muscle strength for HIV negative and HIV positive female Table subjects on HAART by age band (n=26).

Table 4.13a: Comparison ofLower Limb Muscle Strength by Age Bands

Muscle Group (20-24)	HIV Positive Female Mean Muscle Strength (kg/m^2) (n=13)	HIV Negative Female Mean Muscle Strength (kg/m^2) (n=13)	P-Value
Ankle plantar flexors	11.7	16.17	0.01
Ankle dorsiflexors	8.78	13.67	0.0001
Knee Flexors	10.96	11.35	0.68
Knee extensors	14.85	19.38	0.05
Hip flexors	9.08	13.67	0.03
Hip extensors	14.53	19.33	0.09
Hip abductors	10.08	20.00	0.0001
Hip adductors	9.55	18.67	0.0001

Table 4.13b: Comparison ofLower Limb Muscle Strength by Age Bands *(Continued)*

Muscle group (25-29)	HIV Positive Female Mean Muscle Strength (kg/m^2) (n=13)	HIV Negative Female Mean Muscle Strength (kg/m^2) (n=13)	P-Value
Ankle plantar flexors	11.70	16.17	0.01
Ankle dorsiflexors	8.78	13.67	0.0001
Knee Flexors	10.96	11.35	0.68
Knee extensors	14.85	19.38	0.05
Hip flexors	9.08	13.67	0.03
Hip extensors	14.53	19.33	0.09
Hip abductors	10.08	20.00	0.0001
Hip adductors	9.55	18.67	0.0001

Table 4.13c: Comparison of Lower Limb Muscle Strength by Age Bands *(Continued)*

Muscle group (30-34)	HIV Positive Female Mean Muscle Strength (kg/m^2) (n=13)	HIV Negative Female Mean Muscle Strength (kg/m^2) (n=13)	P-value
Ankle plantar flexors	9.13	13.25	0.0001
Ankle dorsiflexors	7.40	9.00	0.15
Knee Flexors	8.03	10.63	0.0001
Knee extensors	9.68	13.25	0.0001
Hip flexors	8.35	9.50	0.02
Hip extensors	8.73	9.75	0.43
Hip abductors	9.38	11.50	0.06
Hip adductors	7.55	9.25	0.03

Table 4.13d: Comparison of Lower Limb Muscle Strength by Age Bands *(Continued)*

Muscle group (45-49)	HIV Positive Female Mean Muscle Strength (kg/m^2) (n=13)	HIV Negative Female Mean Muscle Strength (kg/m^2) (n=13)	P-value
Ankle plantar flexors	12.30	11.50	0.46
Ankle dorsiflexors	10.53	7.50	0.0001
Knee Flexors	12.63	10.63	0.26
Knee extensors	14.78	12.88	0.22
Hip flexors	10.95	8.88	0.06
Hip extensors	14.50	14.75	0.83
Hip abductors	11.50	13.13	0.54
Hip adductors	12.35	8.75	0.09

The results show that in the age band 20-24 years, there is significant difference in lower limb muscle strength in the ankle plantar flexors, dorsiflexors, hip flexors, hip abductors and adductors; knee flexors, knee extensors and hip extensors show no significant difference. In age band 25-29 years, there is significant difference in muscle strength in knee flexors, knee extensors, hip flexors, hip extensors and hip adductors while there is no significant difference in the ankle plantar flexors, dorsiflexors and hip abductors. The 30-34 age bands show significant difference in ankle plantar flexors, knee flexors and extensors, hip flexors and adductors while there is no significant difference in the rest of the groups. There is no significant difference in muscle strength all muscle groups except ankle dorsiflexors in the 45-49 years age band.

4.3.7 Results of Lower Limb Function in HIV Positive Subject son HAART

Lower limb functional scores are shown in graphs below.

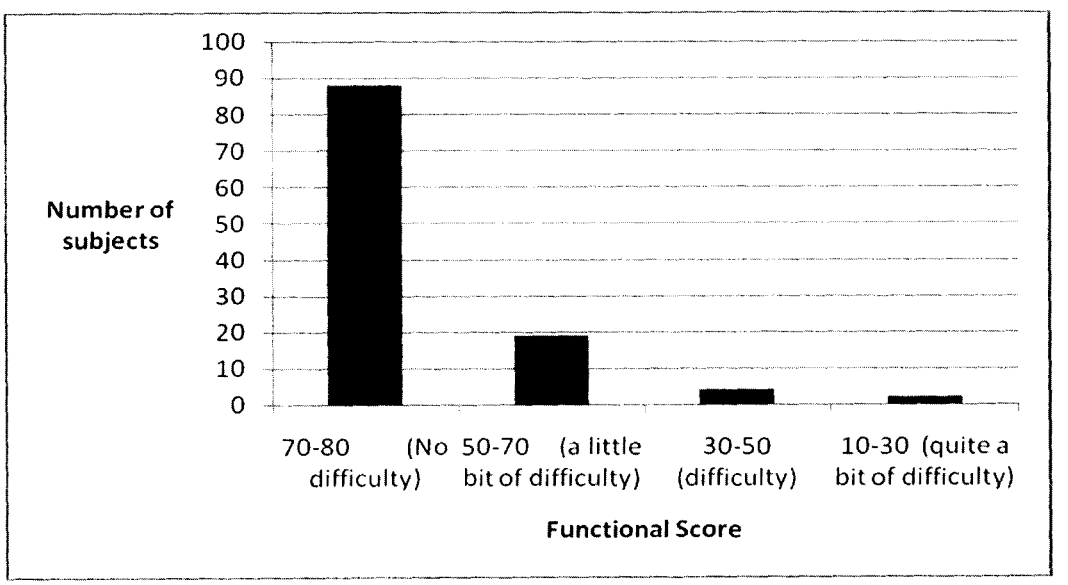

Figure 4.1: Lower Limb Function in HIV Positive Subjects on HAART (n=113)

The majority 78% (n= 88) had no difficulty, 15% (n =17) had a little bit of difficulty, 5% (n=6) had difficulty and only 2% (n=2) of HIV positive patients on HAART had quite a bit of difficulty with lower limb functional activities.

Results of lower limb function in HIV positive male subjects on HAART

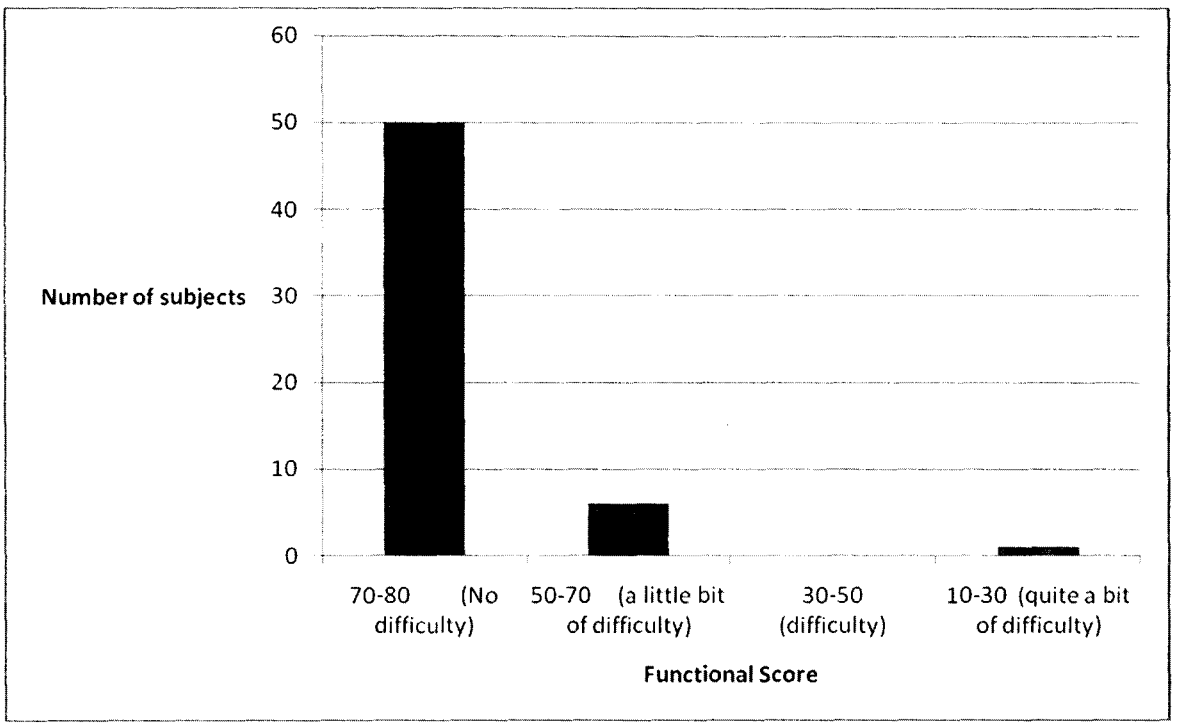

Figure 4.2: Lower Limb Function in HIV Positive Male Subjects on HAART (n=57)

Just over 88% (n=50) had no difficulty with lower limb function, 11% (n=6) had a little bit of difficulty while only 0.02% (n=1) had quite a bit of difficulty. Further analysis was done on lower limb function in HIV positive male subjects on HAART by age bands, only the age bands 45-49 and 50-54 had most people without difficulty.

Results of lower limb function in HIV positive female subjects on HAART

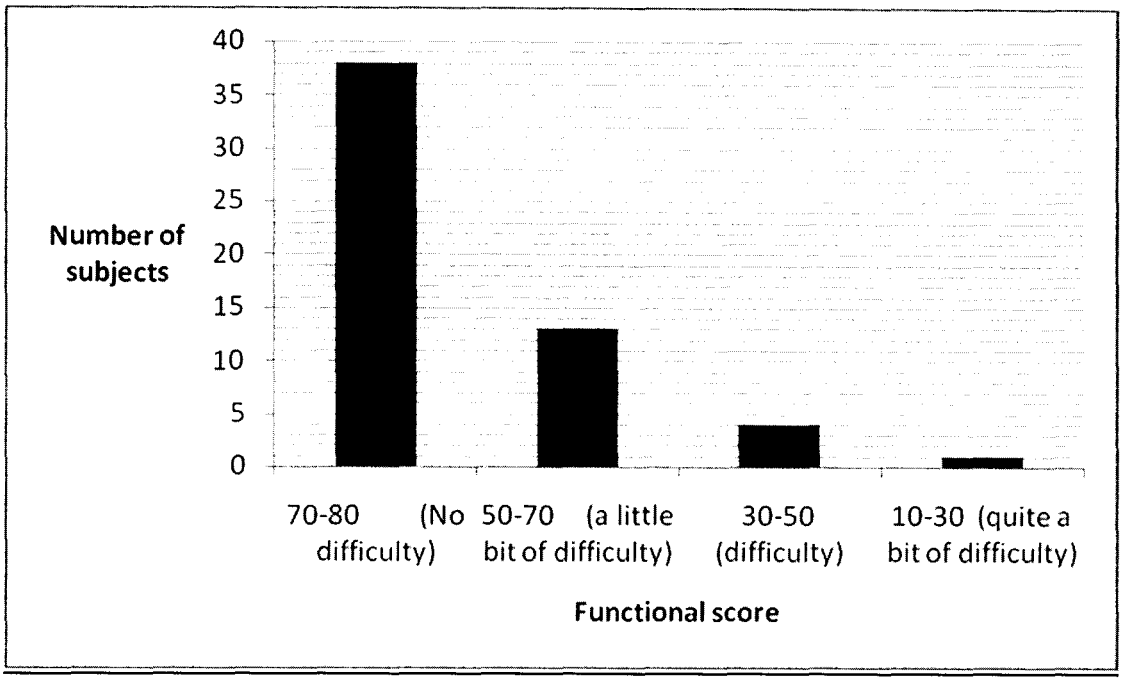

Figure 4.3 Lower Limb Function in HIV Positive Female Subjects on HAART (n=56)

The results show that 68%(n=38) had no difficulty with lower limb function and only 2%(n=1) had quite a bit of difficulty. Further analysis revealed that no age bands had high levels of difficulty.

4.3.8 Relationship between Lower Limb Muscle Strength and Lower Limb Function in HIV Positive Patients on HAART

Table 4.14a is multiple regression summary showing the relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART.

Table 4.14a: Multiple Regression Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0.71[a]	0.50	0.46	8.90

p-value= 0.00000

There is a positive correlation (correlation coefficient r=0.71) between lower limb muscle strength and lower limb function in HIV positive people on HAART. The correlation coefficient is significant at p-value =0.00 showing a high level of significance. The coefficient of determination (0.50 or 50%) means that 50% of lower limb function in HIV

positive people on HAART is a result of lower limb muscle strength. This means other variables contribute to lower limb function in HIV positive people on HAART.

A detailed logistic regression (Table 4.14b) was done for the relationship between lower limb muscle strength and lower limb function. Ankle plantar flexors were established to be the most active group of muscles in lower limb functional activities in HIV positive people on HAART.

Table 4.14b: Detailed Regression Model of Lower Limb Functional Status against Specific Lower Limb Muscle Groups

Model	Unstandardized Regression Coefficients		Standardized Regression Coefficients
	B	Std. Error	Beta
Functional status	33.90	4.26	
Ankle plantar flexors	1.49	0.52	0.32
Ankle dorsiflexors	1.43	0.57	0.29
Knee Flexors	0.18	0.42	0.05
Knee extensors	-.64	0.33	-.27
Hip flexors	0.88	0.44	0.26
Hip extensors	0.13	0.34	0.05
Hip abductors	0.03	0.58	0.01
Hip adductors	0.19	0.47	0.06

The Spearman's rho correlation was also done to establish the order in which each muscle group was contributing towards lower limb functional activities (Table 4.15). The Spearman's rho correlation coefficient confirmed the order of how much each lower limb muscle group is contributing to lower limb function.

Table 4.15: Order of Contribution of Muscle Groups to Lower Limb Function

	Independent Variable							
	Ankle plantar flexors	Ankle dorsiflexors	Knee flexors	Knee extensors	Hip flexors	Hip extensors	Hip abductors	Hip adductors
Dependent variable								
Functional status	0.56	0.45	0.54	0.40	0.54	0.46	0.51	0.50
Correlations ranked	1	7	2	8	3	6	4	5

4.4 CONCLUSION

The results established that lower limb muscle strength contributes 50% to lower limb function. Gender,walking, being employed and housing environment also positively influenced lower limb function. Ankle plantar flexors are the most active muscles when performing lower limb functional activities in this cohort, while knee extensors are the least (8th) active. Hip flexors are third in terms of activity level while hip extensors are the 6th most active in lower limb functional activities.

The results suggest that hip extensors are the strongest lower limb muscles in both HIV positive and negative subjects. Hip extensors mean muscle strength in HIV positive people on HAART was 15.80kg/m^2 whereas for the HIV negative people it was 17.70kg/m^2. Ankle dorsiflexors were the weakest lower limb muscle group in both HIV positive participants on HAART and HIV negative people with a mean muscle strength of 11.20 kg/m^2 in HIV negative people and 10.10kg/m^2 for the positive group on HAART. All Lower limb muscles' strength is significantly less for HIV positive people on HAART when compared to the HIV negative group except knee extensors with a p-value of 0.08.

This study established that 77% (n=88) had no difficulty with lower limb function, 22% (n=17) had difficulty, while only 2% (n=2) having quite a bit of difficulty with functional activities.

This study had equal number of HIV positive females on HAART (n=56) and males (n=57) as subjects. Seventy three (65%) of the HIV positive people on HAART were formally employed, 26% (n=29) was not employed and 10% (n=11) were retired. The majority (n=20) of HIV positive people on HAART were in the 45-49 year age category while the majority of the HIV negative (n=10) were in the 25-29 year category. Walking was the

dominant mode of transport used by most HIV patients on HAART 79% (n=89) even for urban dwellers who constituted 69% (n=78) of this study. The remainder 31% (n=35) were rural dwellers. For the urban dwellers 22% (n=24) lived in shacks or shared their accommodation, 18% (n=20) stayed in a hostel/flat or Hlalani Kuhle (RDP) housing while 30% stayed on a residential stand.

CHAPTER 5

5. DISCUSSION

The primary aim of this study was to establish the relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART.

Male and female ambulant adult HIV positive patients who were on HAART aged between 18- 70 years were included in the study.

Since the aim of this study was to look at the relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART, findings would contribute to understanding possible factors affecting decreased lower limb functional status in this population. Low cost rehabilitation intervention programmes would then be designed so as to be implemented at primary care level. This is because the integration of antiretroviral therapy into HIV care has dramatically extended the life expectancy of those living with HIV (Erlandson et al., 2014). Approximately one half of the people living with HIV in the United States are fifty years or older (Effros et al., 2008). With an increasing life expectancy in HIV infected patients (Lewden et al., 2012), age-related changes and co-morbidities have become a concern as they occur relatively early in this population (Capeau, 2011). Poor locomotor performance is highly prevalent in middle-aged ambulatory HIV-infected patients on HAART who had well-controlled viral load (Richert et al., 2014).

5.1 RELATIONSHIP BETWEEN LOWER LIMB MUSCLE STRENGTH AND LOWER LIMB FUNCTION IN HIV POSITIVE PATIENTS ON HAART

The relationship between lower limb muscle strength and lower limb function in HIV positive cohort in Manicaland Zimbabwe was established using multiple regression. The results established that there is a positive correlation (correlation coefficient (r)=0.71) (p-value=0.00) between lower limb muscle strength and lower limb function in HIV positive people on HAART. The coefficient of determination (0.50 or 50.00%) means that 50% of lower limb function in HIV positive people on HAART is a result of lower limb muscle strength. Gender, being employed, housing environment and mode of transport also positively affected lower limb function in this cohort.

A detailed regression model of lower limb functional status against specific lower limb muscle groups was done. The results showed that lower limb ankle plantar flexors

contribute the most to lower limb function in HIV positive people on HAART. International literature says hip flexors are the dominant factor in lower limb functional activities (Fotoohabadi et al.,2010)

It is imperative to look at the biomechanics of standing up from a sitting position since the majority of lower limb functional activities lower limb functional activities such as getting up from a chair and walking depend on an individual's ability to perform sit to stand.

The activities of rising from a sitting position into standing is an essential prerequisite for walking and therefore, lower limb functional independence (Tiedemann et al., 2008). It has been reported that people who have difficulty rising to a standing position have a greater likelihood of falling during ambulation (Yamada et al.,2009) and to need help with daily lower limb functional activities (Puthoff et al., 2007).Coming from sitting to a standing position is a coordinated sagittal movement between the hips, knees, lumbar spine and thoracic spine in a healthy individual. Hip joint flexion is the **dominant** factor in bringing the body mass forward, and a small degree of lumbar flexion is also a component of trunk forward lean (Fotoohabadi et al.,2010).

Fotoohabadi et al (2010) did a study on kinematics of rising from a chair. They had a sample of convenience of 41 community-dwelling elderly people (22 female and 19 male). The study established that full available hip flexion (90%) was used by these participants during the pre-lift off phase of coming from sitting to standing. This demonstrates that hip flexion limitation would pose a major challenge in the kinematic chain. Possible compensation would include increased lumbar flexion instead of extension to bring the trunk sufficiently forward at an appropriate velocity (Fotoohabadi et al., 2010). Trunk movement must be sufficient to propel the upper body mass forward (Riley et al., 1991). This trunk movement must be limited to prevent the possibility of falling forward at the lift-off phase (Mourey et al., 2000).

The importance of postural stability around the lift-off phase of sit to stand by controlling the centre of mass in relation to the foot support area has been emphasized (Carr et al., 2003). The above discussed sequence happens in healthy individuals. What this means is in healthy HIV negative population, the most active muscles during lower limb functional activities are the hip and trunk muscles which represent proximal stability. In the current study we established that in HIV positive people on HAART, ankle plantar flexors are the most active lower limb muscle group during lower limb functional activities. Ankle plantar flexors are distal musculature of the lower limb. This cohort could possibly be compensating

by increasing lumbar flexion or thoracic flexion instead of extension to bring the trunk forward to perform lower limb functional activities (Carr et al., 2003).

These results are showing proximal weakness which is consistent with Myezwa et al's (2009) findings. Myezwa et al (2009) found that HIV affects function in general. Proximal weakness which compromises function is a common feature when HIV patients were tested using dynamometry. None of the studies reviewed that have examined lower limb muscle strength and lower limb function has established how much each lower limb muscle group contributed to lower limb function. Therefore this is the first study to the researchers' knowledge that has explored the relationship between lower limb muscle strength and lower limb function in HIV positive patients on HAART.

5.2 LOWER LIMB MUSCLE STRENGTH

The mean muscle strength obtained in this cohort of HIV positive patients on HAART ranged from 9.30kg/m^2 to 15.80kg/m^2 in all muscle groups tested. The muscle groups included were ankle plantar flexors, ankle dorsiflexors, knee flexors, knee extensors, hip flexors, extensors, abductors and adductors. These values were compared to an equally matched HIV negative group. The findings showed that in the HIV negative matched group, the mean muscle strength ranged from 11.20 kg/m^2 to 17.70kg/m^2 for the same muscles. The difference between the group values had a statistically significant difference as follows: ankle plantar flexors (0.001), Ankle dorsiflexors (0.0001), Knee flexors (0.47), Knee Extensors (0.02), Hip flexors (0.0001), Hip extensors (0.0001), Hip abductors (0.0001) and Hip adductors (0.0001).

Bahannon (1997) in his reference values for extremity muscle strength obtained by hand-held dynamometry from adults aged 20 to 79 years had a similar finding among the HIV negative group. In Bahannon's (1997) subjects from a convenient sample of 106 men and 125 women, who on entrance into the study were without any neuromuscular, musculoskeletal or cardiovascular pathology established that muscle strength ranged from (95.90N) 9.80kg/m^2 in dorsiflexors to (218.40N) 22.30 kg/m^2 in hip abductors in female subjects. No reading for hip extensors was given in this study.

This study's results show that lower limb mean muscle strength for matched HIV negative group was significantly greater (p-value= 0.0001) than that of the HIV positive group on HAART except knee flexors and knee extensors whose p values were 0.46 and 0.08 respectively. This is consistent with Mascolin (2011) finding in HIV positive people in a French Acquaintance cohort, where he established that HIV positive people had poor leg

muscle strength when compared to the general population. Sagui (2005) also established that lower limb muscle weakness was a common complaint among HIV positive patients on HAART presenting to family physicians.

In contrast Kinsey (2007) reported that there was no significant difference (p-value=0.78) between HIV positive females on HAART for seven months and their HIV negative counterparts. In the current study sample, patients had been on HAART for an average of four years while Mascolin (2011) and Sagui (2005)'s samples had been on HAART for an average of three to five years. There is a difference between Kinsey's (2007) findings that there was no difference in lower limb strength in HIV positive females on HAART for seven months and our finding that there is a significant difference. This disparity is explained by Carter et al's (2011) study showing that each year of infection with HIV increases the risk of poor lower limb strength by 8.00%. Lower limb muscle weakness in HIV positive people on HAART is a result of mitochondrial toxicity (Kohles et al., 2007), limited extraction/ use of oxygen in the lower limb musculature (Menders et al., 2013; Mascolini, 2011). Guazzi (2000) suggested that there were structural changes to capillaries in lower limb muscles leading to "stress failure" of the capillary membranes. This "stress-failure" of the capillary membranes in lower limb muscles progresses to thickening of the capillary enterstium and increased permeability of water and ions. There is a consequent disruption of local regulatory mechanism for gaseous exchange leading to lower limb muscle fatigue secondary to diminished oxygen availability and poor cell regeneration leading to cachexia (Guazzi,2000).

Furthermore, another mechanism that affects muscle function is explained by Russ et al (2010) that contractile properties of knee extensors indicated potential intra-muscular impairments. Gene expression analysis in the muscle tissue of HIV-infected patients suggests alterations similar to those observed with aging (Kusko et al., 2012). There is a resultant impairment of locomotor function, deterioration of lower limb functional ability and limitations in activities of daily living (Richert et al.,2011).

5.3 LOWER LIMB FUNCTION

The international classification of function, defines function as what a person with a healthy condition can do in a standard environment (their level of capacity) as well as what they actually do in their usual environment (their level of performance) (WHO,2002). Functioning refers to all body functions, activities and participation including environmental factors that interact with all these components (WHO, 2002).

The lower extremity functional scale (LEFS) which was used to measure lower limb function in this study established that the majority (78%), n=88) had no difficulty with lower limb function, 22% (n=17) had difficulty. Only 2% (n=2) of HIV positive patients on HAART had quite a bit of difficulty with lower limb functional activities. This is a total 24% experienced functional difficulty similar to Oursler et al (2009) who found that lower limb function is preserved in almost 90% of HIV positive people on HAART. In a study by Van As et al (2008) they found that there is loss of lower limb functional capacity in this group consequently affecting their Health Related Quality of Life (HRQOL).

Loss of lower limb functional activities in HIV positive people on HAART could be explained by the disablement model originally conceptualized by Nagi et al (1964) and extended by Verbrugge et al (1994). They linked pathology, physical impairment, functional limitation and disability (Nagi et al., 1964; Verbrugge et al., 1994). According to this model, an underlying pathology, in this case mitochondrial toxicity, limited extraction/use of oxygen in the lower limb musculature or "stress failure" of capillary membranes will lead to "impairment" at the tissue, organ or body system level (Erlandson et al., 2014). The "impairment" in our current study is loss of lower limb muscle strength. This impairment results in "functional limitation" which could be slow gait speed or difficulty rising from a chair (Puthoff et al., 2007). Ultimately disability sets in, in which the patient is eventually confined to a wheelchair (Erlandson et al., 2014).

One of the strengths of this study was the equal representation of the genders 50% (n=56) females and 50% (n=57) males. This is unlike other studies that have studied HIV populations. An example is the study done by Raso et al (2013) on Handgrip Force after a measure of physical function in individuals living with HIV/AIDS. Their sample consisted of 40 carefully screened male patients recruited from an ambulatory outpatient HIV/AIDS clinic. Roos et al (2014), however, in the study "not easy at all but I am trying": barriers and facilitators to physical activity in a South African cohort of people living with HIV participating in a home-based pedometer walking program had a closer representation of males and females.

The study setting Mutare Provincial Hospital is a public hospital situated in the Eastern part of Zimbabwe serving a population of 1.20 million people. The participants' age ranged between 18 and 70 years. Over nine percent (n=22) of HIV positive participants on HAART were in the age band 45-49 years, close to six percent (n=7) was between 65 and 69 years. This demographic data is consistent with other studies on HIV that HIV positive people on HAART are aging (Hanass-Hancock et al., 2003, Cade et al., 2003, Hunter et al., 2004).

Erlandson et al (2014) noted that the integration of HAART into HIV care has dramatically extended the life expectancy of those living with HIV.

Approximately one half of the people living with HIV/AIDS on HAART are not only concerned with a treatment's ability to extend life but also with the quality of life they are able to lead (Gale, 2003). The health related quality of life (which includes the ability of an individual to function) of people living with HIV/AIDS in South Africa and elsewhere has been found to be severely compromised (Myezwa et al., 2011). The need for designing rehabilitation strategies to improve lower limb muscle strength and consequently function is thus further justified by this study. In any case; physiotherapy is a profession providing services to people and populations to develop, maintain and restore maximum movement and functional ability throughout their life span (Kumar, 2010).

Pebody (2009) found that with improved treatments, a majority of the people living with HIV are able to remain in employment. This is consistent with our finding where we found 65% (n=73) was gainfully employed while 26% (n=29) was not employed and over nine percent (n=11) was retired. Pebody's (2009) findings only related to gays and bisexual men living with HIV in the United Kingdom. Our study population shows that HIV positive people on HAART are gainfully employed with some reaching retirement.

The majority of our study participants 79% (n=89) walked as their mode of transport. They walked because they could not afford the transport cost which on average was R10.00 (approximately one United States dollar). Most participants would walk in order to save their earnings for essentials like food, nutrition and school fees for their children. Wheeled transport was used by 21% (n=24) of the study population. The wheeled transport was primarily buses and taxis.

Brisk walking or jogging to a threshold of 24 to 32 kilometers per week results in an energy expenditure of 1200 to 2200 kilocalories per week. It improves function and is beneficial to healthy living (Durstine et al., 2001). It is possible that the respondents in this study were engaging in brisk walking which met the beneficial threshold. Roos et al (2014) clearly states that prescription guidelines do not influence adherence to physical activity programmes but personality, social and environmental factors played a larger role. This can possibly explain the high functional status which was observed in this study; the social and environmental factors were influencing our study participants to engage in lots of walking. We established that 78% (n=88) of HIV positive subjects on HAART had no difficulty with

lower limb functional activities while only 2% (n=2) had quite a bit of difficulty. The majority of the participants 79% (n=89) walked as their mode of transport.

Lower limb muscle strength was responsible for 50% of lower limb function in our study participants while gender, being employed, housing environment and mode of transport also positively influenced lower limb function. The most active lower limb muscle group was ankle plantar flexors meaning HIV+ people on HAART would compensate proximal muscle weakness during lower limb functional activities. There is proximal weakness in this cohort. Lower limb muscle strength was significantly less in HIV positive people on HAART when compared to the negative group. A total of 24% had difficulty with lower limb function.

CHAPTER 6

6. CONCLUSION, LIMITATION AND RECOMMENDATIONS

6.1 CONCLUSION

This study was beneficial in highlighting that 50.00% of lower limb function is a result of lower limb muscle strength in HIV positive people on HAART attending an outpatient clinic in Mutare, Zimbabwe. Walking, employment and housing environment also contributed positively to this cohort's lower limb function.

This project highlighted that ankle plantar flexors were the most active muscle group during lower limb functional activities. Literature on lower limb function indicates that hip flexors are the most active muscle group during lower limb functional activities (Fotoohabadi et al., 2010). It therefore means exercise prescription to activate/strengthen hip flexors and other proximal muscles will benefit this population since exercises have been proved to strengthen muscles (O'Brien et al., 2004).

International literature suggests that HIV positive people on HAART have lower limb muscle strength compared to their HIV negative counterparts (Mascolin, 2011; Sagui, 2005). The current study confirmed that lower limb muscle weakness is prevalent in HIV positive people on HAART. Most participants in this study were walking as their main mode of transport and walking is a recommended exercise regime (Roos et al., 2014). They reported walking long distances which could be more than 10000 steps per day because of their social and environment factors. This walking could be responsible for why a large number of these HIV positive people on HAART 78% (n=88) had no difficulty with lower limb function.

The study contributes to literature related to HIV and function in individuals who are HIV positive on HAART.

6.2 LIMITATIONS

The research project was done in Zimbabwe while the country was undergoing a challenging economic situation. The study setting made the study difficult to implement as the participants were experiencing a difficult socio-economic situation such that participants were walking long distances and would be tired or hungry during measurements. We could have controlled this by giving them a snack but the researcher failed to obtain funding to do

so. This possibly negatively affected our results in that we would get reduced lower limb muscle strength.

6.3 RECOMMENDATION

The research project highlighted several areas where research is needed.

- The study highlighted that participants found the muscle testing and lower limb functional scoring beneficial. Muscle testing and lower limb functional scoring in current HAART management and prescribing strengthening exercises could be beneficial.

- The project focused on assessing lower limb muscle strength and lower limb function on people living with HIV/AIDS on HAART at an outpatient clinic. Research is needed in newly' diagnosed on HAART and HIV+.

- Research could be carried out to see how Zimbabweans who are HIV positive on HAART perceive documented exercise interventions which are known to be beneficial.

- Research could be conducted to ascertain how much walking or physical activity level of HIV positive patients on HAART undertake on a daily basis and encourage this low-cost beneficial exercise programme.

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APPENDIX A

- **CLEARANCE CERTIFICATE**

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

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R13/49 Peter Mhariwa

CLEARANCE CERTIFICATE	M120715
PROJECT	The Relationship between Lower Limb Muscle Strength and Lower Limb Function in HIV Patients on Highly Active Antiretroviral Therapy (HAART)
INVESTIGATORS	Peter Mhariwa.
DEPARTMENT	Department of Physiotherapy
DATE CONSIDERED	27/07/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

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

DATE 23/08/2012 CHAIRPERSON ..... (Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor: Dr Morake Maleka

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

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.

APPENDIX B

▪ MEDICAL RESEARCH COUNCIL APPROVAL

Telephone 791792 791193 792717
Telefax (263) - 4 - 790715
E-mail mrcz@mrcz.org.zw
Website www.mrcz.org.zw

Medical Research Council of Zimbabwe
Josiah Tongogara / Mazoe Street
P. O. Box CY 573
Causeway
Harare

APPROVAL LETTER

Ref: MRCZ/B/514 25 June 2013

Peter Mharirwa
Premier Service Medical Investments
86 Baines Avenue
Harare

RE: The relationship between lower limb muscle strength and lower limb function in HIV patients on Highly Active Antiretroviral Therapy.

Thank you for the above titled proposal that you submitted to the Medical Research Council of Zimbabwe (MRCZ) for review. Please be advised that the Medical Research Council of Zimbabwe has reviewed and approved your application to conduct the above titled study. This is based on the following documents that were submitted to the MRCZ for review

a) Research proposal and summary
b) Informed Consent Form (English and Shona)
c) Questionnaire (English and Shona)

- **APPROVAL NUMBER** :MRCZ/B/514

This number should be used on all correspondence, consent forms and documents as appropriate

- **APPROVAL DATE** : 25 June 2013
- **TYPE OF MEETING** : Expedited
- **EXPIRATION DATE** : 24 June 2014

After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ website or our website should be submitted three months before the expiration date for continuing review.

- **SERIOUS ADVERSE EVENT REPORTING**: All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 5 working days using standard forms obtainable from the MRCZ website www.mrcz.org.zw
- **MODIFICATIONS**: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ website is required before implementing any changes in the Protocol (including changes in the consent documents)
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ website
- **QUESTIONS**: Please contact the MRCZ on Telephone No. (04) 791792, 791193 or by e-mail on mrcz@mrcz.org.zw

Other:

- Please be reminded to send in copies of your final research results for our records as well as for the Health Research Database
- You are also encouraged to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study

Yours Faithfully

MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

MEDICAL RESEARCH COUNCIL OF ZIMBABWE
2013 -06- 25
APPROVED

APPENDIX C

- **MUTARE PROVINCIAL HOSPITAL APPROVAL**

Telephone: +263-020-64321
Fax: +263-020-67048
E-mail: mphosp@syscom.co.zw

ZIMBABWE

Reference:
MINISTRY OF HEALTH & CHILD-WELFARE
Mutare Provincial Hospital
SCHOOL OF NURSING
P O Box 30
Mutare
MANICALAND
ZIMBABWE

24 May 2013

Mr Peter Mhariwa
8 Perth Circle
Westlea
MUTARE

CLEARANCE FOR MR PETER MHARIWA STUDENT NO. 573596 TO CARRY OUT RESEARCH STUDY: MUTARE PROVINCIAL HOSPITAL

Permission is hereby granted for the above-named to conduct a study titled "**The Relationship between lower limb muscle strength and lower limb function in HIV patients on Highly Active Antiretroviral Therapy (HAART)**".

24 MAY 2013
P.O. BOX 30, MUTARE
ZIMBABWE

DR S.M.NYADUNDU
MEDICAL SUPERINTENDENT

cc. The Chairperson: MPH Research Committee

APPENDIX D

- **INFORMED CONSENT FORM**

INFORMED CONSENT FORM

INFORMED CONSENT

I hereby confirm that I have been informed about the nature, conduct, benefits and risks of the above study: **THE RELATIONSHIP BETWEEN LOWER LIMB MUSCLE STRENGTH AND LOWER LIMB FUNCTION IN HIV PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)**. I have also received, read and understood the above information regarding the study.
I have had sufficient opportunity to ask questions and declare myself prepared to participate in this study.
PARTICIPANT:

Printed name Signature/ Mark or thumbprint
Date and time

I Peter, Clever Mhariwa herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

RESEARCHER:

Printed name Signature
Date and time

APPENDIX E

- **INFROMATION SHEET**

APPENDIX : INFORMATION SHEET

INFORMATION SHEET

THE RELATIONSHIP BETWEEN LOWER LIMB MUSCLE STRENGTH AND LOWER LIMB FUNCTION IN HIV PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART).

Introduction

Good day, my name is **Peter, Clever Mhariwa**, I am a physiotherapist and currently a postgraduate student at the University of the Witwatersrand Johannesburg. I would like to invite you to participate in a research study titled **THE RELATIONSHIP BETWEEN LOWER LIMB MUSCLE STRENGTH AND LOWER LIMB FUNCTION IN HIV PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY(HAART)**. Before agreeing to participate, it is important that you read and understand the following study, the study procedures, benefits and risks. If you have any questions, do not hesitate to ask.

Purpose of Study

The purpose of this study is to establish the relationship between muscle strength and lower limb function in HIV positive patients on HAART.

Procedures

If you agree to participate in this study your lower limb muscle strength will be measured by a hand held dynamometer. You will also be asked questions to establish your lower limb function. Measuring your muscle strength and establishing your lower limb functional status will take approximately 45 minutes.

Risks and discomforts

This study has no risks or discomforts

Benefits and Compensation

This study may contribute to understanding status of muscle strength and its relationship to lower limb function in adults with HIV infection. It will also contribute to designing interventions for counteracting reduction in lower limb function. You will not be paid to participate in this study.

Voluntary Participation

Participation in this study is voluntary. If you decide not to participate in this study, your decision will not involve a penalty and you are free to withdraw at any time. You have the right to decline to answer questions you are not comfortable with.

Confidentiality

Efforts will be put to ensure absolute confidentiality. Your name and personal information will not be used in the course of this study.

Contacts and Questions

For further information and questions, the researcher can be reached at the Department of Physiotherapy, University o f the Witwatersrand, Johannesburg South Africa, tel: +27 11 717 1030 or by email at petrosmhariwa@yahoo.com. Information on questions on ethical considerations and approval can be obtained from the chairman of the Human Research Ethics Committee (Medical), University of the Witwatersrand, Johannesburg, South Africa, Prof P.E. Cleaton-Jones tel: +27 717 1234, fax- +27 11 717 1265

APPENDIX F

- **MUTARE PROVINCIAL HOSPITAL PERMISSION APPLICATION LETTER**

The Medical Superintendent
Mutare Provincial Hospital
Mutare
Zimbabwe

11 February 2013

8 Perth Circle
Westlea
Mutare

Dear Sir

RE:APPLICATION FOR PERMISSION TO DO MY RESEARCH PROJECT AT MUTARE PROVINCIAL HOSPITAL.

I hereby apply for permission to carry out my research project at Mutare Provincial Hospital. I am a final year Msc Physiotherapy student at the University of Witwatersrand in South Africa. My research topic is **"THE RELATIONSHIP BETWEEN LOWER LIMB MUSCLE STRENGTH AND LOWER LIMB FUNCTION IN HIV PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)"**

The aim of the research is to establish the relationship between lower limb muscle strength and lower limb function in patients who are HIV positive on HAART.

The sample size will be 137 patients who are going to be sampled using systematic random sampling. An equal number of males and females will be targeted.

The procedure involves measuring lower limb muscle strength using a hand held dynamometer. Patients will also be asked questions to establish lower limb function. Measuring a singe patient" lower limb strength and establishing there lower limb function will take approximately 45 minutes.

This study may contribute to understanding the status of muscle strength and its relationship to lower limb function in adults with HIV infection. It will also contribute to designing interventions for countering reduction in lower limb function.

This study has no risks or discomforts. Participation is voluntary and patients will be free to withdraw at any time if they so wish.

Efforts will be put to ensure absolute confidentiality. Names and personal information of patients will not be used in the course of this study.
Hoping to hear from you at earliest convenience

Yours Faithfully

Peter Mhariwa
(Msc Physiotherapy Student)

APPENDIX G

- **DYNAMOMETRY FOR LOWER LIMB MUSCLE STRENGTH**

DYNAMOMETRY FOR LOWER LIMB MUSCLE STRENGTH

Positions for Muscle Groups to be tested

Muscle group	Patient position	Limb positions	Manually stabilized part	Dynamometer placement
Ankle plantar flexors	supine	Hip and knee extended	Lower limb proximal to ankle	Just proximal to the metatarsophalangeal joints on plantar surface of foot
Ankle dorsiflexors	Supine	Hip and knee extended	Lower limb proximal to ankle	Just proximal to the metatarsophalangeal joints on dorsal surface of foot
Knee flexors	sitting	Knee and hip flexed at 90 degrees	Thigh	Just proximal to ankle on posterior surface of leg
Knee extensors	Sitting	Knee and hip flexed at 90 degrees	Thigh	Just proximal to ankle on anterior surface of leg
Hip flexors	Supine	Hip flexed to 90 degrees, knee relaxed	Trunk	Just proximal to knee on extensor surface of thigh
Hip extensors	Supine	Hip flexed to 90 degrees, knee relaxed	Trunk	Just proximal to knee on flexor surface of thigh
Hip abductors	Supine	Knee extended, hip in neutral abduction	Contralateral lower extremity	Just proximal to knee on lateral surface of thigh
Hip adductors	Supine	Knee extended, hip in neutral abduction	Contralateral lower extremity	Just proximal to knee on medial surface of thigh

APPENDIX H

- **LOWER EXTREMITY FUNCTIONAL SCALE**

The Lower Extremity Functional Scale:

We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your lower limb problem (s). Please provide an answer for each activity. Today, do you or would you have any difficulty with:
(Circle one number on each line that corresponds to your appropriate answer)

Activity	Unable to perform activity	Quite a bit of difficulty	Moderate difficulty	A little a bit difficulty	No difficulty
1. Any of your usual work, (e.g. work that earns you income, or any other work you do) housework, or school activities	0	1	2	3	4
2. Your usual hobbies, recreational or sporting activities, e.g. attending weddings, church or visiting friends	0	1	2	3	4
3. Getting into or out of the bath/taking bath.	0	1	2	3	4
4. Walking between rooms (such as walking from your room to toilet, bath room, kitchen, etc)	0	1	2	3	4
5. Putting on any kind shoes or socks you want, including slippers or open shoes, if applied.	0	1	2	3	4
6. Squatting (e.g. squatting on pit latrine/doing any squatting activity)	0	1	2	3	4
7. Lifting an object, like a bag of groceries or a small container like 5 liters container full of water, basket of potatoes, etc, from floor	0	1	2	3	4
8. Performing light activities around your home(such as prepare a meal, cleaning a house, making bed, or any other light activity at home)	0	1	2	3	4
9. Performing heavy activities around your home (digging, lifting a heavy bag of potatoes, 20 litres gerrican of water, shifting big items, etc	0	1	2	3	4
10. Getting into or out of a car/taxi.	0	1	2	3	4
11. Walking across from your home to neighbors or walk like 100m across	0	1	2	3	4
12. Walking a Km, such as going to market, church or any other place where you walk	0	1	2	3	4
13. Going up or down 10 stairs (about 1 flight of stairs) or walking up a steep and irregular ground	0	1	2	3	4
14. Standing for 1 hour,	0	1	2	3	4
15. Sitting for 1 hour, like when in church, tax, or meetings	0	1	2	3	4