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THE EFFECTS OF PROGRESSIVE RESISTED EXERCISES ON PERFORMANCE- ORIENTED MOBILITY IN PERSONS WITH HIV RELATED POLY-NEUROPATHY

KHUMBULA MKANDLA

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

Johannesburg, 2012

DECLARATION

I, Khumbula Mkandla declare that this dissertation is my own work. It is submitted for the degree of Master of Science in Physiotherapy at 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 candidate)

.....25TH..... day of..OCTOBER..., 2012.

DEDICATION

This work is dedicated to my family and friends for blessing me with so much love.

ABSTRACT

Key words: Peripheral neuropathy, HIV/AIDS, Progressive resisted exercise, Performance oriented mobility, Quality of life.

Background: Distal symmetrical poly-neuropathy (DSP) has emerged as one of the major neurological complication associated with HIV/AIDS and antiretroviral therapy. People with DSP commonly have problems with pain, mobility, altered gait and balance all which affect their quality of life. While therapeutic strengthening exercise has been reported to attenuate these impairments in other co-morbid conditions like diabetes mellitus and in HIV/AIDS, there is no evidence available on the effects of exercise on DSP in people living with HIV/AIDS (PLWHA).The purpose of this study was to determine the effects of progressive resisted exercises (PRE) on performance oriented mobility and health related quality of life in (PLWHA) related DSP. Objectives of this study were to determine the effects of PRE on gait, balance and pain levels and establish if there is a relationship between performance-oriented mobility and health-related quality of life in PLWHA related DSP. **Methods:** In order to fulfil the objectives, an assessor-blinded randomized controlled trial was conducted over two studies, with a combined sample of 160 participants sourced from two family care clinics at two central hospitals and ten anti-retroviral therapy dispensing municipal clinics in Harare, Zimbabwe. While the experimental group with 80 participants had an intervention program of PRE sessions of one hour for the lower limbs, done twice per week over 12 weeks, the control group of 80 participants was given advice to walk unsupervised at home. Loss to follow up in this study was at 60% (n=97) and the data was analysed using an intention to treat analysis approach. **Results:** Participants of an average age of 42.2 years (SD=8.5) constituted of 70.6% (n=113) female participants. Combination antiretroviral therapy containing stavudine, was used by 59% (n=94) of the participants and 59% (n=94) of the participants had moderate to severe neuropathy. Proximal muscles exhibited weakness (hamstring muscles strength = 3.43 kg force (SD=1.5)) when compared to leg muscles (gastrocnemius muscles strength = 12.8 kg force (SD=2.0)). Gait and balance scores did not show differences in effect between the intervention and the control group (95%CI 0.00-0.02, p = 0.8). Similarly there were no differences of effect for muscle strength (95%CI 0.00-0.08, p=0.13-0.8) and pain (95%CI 0.0-0.06, p>0.13). However the effect on quality of life changes were significantly different between the two

groups (95%CI 0.00-0.12 p= 0.04). Quality of life was positively associated with gait, odds ratio 1.01 (95%CI 1.00 – 1.04), moderately associated with balance odds ratio 0.68, (95%CI 0.52 – 0.93) negatively associated with pain odds ratio 0.98 (95%CI 0.97 – 0.99). **Conclusion:** This research study established that progressive resisted exercises have positive effects on the health related quality of life in PLWHA related DSP. However this study did not show a difference of the effects of progressive resisted exercises on performance oriented mobility in PLWHA related DSP when compared to advice to exercise at home. The study findings may not be generalized to all individuals living with HIV/AIDS who have DSP as the participants were from a particular demographic setting. This project may be continued at the participating family care clinics as a roll on of the perceived benefits of exercise for people with HIV related DSP.

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CHAPTER 1

1. INTRODUCTION

1.1 Background

There are 34 million people living with Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome (HIV/AIDS) globally (UNAIDS, 2011). Of this population, the Sub Saharan region has the highest prevalence rate of 68% (UNAIDS, 2011). However, prevalence rates declined in Botswana, Rwanda and Uganda. In Zimbabwe, the rates declined from 26% in 2002 to 14.3% in 2009 (UNAIDS, 2011).

While global mortality stood at 1.8 million deaths in 2010 (UNAIDS, 2011) the introduction of highly active antiretroviral therapy (HAART) has led to longer life expectancy. The complications of HIV infection, opportunistic infections and side effects of HAART has emerged as the most common cause of HIV associated morbidity (Dudgeon, et al., 2004). One of the common neurological conditions associated with HIV complications is peripheral neuropathy (Verma and Simpson 2007). Peripheral neuropathy can also be caused by diabetes mellitus, alcoholism, and neuro-toxic drugs (Keswani, et al., 2003). Distal symmetrical poly-neuropathy (DSP) is the most prevalent form of peripheral neuropathy occurring in 50% of cases with HIV/AIDS (Simpson, et al., 2006). In Zimbabwe 60% of people living with HIV/AIDS are experiencing the complications of peripheral neuropathy (Robertson, et al., 2008). Other forms of peripheral neuropathy include mono-neuropathy multiplex, inflammatory demyelinating poly-neuropathy (Gullain Barre Syndrome), progressive poly-radiculopathy, autonomic neuropathy and mono-radiculopathy (Nicholas, et al., 2007b).

Distal symmetrical poly-neuropathy is a complex of symptoms that occur as a result of peripheral nerve damage (Nicholas, et al., 2007b). The primary damage occurs mostly in the sensory neurons leading to axonal degeneration (dying back process) and the manifestations of sensory dysfunction (Hahn, et al., 2008). Electrophysiological data has been used to confirm peripheral nerve axonal loss, demylenation and muscle denervation in HIV infected patients (Schifitto, et al., 2002).

HIV infected macrophages damage dorsal root ganglia by secreting antigens and pro-inflammatory cytokines (Hahn, et al., 2008). Stavudine, didanosine and zidovudine were part of the standard first line HAART drugs used in Zimbabwe in the first decade of the HAART roll-out (EDLIZ 2006). These drugs which are classified as dideoxy-nucleoside reverse transcriptase inhibitors (NRTI) are believed to cause neuronal damage. Their pharmacological mechanisms interfere with mitochondrial oxidative metabolism of the neuronal cell body and growth factors production (Keswani, et al., 2007).

While it normally requires technical capacity or specialised medical training to make a diagnosis of distal peripheral neuropathy, a brief peripheral neuropathy screen (BPNS) can be used in clinical settings (Schiffito, et al., 2003). This test can be used by the medical doctor, trained nurses or therapists (Cherry, et al., 2005). Symptoms of pain, the presence of distal bilateral symmetrical burning sensation, parasthesia, or numbness, cramping in the legs, and muscle weakness in the foot can be used to confirm distal symmetrical poly-neuropathy (Schiffitto, et al., 2003). A neurological examination will reveal absence of or diminished ankle reflexes compared to knee reflexes and distal reduction of vibratory pain or temperature perception in a glove and stocking distribution (Cherry, et al., 2005). Further tests which can be used are skin biopsy for epidermal nerve fiber density quantitation (Hahn, et al., 2006), nerve conduction tests consisting of compound muscle action potentials and sensory nerve action potentials (Simpson, et al., 2006).

People with peripheral neuropathy commonly present with pain, altered sensation, muscle weakness and increased fatigue (White, Pritchard and Turner-Stokes 2004). These impairments may lead to immobility, altered gait, increased risk of fall and psychological dysfunction (Dudgeon, et al., 2004).

Distal symmetrical poly-neuropathy impairments may be managed pharmacologically, non-pharmacological or by self-care strategies depending on severity of symptoms, preference or availability (Nicholas, et al., 2007a). In physiotherapy practice, a non-pharmacological approach, these impairments can be addressed by use of functional electrical stimulation, transcutaneous electrical nerve stimulation (TENS), interferential therapy, heat therapy, ice, massage, acupuncture, hydrotherapy and therapeutic exercise (Nicholas, et al., 2007b). Therapeutic exercise can be defined as the prescription of a physical activity or program that involves the

client to undertake voluntary muscle contraction and or body movement with the aim of relieving symptoms or improving, retaining or slowing deterioration of health (Taylor, et al., 2007).Therapeutic exercise includes progressive resisted exercise, aerobic exercise, individualized exercise programs and general home programme (Fillipas, et al., 2006).

The benefits of therapeutic exercise are well documented in randomized clinical trials and systemic reviews (Taylor, et al., 2007; O'Brien, et al., 2008, 2010). Strengthening exercises have been reported to improve muscle strength in people with peripheral neuropathy (White, et al., 2004; Richardson, Sandman and Vela, 2001). Supervised aerobic exercise, done at sub-maximal age predicted maximal heart rate levels of 70% and resistance exercise program in people with HIV is safe and improves cardio vascular fitness (O 'Brien , et al., 2008, 2010). The recommended intensity for progressive resisted exercise is one to three sets of 8-12 repetition maximum with rest of one to three minutes between the sets done two to three times a week (ACSM, 2011). Exercise reduces central adiposity, improves metabolic indices (Mutimura, et al., 2008) and significantly improves immunology and virology outcome measures (Dudgeon, et al., 2004).

Various outcome measures have been used to evaluate mobility and effectiveness of intervention used. For the requirements of this study, the modified Performance Oriented Mobility Assessment (POMA) was selected (Tinneti 1986; Kegelmeyer, et al., 2007; Faber, et al., 2006). It is used for rating gait and balance and a total score is derived as an aggregate of the two subscales (Faber, et al., 2006). The value of the minimal detectable change (MDC) at 95% confidence level, following an intervention for individuals was at least five (5) points and 0.8 points for group scores for the change to be considered significant (Faber, et al., 2006). The Euro Quality of Life – 5 (Five) Dimensions (EQ-5D) state of health questionnaire was used to assess the functional health related quality of life status (Jelsma, et al., 2005). Within its domains is a general assessment of pain and mobility. A Shona version of the questionnaire was developed by Jelsma, et al., (2001). It is reliable with a high measure of agreement range of 0.78 to 1.00 (kappa statistic), for the different domains of activity.

1.2 Problem statement

There is currently insufficient evidence available to draw the best clinical practice guidelines for the management of the effects of DSP in adults living with HIV/AIDS.

1.3 Research question

What is the effect of progressive resisted exercises on the performance oriented mobility and health related quality of life of patients with HIV and AIDS related DSP?

1.4 Aim of study

To determine the effects of progressive resisted exercises on performance oriented mobility and health related quality of life in patients with HIV/AIDS related (DSP).

1.4.1 Objectives of the study:

1. To determine the effects of progressive resisted exercises on gait in patients with HIV/AIDS related DSP.
2. To determine the effects of progressive resisted exercises on balance in patients with HIV/AIDS related DSP.
3. To determine the effects of progressive resisted exercises on pain levels in patients with HIV/AIDS related DSP.
4. To establish if there is a relationship between performance-oriented mobility and health related quality of life in people with HIV/AIDS related DSP.

1.5 Hypothesis

Research Hypothesis: progressive resisted exercises have positive effects on performance oriented mobility and health related quality of life in subjects with HIV/AIDS related DSP.

Null Hypothesis: progressive resisted exercises have no effect on performance oriented mobility and health related quality of life in subjects with HIV/AIDS related DSP.

1.6 Significance of the study

The number of people living with HIV who are experiencing peripheral neuropathy complications (Simpson, et al., 2006) makes it necessary to research the effect of exercise therapy on the mobility and quality of life of those affected (UNAIDS, 2010).The study results may be useful in improving our understanding of how progressive exercise may be harnessed for other conditions where peripheral neuropathy is a major complaint (White, et al., 2004).

1.7 Justification of study

While the Zimbabwe HIV and AIDS strategic plan 2006-2010 (NAC UNAIDS, WHO 2006), a policy document, recommends the mainstreaming of nutrition, it is silent on physical fitness, wellness and quality of life as a measure to improve the state of health in people living with HIV and AIDS. Considering that 60% of people living with HIV and AIDS in Zimbabwe, are experiencing the complications of peripheral neuropathy (Robertson, et al., 2008), a research study on the effects of therapeutic exercise on mobility and the quality of life of the affected is therefore necessary and relevant (UNAIDS, 2010).

1.8 Procedure, instruments and data analysis

The study was of an assessor-blind randomized controlled clinical trial design. The experimental group had an intervention program of progressive resisted exercises while the control group was given advice to walk as with the usual method. Whereas the initial protocol plan sought to source participants from the three main hospitals, when this was done, the study had a high loss to follow-up. Thus the study was repeated using the same methodology and a higher sample size with participants sourced from antiretroviral dispensing clinics in the community.

Upon pooling of the data from the studies completed, one hundred and sixty participants were randomized into these two groups. Eighty participants per group had been sourced from the anti-retroviral therapy dispensing clinics and the family care clinic at Wilkins Hospital of the Municipal of Harare and family care clinics at Parirenyatwa and Harare Central Hospitals in Zimbabwe. Baseline assessments consisted of demographic information including HIV measures; CD4+ counts; medication; length of time on anti-retroviral drugs and history. The Brief peripheral neuropathy screen questionnaires were administered to ascertain diagnosis of peripheral neuropathy using scores of neural deficits and symptoms. Muscle strength was measured using a hand held dynamometer while pain was assessed using a pictorial Likert like scale. While Performance oriented mobility was based on the POMA scores, health-related quality of life levels were ascertained using the Shona or English EQ-5D questionnaire. The researcher did all assessments and trained the research assistants to implement the intervention.

Data was analysed using an intention-to-treat approach. The mean change in all the outcomes was analysed with respect to the objectives of the study using the STATA v10 statistical software after cutting and pasting into the STATA v10 program from data logged in the Excel program. An intention-to-treat analysis captures the real life situation, where the participants who may not have been as compliant and adherent to the intervention are also included thereby reducing occurrence of possible bias about the effectiveness of the intervention (Petroczi, et al., 2010).

CHAPTER 2

2. LITERATURE REVIEW

2.1 Introduction

This review of literature will briefly outline the situation regarding HIV/AIDS and how peripheral neuropathy has emerged as a major complication of HIV/AIDS and anti-retroviral therapy. A focused discussion will be presented on the effects of peripheral neuropathy in people living with HIV/AIDS and how the strategies have been developed by practitioners involved in managing these effects. Methods chosen to assess the effects of peripheral neuropathy will be reviewed, highlighting the reasons why these methods were chosen for use in this study.

Articles reviewed in this chapter were sourced from physiotherapy journals, publications, Pubmed, the Cochrane collaboration, and Google search engine. Keywords in the literature search included HIV, peripheral neuropathy, HAART, therapeutic exercise, progressive resisted exercise, balance, gait, pain and quality of life.

2.2 HIV/AIDS situation

There are 34 million people globally who are living with the Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome (HIV/AIDS) (UNAIDS, 2011). Of this population, the Sub Saharan region has the highest prevalence of 68% (UNAIDS, 2011). Concerted intervention efforts by different organizations and the governments have seen a decline in the rates in Botswana, Rwanda and Uganda (UNAIDS, 2010). In Zimbabwe, the prevalence rate reduced from 26% in 2002 to 13.9% in 2009 (UNAIDS, 2010). Although the global mortality rate stood at 1.8 million deaths in 2010 (UNAIDS, 2011), widespread availability of highly active antiretroviral therapy (HAART) has led to longer life expectancy, transforming HIV from a terminal to an episodic chronic illness (Rusch, et al., 2004). Associated HIV co-morbidity has emerged as the major medical challenge from the complications of HIV infection, opportunistic infections, and the neurotoxicity of some classes of HAART drugs (Nicholas, et al., 2007b).

2.3 Peripheral neuropathy

Peripheral neuropathy (PN) is the most common neurological complication emerging from the era of HAART (Keswani, et al., 2002) with distal symmetrical peripheral neuropathy (DSP) being the most common form of peripheral neuropathy (Verma and Simpson, 2007). In Zimbabwe, 60% of people with HIV who were yet to commence on antiretroviral therapy were found to have peripheral neuropathy (Robertson, et al., 2008).

Peripheral neuropathy presents and consists of several patterns and forms namely mono-neuropathy multiplex including vasculitis neuropathy, brachial and lumbar plexopathy, inflammatory demyelinating polyradiculo-neuropathy (also known as Guillain Barre Syndrome), progressive poly-radiculopathy including cytomegalovirus polyradiculopathy and myeloradiculopathy, autonomic neuropathy, mono-radiculopathy, diffuse infiltrative lymphocytosis syndrome and distal symmetrical polyneuropathy (Keswani, et al., 2002; Nicholas, et al., 2007b; Verma and Simpson, 2007).

Distal symmetrical polyneuropathy is a complex of manifestations of sensory dysfunction as a result of peripheral nerve damage (Hahn, et al., 2008). The primary damage occurs to nerve structures like the myelin (insulating sheath of the nerve) and the axon (the central fibre of the nerve) leading to axonal degeneration (termed dying back process) or it may involve both as well as the dorsal root ganglia (White, Pritchard and Turner- Stokes, 2004). Damage occurs mostly in the sensory neurons, with the resultant sensory dysfunction presentation (Keswani et al., 2002). Motor activity may also be affected by the alteration of motor nerve function, leading to motor activity dysfunction which presents as cramping in the legs and muscle weakness in the foot (Cherry, et al., 2005; Nicholas, et al., 2007b).

Diagnosis of distal symmetrical polyneuropathy (DSP) can be drawn from the most commonly observed neurological signs (Schifitto, et al., 2002). On examination there are dampened or absent ankle reflexes while the patellar reflexes are usually intact (Verma and Simpson, 2007). Pinprick, temperature and vibration are impaired or reduced distally (Verma and Simpson, 2007). While DSP was previously commonly associated and prevalent in patients with diabetes mellitus it has been known to present concomitantly in patients who have alcohol abuse, cancer, multiple sclerosis,

spinal cord disorders, cognitive problems, hypothyroidism, hereditary neuropathy, Vitamin B12 and thiamine deficiency, uremia, significant weight loss, low albumin, low haemoglobin and neurotoxic agents or drugs like anti-tuberculosis drugs such as isoniazide (Verma and Simpson, 2007). Currently, DSP is strongly associated with HIV/AIDS and antiretroviral therapy complications.

2.4 HIV associated peripheral neuropathy

2.4.1 The general effects of HIV on body systems

HIV has many effects on the human body and its systems (Dudgeon, et al., 2004). Skeletal muscle wasting was the identifying effect of HIV before HAART, (which gave HIV/AIDS the name; slimming disease) mainly caused by the catabolic effects of increased circulating gluco-corticoid levels (Dudgeon, et al., 2004). Increased blood gluco-corticoid levels slow down protein synthesis while increasing the processes that breakdown muscle content (Dudgeon, et al., 2004). Weight loss is influenced by the combination of episodes of infection which lead to a significant rise of circulating cytokine and gluco-corticoid levels causing an increased level of resting energy consumption and reduced food intake as a result of several factors including loss of appetite (Dudgeon, et al., 2004).

While HIV has a well-documented and often cited effect on the immune system, it is also generally recognized as having adverse effects on most body systems including the nervous, musculoskeletal and cardiopulmonary systems (Cherner, et al., 2004). Myezwa, et al., (2009) found that 69% of the participants in a suburban setting study in South Africa had mental function impairment. This is consistent with the review findings by Wright, et al., (2008) which show that HIV associated neuro-cognitive dysfunction (HAND) including dementia was the most commonly observed effect of HIV.

HIV associated cardiopulmonary effects were among the first systemic effects to be noticed and as shown in Myezwa, et al., (2009)'s study, respiratory problems were reported in 22% of the participants. Most of the opportunistic infections are in the form of tuberculosis. Mutimura, et al., (2008) in a random controlled trial, where they investigated the use of exercise training to reduce central adiposity, demonstrated the negative effects of HIV on the metabolic indices on the baseline measures in

lipodystrophy in HAART-treated HIV-positive participants. Furthermore, Gabuzda and Wang (2000), in a scholarly review, postulate that HIV tends to have a high affinity for the neural cells since it appears to affect the central and peripheral nervous system more often.

2.4.2 HIV as a cause of peripheral neuropathy

The pathogenesis of peripheral neuropathy is hypothesised to evolve by two main pathways. The first pathway proposes that the HIV glycoprotein 120 (GP120) envelope has a toxic effects when it binds to a certain vanilloid receptors on the CD4+ receptor of the macrophage thereby interfering with immune responses (Keswani, et al., 2002). The second pathway proposes that, HIV infected macrophages damage dorsal root ganglia by secreting antigens and pro-inflammatory cytokines (Hahn, et al., 2008). Chemotactic cytokines (chemokines) like the TNF- alpha, Interleukin-1 (IL-1) and IL-6 cathepsin S and fractalkine, which are released locally as a result of the presence of macrophages, serve as coordinators of the nervous system, signalling and controlling the movements of leukocytes into the neural tissues during an inflammatory response process (Abbadie, et al., 2009; White, Jung, and Miller 2007; Gabuzda and Wang 2000). An appropriate inflammatory response is required for the clearance of pathogens but can become pathological if this response is prolonged or excessive (Keswani, et al., 2002). Thus Nicholas, et al., (2007b), in a review, concluded that DSP is a complex of symptoms that occurs at any stage of HIV/AIDS and is associated with exposure to viral load and mitochondrial toxicity, disease duration and exposure to neurotoxic antiretroviral therapy.

2.4.3 Anti-retroviral therapy toxic neuropathy (ATN)

While antiretroviral therapy (ART) is critical in containing the viral load and promoting increased CD4+ count, it has been shown that some ART regimens used in Zimbabwe and in some developing countries in the first decade of the twenty-first century (National Drug and Therapeutics Policy advisory Committee, NDTPAC 2010) are neuro-toxic.

Anti-retroviral therapy regimens

Below is a summary of the different antiretroviral drugs used in Zimbabwe and their side effects on the neuro-musculoskeletal system (NDTPAC, 2010).

Table 1.1 Antiretroviral drugs used in Zimbabwe and their side effects on the neuro-musculoskeletal system (NDTPAC, 2010)

Class	**Drug**	**musculoskeletal/ major side effects**
Nucleoside reverse transcriptase inhibitors (NRTIs)	Zidovudine (AZT),	Anaemia, myopathy, lactic acidosis
	Didanosine (ddI),	Peripheral neuropathy, lactic acidosis
	Zalcitabine (ddC),	Peripheral neuropathy
	Stavudine (d4T),	Peripheral neuropathy, fatigue, lactic acidosis
	Lamuvidine (3TC)	Nil
	Abacavir (ABC)	Hypersensitivity
Nucleotide reverse transcriptase inhibitors (NRTIs)	Tenofovir (TDF),	Renal complications
Fusion inhibitor	Enfuvirtide	Nil
Non- nucleoside reverse transcriptase inhibitors (NNRTIs)	Nevaripine (NVP),	Fatigue, nausea
	Efavirenz (EFV)	Confusion, headache, sleep disturbance
	Delavirdine (DLV).	Nil
Protease inhibitors.	Saquinavir (SQV),	Lipodystrophy, tiredness dizziness
	Ritonavir (RTV),	Lipodystrophy
	Indinavir (IDV),	Lipodystrophy, muscle pain, headache, blurred vision
	Nelfinavir (NFV),	Nil
	Amprenavir (APV)	Nil
	Lopinavir (LPV)	Lipodystrophy
	Atazanavir	Headache, nausea

Antiretroviral drugs are classified as nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors (Bartlett & Gallant 2003). The nucleoside/ nucleotide reverse transcriptase inhibitors (NRTIs) are also

known as dideoxy-nucleosides (ddN) (Bartlett and Gallant, 2003). These drugs act by blocking the HIV reverse transcriptase enzyme and prevent the copying of the viral RNA into the DNA of infected host cells by presenting deceptive building blocks of the DNA chain (NDTPAC, 2010). The resulting DNA chain is incomplete and therefore unable create new viruses (NDTPAC, 2010). The non- nucleoside reverse transcriptase inhibitors (NNRTIs) have the same modality of function with more resistant profile than the nucleotide analogues and protease inhibitors are not yet publicly the available in Zimbabwe (NDTPAC, 2010). The intergrase inhibitor, fusion inhibitor and the CCR5 inhibitor classes of antiretroviral drugs are not yet in use in Zimbabwe (NDTPAC, 2010).

Mechanisms of neurotoxicity in antiretroviral therapy neuropathy (ATN)

Stavudine (d4T), didanosine (ddI), zalcitabine (ddC) are dideoxy-nucleoside reverse transcriptase inhibitors (ddN or NRTI) drugs, which were widely and commonly used in the developing world as recommended by World Health Organisation (WHO) (NDTPAC, 2003; Bartlett and Gallant, 2003). These drugs have been observed to be a cause of toxic neuropathy as shown in Table 1.1. Menez, et al., (2011) in a South African study with a large study of 9040 participants on HAART showed that Stavudine was associated with co-morbidities which seemed to outweigh the drugs benefits. However, Keswani, et al., (2002) in their review of clinical trials and expert - opinion, feel that since DSP and ATN are similar in their presentation, it may be possible that dideoxy-nucleoside only serve to unmask the latent asymptomatic DSP thereby worsening the damage to the neuronal cells. Other classes of HAART have been trialed to establish their possible contribution to peripheral neuropathy. For example, Ellis et al., (2008) showed that, exposure to protease inhibitors drew a negligible risk of peripheral neuropathy in a prospective study in North American locations involving a sample of 1159 HIV infected participants.

The nucleoside inhibitors' become toxic by way of their activity when they interfere with the mitochondrial oxidative metabolism of the neuronal cell body as well as with growth factor production (Nicholas, et al., 2007b; Hahn, et al., 2008). Keswani, et al., (2002) outlines a possible mechanism of how the NRTI interacts with triphosphate thereby inhibiting deoxyribonucleic acid (DNA) polymerase gamma leading to reduction in mitochondrial DNA levels. Other mechanisms involves drug toxicity

emanating from anti-retroviral drug interference in the activity of adenylate kinase, an enzyme responsible for catalyzing the oxidative phosphorylation of adenosine diphosphate, a nucleoside diphosphate to adenosine triphosphate (Keswani, et al., 2002). This process is critical for the energy requirements of a cell (Keswani, et al., 2002). The NRTI is also thought to actively interfere with the activity of other respiratory complexes that form the electron transport chain thereby impairing the process of oxidative phosphorylation, which is required in the formation of energy (Keswani, et al., 2002). This reduces the available energy levels for cellular activity leading to a cascade of other harmful corrective processes leading to neuronal cell death (Keswani, et al., 2002).

Anti-retroviral therapy in Zimbabwe is based on WHO guidelines (NDTPAC, 2010).The first line of treatment for adults in Zimbabwe in the first decade of the HIV pandemic after the introduction of HAART consisted of stavudine, lamivudine and nevirapine (NDTPAC, 2003). This was normally given as a combination product Stalanev or Triviro with cotrimoxazole prophylaxis (NDTPAC, 2003). However this is in the process of being phased out with a new regime of first line therapy now consisting of a first line of tenofovir and zidovudine combined with lamivudine and nevirapine (Zidolan) (NDTPAC, 2010). This is consistent with the findings in Griensven, et al., (2010)'s study, where in a cohort in which 2190 participants who had used stavudine were re-assessed after its substitution for a variety of toxic effects. They found that one of the major side-effects of stavudine was DSP thus concurring with the WHO position.

Hence while HIV may have initiated the DSP through pathological inflammation and macrophage activation in the peripheral nerves and dorsal root ganglia, the use of dideoxy-nucleoside in antiretroviral therapy worsens the DSP, unmasking its presence (Keswani, et al., 2002). It remains to be established if the peripheral neuropathy experienced in diabetes mellitus and co-morbidities is phenotypically identical to the HIV- associated peripheral neuropathy.

2.5 The effects of HIV-associated peripheral neuropathy

2.5.1 Introduction

Effects of DSP consist of various degrees and forms of sensory impairments, pain, gait dysfunction and imbalance, fatigue, muscle weakness and impaired health related quality of life (Nicholas, et al., 2007b). The International classification of function (ICF) is going to be used to describe the presentations of the effects of HIV-associated peripheral neuropathy found in the literature.

The ICF is a classification system developed by the World Health Organization (WHO) to improve communication between stakeholders, who include health professionals and people with disabilities (Hwang and Nochajski, 2003). Dimensions of human function are considered as different domains, thereby capturing the factors which allow for wholistic approach to assessment and intervention. Impairments are defined by the ICF (WHO, 2001) as problems in body function or structure such as a significant deviation or loss (WHO, 2001). Major impairments in PLWHA occur in mental, neuro-musculoskeletal and movement related functions (Myezwa, et al., 2009). Activity limitations are seen as the difficulties an individual may have in the performance of activities, previously termed disability (WHO, 2001). Furthermore, participation restrictions are problems an individual may have in the manner or extent of involvement in life situations and these were previously termed handicaps (WHO, 2001).

2.5.2 Sensory impairments related to peripheral neuropathy

As already identified, one of the major impairments for PLWHA, is neuro-musculoskeletal function. Hahn, et al., (2008) and White, Pritchard and Turner-Stokes, (2004) explain that primary damage in peripheral neuropathy occurs mostly in the sensory neurons, leading to axonal degeneration and alteration of nerve function. The major manifestations of sensory impairment as outlined by Cherry, et al., (2005) include pain, aching, symmetrical distal burning, numbness (loss of feeling of an area), pins and needles (paraesthesia) and loss of perception of vibration. While pain will be reviewed in the next section, numbness is an equally important

sensory impairment with serious implications on activity limitations. As shown by Tannenburg, (2009) in a review, peripheral neuropathy can present as a contradiction of painful neuropathy or painless neuropathy (numbness). Nerve function alteration also results in allodynia where PLWHA with DSP become overly sensitive to touch, and cannot tolerate contact with blankets/ covers during sleeping time and to socks or shoes (Simpson, et al., 2006; Keswani, et al., 2002). Sensation to temperature becomes impaired with the affected PLWHA with DSP being unable to tell hot from cold, often denoted by inability to tell a hot bath/shower from a cold one (Verma and Simpson, 2007). Cherry, et al., (2005) clarify that these sensations may be of sharp stabbing, lancinating or shooting pain quality with the legs sometimes experiencing electric shock like pain**.** The physiology of pain will be briefly explained in the section on neuropathic pain.

2.5.3 Neuropathic pain

Pain is a complex symptom of the sensory impairments which occur as a result of injury to the sensory neurons. As such pain is defined as a sensation of unpleasant feeling indicating potential or actual damage to some body structure and is classified as impairment by the ICF (WHO, 2001).

Pain is primarily a subjective symptom based on mostly an individual experience which requires a multidisciplinary approach to comprehend its complex presentation (Campbell, Clauw, and Keefe, 2003). It may also be defined using the biomedical or the bio psychosocial model or a combination medical-psychosocial approach (Campbell, Clauw, and Keefe, 2003). In the biomedical framework, pain perception is modulated by nociceptors through a neurone network to the thalamus and to the somatosensory centres in the cortex (White, Jung and Miller, 2007). A feedback loop in the pathways initiates a pain withdrawal reflex while an efferent impulse leads to a local release of neuropeptides which is believed to offset an inflammatory response which is augmented by the immune response (White, Jung and Miller, 2007).

In neuropathic pain the initial inflammatory response activates spinal sensitisation through involvement of other nociceptive mediators and pathways still being investigated (Abddie, et al., 2005). Once spinal sensitization has occurred a phenomena involving chemokines and the immune mediators is set in motion, where pain continues to be propagated in the absence of a pain stimulus (White, Jung and

Miller, 2007). While the biomedical model assumes that pain is equivalent to nociception, it fails to fully explain phantom limb pain, pain in the absence of pathology or pathology without pain (Abddie, et al., 2005).

Hence a more integrative conceptual model with a multi-disciplinary understanding is required to explain chronic pain which has proved to be a difficult symptom to manage leading to concerted attempts to understand its propagation (Campbell, Clauw, and Keefe, 2003). Chronic pain, which is similar to neuropathic pain, is associated with depression which may manifest as maladaptive coping responses for example catastrophizing, perceived helplessness, and low self-efficacy and pain related fear and anxiety (Keefe, et al., 2004).

Considering that people adjust themselves to pain in different ways Keeffe, et al., (2004), found that an adjustment response to chronic pain was dependent on factors like: self-efficacy, acceptance, coping mechanisms, and the readiness to change. Group support and interaction are known to be as effective management approaches for adjustment to chronic situations like pain (Lucey, et al., 2011). Keeffe, et al., (2004) explains that differing coping mechanisms to persistent pain also yield different perceptions to pain. Catastrophizing is occasionally used as a coping mechanism where one may take advantage of their pain with the hope that society members might help them (Lucey, et al., 2011). Ownby and Dune (2007), applying a grounded theory approach concur with these findings adding that there is need for the health care workers to research more on the problems associated with DSP so as to develop effective strategies for reducing associated activity limitation and participation restrictions. The study by Ownby and Dune (2007) also suggest that activity in the form of exercise may be used to mediate chronic neuropathic pain. As shown in a study covering three continents done by Nicholas, et al., (2007a), PLWHA who had DSP and experiencing neuropathic pain, tried all self-help activities or available methods to control pain.

2.5.4 Gait

One of the major complaints received from participants in studies for the effects of peripheral neuropathy is that of gait instability (Ites, et al., 2011). The factors involved in the quality of gait include, proprioception, numbness, balance, muscle

strength and co-ordination (Bensoussan, et al., 2008; Tannenburg, 2009). Mobility is defined as the muscles ability to initiate movement, and the flexibility in movement thereafter (American College of Sports Medicine (ACSM), 2006). It can be maintained by postural stability which may be improved by muscle strengthening of postural muscles (Bensoussan, et al., 2008). Strength is defined as the force to propel or withstand against force and to lift a mass and is measured using electromyography, myometry or dynamometers (ACSM, 2011). Whereas mobility generally refers to the ability to walk with or without the assistance of walking aids, the ICF (WHO, 2001) defines walking as moving along a surface on foot step by step so that one foot is always on the ground such as when standing (WHO, 2001). This includes; walking short distance; long distance walking on different surfaces domain [d4502] or walking around obstacles [4503] (WHO, 2001). Mobility is a d4 domain of activities and participation. It is essential for people with peripheral neuropathy to remain mobile as this is also accepted as one of the palliative modalities for neuropathic pain (Nicholas, et al., 2007a).

Walking is a cycle of feedback loops as a skill and in adults, supraspinal control mechanisms are utilized in generalized motor programmes (Gates and Dingwell, 2007). During normal gait, central processing mechanisms control the stride over long range walking; however in the elderly people, people with Huntington's disease and people with Parkinson disease, long range striding is affected (Gates and Dingwell, 2007). Long range factors in stride intervals are believed to be controlled by supraspinal control mechanisms. Thus where there is central control deterioration gait stride becomes uneven (Gates and Dingwell, 2007).

Gates and Dingwell (2007) carried out a comparative study with a sample of 14 participants with severe peripheral neuropathy and 12 gender, age, height and weight matched non-diabetic controls. Gates and Dingwell (2007) hypothesised that if loss of long range correlation indicates that inability has been caused by central control of gait then peripheral change would have no effect. However if loss of long range correlation indicated general inability to regulate gait cycle timing then similar loss of long range timing would occur in patients with peripheral movement disorders ability to regulate gait. They found that there was no difference in stride times between the peripheral neuropathy and control subjects $p=0.95$ and 0.97 respectively. However participants with peripheral neuropathy also exhibited a slower gait speed, which is a cognitive adaptive coping strategy (Gates and Dingwell, 2007).

2.5.5 Balance

Factors known to influence balance namely; decreased sensation, proprioception, reflexes and strength in the lower limbs, are all negatively affected by DSP (Ites, et al., 2011). Hess and Woollacott (2005) demonstrated in their study on an elderly population that strength training can improve their balance by improving muscle strength of the lower limb muscles especially ankle stabilizers. In their discussion, Hess and Woollacott (2005) demonstrate how by eccentric contraction, the hamstrings, gastrocnemeius, tibialis anterior and the quadriceps all act in symphony to reduce sway and maintain the centre of gravity.

On the other hand, Kanekar, Santos, and Aruin, (2008) investigated how the body responds to fatigued muscles and found that there was also cognitive compensation in form of anticipatory postural adjustment to this effect. Although their sample was small (n=9), they used the deltoid anterior and hamstring muscle to determine how adjustment occurs, and concluded that there existed effective mechanisms which can easily be employed (Kanekar, Santos, and Aruin, 2008). Hence while balance dysfunction is a result of factors which include decreased sensation, proprioception, reflexes and strength in the lower limbs (Ites, et al., 2011) it may be attenuated by cognitive processes.

2.5.6 Muscle dysfunction

Muscle dysfunction which presents as cramping in the legs and muscle weakness in the intrinsic muscles of the foot occurs as a result of the alteration of motor nerve function (Cherry, et al., 2005; Nicholas, et al., 2007b).This is explained by the changes in the metabolic functions of muscle and primary lactate accumulation which occurs as a result of HIV and as a side effect of ART depending on the type being used Dungeon, et al., (2004) In people with peripheral neuropathy this does not necessarily translate to reduced muscle strength for the affected muscles (White et., al). In their review of studies where PRE was employed as a method of management and intervention in PLWHA, Dungeon, et al., (2004) indicate that muscle adapt to the stress loads and type of training it is exposed to.

2.5.7 Health related quality of life

When there is activity limitation and participation restriction, health related quality of life is compromised. Bril, et al., (2010) feel that health related quality of life is a relevant dimension of functional outcomes which should be investigated to acquire a better evaluation of the effectiveness of intervention in the management of conditions which affect the activity of PLWHA. Considering the multi-faceted context of quality of life Rusch, et al., (2004), several dimensions/domains, form the integral part of quality of life (Miners, et al., 2001).

In their review, Hwang and Nochajski (2003) outline the major areas of activity limitation and participation restriction for PLWHA as mobility, self care and domestic life. People with peripheral neuropathy commonly present with pain, altered sensation, loss of proprioception, muscle weakness, and increased fatigability and psychological dysfunction (White, Pritchard and Turner- Stokes, 2004). These impairments may lead to immobility, altered gait and increased risk of falling secondary to impaired balance, as explained by Ites, et al., (2011) and also by Hwang and Nochajski (2003). Activity limitations commonly experienced by persons with peripheral neuropathy are walking, activities of daily living like bathing, sleeping and other usual activities, factors which all may change the quality of life (Myezwa, et al., 2009). Limitation in aspects of health related quality of life as drawn up by the European Quality of Life group include; mobility, self-care and usual activities (Miners, et al., 2001). O'Brien, et al., (2008b) demonstrated how episodes of activity limitation eventually lead to participation restriction and ultimately disclose to the employer and colleagues and the community, the possible status of an individual, leading to stigmatization. The main areas of possible participation restriction include role fulfillment, like being at work, being a parent or spouse (Miners, et al., 2001). (Hwang and Nochajski, 2003) using the ICF explains that the major environmental barriers for human function are found in the attitudes and beliefs of the society. The available services, systems and policies create an enabling environment upon which performance is based (Hwang and Nochajski, 2003).

2.6 Management of peripheral neuropathy

2.6.1 Introduction

Distal symmetrical poly-neuropathy impairments may be managed using pharmacological, non-pharmacological or self-care strategies depending on the severity of symptoms, preference, or availability of approach (Nicholas, et al., 2007b). Pharmacological approaches include analgesics and some of the ARV drugs. Non pharmacological approaches include physiotherapy, which addresses these impairments by way of electrotherapy, massage, acupuncture and therapeutic exercise (Verma and Simpson, 2007). Therapeutic exercise includes progressive resisted exercise, aerobic exercise, individualized exercise programs and generalized home exercise programs including walking (Philipas, et al., 2006).

2.6.2 Pharmacological management

While analgesics are the commonly used approach, certain anti retroviral therapy drugs are also known to alleviate DSP symptoms. These therapeutic drugs include zidovudine, which has been shown to ameliorate symptoms of DSP (Keswani, et al., 2002).The main approach utilized is symptomatic relief of pain based on the WHO ladder of pain management (Verma and Simpson, 2007; Nicholas, et al., 2007b). Anti convulsants like carbazapine has shown good relief of neuropathic pain while drugs like lamotrigine and gabapentin are used internationally but are not available locally (Verma and Simpson, 2007). The American Association of neuromuscular and electrodiagnostic medicine, the American Academy of neurology and the American Academy of Physical Medicine and Rehabilitation approved a report by Bril, et al., (2011). This report recommends the use of anti-convulsants, especially pregabalin as treatment of painful diabetic neuropathy where clinically appropriate as they are equally effective in relieving pain (Bril, et al., 2011). The same report also recommends that Gabapentin and sodium valproate should be considered. However they do not recommend Oxcarbazepine, lamotrigine and lacosamide. Bril, et al., (2011) reviewed the use of antidepressants and recommend that amitrypyline, venlafaxine, and duloxetine be considered based on their review of well-designed clinical trials.

2.6.3 Non -pharmacological management

Electrotherapy

Physiotherapists commonly manage pain using electrotherapy agents which include functional electrical stimulation, trans-cutaneous electrical nerve stimulation (TENS), interferential therapy, heat therapy and cryotherapy (Pieber, Herceg and Partenostro-Sluga, 2010). There is limited evidence from clinical studies conducted to establish the effectiveness of electrotherapeutic agents in reducing HIV related neuropathic pain. However patients have been shown to use heat in warm baths and cold water as a form of cryotherapy in self-management of their chronic pain (Nicholas, et al., 2007b). Most literature linked to neuropathic pain management using electrotherapy is cited in the management of painful diabetic neuropathy (Pieber, Herceg and Partenostro-Sluga, 2010; Bril, et al., 2011). In a review of fifteen studies done to determine the efficacy of electrotherapeutic modalities, Pieber, Herceg and Partenostro-Sluga, (2010) found that transcutaneous electrical nerve stimulation was consistently beneficial in three of the large randomized controlled trials studies. Bril, et al., (2011), also recommend the application of percutaneous electrical nerve stimulation based on a review of one well designed clinical trial. Frequency modulated electromagnetic neural stimulation registered clinical important reduction of pain in the other reviewed studies (Pieber, Herceg and Partenostro-Sluga, 2010). Nonetheless conflicting results emerged from studies where pulsed and static electromagnetic fields were trialed thereby leaving a need for further studies in this arena (Pieber, Herceg and Partenostro-Sluga, 2010). Bril, et al., (2011) concurs with this finding and recommends that electromagnetic field treatment should probably not be considered for treating painful diabetic neuropathy. More work has been done by acupuncturists and alternative medicine practitioners in showing evidence of providing relief for neuropathic pain as discussed in the next section.

Massage

It is estimated that there are over 100 types of massage (Hillier, et al., 2010). The most commonly used form of massage in the western world is the Swedish or muscular massage which comprises of different techniques used to manipulate the soft tissues (Hillier, et al., 2009). These include slow rhythmic stroking; effleurage,

circular compressions also known as kneading, forceful skin/tissue rolling also called petrissage, and penetrating pressure from finger tips with circular or transverse movements like trigger point or friction massage and tapotment where there is rapid striking of the tissues by the hand (Ashton and Cassel 2002). However in a study to establish the effects of massage in 30 participants, who had cold induced pain with no known pathology, Kessler, Marchant and Johnson (2006), showed that there was a trend towards significance when the massage effect was compared to touch where soft tissue below it was not manipulated. When discussing their results, Kessler, Marchant and Johnson (2006), suggest that massage reduces transmission of pain impulses as mediated by the stimulation of mechano- receptors. Swedish massage or western massage has been shown to have an effect on peripheral neuropathy when used with topical agents like lidocaine or capsaicin (Wolfe and Trivedi, 2004). The results of the review by Hillier, et al., (2010) suggest that massage may be used with other modalities like acupuncture, Tai Chi, meditation and relaxation to improve the quality of life and deal with stress associated with pain in PLWHA (Galantino, et al, 2005).

Acupuncture and Tai Chi

Whereas acupuncture has been used extensively in the alleviation of pain, it is only recently that research has sought for evidence on how acupuncture works and if it works for symptoms of pain in PLWHA. Phillips, Skelton, and Hand (2004) examined the effect of acupuncture on pain associated with HIV by carrying out a pre-test /post test pre-experimental study designed to assess the effects of acupuncture in a group setting on subjective pain and symptoms of peripheral neuropathy in PLWHA. A certified acupuncturist performed the acupuncture to twenty one participants over a five week period and all scores of pain showed significant reduction post acupuncture of between 39% to 50% points (Phillips, Skelton, and Hand, 2004). The results show that the Subjective Peripheral Neuropathy Screen (SPNS) score was reduced by between 43% to 56% points in the intervention group (Phillips, Skelton, and Hand, 2004). However the intervention did not address muscle weakness associated with peripheral neuropathy. All measures used in the study were subjective and placebo factors were not controlled for (Phillips, Skelton, and Hand, 2004). Other forms of therapy have been researched with some progress. Galantino, et al., (2005) compared the effects of group aerobic exercise and Tai Chi done twice per week for

eight weeks, with a sample of thirty eight participants in an outpatient setting at two clinics. They found that aerobic exercise and Tai Chi improved flexibility, balance, endurance, the quality of life and some physiological measures. Some of the interventions used by individual PLWHA are remedies recommended traditionally by relatives or friends, which have been utilised as self-care strategies (Nicholas, et al., 2007a).

Self- care strategies

Nicholas, et al., (2007a) carried out a study with a sample of 450 participants in American, European, Caribbean and Asiatic cities so as to establish the patterns of self-care activities PLWHA use to manage peripheral neuropathy. Their study found that 292 of participants took a hot bath, while others strategies included staying off the feet (n=258), rubbing the feet with cream (n=177, walking (n=262), elevating the feet (n=236). These results concur with findings by Ownby and Dune (2007) who found that people with peripheral neuropathy tended to develop individual strategies to manage their symptoms. In a grounded theory approach, they interviewed 19 people with peripheral neuropathy and listed the categorized strategies as follows: humor, exercise, massage and lotion, heat and cold modalities, rest, environmental /personal changes, herbal/ marijuana, prescribed medications, TENS, prayer, meditation and guided imagery (Ownby and Dune, 2007). However, Nicholas, et al., (2007) is of the opinion that some of the management behaviors which were employed by participants in his study including, use of marijuana, cigarette smoking and street drugs may be deemed unhealthy. As shown by these findings some form of exercise, e.g. walking was adapted by the participants of these studies as a strategy to manage peripheral neuropathy (Ownby and Dune, 2007). In the following section, therapeutic exercise will be explored as a management approach to peripheral neuropathy.

Therapeutic exercise

Therapeutic exercise can be defined as the prescription of a physical activity or program where the client carries out voluntary muscle contraction and or body movement with the aim of relieving symptoms or improving, retaining or slowing deterioration of health (Taylor, et al., 2007). However medical practitioners advise

their clients to avoid physical exertion and therefore will not refer them for exercise for fear of further immune-compression arising from over-exertion and fatigue (Bopp, Philips and Fulk, 2003). Nonetheless there is compelling evidence in well documented randomized clinical trials to the benefits of therapeutic exercise without excessive effects on immunity (O'Brien, et al., 2008, 2010; Taylor, et al., 2007). Strengthening exercises have been shown to improve muscle strength in people with peripheral neuropathy (White, Pritchard and Turner-Stokes 2008). Supervised aerobic exercise done at sub-maximal age predicted maximal heart rate levels of 70% and resistance exercise programs in PLWHA has been shown to be safe and is known to improve cardiovascular fitness (O' Brien, et al., 2010). Exercise reduces central adiposity, improves metabolic indices (Mutimura, et al., 2008) and significantly improves immunology and virology measures as defined by CD4+ counts (Dudgeon, et al., 2004).

Muscle strengthening programmes involve progressive resisted exercise utilising repetitions of specific muscle contractions. These can be isometric (performed against maximal resistance where no associated joint movement is possible), isotonic (performed against a sub maximal known resistance, this is typically greater than 70% of the maximal load possible, where joint movement and limb excursion is permitted) or isokinetic (performed against variable resistance but where the speed of contraction is constant) ACSM (2011). Endurance programmes involve gradually increasing the duration and intensity of aerobic activity for example cycling, running, or walking. Specific muscle endurance programmes may also involve the use of low load high repetition muscle contractions (White, Pritchard and Turner-Stokes, 2006)

Taylor, et al., (2007) conducted a systematic review on the use of therapeutic exercise on a variety of conditions as commissioned by the Australian Physiotherapy Association, They found 47 trials which confirmed that therapeutic exercise can improve muscle performance and mobility in people with multiple sclerosis and reduce pain and improve activity levels in people with chronic osteoarthritis of the knee, and chronic low back pain (Taylor, et al., 2007). Therapeutic exercise is beneficial in conditions which include heart conditions, geriatric, and peripheral neuropathy and in HIV (Taylor, et al., 2007). Meanwhile O 'Brien, et al., (2010) in a Cochrane review, carried out a meta analyses of all studies they had retrieved using Rev Man 4.2.2 software and showed that exercise improves cardio vascular fitness and is safe. However, the results of O 'Brien, et al., (2010)'s study review showed no

significant changes in immunology or virology outcome measures. Weight, body composition, body mass index, strength, amount of weight resisted were analysed in most studies which were male dominated (O 'Brien, et al., 2010). This meta-analysis reveals that most studies had a high loss to follow-up of more than 15% withdrawals and data in the studies was analysed using a per protocol analysis whereas an intention to treat analysis would add value.

Fillipas, et al., (2006) carried out a single blind, randomised, controlled trial to determine the effects of two six month supervised aerobic and resistance exercise programs for HIV infected participants. Outcome measures in this trial by Fillipas, et al., (2006) included a self-efficacy scale, cardiovascular system fitness using Kasch pulse recovery test which tests fitness by checking the recovery rate of the cardiopulmonary system after exertion and they used the Medical Outcomes Study HIV Health Survey to evaluate Health related quality of life. Participants' health status was ascertained using CD4+ count and viral load values. This study confirmed the known effects of exercise which include improved self-efficacy and cardiovascular fitness. Results from this study by Fillipas, et al., (2006) remind researchers that the need for supervision in exercise is important and reveals that a twice weekly program can be comparable in effects to a thrice weekly program. The exercise was run by an experienced therapist with knowledge in HIV and therefore counseling in an exercise setting may have been an extenuating factor value adding to the exercise. White, Pritchard and Turner-Stokes (2004) also performed a review of three clinical trials done on the use of exercise in the management of peripheral neuropathy in diabetes mellitus. In three studies they found suitable, White, Pritchard and Turner-Stokes (2004) observed that the methodological quality of two of the studies was poor. Less than eight weeks of intervention had been used while the outcomes and diagnostic groups of these studies were not similar therefore could not be compared (White, Pritchard and Turner-Stokes 2004). One of the studies found to be methodological proper, was done by Richardson, Sandman and Vela (2001) and had a sample size of 20 participants, ten in the control and ten in the experimental group. This study used an exercise program which focused on strengthening the lower limb muscles without using a proper PRE. Their findings indicated that a focused strengthening programme was effective in increasing muscle strength and improving balance Richardson, Sandman and Vela (2001).

Progressive resisted exercises (PRE)

Progressive resisted exercise is defined as an exercise regimen where physical resistive activity is performed at least three times per week for at least four weeks (O'Brien, et al., 2008). In their meta-analysis, O' Brien, et al., (2008) demonstrates by the results of different clinical trials that an effective exercise regimen must ideally be at least six weeks long. The ACSM (2011) paper, in a review of studies, found that PRE has positive effects on muscle strength, balance and quality of life in apparently healthy adults. This is consistent with the findings by O'Brien, et al., (2008), where the studies reviewed reveal that PRE is similarly effective in improving muscle strength, balance and quality of life in PLWHA. However these studies had small samples sizes, and were of predominantly male constitution, and did not include quality of life in their outcomes. A small number of the studies reviewed by O'Brien, et al., (2008) analysed the data using an intention to treat analysis approach. In a study done by Bhasin, et al., (2000), where only male participants were used, PRE was compared with PRE augmented with testosterone, testosterone only and a control group. They found that PRE was effective in improving muscle strength and quality of life without the need for augmentation with testosterone. This concurs with the findings by Agin, et al., (2001)'s study that tested PRE on a women only sample in PLWHA and compared PRE and PRE with whey protein supplements. The study by Agin, et al., (2001) found that PRE improved muscle strength and quality of life in a similar manner as when supplemented with protein. Some studies have used different forms of nutritional supplements to augment exercise based on muscle hypertrophy physiology as done in a study by Hess and Woollacott (2005). However the results of other studies seem to defy this generalization. Agin, et al., (2001) using whey protein in female participants to augment exercise and found that there was no value addition. Sakkas, et al., (2009) in a study where they used creatinine supplements found results similar to the study done by Agin, et al., (2001).

Furthermore, Hess and Woollacott, (2005) showed that PRE increases strength and improves balance in 27 elderly men and women after carrying out a high intensity PRE program over ten weeks. Both studies by Agin, et al., (2001) and Hess and Woollacott, (2005) looked at the effects of PRE on other variables including immunological and virological indices and found that these indices were improved by PRE. On the other hand Dolan, et al., (2006) also used a women only sample to

show that when combined with aerobic exercise PRE was effective in improving muscle strength and the body composition.

On the other hand literature on people with diabetic DSP which is believed to be similar to DSP in PLWHA was reviewed in a study by White, Pritchard and Turner-Stokes, (2004).This review cites flaws in methodology used, but concludes that strengthening exercise moderately improve the functional abilities of people with diabetic DSP (White, Pritchard and Turner-Stokes, 2004).

Progressive resisted exercise protocol

Literature was reviewed to establish the recommended procedures for PRE and found that the intervention exercise program consists of warm up, stretching and progressive resisted exercise (ACSM, 2006). Participants carried out exercise sessions based on the established baseline strength. While several protocols may be used, Hess and Woollacott, (2005) used a simple protocol where the weights are then increased for each participant as the participant could tolerate every two weeks to allow for adaptation. The sets were increased to three (3) on the following week while the weight was maintained. A resting period of 2 minutes was allowed between the sets so that the muscles could recover (ACSM, 2011).

While the studies reviewed by O'Brien, et al., (2008) used a regimen of three sessions per week, other studies have used the twice per week regimen. Fillipas, et al., (2006), in a study with PLWHA used the twice weekly regimen over a period of six months equally and found that the regimen was equally effective. Furthermore the ACSM, (2011) position paper concurs and states that a twice to thrice per week regimen is effective for the purpose of muscle strengthening (ACSM, 2011).

Adherence to exercise

Adherence to exercise can influence the actual results of the study as with findings by Petrozsci, et al., (2010) that the perception of well-being, lifestyle and cultural beliefs are major contributors to compliance in studies. The withdrawal rates in the studies reviewed by O' Brien, et al., (2008), range from 0 -76 % and different reasons including, employment, illness, relocation, loss of interest, transportation difficulties, personal issues, lack of motivation, lack of time, economic reasons.

Basta, Reece and Wilson (2008), in their study propose the use of the trans-theoretical model to predict how PLWHA adjust to an exercise program. They used this model of approach in a study and found that this model may explain how PLWHA go through the stages of change to become compliant to management (Basta, Reece and Wilson, 2008). Using such a model implies the factoring in of motivation as a crucial factor in behavior modifications and as such, so as to exercise PLWHA need to have a good reason to commit to this undertaking.

2.7 Methods of Assessment of the Effects of HIV-associated Peripheral Neuropathy

2.7.1 Introduction

An outcome measure is a test or scale administered and interpreted by the therapist that has been shown to measure accurately any aspect of interest, which is expected to respond to an intervention (Hammond, 2000). As such, this study required instruments to measure the effect of the intervention that had been set.

The choice of instrumentation is dependent on reason for measuring, the preference and need of the outcome measure and who the end user of the information (Hammond, 2000). An instrument may be discriminative, predictive or evaluative in nature. Occasionally diagnostic relevance and specifity does not necessarily reflect the result of specific intervention (Hammond, 2000). Outcome measures need to be standardized to allow for comparison of results from different intervention studies (White, Pritchard and Turner-Stokes 2004).

The measure should be reliable, valid and responsive to changes. It should be convenient to use by the clinician while being comfortable and painless to the subject (Hammond, 2000). In the literature, the participants' health status was one of the outcomes measures assessed and the outcomes include: the participants' health status outcomes were assessed using body composition changes like the body mass index while immunology was measured using CD4+ count. Physical performance tests include cardiovascular system fitness and muscle strength assessment. Chester step test and force transducers like the dynamometer are used. Functional performance measures are the clinician's choice for assessment as they have to be relevant. In this study there was need to choose a suitable assessment tool to measure the appropriate changes which would occur as a result of the intervention.

2.7.2 Definitions

Some of definitions considered important in the process of choosing the assessment tools for this study included:

Validity indicates whether the instrument does indeed measure what it is intended to measure; therefore the right questions have been asked (Faber, et al., 2006).

Reliability is how uniformly the test can be repeated when administered on more than one occasion that is stability overtime (test-rater reliability). *Reliability* also refers to the extent to which the measurements can be objectively administered (inter-rater reliability) (Bruton, Conway and Holgate, 2000).

Responsiveness is defined as the ability of an instrument to accurately detect true change in subjects when it has occurred (Hammond, 2000).

Predictive validity was expressed in terms of sensitivity and specificity where s*ensitivity,* is defined as the probability that an event is indeed predicted to occur, whereas *specificity* is defined as the probability that a non-event is indeed a non-event (Faber, et al., 2006).

Ceiling effect is a measurement limitation of an instrument which renders the instrument unable to determine an increased performance beyond a certain level.

As the process of choosing the tools is reviewed in the following section, these terms defined will be used accordingly.

2.7.3 Dynamometry and muscle strength assessment

While manual muscle tests like the Oxford scale may be used, they are highly subjective and unreliable (Bohannon, 1997). A one-repetition maximum (1RM) is the weight as adjusted to ensure that the participant can only lift that weight once through a full range of motion (ACSM, 2006). The 1RM is established by asking the participant to lift a weight. If the person can barely lift the weight, it is adjusted until the person can just lift it through range of motion (ACSM, 2006). Dynamometry may also be used in the place of 1RM as its values are equivalent to 1RM as established by Verdjk, et al., (2009), in a randomized controlled trial, The make test (Bohannon, 1997) is performed when the assessor holds the dynamometer and matches the participant's maximal force exertion until the joint gives in (Bohannon, 1997). This is to allow the weakened participant to initiate and exert a force they can generate and each movement is repeated three times and the mean recorded (Bohannon, 1997).

The Jamar Dynamometer was used in the assessment of muscle strength and it features a strain gauge mechanism while allowing for digital output.

O'Brien, et al., (2008) explains that using isometric testing for muscle strength, may underestimate muscle strength. This position is consistent with the results from five out of the seven of the studies reviewed by O'Brien, et al., (2008) which had used isotonic muscle strength testing.

Studies have shown that people living with HIV and AIDS have a physiologic performance level of 70% of usual level which is equivalent to a 12RM and approximately 75% of a 1RM (ACSM, 2006). Use of the 12 repetition maximum also reduces the risk of injury to the person.

2.7.4 Performance Oriented Mobility Assessment

While functional performance tests have been used to evaluate mobility and effectiveness of clinical interventions, for the requirements of this study, the modified Performance Oriented Mobility Assessment (POMA) (Faber, et al., 2006) was selected. The Performance Oriented Mobility Assessment, also referred to as the Tinnetti Mobility Test (TMT) was developed by Mary Tinnetti in 1986 for use with the elderly population who are at risk of falling.

The TMT can be administered in less than five minutes making it easier than the Berg balance scale (BBS) which takes 15 to 20 minutes. It may be used as proficiently by experienced physiotherapists as by physiotherapy students (Faber, et al., 2006). The POMA is an easily administered task-oriented test that consists of eight items of gait and eight items on balance. (Faber, et al., 2006).It requires basic equipment including a hard armless chair, Stopwatch or wristwatch and a 6 meter walkway (Faber, et al., 2006). It is used for rating gait (POMA- G) and balance POMA –B and a total score POMA-T is derived as an aggregate of the two subscales. Balance Score = 16, Gait Score = 12 and the Total Test Score = 28. The Performance Oriented Mobility Assessment is interpreted as: 25-28 = low fall risk 19-24 = medium fall risk < 19 = high fall risk. There is no literature found showing the use of the POMA in a study involving participants with peripheral neuropathy and

HIV/AIDS hence while the POMA has been used for other conditions it has not been applied or validated for peripheral neuropathy.

The studies found in literature sought to establish the POMA as a predictor of the risks of falls in the elderly for geriatric participants (Tinnetti, 1986, 1988; Lin, et al., 2004; Baloh, et al., 2006; Faber, et al., 2007; Panzer, et al., 2011). Kegelmeyer, et al., (2007) used the POMA to assess the risk of falls as well as the testing the reliability and the validity of the POMA in participants with Parkinson's disease. Kloos, et al., (2010) carried out a study to also assess the responsiveness of the POMA in participants with Huntington's chorea Kloos, et al., (2010). However, other studies were done to determine the reliability and validity of the POMA against the tools considered gold standards when used for different neurological conditions.

Reliability and validity of the Tinnetti Mobility Test for individuals with mobility dysfunction was tested for in two studies by Kegelmeyer, et al., (2007) and Faber, et al., (2006). In a study which had a sample size of 30 individuals from a movement disorders clinic, Kegelmeyer, et al., (2007) found that the Tinnetti Mobility Test has the best predictive validity with reference to falls in the elderly. Kegelmeyer, et al., (2007) also detailed the validity and reliability of the POMA against the other gold standard tests and in different populations which showed good reliability levels and showed that the TMT was a valid measure of balance. In another randomised clinical trial to investigate the effects of exercise on elderly with participants drawn from 15 self-care and nursing care residences Faber et al 2006, found a similar outcome. Faber, et al., (2006) assessed the POMA for validity, reliability and responsiveness against gold standard test/ reference tests which included the timed ''Up and Go'' test (TUG), the six minute walk, the balance test from Frailty and injuries Co-operative studies of Intervention Techniques (FICSIT). Other comparable physical performance and functional tests include gold standard tests like: the functional Reach Test (FRT) for balance, sit and reach test for flexibility, the sit up test for endurance (Galatino, et al., 2004), the Dynamic Gait Index, the Berg Balance Scale and the Groningen Activity Restriction Scale GARS and the Southampton Mobility Assessment. The Spearman correlations between the scores when it was tested for intra rater and inter rater reliability on the POMA scales and the scores on the reference test indicate moderate current validity of scores for the scales Spearman's rho score of .74 to .93 with levels of agreement at -4 to 4 points (Faber, et al., 2006).The value of the minimal detectable change (MDC) at 95% confidence level, following an intervention

for individuals was at least five (5) points and 0.8 points for group scores for the change to be considered significant (Faber, et al., 2006). However while the POMA is sensitive to fallers it is not specific enough with a sensitivity of 64% and specificity of 66%, (Faber, et al., 2006). This is interpreted as a moderate predictive validity for the POMA (Faber, et al., 2006). This tool was therefore recommended for use in the study to assess gait and balance in participants as it was the most suitable for the requirements of the study as shown by studies by Faber, et al., (2006), Kegelmeyer, et al., (2007) detailing the validity and reliability of the POMA against the other gold standard tests in different populations.

2.7.5 Wong Baker faces

One of the recommendations by Bril, et al., (2011) in their report, is that non-ambiguous pain rating scales for use in clinical trials should be developed. Different scales have been used before in the assessment of pain and the Likert scales are the most popular. Wong Baker faces were found useful when assessing young participants of three years of age and also suitable for people who are older and illiterate as the concept of a scale using numbers may not be reliable (Jackson, et al., 2006; Wong, et al., 2001). This pictorial visual analogue scale is modelled along the six point Likert scale from no pain to worst pain imaginable and employs a representative face for each level of pain (Wong, et al., 2001). The respondent then chooses the face which best matches how they would describe their pain. Their pictorial presentation of pain using expression faces reduces confusion associated with interpretation of visual analogue scales which use numbers (Jackson, Kersten and Turner- Stokes 2006). Using the Wong Baker is therefore recommended as it is simple clear and reduces the misunderstanding and bias which may arise with illiterate or cognitively impaired participants.

2.7.6 Brief Peripheral Neuropathy Screen (BPNS)

While it may be difficult to make a diagnosis of distal peripheral neuropathy, a brief peripheral neuropathy screen (BPNS) can be used in clinical settings (Cherry, et al., 2005). Symptoms of shooting pain, the presence of distal bilateral symmetrical burning sensation, parasthesia, or numbness, cramping in the legs, and muscle

weakness in the foot can be used to confirm distal symmetrical poly-neuropathy (Nicholas, et al., 2007b). This is a non-invasive method of diagnosis, which is fast and easy to perform and has excellent sensitivity to DSP (Hahn, et al., 2006). This study did not differentiate the underlying cause of neuropathy but demonstrated the tools' sensitivity to small fiber evoked potentials/ pain fibers, which indicate the presence of DSP (Hahn, et al., 2006). Non-neurologist clinicians, like a general practitioner, trained nurses or therapists could use the Brief Neuropathy Screen Test to diagnose peripheral neuropathy (Cherry, et al., 2005); (Schifitto, et al., 2006). Severity of neuropathy is assessed using the neural deficit score and the neuropathy symptom score (Cherry, et al., 2005). The study correlated sensory neuropathy with the symptoms of pain in HIV associated sensory neuropathy and found (Schiffito et al 2002). It is reliable in identifying symptomatic peripheral neuropathy (Cherry et al., 2005). Cettamoi, et al., (2010) piloted the use of the BPNS against quantitative sensory testing and found that using only one of the questions (do you feel numb in your feet) as a single question neuropathy screen was 83% sensitive in identifying DSP in PLWHA. Hence this tool was found to be suitable and cost effective in identifying participants for this study.

2.7.7 The European Quality of Life in 5 Domains (EQ-5D) Questionnaire

O'Brien, et al., (2010) observed that the studies in their Cochrane review lacked a standard outcome measure of the health related quality of life. Bril et al., (2011) in their review of the management of painful diabetic neuropathy concurred and recommended that health related quality of life should be included in clinical trials with standardized measurements (Bril, et al., 2011). As this measure focuses on individual PLWHA understanding of their own quality of life, a thematic approach was been used by previous studies to construct this measure, successfully providing researchers with choice of tools tailor-made for the requirement of the research (Robberstad and Olsen, 2010).

Robberstad and Olsen, (2010) in a review of the studies on quality of life in Southern Africa found that the EQ5D was the most appropriate instrument used recently to evaluate the quality of life in PLWHA in this region. In a study with PLWHA Miners, et al., (2001) sought to validate the European Quality of Life in 5 Domains (EQ-5D) state of health questionnaire against the Medical Outcomes Survey HIV (MOS-HIV),

which is accepted as a gold standard in the evaluation of quality of life in PLWHA. The Medical Outcomes Survey HIV Health Survey is a 35 item self-administered questionnaire with 10 dimensions of health and eight subscales physical health summary which include pain, health perception, physical role and social function, mental health summary, with mental health, health distress, overall quality of life, cognitive function and energy or fatigue scale (Miners, et al., 2001). The EQ-5D is a simplified and practical form of a health related quality of life which explores and summarizes the ten dimensions of living included in the Medical Outcomes Survey–HIV into five domains (Miners, et al., 2001). These domains include mobility with regards to being able to walk about or being confined to bed. Other domains are self-care, where one may have problems with washing or dressing self; problems with usual activities (e.g. work, study, housework, family or leisure activities); pain/discomfort measuring levels of pain or discomfort and anxiety/depression (Jelsma, et al., 2001). Miners, et al., (2001), in across sectional study, compared the use of the Medical Outcomes Survey HIV Health Survey (MOS –HIV) with the use of the Euro-Quality of life questionnaires in a developed country setting with a sample of 128 participants. Their findings indicate that EQ-5D can be used effectively to assess the level of quality of life in PLWHA. Jelsma, et al., (2005) assessed the quality of life in 117 participants in a resource poor setting who had been commenced on highly active anti-retroviral therapy and found that the EQ-5D was a valid instrument for evaluating quality of life in PLWHA. They found that quality of life was an important measure of the possible effects of a HAART intervention.

A Shona version of the questionnaire which was developed a by Jelsma, et al., (2001) using the Euro-Qol group protocol, which involved translation and back translation, showed a high level of reliability with a level of agreement of 0.78 to 1.00 using kappa statistic for the different domains of activity (Jelsma, et al., 2001). Hence the EQ5D was chosen for use in this study as it had already been translated into Shona using the required methods by Jelsma, et al, (2001) and shown that it was comparable to the MOS-HIV which is regarded as the gold standard in evaluating the health related quality of life by Miners, et al, (2001).

CHAPTER 3

3. METHODOLOGY

3.1 Introduction

In this chapter the research design, instruments, the procedure and statistical analysis of the study will be discussed. Discussed, are the most suitable measuring instruments, and the reason why they were used. The validity and reliability of all the measuring instruments in this study were assessed according to the literature.

3.2 Study design

The study was an assessor-blinded randomized controlled clinical trial. The participants in the experimental group underwent an intervention program of progressive resisted exercises while the participants in the control group were given advice as usual by the doctors and nurses to walk as a home exercise program.

3.2.1 Study population

Participants for the pilot study were sourced from the family care clinics (FCC), previously known as opportunistic infections (OI) clinics at Wilkins Hospital of the Municipal of Harare and family care clinic clinics at Parirenyatwa and Harare Central Hospitals in Zimbabwe. The participants for study 1 were sourced from the same sites as for the pilot study. However the participants for study 2 were sourced from ten selected antiretroviral therapy dispensing local clinics of the Municipality of Harare. (The research team had to do Study 2 because the Study 1 had experienced a high loss to follow-up rate and therefore a Study 2 was essential to achieve the required sample size as calculated in the initial protocol).

3.2.2 Sample selection and size

Inclusion Criteria

Both female and male residents in Harare aged between 18 to 70 years were recruited by way of an invitational English or Shona Brief Peripheral Neuropathy Screen (BPNS) questionnaire. Participants who had been on first line antiretroviral therapy (including d4T / Stavudine) for at least six months were selected. CD4+ counts of any level were included in the study as they were not reliable or in some cases current. The strength of knee and ankle muscles on quick assessment was expected to be grade 3 (antigravity) or greater by the manual muscle testing. The assessors required participants to be able to walk without assistance or with a walking aid. Willing and able participants signed consent forms before the diagnosis of distal symmetrical peripheral neuropathy was reached at by use of a Brief Peripheral Neuropathy Screen Test (BNST).

Exclusion criteria

Participants with a history of central nervous system dysfunction, hemiparesis, myelopathy or cerebellar ataxia (Richardson, Sandman and Vela, 2001), were disqualified. Alternative causes of distal symmetrical neuropathy – alcohol, other drugs, other chronic illnesses like diabetes were screened for. Participant on isoniazide, either as prophylaxis or as part of TB treatment were excluded. Other exclusion factors as noted by Richardson, Sandman and Vela, (2001), included: musculoskeletal deformity, amputation, scoliosis and inability to actively and functionally move ankle and knee joints lower extremity arthritis or pain that limited standing and foot ulcers at the time of assessment.

All those who had already been receiving physiotherapy prior to the study were not considered.

3.2.3 Sample size determination

The sample size was calculated using the Microsoft Excel Sample size calculator (v4 draft). Assuming a standard deviation of 5.5, (Faber, et al., 2006), in study 1, a sample of 34 participants per group gave 90% power to detect a 5 point change on the POMA scores with a confidence interval of ±1.54. A 25% potential loss due to follow up was factored into this calculation. However in the second study while still assuming a standard deviation of 5.5, a sample of 58 participants per group had 90% power to detect a 5 point change on the POMA scores with a confidence interval of ±1.54. A 45% potential loss to follow up and 10% to noncompliance was considered.

3.2.4 Randomisation

A computer generated randomization system of numbers was used to allocate the participants to their respective intervention groups in the pilot phases. In the main study, the selected clinics were paired by cross matching the participants at the clinics for sex and age of within five years of each other. The research assistant was then given the matched clinic pairs which were then randomly allocated for each pair by picking from a hat, into either intervention group or control group. Each clinic drawn first from each hat was taken as the intervention clinic. The second drawn clinic was the control clinic.

3.2.5 Assessor blinding

The principal investigator, who was the assessor, was blinded to the allocation of participants by a qualified registered physiotherapist, appointed to work as the research assistant at each phase through the study. The research assistant kept the names of the randomised participants in a centrally locked drawer, coded them and passed the coded participants on to the assessor without informing him which of the groups a participant belonged to. During the intervention period, the research assistants carried out the progressive resisted exercise program and did not allow the assessor access to any of the clinics. Thus on reassessment of the participants,

the researcher was not aware if the participants had been in the experimental group or control group.

3.3 Study instruments

3.3.1 Study instruments and procedures

The study instruments, the outcome variable to be tested, the procedure or the tool and the instrument validity and reliability will now be summarised in the tables according to the variable they test.

Brief Peripheral Neuropathy Screen (BPNS) (Appendix A1, A2 and A4)

The Brief Peripheral Neuropathy Screen, is summarized below in Table 3.1

Table 3.1 Brief Peripheral Neuropathy Screen (BPNS)

Study instrument:	**Outcome Variables tested:**	**Tool/Procedures:**
Brief Peripheral Neuropathy Screen (BPNS) (Appendix A1 and A4)	Level of severity of peripheral neuropathy symptoms in participants	Invitational Questionnaire Potential participants were invited to contact the researcher if they answer yes to more than 4 of the 15 questions.
Brief Peripheral Neuropathy Screen (BPNS) (Appendix A2)	Demographics including age, sex, marital status, education and HIV related information	Questionnaire to identify patients with or without peripheral neuropathies related to ART. Used to screen participants for exclusion

A self-administered modified Brief Peripheral Neuropathy Screen (BPNS) (AIDS Clinical Trials Group 2004) questionnaire (Appendix A1, A4) was used as an invitational questionnaire. As there was no Shona version of the questionnaire (Appendix A4), the research team translated the English version into Shona. The Shona version was then back translated into English. It is a checklist for muscular

cramping, numbness, tingling sensation inability to tell hot from cold especially when bathing, burning or aching pain, sharp, stabbing, shooting or sudden electric shock like pain and allodynia during sleep. It checks for foot sensation patterns when walking and if the skin becomes so dry it cracks.

The Questionnaire for Screening of Peripheral Neuropathies related to HIV and ART (Appendix A2), was used to provide demographic history of the participants among those showing willingness to participate in the study. It is an informational nurse-aide administered questionnaire which also serves to screen for exclusion criterion. Demographic characteristics consisted of gender, age, and highest level of education, occupation, marital status. General health status of the participant included HIV diagnoses period, the CD4+ count, the specific type(s) of anti-retroviral drug, duration of treatment and presence of common co-morbidities. The questionnaire also established when the symptoms commenced (before start or after starting ARVs), based on the participant memory or records on the hospital cards. If it was after starting ARVs, clarification on after how long on ARVs the symptoms had commenced was made.

Brief peripheral neuropathy screen tool (BNST) (Appendix A3).

The Performance Oriented Mobility Assessment, is summarized below in Table 3.2

Table 3.2 Brief peripheral neuropathy screen tool (BNST) (Appendix A3).

Study instrument:	**Outcome Variables tested:**	**Tool/Procedures:**
Brief peripheral neuropathy Screen Tool (BNST) (Appendix A3).	Level of severity of peripheral neuropathy in participants	Diagnosis of peripheral neuropathy by physical examination. Symptoms rated on a VAS and location 128 Hz tuning fork was used to evaluate perception of vibration as rated by duration of vibration felt. - Reflex hammer was used to strike the Achilles tendon so as to evaluate of tendon reflexes in the ankle.

While the subjective part of the BPNS was used to invite participants into the study, the Brief Neuropathy Screen Test (BNST) of the BPNS was used in confirming the

diagnosis of peripheral neuropathy. The examiner scored for neuropathy symptoms by checking for muscular cramping, numbness and abnormality in sensing of temperature, tingling sensation, burning pain, aching pain and irritation by bedclothes in the lower legs and feet (Cherry, et al., 2005; Schifitto, et al., 2006). The subject rated the severity of each symptom of pain, aching, or burning, “pins and needles” and numbness (lack of feeling) in feet; legs. These were graded using subjective elicited symptoms to form the subjective sensory neuropathy score. Location of symptoms was used to score depending on where the symptoms were e.g. feet, legs. Neuropathy deficit score focused on presence of the ankle tendon reflex and the vibration sensation (128Hz tuning fork) (Simpson, et al., 2006). The neurologist at Parirenyatwa Hospital (there was only one at the time of study), concurred with the findings from literature that clinicians besides the neurologists could use the Brief Neuropathy Screen Test (Cherry, et al., 2005; Schifitto, et al., 2006)

The Wong Baker Faces (Appendix E)

The Wong Baker faces are presented below in Table 3.3

Table 3.3 The Wong Baker faces

Study instrument:	**Outcome Variables tested:**	**Tool/Procedures:**
The Wong Baker Faces (Appendix E),	Pain as viewed subjectively by the participant on a Likert scale 0-5	Visual analogue scale Representative faces used for each level of pain. Participant chooses the best descriptive face

Performance Oriented Mobility Assessment (POMA) (Appendix B)

The Performance Oriented Mobility Assessment, is summarized below in Table 3.4

Table 3.4 Performance oriented mobility assessment tool

Study instrument:	Outcome Variables tested:	Tool/Procedures:
Performance Oriented Mobility Assessment (POMA) Tinnetti, 1986 (Appendix B)	Level of gait performance score out of 12 and level of balance performance score out of 16, the total Mobility Assessment is interpreted as: 25-28 = excellent 19-24 = good < 19 = poor mobility. For gait poor (<9) good (9-10) Excellent (11-12) For balance Poor (<10) Good (11-13) Excellent (14-16)	When assessing gait, the subject stands with the examiner, walks down the hallway or room at the usual pace. The subject is asked to walk down the walkway, turn, and walk back after being instructed to go. The subject should use the usual walking aid. The characteristics scored: -Initiation of gait -Step length, continuity and symmetry. -Turning while walking (180°) -Height clearance and path deviation -Trunk sway and walking stance. When assessing balance the subject is seated on a hard, armless chair and the manoeuvres tested are: -Sitting balance posture, ability to arise smoothly, immediate standing balance. -Standing balance and when balance when nudged on the sternum. -Standing balance with eyes closed -Turning 360º or 180° continuity of steps. -Safety in the manoeuvre to sit.

The Performance Oriented Mobility Assessment also referred to as the Tinnetti Mobility Test (TMT) was developed by Mary Tinnetti in 1986 for use with the elderly population who are at risk of falling. The POMA is an easily administered task-oriented test that consists of eight items of gait and eight items on balance. It requires basic equipment, which includes a hard armless chair, stopwatch or wristwatch and a 6 meter walkway (Faber, et al., 2006).

Health related quality of life.

The health related quality of life EQ5D questionnaire is summarized below in Table 3.5

Table 3.5 The EQ5D questionnaire (Appendix C and D)

Study instrument:	Outcome Variables tested:	Tool/Procedures:
EQ-5D questionnaire (Appendix C English, Appendix D Shona)	Health related quality of life, on five dimensions -mobility - usual activity - self care -pain or discomfort -anxiety or depression	It is a questionnaire with five dimensions where participant rate level of problem in domain: mobility (ability to walk about or being confined to bed), self-care problems like with washing or dressing oneself, problems with usual activities (e.g. work, study, housework, family or leisure activities), levels of pain or discomfort and anxiety or depression. The participant indicates in their opinion their state of health on that day using a scale on which the best state imaginable is marked 100 and the worst state imaginable is marked 0.

This questionnaire has undergone rigorous validation and reliability tests by the European quality of life group and the Shona version was coined by Jelsma, et al., (2001), following the European quality of life group protocol for translations.

Muscle strength assessment

Hand held dynamometer (Appendix I)

Table 3.6 below summarises the details of process of using the hand held dynamometer.

Table 3.6 Details of the dynamometer

Study instrument:	**Outcome Variables tested:**	**Tool/Procedures:**
Dynamometer (Appendix I)	The muscle strength assessment (measured in kilograms of force) of quadriceps , the hamstring, the tibialis anterior and the gastrocnemius	Jamar® hand held dynamometer Each tested movement was repeated three times and the mean recorded. The make test used requires the assessor to hold the dynamometer and match the participant's maximal force exertion until the joint gives

In the main assessment, muscle strength was measured using dynamometry by way of the Jamar Dynamometer. It has a strain gauge mechanism and allows for digital output. The make test (ACSM) which was used allows the weakened participant to initiate and exert a force they can generate (Bohannon, 1997). In the initial quick screen test, participants were tested using the manual muscle test as a criterion for entry.

Table 3.7 below summarises the assessment positions, Bohannon (1997) used when assessing muscle strength using a dynamometer.

Table 3.7 assessment positions for muscle strength dynamometry

Muscle group and action	Limb joint position	Dynamometer placement	Stabilization of participant
(quadriceps muscles) knee extensors	Hips and knees flexed at 90° hand resting on lap	2cm proximal to malleoli	Stabilized at shoulder by assistant
(hamstring muscles) knee flexors	Hips and knees flexed at 90° hand resting on lap	2cm proximal to malleoli	Stabilized at shoulder by assistant
(tibialis anterior muscles) ankle dorsiflexors	Hip and knee and ankle at 0°	2cm proximal to metatarsophalangeal joints	Foot is just off the couch and the leg is stabilized by assistant
(gastrocnemius muscles) ankle plantarflexors	Hip and knee and ankle at 0°	2cm proximal to metatarsophalangeal joints	Foot is just off the couch and the leg is stabilized by assistant

3.4 Intervention

3.4.1 Introduction

The intervention exercise program consisted of warm up, stretching and progressive resisted exercise. Participants carried out exercise sessions based on the established baseline strength assumed to define the one repetition maximum (1RM) value. As the programme assumes to use moderate exertion, an eight repetition maximum (8RM) to twelve repetition maximum (12RM) was used. A calibrated set of sandbags ranging from 500g, 1kg, 2kgs and 5kgs were combined to make up the required weight.

Description of intervention exercises

The procedure for progressive resisted exercises is summarised below in Table 3.8

Table 3.8 Summary of a progressive resisted exercise sessions

Procedure week	**Frequency**	**Progression**
Week one (Load less)	10 reps by 2 sets	No Load
Week two		Increase to 10 reps by 3 sets
Week three	10 reps by 2 sets	Start with 2kg/Ikg load
Week four		Increase to 10 reps by 3 sets
Week five	10 reps by 2 sets	Increased load by 1 kg
Week six		Increase to 10 reps by 3 sets
Week seven	10 reps by 2 sets	Increased load by 1 kg
Week eight		Increase to 10 reps by 3 sets
Week nine	10 reps by 2 sets	Increased load by 1 kg
Week ten		Increase to 10 reps by 3 sets
Week eleven	10 reps by 2 sets	Increased load by 1 kg
Week twelve		Increase to 10 reps by 3 sets

The exercise sessions were done twice a week such as on Mondays and Thursdays or Tuesdays and Fridays. The weights were increased as the participant could tolerate at increments of 1kg per after every two weeks (ACSM, 2006). On the week the weight was increased, two (2) sets of repetition were used. The sets were increased to three (3) on the following week while the weight was maintained.

Session format

Table 3.9 below highlights the phases followed within a session.

Table 3.9 Summary of an exercise session

Procedure	Duration	Progression
Warm up and general static stretching	5 min	Easy walking Arm swinging Walking sideway and backwards
Specific static stretching to the lower limb described in Table 3.9	10 min	As described in stretching a hold of 30 seconds at the point of mild discomfort per stretch.
Progressive resisted exercises	30 min	As described in PRE section
Warm down	5 minutes	Walking around the gym and combined stretching.

Warm up

The specific static stretching to the lower limb is summarised in Table 3.10.

Table 3.10 Specific static stretching to the lower limb

Muscle	**Starting position**	**Movement/ name of stretch**
Hamstring muscles	Sitting	modified hurdlers stretch
Quadriceps	side lying	Upper leg is self-stretched by bending the knee and pulling the leg back.
Calf stretches	Standing	Lunge forward keeping the feet firm on the floor
Tibialis anterior	in standing	front of leg stretches- lift the leg bending it back
The back muscle	in side lying	using the back curls/ knees to chest tuck

A general warm up activity was done before participants commenced on the specific static stretching to the lower limb.

Main progressive resisted exercises

The progressive resisted exercise session procedure is summarized in Table 3.11 below

Table 3.11 Progressive resisted exercise session procedure

Muscle group	**Starting position**	**Activity**
Quadriceps femoris muscles	Seated on a plinth, weight fixed at the ankle. Feet must clear the ground with the knee bending.	Knee extensions – straightening the knee
Hamstring muscles	Lying in prone on mat, weight fixed at the ankle. Legs will be straight on the mat with a pillow under the ankle.	Knee flexion – (bending the knee) as per schedule
Tibialis anterior muscles	Seated on a plinth, weights fixed near the toes. Feet must clear the ground with the knee bending.	Foot lifting as per schedule ankle dorsi-flexors
Gastrocnemius muscles	Lying in prone on mat, weight fixed near the toes. Knees bent at 90.	the ankle plantar-flexors Foot pushups getting toes to point up to ceiling

The core muscles underwent a general strengthening exercise programme using self body weight. The Erector Spinae muscles were exercised in prone on mat, while the abdominals were exercised in supine crook lying on the mat. The core muscles were exercised generally to stabilize the trunk; however no assessment was done as this was not objectively feasible in our setting or primarily part of the objectives. On commencing sessions, each muscle group in the lower limbs was taken through two sets of ten (10) repetitions using the mean weight at 12RM. The weight was fixed in a safe manner on the participants' body with Velcro or crepe bandage depending on movement to be performed. A resting period of 2 minutes was allowed between the sets so that the muscles could recover (ACSM, 2006). Non- compliance was defined as not attending more 50% of the sessions, which in this case is twelve sessions.

3.5 Data collection and recording procedure

3.5.1 Introduction

The procedure of how the data were collected, recorded and analysed as well as the intervention procedure will be outlined in the following section.

Ethical considerations: / ethical clearance (Appendix J and Appendix K)

Approval and ethical clearance of the protocol was sought from both the Human Research Ethics committee of the University of the Witwatersrand registration No: M090214 and the Human Medical Research Council of Zimbabwe registration No: MRCZ/B/62 through application for registration of protocol after approval by the school. Approval and ethical clearance of the research protocol was sought from the Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics registration No: JREC/23/09, through application for permission. Permission to access the municipal clinics was sought from the Medical Director of City of Harare. Permission to access the Municipality of Harare clinics was granted in December 2010 by the Medical Director. Permission by the Medical Research Council of Zimbabwe was granted in September 2009, after approval and ethical clearance of the research protocol by the responsible ethical boards and councils. Participant's written consent to participate in the study was sought using an information sheet (Appendix K). Participants in the control group were switched to do the experimental intervention at the end of the trial. Confidentiality was maintained to address HIV/AIDS associated stigma. An annual renewal of ethical clearance with the Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Zimbabwe and Medical Research Council of Zimbabwe was observed in 2010 and 2011.

3.6 Pilot study

3.6.1 Pilot study objectives

The main purpose for the pilot study was to establish the intra-rater reliability of the Performance Oriented Mobility Assessment tool and of the hand held dynamometer. The study sought to establish the usual treatment method used while allowing the

principal researcher and research assistant to familiarise with the study process and to adjust logistical preparations.

3.6.2 Procedure of pilot study

The pilot study was completed in four weeks using a sample of seven (7) participants determined by using the equivalent of 10% of total sample required for main study so as to determine the intra-rater reliability.

The pilot was commenced in January 2010 with prospective participants being invited in person by the researcher using the Brief Peripheral Neuropathy questionnaire. All the invited persons had an initial assessment done immediately on the day, or when they presented at the physiotherapy department. A reassessment for all the participants was carried out within 48 hours for intra rater reliability tests. The research assistant took the experimental group of four participants through a program of four progressive resisted exercises sessions as described in the intervention method. Seven of the participants were reassessed at the end of the experimental groups four sessions of progressive resisted exercises.

3.6.3 Results of pilot study

The results intra rater reliability tests are summarised in Tables 3.12 and Table 3.13 below. The results intra rater reliability tests for muscle strength are summarized in Table 3.12.

Table 3.12 Correlation of muscle strength scores

Muscle	Spearman Rho	p value
right quadriceps	0.87	0.01
left quadriceps	0.80	0.03
right hamstrings	0.96	0.001
left hamstrings	0.70	0.08
right gastrocnemius	0.88	0.01
left gastrocnemius	0.53	0.22
right tibialis anterior	0.33	0.47
left tibialis anterior	0.46	0.30

Intra-rater reliability of the dynamometer was high for the quadriceps, hamstring and right gastrocnemius muscles with Spearman rho range of 0.70 to 0.96.with p= 0.08 to p=0.001. Both tibialis anterior muscles and left gastrocnemius muscle were poorly correlated p=0.2, p=0.29 and p=0.47.

Table 3.13 Correlation of POMA gait and balance and pain scores

Variables	Spearman Rho	P value
Wong Baker faces		
Pain	0.94	0.002
POMA		
Balance score	0.82	0.03
Gait score	0.37	0.42
Total score	0.58	0.17

The Performance Oriented mobility assessment balance scores showed a reliability quotient, Spearman's rho = 0.82, which is significant p= 0.03. The gait score had a Spearman's rho = 0.37, p=0.42 and the total mobility score was Spearman's rho = 0.58, p= 0.17. The Wong baker faces pain score showed a reliability quotient, Spearman's rho = 0.94, (p= 0.002).

3.6.4 Implications for the study

The pilot study showed that inviting participants by using the first part of the BPNS was more efficient in recruiting participants. The analysis of the results suggested that instruments were reliable as shown by high correlation co-efficient realised. The dynamometry measurements were appropriate for determining muscle strength. However the dynamometer needed a cushion pad to be used to reduce contact pain during testing. The pilot study revealed that not all participants who attended at the central hospitals were residents of Harare; they had only sought accommodation with their relative's resident in Harare while they accessed drugs which were more readily available at these centers. The CD4+ count was unreliable as most of these clinical results were more than one year old since an actual test had been done making these results stale. A high percentage of the participants were employed and once they felt better they stopped attending and went back to work in Harare or other

towns while others were self-employed and therefore could not afford to attend as many sessions. Eligible numbers were lowered by co-morbidity especially tuberculosis which made them ineligible for the study. The working space in the gym for the exercise classes would be able to accommodate only 15 clients per session.

Study setting

The experience we had when sourcing for our participants showed that our approach of assessing patients at source sites was time consuming and unfriendly to the prospective participants. On corresponding with the medical consultants responsible at the family care clinics, we were advised that the local doctors would be too busy to assist in the diagnosis of poly-neuropathy for the study. We therefore had to use a different approach in recruitment, where participants were invited to attend a full assessment using an invitation questionnaire for main study compared to the pilot study approach.

Performance oriented mobility assessment and dynamometry reliability

The gait scoring showed volatility consistent with its ability to discriminate change and a possible training effect from the first session. The results show that the dynamometer and the performance oriented mobility assessment are reliable instruments when assessed by the same assessor.

Usual method of treatment

Most participants interviewed showed that the usual treatment method used by clinics was to be advised by the nurse or doctor to go and do exercises like walking while at home. Pain was managed using medication usually in the form of amitryptiline. Rarely were these participants referred to the physiotherapist for exercise prescription. Participants had knowledge of the need to exercise but not the information on how to exercise or they would go to the gym or taking walks. The study found that some participants with symptoms of peripheral neuropathy had been referred for physiotherapy to address the neuropathic pain and activity limitation emanating from the impairments of pain weakness and numbness. However, when they presented at the Physiotherapy department they were asked to pay US$10 for each session. The participants did not have the money to pay for this service as they were getting the antiretroviral drugs for a token fee or for free. These participants were included in the study because they had not received therapy as they were

unable to pay for the service. This may be one of the reasons why the usual method used advice from the doctor or nurse for the patient to exercise at home.

3.7 Main Study

The main study was fulfilled in two phases; Study 1 and Study 2 because the Study 1 had experienced a high loss to follow-up rate and therefore a Study 2 was essential to achieve the required sample size as calculated in the initial protocol.

3.7.1 Study 1

Study 1 was completed over thirty weeks from March to August 2010. Participants were invited for baseline assessments using the English and Shona versions of the BPNS at Wilkins clinic and Opportunistic Infections clinics at Parirenyatwa and Harare Central Hospitals. Baseline assessments as per pilot study were carried out on a sample of forty six participants over eleven weeks, at the physiotherapy department at Parirenyatwa Hospital. The control group was advised to exercise using walking at home. The selected experimental group participants were informed by phone call to attend exercise sessions by the assistant. The research assistant took the experimental group of participants through of twenty four sessions of progressive resisted exercises as described in the intervention method. After the twelve weeks reassessments were done for both the control group and the experimental group.

3.7.2 Study 2

The researcher selected ten clinics with functional support groups from the ART dispensing local clinics of the Municipality of Harare. Baseline assessment of the one hundred and fourteen participants was completed over fifteen (15) weeks as they are identified using the BPNS questionnaire at the local clinics. The baseline assessments were completed in the same manner as in the pilot study. The ten groups were cross matched for sex and age and then randomized to five (5) interventional groups and five (5) control groups. The experimental group of fifty seven participants in their five different home support groups (eleven+/-two participants per group) was taken through a program of progressive resisted exercise sessions described earlier in the intervention method by a research assistant. The other five (5) control groups' participants were given advice to walk as a home

exercise programme. All the participants were then reassessed within three weeks at the end of twelve weeks of trial intervention. The reassessments also included focus group discussions to get insight on the reasons for failing to attend the exercise sessions. Participants who could not attend the reassessments sessions were interviewed on the phone to get insight on the reasons for failing to attend the exercise sessions. The participants were asked the question:
What are/were your reasons for failing to attend the assessment exercise sessions?

3.8 Data analysis

Each participant was given a unique identifying code number so that they are identified on their result forms and questionnaires. All raw data was recorded on these prepared assessment forms and questionnaire forms and logged using a prepared Excel software spread sheet. The data logged into the Excel program was analysed after cutting and pasting into the Stata V10 statistical software program.

The statistical tests used on this data are summarised in Table 3.14 and Table 3.15.

Table 3.14 Variables analysed and the tests applied.

Variables analysed:	**Test**
Intra-rater reliability of the Performance Oriented Mobility Assessment tool.	Spearman rho
The intra-rater reliability of dynamometer	Pearson r
Differences in the mean change in the muscle strength scores within groups	Paired t-test
Differences in the mean change in the performance oriented mobility gait scores	Paired t-test
Differences in the mean change in the performance oriented mobility balance scores	Paired t-test
Differences in the mean change in the pain scores within groups	Wilcoxon's rank sum test
Differences in the mean change in the health related quality of life scores within groups	Paired t-test

Table 3.15 Variables analysed and the tests applied for between group and association analysis.

Variables analysed:	**Test**
Differences in the mean change in the muscle strength scores between groups	Analysis of variance
Differences in the mean change in the performance oriented mobility gait scores between groups	Analysis of variance
Differences in the mean change in the performance oriented mobility balance scores between groups	Analysis of variance
Differences in the mean change in the pain scores between groups	Analysis of variance
The mean change in the health related quality of life between groups	Analysis of variance
Relationships between muscle strength changes, the mobility level change and the health related quality of life.	Logistic regression model using generalised estimating equations

Intention to treat analysis was applied to the raw data. The EQ5D-utility score was analysed using pre-calculated tables from the results of the EQ5D –profile scores. Upon analysis, the EQ5D profile scores defines 243 states of health pre-calculated using a regression analysis to produce Euro-quality of life a utility scores (Appendix F). The outcomes were then multiplied by 100 to give a percentage rating which allows for ease of analysis. Baseline similarities were determined using unpaired t-tests for muscle strength and quality of life utility scores, while Wilcoxon Rank sum tests were used for gait, balance and pain. The results of the study was analysed to establish the effect of progressive resisted exercises on the different variables as outlined in the objectives. The levels of difference between the change in the scores in the experimental group and the control group after intervention were analysed using analysis of variance on a logistic regression model generated using a generalized estimating equations. The association levels between variables were analysed using univariate models, temporal and group adjusted models and multivariate logistic regression models.

CHAPTER 4

4. RESULTS

4.1 Introduction

In this chapter the results of the data collected as well as the outcomes of the intervention will be presented and analysed according to the study objectives. The aim of the study was to determine the effects of progressive resisted exercises (PRE) on performance oriented mobility and on health related quality of life in people with HIV/AIDS related distal symmetrical poly-neuropathy (DSP). The first objective in the study sought to determine the effects of PRE on the aspect of gait in participants with HIV/AIDS related DSP. The second objective was to determine the effects of PRE on balance in the above same participants. The third objective sought to determine how PRE affect the pain levels in the said participants. The fourth objective was to establish if there is a relationship between the levels of performance-oriented mobility and health related quality of life in participants with HIV/AIDS related DSP.

4.2 Pilot Study Results

In summary, the purpose of the pilot study was to establish the feasibility and intra-rater reliability of the Performance Oriented Mobility Assessment (POMA) tool and that of the hand held dynamometer. It also sought to establish the usual method used to treat peripheral neuropathy in Zimbabwe. The POMA balance scores showed a high intra-rater reliability, Spearman rho (rho = 0.82, p= 0.03) while gait score was low, (rho = 0.37, p=0.42). Intra-rater reliability of the dynamometer was high for the quadriceps, hamstring and right gastrocnemius muscles with Pearson r of 0.7 to 0.96 and p= 0.07 to p=0.001. The pilot study showed that the usual treatment for peripheral neuropathy was advice given by doctor or nurse to exercise at home and medication for pain. The full results of the pilot study are reported in detail in Chapter Three under section 3.10.

4.3 Main study results

4.3.1 Introduction

The main study was conducted in two separate studies as Study 1 and Study 2. Study 1 was conducted during the period March to August 2010. This study was completed and experienced very high dropout rates of above 33% (n=16). Due to the high dropout rate the researcher undertook to repeat the study using the same methodology but located the study closer to the participants. Hence Study 2 sought to recruit a sample size of 120 participants calculated using a dropout rate of 45% and the same power at 90% (as described in Section 3.4.3) so as to take into account the high dropout experienced in Study 1. Study 2 was conducted during the period January to September of 2011.

The per protocol analysis is presented as Appendix G and Appendix H. The results using an intention to treat analysis approach will be presented under the following headings

i) Description of the study participants

ii) Baseline assessments results of main study.

iii) Post intervention results between the control group and the experimental group.

iv) Post intervention results within the control and within the experimental group.

v) Correlation and associations between the study variables.

vi) Reasons for non-compliance or withdrawal from study

4.3.2 Description of the study participants

Flow of participants

Figure 4.1 is a flow diagram of the participants through the combined Study 1 and Study 2 using the Consolidated Standards for Reporting Trials (CONSORT) template for flow diagrams recommended for reporting outcomes of trials (Moher et al 2010).

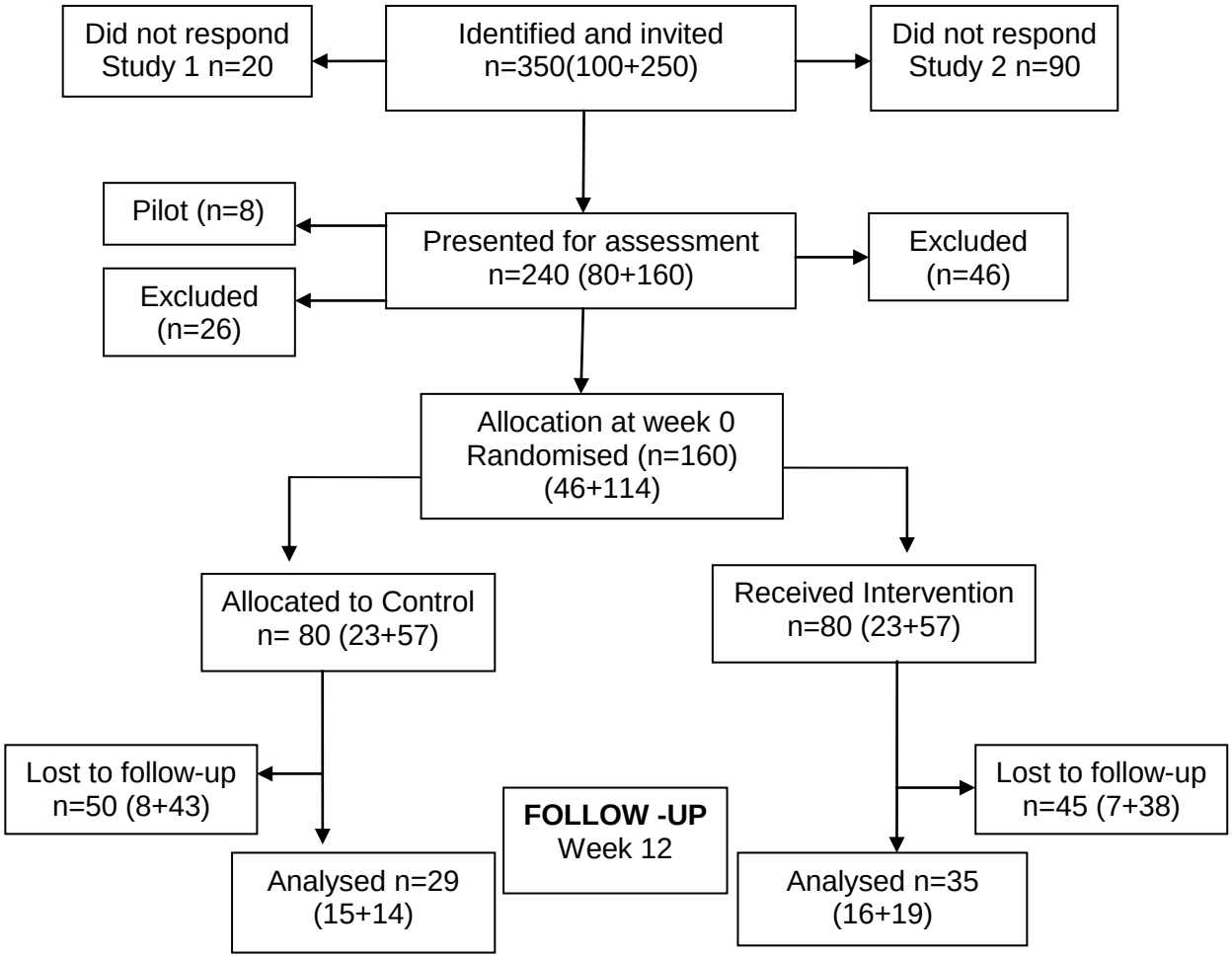


Figure 4.1 Flow of participants through the main study showing loss to follow-up (n =160)

Baseline assessments in Study 1 were carried out on 80 participants, eight were excluded from the study for being non-resident in Harare n=8, declined to participate n=6, diabetic n=3, period on ART less than six months n=6, were moving n=5, getting employed n=3 or were pregnant n=3. Therefore 46 participants were randomised for the Study 1, 23 in the control group and 23 in the experimental group. Reassessments were done on follow-up for thirty-one participants, 15 controls and 16 in the experimental group. Baseline assessments in Study 2 were carried out on a sample of one hundred and fourteen (114) participants at sites at the selected city of Harare clinics, over eleven weeks. Participants were excluded for not being residents of Harare n=16, declining to participate n=6, being diabetic n=4, less than six months

on ART n=12, planning to move n=1, being too ill and requiring hospitalisation n=1, getting employed n=2 and being pregnant n=4. Reassessments were done for 33 participants, 14 controls and 19 participants from the experimental group. Of the 114 participants who were randomised, 71% (n=81), were lost to follow up.

Demographic information of Study 1 and Study 2

The demographic characteristics of the participants in the study is described below in Table 4.1

Table 4.1 Demographic characteristics of the participants (n=160)

Characteristic	Control group (n=80) n (%)	Experimental group (n=80) n (%)
Gender		
Females	56 (70)	57 (71.3)
Males	24 (30)	23(28.7)
Marital status		
Single	11 (13.7)	11 (13.9)
Married	45 (56.3)	43 (54.4)
Divorced	6 (7.5)	3 (3.8)
Widowed	18 (22.5)	22 (27.9)
Age		
<30 years	6 (7.5)	5 (6.3)
31-40 years	29 (36.3)	30 (37.5)
41-50 years	30 (37.5)	32 (40)
>51 years	15 (18.7)	13 (16.2)
Occupation		
Unemployed	12 (15)	7 (8.8)
Self employed	33 (41.3)	32 (40)
Employed	35 (43.7)	41 (51.2)
Education (years)		
Nil	1 (1.2)	1 (1.2)
1-7 (primary)	22 (27.5)	21 (26.3)
8-11 (secondary)	53 (66.3)	57 (71.3)
12+ (tertiary)	4 (5)	1 (1.2)

The above results show that 55% (n=88) participants were married and female participants constituted 70.6% (n=113) of the total study sample.

HIV related information of the participants

Table 4.2 shows HIV related information of the participants in the main study.

Table 4.2 HIV related information of the participants (n=160)

HIV Information	Control group (n=80) n (%)	Experimental group (n=80) n (%)
Period after diagnosis		
6-12 months	47 (58.7)	45 (56.3)
13-24 months	6 (7.5)	8 (10)
25-36 months	6 (7.5)	7 (8.7)
>37 months	21 (26.3)	20 (25)
CD4+ count (cells per mm3)		
>100	27 (33.7)	16 (20)
101-200	18 (22.5)	24 (30)
201-300	11 (13.8)	7 (8.8)
301-400	4 (5)	5 (6.3)
>401	11 (13.7)	11 (13.7)
Missing values	9 (11.3)	17 (21.2)
Type of Antiretroviral Therapy		
Stalanev	59 (73.7)	59 (73.7)
Combivir/coviro	12 (15)	7 (8.8)
Zidolan	9 (11.3)	14 (16.5)
Period on Antiretroviral Therapy		
6-12 months	32 (40)	26 (32.5)
13-24 months	11 (13.7)	9 (11.3)
>25 months	37 (46.3)	45 (56.2)

The results above show that 70 % (n=112) had a CD4+ count of less than 300 cells per cubic mm. Combination antiretroviral therapy of Stavudine, Lamivudine and Nevirapine was used by 59% (n=94) of the participants.

Levels of peripheral neuropathy in the participants

The levels of peripheral neuropathy in the participants, using the subjective peripheral neuropathy screen (PNS) scores are shown in Table 4.3 below.

Table 4.3 Subjective peripheral neuropathy screen (PNS) scores in the participants (n=160)

PNS score	Control group (n=80) n (%)	Experimental group (n=80) n (%)
minor (1-3)	5 (6.3)	4 (5)
mild (4-7)	25 (31.3)	32 (40)
moderate (8-11)	43 (53.7)	30 (37.5)
severe (12-15)	7 (8.7)	14 (17.5)

The subjective peripheral neuropathy screen score show that 59% (n=94) of the participants had moderate to severe neuropathy. The results highlight the similarities in severity of neuropathy between the control and the experimental groups.

Numbness

During the assessments of peripheral neuropathy the signs and symptoms required further clarification. Participants reported having problems with numbness a symptom of peripheral neuropathy where participants did not have pain but could not feel their feet. Participants described not feeling their feet and losing their footwear and walking for a distance before realizing they had forgotten their footwear. Five of them were public vehicle drivers and related experiences associated with the loss of feeling in the feet. These drivers indicated that they had difficulty feeling the clutch and brake pedals during driving. One of participants was a haulage truck driver who occasionally had to rely on visual check when braking. Two of the participants were public commuter or taxi drivers. They reported that the numbness was worse as the day progressed and as they got tired. All of the participants walked over two

kilometers per day and they complained of fatigue as the day progressed. All the research assistants reported that during the exercise sessions participants would discuss their problems with pain and numbness while sharing ideas on how to manage these problems.

Comparison of participants' demographic and clinical characteristics between the control and experimental groups

Table 4.4 compares the demographic and clinical characteristics between the control and experimental groups.

Table 4.4 Comparison of the participants at baseline (n=160)

Characteristic	Control group (n=80) mean (SD)	Experimental group (n=80) mean (SD)	Mean Difference (SE)	p value	(95%) Confidence intervals
Age (yrs)	42.4 (8.5)	42.2 (8.0)	0 (1.3)	1.0	-2.6 – 2.6
Education (yrs)	9.3 (2.3)	9.1 (2.7)	0.25 (0.4)	0.5	-0.5 – 1.0
Period of diagnosis (months)	26.6 (30)	26.6 (23)	0 (4.2)	1.0	-8.4 – 8.4
CD4+ count (per mm3)	211.4 (193)	222.9 (198)	-11.5 (33.8)	0.7	-78.4 – 55.5
Peripheral neuropathy score	8.2 (2.8)	8.1 (2.9)	0.15 (0.5)	0.7	-0.7 – 1.1

The participants in the experimental group and the control group showed similarities in most characteristics tested for including: gender, age, education level, period of diagnosis and if on ARVs, CD4+ count and peripheral neuropathy scores with a ($p > 0.5$).

4.3.3 Results of baseline assessments

The baseline assessment results for muscle strength, gait, balance and health-related quality of life the participants in the study will be presented in Tables 4.5 – 4.7b.

Baseline muscle strength

A comparison of the muscle strength means between the control groups and the experimental group is presented in Table 4.5.

Table 4.5 Muscle strength means comparing the control groups and the experimental groups (n=160)

Muscles in kg of force	Control group (n=80) mean (SD)	Experimental group (n=80) mean (SD)	Difference mean (SE)	Confidence intervals (95%)	p value
Rt quadriceps	7.96 (4.6)	7.99 (3.6)	-0.03 (0.7)	(-1.3 – 1.2)	0.96
Lt quadriceps	7.25 (3.65)	7.55 (4.4)	-0.30 (0.6)	(-1.4 – 0.8)	0.60
Rt hamstrings	3.43 (1.5)	3.65 (2.0)	-0.23 (0.74)	(-0.8 – 0.3)	0.41
Lt hamstrings	3.49 (1.7)	3.54 (1.9)	-0.05 (0.3)	(-0.6 – 0.5)	0.87
Rt gastrocs	12.84 (2.0)	12.88 (5.3)	-0.58 (0.8)	(-2.1 – 1.0)	0.47
Lt gastrocs	12.11 (4.4)	12.26 (4.7)	-0.15 (0.7)	(-1.6 – 1.3)	0.84
Rt tib anterior	8.2 (3.5)	8.6 (4.3)	-0.39 (0.6)	(-1.6 – 0.8)	0.53
Lt tib anterior	7.71 (3.2)	7.95 (4.0)	-0.24 (0.6)	(-1.6 – 0.9)	0.68

Abbreviations: Rt = right, Lt = Left, gastrocs = gastrocnemius, tib = tibialis

The muscle strength profile showed that the hamstring generated the least mean force at 3.43 (1.5) kilograms of force in contrast to the right gastrocnemius muscles which exhibited the highest mean muscle strength at 12.8 (2.0) kilograms of force. Mean muscle strength of the control group were not statistically different to the mean muscle strength of experimental group at baseline, (p=0.41 – 0.96).

Gait, balance and pain baseline scores

The gait and balance scores at baseline assessed using the POMA reported in Table 4.6 below.

Table 4.6 Gait, and balance scores at baseline in the participants (n=160)

Score	Control group (n=80) mean (SD)	Experimental group (n=80) mean (SD)	Difference mean (SE)	(95% confidence interval)	p value
Gait	11.5 (1.0)	11.4 (0.9)	0.06 (0.2)	-0.23 – 0.36	0.68
Balance	14.4 (1.2)	14.3 (1.6)	0.05 (0.2)	-0.39 – 0.49	0.82
Total	25.7 (2.3)	25.8 (2.1)	0.04 (0.4)	-0.73 – 0.60	0.91

The mean difference in the gait score of 0.06 (p=0.68) and in the balance score of 0.05 (p=0.17) show there was no difference statistically between the two groups When pain was tested using Wilcoxon's rank sum test, the results showed similarity between the control group and the experimental group (p=0.96).

Health related quality of life levels at baseline

The health related quality of life levels at baseline assessed using the EQ-5D scores in the participants in the study are shown in Table 4.7a below.

Table 4.7a Health related quality of life (EQ-5D) scores at baseline in the participants (n=160)

Scores	Control group (n=80) mean (SD)	Experimental group (n=80) mean(SD)	Mean Difference (SE)	p value	(95% confidence interval)
EQ5D VAS	63.5 (15.1)	66.8 (14.5)	-3.30 (2.3)	0.16	-7.93 – 1.33
EQ5D utility	57.5 (29.9)	50.8 (30.9)	6.63 (4.8)	0.17	-2.86 – 16.1

The EQ-5D visual analogue score mean difference of -3.3 (SE 2.3) p=0.16 and the health related quality of life utility score mean difference of 6.6 (SE=4.8) p=0.17, showed similarity between the control group and the experimental group. Table 4.7b is a profile of the EQ-5D health related quality of life levels results showing the scores in the five domains at baseline for the participants.

Table 4.7b EQ-5D profile scores at baseline (n=160)

EQ5D scores	Control group (n=80) n (%)	Experimental group (n=80) n (%)
ED-5D mobility		
No problems	51 (63.7)	42 (52.5)
Some problems	29 (36.3)	36 (45)
Confined to bed	0	2 (2.5)
EQ-5D self-care		
No problems	71 (88.7)	74 (92.5)
Some problems	9 (11.3)	6 (7.5)
Unable	0	0
EQ-5D usual activity		
No problems	43 (53.7)	47 (57.8)
Some problems	29 (36.3)	19 (23.7)
Unable	8 (10)	14 (17.5)
EQ-5D pain or discomfort		
None	13 (16.3)	10 (12.5)
Moderate	56 (70)	51 (63.8)
Extreme	11 (13.7)	19 (23.7)
EQ-5D anxiety/depression		
None	32 (40)	40 (50)
Moderate	38 (47.5)	30 (37.5)
Extreme	10 (12.5)	10 (12.5)
EQ-5D state of health level		
Better	61 (76.2)	56 (70)
Much the same	10 (12.5)	16 (20)
Worse	9 (11.3)	8 (10)

The health related quality of life profile shows that 42% (n=67) of the participants had some problems with mobility and completion of usual activities. Self-care was a problem in 9 % (n=14) of the participants. The study showed that 20% (n=32) of the participants reported extreme pain. Participants perceived themselves to be in a better state of health, where state of health median score was one (1).

4.3.4 Post intervention results between the experimental group and the control group

Introduction

The results of the study were analysed to establish the effect of progressive resisted exercises on gait, balance and pain as outlined in the objectives. The analysis determined if there was a difference in the muscle strength change between the control and the experimental groups prior to establishing the effects of progressive resisted exercise.

Muscle strength difference between the control and experimental groups

The difference in mean muscle strength between the combined control group and experimental group post intervention is summarized in Table 4.8 below.

Table 4.8 Mean muscle strength difference between the control group and experimental group after intervention (n=160)

Muscle	F ratio	Standard error	(95% confidence interval)	p value
Right quadriceps	0.07	0.01	(0.00 – 0.02)	0.80
Left quadriceps	1.59	0.02	(0.00 – 0.04)	0.20
Right hamstrings	2.22	0.03	(0.00 – 0.06)	0.13
Left hamstrings	0.13	0.01	(0.00 – 0.02)	0.70
Right gastrocnemius	0.59	0.01	(0.00 – 0.02)	0.44
Left gastrocnemius	0.11	0.01	(0.00 – 0.02)	0.73
Right tibialis anterior	2.78	0.03	(0.00 – 0.08)	0.09
Left tibialis anterior	1.23	0.01	(0.00 – 0.03)	0.26

There was a trend towards a significant difference between the control and experimental group, p=0.09 in the right tibialis anterior muscles. There was no difference in the mean muscle strength change between the control group and the experimental group in the other muscles tested (p= 0.13 – 0.80).

Gait, balance, pain and quality of life differences between the control and experimental groups after intervention

Objectives 1, 2 and 3 of the study focus on the effects of progressive resisted exercises on gait, balance and pain. The differences in the gait, balance, pain and quality of life utility score between the control group and the experimental group after intervention are summarized in Table 4.9.

Table 4.9 Difference in the gait, balance, pain and quality of life (QOL) utility scores and state of health between the control group and the experimental group post intervention (n=160)

Variable	F ratio	Standard error	(95% confidence interval)	p value
Balance	0.00	0.01	(0.00 – 0.02)	0.95
Gait	0.01	0.01	(0.00 – 0.02)	0.94
Pain	2.36	0.03	(0.00 – 0.06)	0.13
QOL Utility score	0.07	0.01	(0.00 – 0.02)	0.79
QOL State of health	4.24	0.05	(0.00 – 0.12)	0.04

There was no difference in the changes in the gait scores of the POMA between the experimental and control groups p=0.94. The change in the balance scores of the POMA between the experimental and control group after the intervention were similar p=0.95. There was a trend towards significance in the pain score change between the control group and the experimental group p=0.13. The health related quality of life changes in the experimental group and control groups after the intervention measured using the utility score showed no differences between the groups p=0.79. However the health related quality of life changes in the experimental group and control groups after the intervention measured using the state of health showed there was a difference between the groups p=0.04.

Within group changes for these same variables were analysed using paired t-tests and Wilcoxon's rank sum test and the results are outlined next.

4.3.5 Within group results pre and post intervention (experimental group and the control group)

Introduction

This section of the results presents the change in the muscle strength, gait, balance and pain within the control group and the experimental group.

Muscle strength change within the control group

The mean muscle strength changes within the control group are shown in Table 4.10 below.

Table 4.10 Mean muscle strength change in the control group (n=80)

Muscle	Mean muscle strength change	95% (confidence interval)	Standard Error	p value
Right quadriceps	0.8	0.17 – 1.43	0.31	0.01
Left quadriceps	1.0	0.29 – 1.71	0.35	0.006
Right hamstrings	0.95	0.52 – 1.38	0.25	0.0001
Left hamstrings	0.8	0.41 – 1.20	0.20	0.0001
Right gastrocnemius	1.75	0.90 – 2.60	0.43	0.0001
Left gastrocnemius	1.36	0.57 – 2.16	0.40	0.001
Right tibialis anterior	1.18	0.45 – 1.89	0.36	0.002
Left tibialis anterior	1.14	0.45 – 1.83	0.35	0.002

The mean muscle strength changes within the control group were significant ranging from p=0.0001 to p=0.01. The highest mean difference occurred in the right gastrocnemius muscle =1.75 kg (95% CI 0.90 – 2.60). The least mean difference of 0.8 kg (CI = 0.41 – 1.2) occurred in the left hamstring muscle and right quadriceps muscle.

Muscle strength change within the experimental group

The mean muscle strength changes within the experimental group are shown in Table 4.11 below.

Table 4.11 Mean muscle strength change within the experimental group

Muscle	Mean muscle strength change	Standard Error	p value	(95% confidence interval)
Right quadriceps	1.75	0.35	< 0.0001	1.05 – 2.45
Left quadriceps	2.16	0.35	< 0.0001	1.47 – 2.86
Right hamstrings	1.39	0.23	< 0.0001	0.94 – 1.83
Left hamstrings	0.93	0.21	< 0.0001	0.51 – 1.34
Right gastrocnemius	2.25	0.51	< 0.0001	1.23 – 3.27
Left gastrocnemius	2.00	0.48	0.0001	1.04 – 2.96
Right tibialis anterior	2.39	0.47	< 0.0001	1.48 – 3.30
Left tibialis anterior	1.78	0.42	0.0001	0.93 – 2.61

The mean muscle strength changes within the experimental group were significant ranging from $p<0.0001$ to $p=0.0001$. The highest change in muscle strength occurred in the right tibialis anterior muscle with 2.39 kg (95% CI 1.48 – 3.30) and the least change occurred in the left hamstrings, 0.93 kg (95% CI 0.51 – 1.34).

Gait, balance and pain changes within the groups

The level of changes in the gait, balance and pain scores of the performance oriented mobility scores within the experimental groups and the control groups are summarised in Table 4.12 below.

Table 4.12 The POMA gait score change within the control group and within the experimental group

Study Group (n=80)	Mean gait score change	Standard Error	(95% confidence interval)	p value
Control group	0.36	0.14	-0.27 – 0.34	0.81
Experimental group	0.25	0.17	-0.1 – 0.6	0.16

There was no difference in the change in the gait scores for both the experimental and the control groups $p=0.16$ and $p=0.81$ respectively.

Table 4.13 The POMA balance score change within the control group and within the experimental group

Study Group (n=80)	Mean balance score change	Standard Error	(95% confidence interval)	p value
Control group	0.8	0.25	0.3 – 1.3	0.003
Experimental group	0.48	0.21	0.6 – 0.9	0.03

Both the control group and the experimental group had a significant difference in the balance score change p=0.003 and p=0.03 respectively.

Table 4.14 The POMA total score change within the control group and within the experimental group

Study Group (n=80)	Mean POMA Total score change	Standard Error	(95% confidence interval)	p value
Control group	0.78	0.36	0.03 – 1.54	0.003
Experimental group	0.55	0.27	-0001 – 1.1	0.05

Both the control group and the experimental group had a significant difference in the balance score change p=0.003 and p=0.05 respectively.

Table 4.15 Level of changes in the gait, balance and pain scores of the performance oriented mobility scores within the experimental groups and the control groups

Variable	Control group (n=80)		Experimental group (n=80)	
	z-score	p-value	z-score	p-value
Pain	1.97	0.05	3.20	0.001

There was a significant change in the pain scores for both the experimental and the control groups p=0.001 and p=0.05 respectively.

Health-related quality of life

Table 4.16 below, shows the quality of life utility score change within the control group and experimental group.

Table 4.16 Quality of life utility score change within the control group and utility score change within the experimental group

Study Group (n=80)	Quality of life utility score change	Standard Error	(95% confidence interval)	p value
Control group	-11.7	7.5	-27 – 0.36	0.13
Experimental group	11.3	3.07	-0.60 – 11.60	0.08

The change in the quality of life utility scores of 11.3 for the experimental group trended to be significant p=0.08 while the control group's quality of life utility scores of -11.7 did not show significant change p=0.13.

4.3.6 The relationships between the gait, balance, pain and quality of life in the study

Introduction

The fourth objective sought to establish if there was a relationship between the levels of performance-oriented mobility and health related quality of life in participants with HIV/AIDS related DSP will be reported in this section.

Relationship of gait, quality of life, level of neuropathy and muscle strength

The relationship between gait and health related quality of life is presented below. Gait also has relationships with the level of neuropathy and muscle strength of the right tibialis muscle as presented in Table 4.17a and Table 4.17b below.

Table 4.17a Univariate model showing the relationship between gait and quality of life, level of neuropathy and strength of the right tibialis muscle (n=160)

Variable	Odds ratio	95% confidence interval	z score	p value
Right tibialis anterior muscle strength	1.30	1.10 – 1.58	2.95	0.003
Quality of life	1.01	1.00 – 1.04	1.94	0.05
Level of neuropathy	0.76	0.61 – 0.96	-2.31	0.02

Table 4.17b Time and group adjusted model showing the relationship between gait and quality of life, level of neuropathy and muscle strength of the right tibialis muscle (n=160).

Variable	Odds ratio	95% confidence interval	z score	p value
Right tibialis anterior muscle strength	1.29	1.11 – 1.63	2.97	0.003
Quality of life	1.01	1.00 – 1.04	0.99	0.05
Level of neuropathy	0.76	0.61 – 0.95	-2.38	0.02

The results of the models depicted in Table 4.17a and Table 4.17b demonstrate a strong positive relationship between the changes in gait and health related quality of life, odds ratio 1.01, p=0.05. There is also a strong positive relationship between gait and muscle strength of the right tibialis anterior muscle, odds ratio 1.29, p=0.003. The change in the level of neuropathy is moderately related to the change in gait scores, odds ratio 0.76, p=0.02.

Table 4.18c Multivariate model showing the relationship between gait and level of neuropathy and strength of the right tibialis muscle (n=160).

Variable	Odds ratio	95% confidence interval	z score	p value
Right tibialis anterior muscle strength	1.31	1.07 – 1.61	2.66	0.008

The time and group adjusted model results are similar to the results of multivariate model above. Gait is strongly positively related to the muscle strength of the right tiabialis muscle, odds ratio 1.31, p=0.008.

Balance and quality of life relationship

The correlation between balance and the level of pain, and muscle strength of the right and left hamstring muscle and quality of life are described in Table 4.19a and Table 4.19b.

Table 4.19a Univariate model showing the correlation between balance and the level of pain, and muscle strength of the right and left hamstring muscle and quality of life (n=160).

Variable	Odds ratio	95% confidence interval	z score	p value
Right hamstring muscle strength	1.19	1.00 – 1.42	1.95	0.05
Left hamstring muscle strength	1.19	0.99 – 1.44	1.86	0.06
Level of pain	0.62	0.46 – 0.83	-3.17	0.001
Quality of life	0.68	0.52 – 0.93	2.76	0.06

Results show that there was a trend towards significance in the association between balance and quality of life odds ratio 0.68, p=0.06. There was significant positive relationship between the level of balance and the level of pain, odds ratio 0.62, p=0.001, muscle strength of the right hamstring muscle odds ratio 1.19, p=0.05 and a trend towards significance in the muscle strength of the left hamstring muscle, odds ratio=1.19, p=0.06.

Table 4.19b Adjusted model showing the relation between balance and level of pain (n=160)

Variable	Odds ratio	95% confidence interval	z score	p value
Level of pain	0.64	0.47 – 0.87	-2.84	0.005

There was significant correlation between the change in balance and the level of pain, odds ratio 0.64 p=0.005 as depicted by the group and time adjusted model. The multivariate model showed a significant positive relationship between balance and the level of pain, odds ratio 0.64 p=0.01.

Pain, quality of life and other relationships

The relationship between pain and the quality of life and the level of neuropathy is shown in Table 4.20a and Table 4.20b.

Table 4.20a Univariate model showing the correlation between pain and the quality of life, level of neuropathy (n=160).

Variable	Odds ratio	95% confidence interval	z score	p value
Quality of life	0.98	0.98 – 0.99	4.35	<0.0001
Level of neuropathy	1.21	1.08 – 1.36	3.36	0.001

The relationship between pain and the quality of life was significant odds ratio=0.98, p= 0.005. The results also show that pain was significantly related to the level of peripheral neuropathy, odds ratio=1.21, p=0.001.

Table 4.20b Multivariate model showing the relationship between pain and the quality of life, and the level of neuropathy (n=160).

Variable	Odds ratio	95% confidence interval	z score	p value
Quality of life	0.98	0.97 – 0.99	-4.03	<0.0001
Level of neuropathy	1.17	1.04 - 1.31	2.71	0.007
Time	0.45	0.22 – 0.92	-2.19	0.03
Experimental group	0.50	0.26 – 0.96	-2.07	0.04

The relationship between pain and the quality of life was significant, odds ratio 0.98, (p<0.0001), time, odds ratio 0.45, p=0.03, exercise group, odds ratio 0.50, p=0.04 and the level of neuropathy was also significant, odds ratio 1.17, p= 0.007 for both the adjusted and the multivariate model.

Health related quality of life relationships with other variables.

The relationship between the quality of life and pain, the level of neuropathy, level of education level of health, muscle strength of the left quadriceps muscles is shown in Table 4.21a Table 4.21b below.

Table 4.21a Univariate model showing the relationship between the quality of life and pain, level of neuropathy, level of health and muscle strength of the left quadriceps muscles (n=160).

Variable	Odds ratio	95% confidence interval	z score	p value
Muscle strength left quadriceps	1.06	0.99 – 1.14	1.79	0.07
Pain score	0.62	0.49 – 0.77	-4.18	<0.0001
Level of health	0.45	0.29 – 0.69	-3.58	<0.0001
Level of neuropathy	0.91	0.82 – 1.01	-1.81	0.07

There were significant relationships between quality of life and pain, odds ratio 0.62, p<0.0001 and the level of health, odds ratio 0.45, p<0.0001. There was a trend towards significance in relationships between quality of life and the level of neuropathy, odds ratio 0.91, p=0.07 and muscle strength of the left quadriceps muscles, odds ratio 1.06, p=0.07.

Table 4.21b Multivariate model showing the relationship between the quality of life, level of health and pain (n=160).

Variable	Odds ratio	95% confidence interval	z score	p value
Level of health	0.50	0.31 – 0.80	-3.86	<0.0001
Pain	0.68	0.53 – 0.87	3.04	<0.0001

The relation between quality of life and pain was significant, odds ratio 0.68 p=<0.0001, as with the level of health, odds ratio 0.50 p=0.004 and muscle strength of the left quadriceps muscles, odds ratio 1.06, p=0.05 in the temporal and group adjusted. The relation between quality of life and pain was significant, odds ratio 0.68 p<0.0001, and with the level of health, odds ratio 0.50 p<0.0001 in the multivariate model.

Relationship structural equation model

The relationships between health-related quality of life and balance, pain, gait, time and level of neuropathy are presented in Figure 4.2. These relationships were generated from structural equation models using Stata v12 and are illustrated by lines of which indicate the p values association between the different related variables.

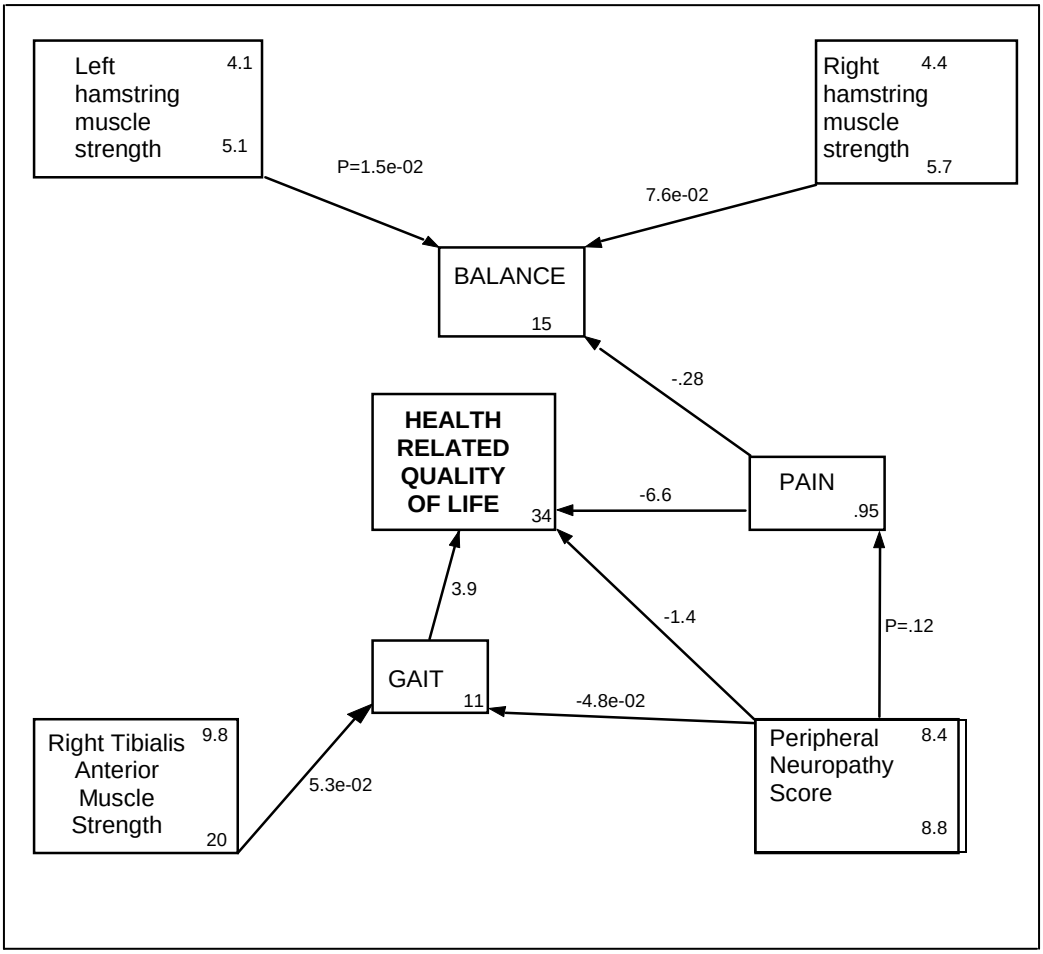


Figure 4.2: The relationships between health-related quality of life and time, gait, pain, balance and level of neuropathy

The structural equation model also shows associations between health-related quality of life and pain, gait and peripheral neuropathy. Pain is associated with quality of life, balance and peripheral neuropathy. This model demonstrates the relationship between the right tibialis anterior muscle and gait as well as the association between balance and the right and left hamstring muscles.

4.3.7 Results of the interviews on participants reasons for withdrawal and non-compliance.

Following a 33% (n=) dropout in study 1 and a 71% (n=) dropout in study 2 (average 60%) and non-compliance participants had failed to attend follow-up assessment sessions or failing to attend their exercise sessions were invited to give their reasons. A total of 20 participants responded to an open ended question.
The reasons given by the participants for withdrawal from the study or non-compliance are listed below in table 4.22.

Table 4.22 Reasons given by participants for withdrawal from study or non-compliance (n=20).

Concept	Specific reasons
Transportation	- Had difficulties getting to the site - Could not afford taxi fare - Can only walk short distances of less than two kilometers - Average taxi fare five rand
Expected incentives	- Had been involved in another study before which provided food and goodies. - This study did not provide goodies/food = no reason for attending. - ‘‘These researchers have lots of money they are making money using us.’ - What do I benefit by being in this study?
Livelihood pressures	- They were trying to earn a living in a very tough economic time - I would rather be at my vegetable and fruit stall making money.’ - They were busy with living chores, cooking, laundry and tending to the family, e.g. the widowed or separated women.
Greater expectations of study	- The equipment being used in this study was not new so there was nothing to “expect” from study. - Had seen what was being done at the exercise sessions and continued doing so at home.
Mistrust	- There have been few cases of unethical research and some participants felt they were being used “again”.
Stigma	- Afraid to be seen in the group as other people would know their status and stigmatise them in the community.

Participants withdrew commonly for transportation expected incentives livelihood pressures greater expectations of study mistrust stigma socio-economic reasons. Stigma was also a threat to participants because a few clinics still had “special days” for ART medication collection, while some clinics have integrated the ART medication as any other chronic condition, like diabetes mellitus.

4.4 Conclusion

Baseline assessments were carried out on a sample of 160 participants sourced from family care clinics in Harare and randomized for the clinical trial with 80 in the control group and 80 in the experimental group for intervention using PRE. After the twelve weeks, reassessments were done for 63 participants, 14 controls and 19 participants from the experimental group with 60% (n=97) of the participants lost to follow up.

While the participants’ demographic results highlight similarities in the control and experimental groups, female participants constituted 70.6% (n=113) of the sample. The results show that 70 % (n=112) had a CD4+ count of less than 300 cells per cubic mm and the combination antiretroviral therapy of stavudine, lamivudine and nevirapine was used by 59% (n=94) of the participants. The subjective peripheral neuropathy screen score show that 59% (n=94) of the participants had moderate to severe neuropathy. The participants in the experimental group and the control group showed similarities in most characteristics tested for including: age, education level, period of diagnosis and on ARVs, CD4+ count and the peripheral neuropathy scores with a p value range of 0.5 -1.0.

The muscle strength profile showed that the hamstring generated the least mean force at 3.43 (1.5) kilograms of force in contrast to the right gastrocnemius muscles which exhibited the highest mean muscle strength at 12.8 (2.0) kilograms of force. The baseline mean muscle strength of the control group was similar to the baseline mean muscle strength of experimental group, p value range of p=0.41 to p=0.96. The gait score mean difference was 0.06, p=0.68 and the balance score mean difference of 0.05 p=0.17, showed similarity between the control group and the experimental group. The pain scores show similarity between the control group and experimental group at baseline, p=0.96. The EQ-5D visual analogue score mean difference of -3.3

p=0.16 and the health related quality of life utility score mean difference of 6.6 p=0.17, showed similarity between the control and the experimental groups.

The results of the study were analysed to establish the effect of progressive resisted exercises on muscle strength, gait, balance and pain as outlined in the objectives. There was a trend towards a significant difference between the control and experimental group, p=0.09 in the right tibialis anterior muscles. There was no difference in the mean muscle strength change between the control group and the experimental group in the other muscles tested p value range 0.13 – 0.80. There was no difference in the changes in the gait scores of the performance oriented mobility assessments between the experimental and control groups p=0.94. The change in the balance scores of the performance oriented mobility between the experimental and control group after the intervention were similar p=0.95. There was no difference in the pain score change between the control group and the experimental group p=0.13. The health related quality of life changes in the experimental group and control groups after the intervention measured using the utility score showed no differences between the groups p=0.79. However the health related quality of life changes in the experimental group and control groups after the intervention measured using the visual analogue score showed a difference between the groups where p=0.04.

Relationship results will be presented as odds ratios with the 95% confidence interval shown in brackets. The results demonstrate a significant relationship between the changes in gait and health related quality of life, odds ratio 1.01 (1.00 – 1.04). There is also an association between gait and muscle strength of the right tibialis anterior muscle, odds ratio 1.31 (1.07 – 1.61). The change in the level of neuropathy is also related to the change in gait scores, odds ratio 0.76 (0.61 – 0.95). There was significant relationship between the level of balance and the level of pain, odds ratio 0.64 (0.46 – 0.83), muscle strength of the right hamstring muscle, odds ratio 1.19 (0.99 – 1.44), muscle strength of the left hamstring muscle, odds ratio 1.19 (1.00 – 1.42). There was relationship between balance and quality of life was significant, odds ratio 0.68, (95%CI 0.52 – 0.93). The relationship between pain and time, odds ratio 0.45 (0.22 -0.92) and exercise group was significant, odds ratio 0.50 (0.26 – 0.96) using both the univariate model and the time and group adjusted model. Pain was significantly related with the level of peripheral neuropathy, odds ratio 1.17 (1.04 – 1.13). There were significant relationships between quality of life and pain, odds

ratio 0.98 (0.97 – 0.99), the level of neuropathy, odds ratio 0.91 (0.82 – 1.01) with some adjustments using the different models.

CHAPTER 5

5. DISCUSSION

5.1 Introduction

Chapter 5 will discuss the results of the data collected and the outcomes of the intervention based on the research question, the objectives of the study and the hypothesis. Therefore the aim of this study was to determine the effects of progressive resisted exercises on performance oriented mobility and on health related quality of life in patients with HIV/AIDS related distal symmetrical poly-neuropathy (DSP) and the specific objectives of the study included:

1. Determine the effects of progressive resisted exercises on gait in participants with HIV/AIDS related DSP.
2. Determine the effects of progressive resisted exercises on balance in participants with HIV/AIDS related DSP
3. Determine the effects of progressive resisted exercises on pain levels in participants.
4. Establish if there is a relationship between the level of performance-oriented mobility and health related quality of life in participants with HIV/AIDS related DSP.

5.2 Discussion of results

While the research hypothesis stated that progressive resisted exercises (PRE) have positive effects on performance oriented mobility and health related quality of life in participants with HIV/AIDS related distal symmetrical poly-neuropathy, the null hypothesis stated that PRE have no effect on performance oriented mobility (POMA) and health related quality of life in subjects with HIV/AIDS related distal symmetrical poly-neuropathy. POMA was used to assess gait and balance on a sample of 160 participants and their characteristics are discussed here. With a seventy percent 70.6% (n=113) female composition, this study was similar to Mutimura, et al., (2008)'s and Jelsma, et al., (2005)'s studies which had high female compositions of 68% and 74.5% respectively. On the other hand these percentages differed from

earlier studies reviewed by O'Brien, et al., (2008) in which women comprised less than 30% (n= 87) of the participants. However in studies done by Dolan, et al., (2003) and Agin, et al., (2001), purposeful targeting of women participants only was practiced to fulfill the aims of these studies. The participants in this study were educated to a high school exit level (which is Ordinary Level in Zimbabwe) comparable to Basta, Reece and Wilson (2008)'s study. Composition of this study also shows an equal proportion of formally employed, not employed and self-employed participants (33% each, n=53). Objectives one and two will be discussed first as they assessed the first two elements.

Progressive resisted exercises effect on the elements in POMA and HRQOL

Although POMA includes balance and gait, muscle strength and pain were also assessed as they are closely linked to the outcomes of POMA and the effects of progressive resisted exercises. Progressive resisted exercises on, gait and balance scored using the POMA did not show differences in effect between the intervention and the control group (CI 0.00-0.02 p = 0.8). Similarly there were no differences of effect for muscle strength (CI 0.00-0.08) p=0.13-0.8) and pain (CI 0.0-0.06 p>0.13). However the effect on quality of life changes were significantly different between the two groups (CI 0.00-0.12 p= 0.04). While PRE has been tested for its effects on muscle strength, gait, balance, pain and quality of life in studies outlined in a recent Cochrane review (O'Brien et al., 2008), no single study testing these variables in combination was found. Similarly no study was found that tested for mobility using the POMA in people living with HIV/AIDS (PLWHA). The results cannot therefore be compared as a unit (POMA) with other studies. Nevertheless, the literature was examined and studies that tested the individual variables were reviewed and will be discussed under each single variable namely muscle strength, gait, balance, pain and quality of life.

The literature was therefore examined for studies in HIV that used PRE as an intervention. ACSM (2011), in a review of studies, found that PRE has positive effects on muscle strength, balance and quality of life in healthy adults ACSM (2011). This is consistent with the findings by O'Brien, et al., (2008), where the studies reviewed reveal that PRE is similarly effective in improving muscle strength, balance and quality of life in people living with HIV/AIDS (PLWHA). However these studies had small samples sizes, and were of predominantly male constituted, and did not

include quality of life in their outcomes. A small number of the studies reviewed by O'Brien, et al., (2008) analysed the data using an intention to treat analysis approach. One of these studies done by Bhasin, et al., (2000), in which male participants only were used had four groups. PRE only was compared with PRE augmented with testosterone, testosterone only and a control group. They found that PRE was effective in improving muscle strength and quality of life without the need for augmentation with testosterone. This concurs with the findings by Agin, et al., (2001)'s study that tested PRE on a women only sample in PLWHA and compared PRE and PRE with whey protein supplements. The study by Agin, et al., (2001) found that PRE improved muscle strength and quality of life in a similar manner as when supplemented with protein. These studies both looked at the effects of PRE on other variables including immunological and virological indices. In a different approach, Fillipas et al., (2006) combined supervised PRE and aerobic exercises over six months and compared this intervention to an unsupervised walking program for PLWHA. They found that there was an improved quality of life and cardiovascular fitness but did not look at muscle strength as a variable. If muscle is loaded as opposed to aerobic training it will adapt to the load and type of training by hypertrophying through increased protein synthesis (Dungeon, et al., 2004). In addition the muscle function (e.g. contraction speed and endurance), mediated by neural factors, will improve. PRE utilizes anaerobic ways of Adenosine Tri-phosphate formation where lactic acid is one of the end products (Dungeon, et al., 2004). On the other hand Dolan, et al., (2006) also used a women only sample to show that when combined with aerobic exercise PRE was effective in improving muscle strength and the body composition (Dolan, et al., (2006) .

No literature could be found that looked at the effects of PRE on peripheral neuropathy in PLWHA. On the other hand, available literature relating to the effects of exercise on peripheral neuropathy focuses on people with diabetic DSP, which is similar to DSP in PLWHA, (Richardson, Sandman and Vela 2001). In their study, Richardson Sandman and Vela (2001) carried out a muscle strengthening program specifically targeting muscles on the lower limb over three weeks using a sample of twenty participants and found that exercise had a positive effect on muscle strength and balance. Furthermore, Hess and Walcott (2005) showed that PRE increases strength and improves balance in 27 elderly men and women after carrying out a high intensity PRE program over ten weeks. While these effects are not questionable even in healthy people (ASCM 2011), Richardson, Sandman and Velas (2001) study

was a controlled pre and post intervention study that used only 10 participants per group over three weeks. Therefore it can be considered to have a small sample size with a short follow up period and the study would need to be repeated with a randomized control trial and sample size calculated in order to be credible for effect of treatment. Another interesting difference with Richardson, Sandman and Velas (2001)'s study is that they deviated from the recommended protocol for PRE implementation (ASCM 2011) by doing PRE daily as opposed to three time weekly. Hess and Walcott (2005) conducted a study in with a sample size of 27 over a longer period of ten weeks and found that PRE had an effect on balance in the elderly population. However their sample size still remains relatively low though larger than Richardson, Sandman and Vela (2001)'s study.

In spite of calculating a sample size of 34 participants per group and repeating the study to try and obtain the appropriate sample size this study still experienced very high dropout rates and non-compliance. Possible reasons for this outcome include the factors involved in the methodological approach to the study and contextual factors. The contextual factors were explored by following up patients who dropped out and were non-compliant and conducting focus groups discussion to explore the reasons for dropping out. Newly qualified therapists, who were engaged as research assistants to conduct the exercise intervention were trained by the researcher to ensure uniformity of implementation approach. However as a safety precaution to ensure patients were not over exerted, the research assistants were given the autonomy to adapt the exercise program according to the principles of exercise therapy prescription after evaluating the participant's condition and ability to complete each session they attended.

This study, one of the first to use PRE in addressing the physical and HRQOL effects of DSP in PLWHA, experienced a high loss to follow-up rate of 53% (n=85) on average. This is higher than similar studies in a Cochrane review by O'Brien, et al., (2008). These studies showed high loss to follow up of between three to 35% (n=60). Some of the reasons attributed to a high dropout rate in this study and non-compliance were related to socio-economic difficulties, problems with transportation, expectation of incentives and greater expectations of study, livelihood pressures, mistrust and stigma. Some of the factors reported by the patient group related to pressures that affected the PLWHA lifestyle and health beliefs. This is consistent with findings by Petrozsci, et al., (2010) who found that the perception of well-being,

lifestyle and cultural beliefs are major contributors to compliance in studies. In comparison O'Brien, et al., (2008), reported similar reasons such as, employment, illness, relocation, loss of interest, transportation difficulties, personal issues, lack of motivation, lack of time, economic reasons. Part of the reason for enhanced socioeconomic difficulties in this study is that it was implemented during the period 2010 to 2011 when the country from which the participants of this study are habitant was going through a recovery period after the economic meltdown of 2006 -2009, unprecedented in history (Ministry of Health and Child Welfare (MoH&CW) 2009). Most of the population was unemployed with rates quoted at 80% (MoH&CW 2009) and most people reporting inability to eat more than one meal a day.

Methodological issues that may have contributed to the reduced effect on the experimental group is that in this study, the researcher decided to conduct two exercise sessions in view of the economic capacity and the participant's potential to exercise. While the studies reviewed by O'Brien, et al., (2008) used a regimen of three sessions per week, using the twice per week regimen is acceptable as stipulated by the ACSM (2011) position paper. Fillipas, et al., (2006), in a study with PLWHA used the twice weekly regimen over a period of six months and found that the regimen was equally effective for the purpose of muscle strengthening.

While the results comparing the control and intervention groups did not show any differences, further analysis to establish within group changes and association between the muscle strength, pain, gait and HRQOL showed significant effects of PRE and significant association between the variables as shown in the structural equation model in figure 4.2. found similar results in, in group analysis when they tested for the effect of PRE on gait, balance and pain in participants with DSP (Ites, et al., 2011). As such the results of the individual variables pre-intervention, within group and their associations will be discussed.

Muscle strength

When the study participants' mean muscle strength was tested for differences between the control group and the experimental group there was a trend towards significance, $p=0.09$ in the right tibialis anterior and right hamstring muscle muscles as summarized in Table 4.8. However the differences in the experimental and control group in the other muscles tested was not significant $p > 0.13$. Meanwhile the

baseline muscle strengths values in this study were lower than the normative values (Bohannon 1997) and in other studies reviewed by (O'Brien, et al., 2008). Moreover the results from five out of the seven of the studies reviewed by O'Brien, et al., (2008) which had used isotonic muscle strength testing, yielded high muscle strength values. O'Brien, et al., (2008) attributes low values in muscle strength to the use of isometric testing, which was also done in this study. Even though this study used isometric muscle strength testing, moderate muscle strength levels were still observed in the participants when compared to the reference normative values for extremity muscle strength dynamometry in a healthy population in a developed country (Bohannon, 1997). Similarly, Dolan, et al., (2006) whose study focussed on female participants only showed higher muscle strength levels for the quadriceps and the hamstring muscles than in this study.

Interestingly, at baseline, the left hamstring muscles generated the least mean force at 3.43 (SD 1.5) kilograms of force in contrast to the right gastrocnemius muscles which exhibited the highest mean muscle strength at 12.8 (SD 2.0) kilograms of force. Participants therefore exhibited weaker proximal muscles as shown by the hamstring values of 3.43 kilograms of force. The leg muscles had better strength with the calf muscles being the strongest. Proximal muscle weakness which was also reported in Myezwa, et al., (2009)'s study done in PLWHA in a mining and inpatient community is different from the findings in Bohannon's (1997)'s for normative values, Hess and Woollacott (2005)'s elderly participants and from O'Brien, et al., (2008)'s review where the proximal muscle showed greater strength. Furthermore, participants who had problems with proximal weakness especially in the hamstring muscle in this study had low balance scores as shown by the association between left and right hamstring muscle strength scores and balance.

Hess and Woollacott (2005) in a study on an elderly participants sample argued that the effectiveness of PRE on muscle strengthening may need to be augmented by nutritional supplementation. However findings in studies with PLWHA appear to contradict this generalisation, as shown by Agin, et al., (2001) where the use of whey protein in female participants to augment exercise brought no added benefits to the participants Agin, et al., (2001). While the possible reason for the similarity between the groups may be that participants in the experimental group exhibited poor adherence to exercise, the effects of PRE on muscle strength are clear in the within group results. Although muscle strength results had not shown an effect difference

between the control and experimental group, within group analysis comparing the pre and post intervention muscle strength showed a significant difference ($p<0.01$.) and ($p<0.0001$) in the control and experimental groups respectively. However one cannot also ignore that all these participants were walking long distances as a mode of transport and consistent walking is recorded in the literature as an effective intervention for general muscle increase and fitness (ACSM, 2011). These results support the hypothesis that PRE, as an exercise program has an effect on muscle strength, as reported in other studies reviewed by O'Brien, et al., (2008). Further analysis also showed a significant association between the muscle strength increase of both the left and right hamstring muscle with balance ($p=0.05$) in both experimental and control groups.

Balance

As already stated in the introduction, change in the balance scores of the performance oriented mobility showed that there was no difference between the experimental and control group after the intervention $p=0.95$. There was however, significant change in balance within the control group ($p=0.002$) and the experimental group ($p=0.04$) which suggests that the usual method and the progressive resisted exercises had a similar effect on balance. All the participants in the study were mobile, where none of them used a walking aid.

The usual method was further augmented as noted before by the long distances that patients were walking (an average of one and half kilometres per day per patient). Most patients could not afford transport costs and thus had to walk. Walking has been reported in the literature as a potentially effective intervention to improve strength, endurance and cardiovascular fitness (ACSM, 2011).

As discussed previously PRE are closely related with increased and balanced muscle strength contributing to maintenance of posture (Zagyapan et al 2011). Related to balance and muscle strength is mobility. In this study, mobility, assessed using POMA was good to excellent (mean score = 25.7(SD=2.3)) as shown in Table 4.6 for all the participants. Literature searches for studies in HIV and peripheral neuropathy which had used the POMA to assess gait and balance in participants with peripheral neuropathy did not yield comparable results. Hess and Walcott (2005) found that an increased muscle strength score improved the balance in the elderly

sample. However Hess and Walcott (2005) used the Berg Balance Scale as their outcome measure for balance instead of the POMA which limits comparability with this study.

Studies found in literature used the POMA as a predictor of the risk of falling in the elderly (Tinnetti 1986, 1988; Lin, et al., 2004; Baloh, et al., 2006; Faber et al 2007; Panzer, et al., 2011). However, other studies were done to determine the reliability and validity of the POMA against the tools considered gold standards when the POMA was used for different neurological conditions. Kegelmeyer, et al., (2007) used the POMA to assess the risk of falls as well as the reliability and the validity of the POMA in participants with Parkinson's disease. Similarly, Kloos, et al., (2010) carried out a study to also assess the responsiveness of the POMA in participants with Huntington's chorea. These studies while assessing gait and balance, differed with this study as the cause of both Parkinson's disease and Huntington's chorea are impairments to central nervous system level whereas this study looked at impairments to the peripheral nervous system. However these studies experience of using the POMA shows that it is a valid and reliable measure of the factors influencing the quality of gait and balance which can be impaired in peripheral neuropathy and therefore it would be the appropriate tool to use.

Considering that the function of the hamstring muscle is mainly to prevent forward sway, an important facet of balance (Hess and Woollacott 2005), it would have been expected that the low strength values found in the hamstring would have also translated into low balance scores. However the results only showed a mild change in the balance scores obtained using the POMA of 14 out of a possible 16 on average to 15.5 out of 16. In contrast, when Kanekar, Santos, and Aruin (2008) investigated how the human body responds to fatigued muscles, their results show that the body may compensate cognitively by form of anticipatory postural adjustment to this effect. Although their sample was small (n=9), they tested the deltoid anterior and hamstring muscle to determine how adjustment occurs, and concluded that there existed effective mechanisms which can easily be employed (Kanekar, Santos, and Aruin 2008). Hence while balance dysfunction is a result of factors which include decreased sensation, proprioception, reflexes and strength in the lower limbs (Ites, et al., 2011) cognitive processes also have a role to play. In fact during this study, the participants appeared to be unaware that they had problems with balance until they were tested. Balance was also found to be associated with level of pain, odds ratio

0.64 (0.46 – 0.83). Taking the previously mentioned fact that the quality of balance is affected by elements which include decreased sensation or proprioception may explain the relationship between balance and pain. Considering that the pain was concentrated in the foot, it follows that pain sensation would interfere with proprioceptive feedback and possibly gait.

Gait

No difference in the changes in the gait scores of the POMA between the experimental and control groups p=0.94 was found. Considering that the scores of gait were already excellent at baseline for this sample, the results of gait scores may have had a ceiling effect, as a result of the small margin for improvement possible for already high scores. As with the between group results, the within group results post intervention also showed no statistically significant difference with the pre-intervention score (p=0.26).

When compared with the results of the gait scores reported in Faber, et al., (2007) and Baloh et al.,'s (2006) with elderly participants, this study's baseline results had a higher level of scores. In Kegelmeyer, et al., (2007)'s study, the participants with Parkinsons' disease had lower gait scores when compared to this study. These findings are consistent with the activity limitations associated with the impairments arising from the central nervous system lesion in comparison with a peripheral nerve lesion (Kegelmeyer, et al., 2007).

Lack of statistically significant differences in the changes in gait between the control and the experimental group may also be attributed to other factors. These factors, which contribute to the quality of gait include, proprioception, balance, co-ordination and muscle strength (Bensoussan, et al., 2008). It is therefore not surprising that the results showed a relationship between gait and muscle strength of the right tibialis anterior muscle, odds ratio 1.31 (1.07 – 1.61). During the swing phase of gait, the tibialis anterior muscle is responsible for ensuring that the foot clears the ground (Bensoussan, et al., 2008). The change in the level of neuropathy, which also assesses proprioception is also significantly associated with the change in gait scores, odds ratio 0.76 (0.61 – 0.95). These associations are not surprising because the function of the tibialis anterior muscle is more energy efficient than its contemporary muscles which use compensatory gait like high stepping gait. Using a

high stepping gait would increase energy expenditure as the use of hip flexors which lift the whole lower limb for clearance, would then be required.

Another reason for the difference in gait scores between these studies is found in the difference in demographic and socio-economic status of this sample to the samples in Kegelmeyer, et al., (2007)'s, Faber, et al., (2007)'s and Baloh et al., (2006) studies. Participants in this study only used public transport when they had to travel distances longer than two kilometers. For example to get to their local clinic 20% (n=4) would use public transport. The other 80% (n=16) walked to the clinic and to all local amenities and social visits. The ACSM (2011) position paper recommends that people who walk at least one and a half kilometers a day, which is equivalent to about 2 000 steps a day, lead a reasonably active lifestyle. Gait results indicate that the assessments were therefore carried out on participants who have an active lifestyle. Furthermore earlier results indicate that the participants had stronger distal leg muscles which include the tibialis anterior, a result that is confirmed by the excellent gait scores posted by the participants.

Gait results also seem to indicate that walking as a home exercise programme even without supervision has a reasonable effect on gait measures, balance, pain and quality of life. This implies that where there are no practitioners to implement an exercise programme, advice given by the health worker to PLWHA who have DSP exercise at home, may be an effective community based intervention to improve mobility and pain. Furthermore all health workers must be trained to advise PLWHA on simple methods of exercising at home, or at least to encourage PLWHA to continue an active lifestyle even when in pain from DSP. Pain was often cited as a reason for reduced activity at times by the participants in this study.

Pain

There were no differences in pain score changes between the control group and the experimental group as reported previously however the within group change in pain for the experimental and in the control groups was significant (p= 0.001 and 0.05) respectively. It is possible that the lack of differences between the experimental and the control groups is a result of the different coping mechanisms employed by participants including self-care strategies in dealing with pain symptoms (Nicholas, et al., 2007a). However taking note of the significant within group changes, we may argue that PRE has an effect on pain but the difficulties discussed earlier may have

impacted on the between group differences. In addition to this Basta, Reece and Wilson (2008)'s study, where they used the trans-theoretical model to predict how PLWHA go through the stages of change when complying with an exercise program allude to motivation as a crucial factor in behavior modification. Correspondingly, Keefe, et al., (2004), found that an adjustment response to chronic pain was dependent on factors like: self-efficacy, acceptance, coping mechanisms, and the readiness to change. Therefore, a greater change would have been expected in the experimental group which offered group support and interaction, both known as effective management approaches for adjustment to chronic situations like pain (Keefe, et al., 2004). However this was not the case and therefore it is possible that the participants' pain got better as they might have used self-care strategies in a manner similar to PLWHA in the study by Nicholas, et al., (2007a).

The majority of participants in this study with the help of the medical practitioners also tried several approaches including amitriptyline prescriptions (Wolfe and Trivedi 2004; Bril, et al., 2010) as this was not controlled for, but the pain especially the allodynia type, continued to disturb their sleep. Lack of sleep in turn, affected their ability to work on the following day as they would be tired and irritable from. The results are a subjective measure and therefore bias by for example using a catastrophizing coping approach may not be dismissed (Lucey, et al., 2011). Nicholas, et al., (2007b), reported similar findings in an extensive study covering three continents indicate a tendency by people experiencing neuropathic pain to use various available methods to combat their pain. Considering that people adjust themselves to pain in different ways Keeffe, et al., 2004), it is not surprising that there were novel approaches by different participants in this study and the study had no control with regard to pain management practiced by the participants.

While it is debatable to ascertain the effects of PRE on pain from the results of this study, these results may be useful for making inferences on the factors which might contribute to the reduction in the symptoms of pain. We may hypothesise that time lapse; being in a group; PRE and the reduction in peripheral neuropathy levels are associated with change in pain levels. These associations may also be because the instruments that assess pain, the Wong -Baker faces; level of neuropathy and the brief peripheral neuropathy screen; have domains which actually assess the levels of pain. Therefore these results are not surprising as the same evaluation has been repeated, as part of the whole in each assessment. However these arguments do not

explain the association between time that had lapsed between pre and post-intervention, and the association of being in the experimental group. Association between pain and belonging to the experimental group agrees with literature which states that being active group support approaches were used effectively in managing neuropathic pain (Keefe, et al., 2004).

As pain is a subjective measure there is risk of bias related to the social context in which the assessments were carried out in bearing in mind that, differing factors contribute to the individual perception of pain (Keeffe, et al., 2004). Hence a participant may catastrophize their pain with the hope that the clinician might help them. The level of self-efficacy may also be inferred from the participant rating of their own pain (Campbell, Clauw and Keefe, 2003). For example during the assessments, a participant who had avoided walking barefoot was asked to remove their shoes for observation. They were surprised that they were able to walk on the floor without shoes and believed they had been given a miracle cure! The participant explained that before this assessment she was in so much pain she had always used shoes with thick socks each time when walking to avoid the pain. Similar responses were expressed by participants in Ownby and Dune (2007)'s study. In this study Ownby and Dune (2007) sought to analyse the concepts involved in neuropathic pain in interviews with 19 PLWHA and form themes for a neuropathic pain management strategies classification. Their findings concur with Nicholas, et al., (2007) in classifying some of the strategies as for example; activities, exercise and prescribed medications.

The results as shown by the generalized equating models show that peripheral neuropathy levels are closely related to pain odds ratio 1.17 (1.04 – 1.13). The results of the brief peripheral neuropathy screen in this study, show that 59% (n=94) of the participants had moderate to severe peripheral neuropathy (score range 8-15) as shown in Table 4.3. Schifitto, et al., (2002) and Cherry, et al., (2005) described similar scores in their study where they sought to establish the risk factors of peripheral neuropathy and evaluate the instrument respectively. In this study the subjective peripheral neuropathy screen was used only as a diagnostic confirmation tool as it had been established as a sensitive tool in identifying peripheral neuropathy (Cherry, et al., 2005). Whereas the association between the severity of peripheral neuropathy and pain may be assumed, it is not clear why this is so since peripheral neuropathy also shows numbness symptoms, which is the opposite of pain. Further

research studies may all the involved partners to understand the fine line between painless and painful neuropathy.

Experiences from using the tools will be discussed briefly as the issues noted are important for future research. Nonetheless the pictorial presentation of the Wong baker faces reduced confusion associated with interpretation of visual analogue scales using numbers (Jackson, Kersten and Turner- Stokes 2006). An interesting fact noted during assessments using the VAS on the BPNS, was that participants would invert the interpretation of the scale. Whereas a ten (10) on the scale means the worst pain, participants would say ten (10) means that “my pain is very good /excellent”, therefore if I am not in pain my score is a ten (10). The assessor had to repeat the explanation and ask the participant what they understood by the score. Furthermore a score of one (1) or zero (0) would be taken to mean that “my pain is very bad/ (poor) therefore its score must be one (1). Furthermore, using the terms employed in the the brief peripheral neuropathy screen they also describe their pain as being constantly worst at night and fluctuating during the day when they are busy and active. This experience shows that the assessor needs to be aware of the different interpretations of Likert scales and the influence of context and past experience when assessing pain.

While pain management was not the focus of this study, participants showed that pain and numbness were of major concern to them and discussed these problems during their exercise sessions. Numbness has important implications for the participants, as it is a critical safety issue both at home and at work especially in the circumstances where the PLWHA is a driver as it showed that they can injure themselves easily if due protective care is not taken. There is need to protect the feet and to give advice to people with peripheral neuropathy who are involved in driving. Public vehicle drivers should be tested for numbness during medical examinations for their driver’s licenses, to mediate in reducing human error caused accidents on the national roads. Previous studies have indicated that splinting and protective padding may be used for protecting the feet (Ites, et al., 2011). However this may be difficult in cases where the individual complains of allodynia, which is also known to affect sleep. Ownby and Dune (2007), applying a grounded theory approach concur with these findings adding that there is need for the health care workers to research more on the problems associated with DSP so as to develop effective strategies for reducing associated activity limitation and participation restrictions. Whereas the

association between pain and quality of life may be deemed natural associations between health-related quality of life, pain and the elements of POMA will now be discussed.

Health related quality of life

As discussed previously, health related quality of life changes in the experimental and control groups after the intervention, when measured using the utility score showed no differences between the groups (p=0.79). Considering the multi-faceted context of quality of life (Rusch, et al., 2004), the difference in the quality of life values found between the experimental and control group in this study will be discussed in the context of its relationships with the other variables. When the relationships between the levels of performance-oriented mobility and health related quality of life in participants were analysed using generalized estimating equations a positive significant association was found between the changes in health related quality of life and gait, odds ratio 1.01 (95%CI 1.00 – 1.04), with balance odds ratio 0.68, (95%CI 0.52 – 0.93), pain odds ratio 0.98 (0.97 – 0.99), and peripheral neuropathy odds ratio 0.91 (0.82 – 1.01) and gait (p=0.001), balance (p=0.03) pain (p=0.02), and the muscle strength of the left quadriceps muscles (p=0.02). The results demonstrate strong associations with variables which form the dimensions/domains, an integral part of quality of life (Miners, et al., 2001). Therefore, since utility score showed no difference between the groups this validates the internal consistency of the quality of life, since gait, balance and pain, form integral components of quality of life, (Jelsma, et al., 2005).

However the health related quality of life changes in the experimental group and control groups after the intervention measured using the state of health visual analogue score showed a difference between the groups where p=0.04. Considering that this measure focuses on individual participants' understanding of their own quality of life, this may be a complex issue to discuss. Robberstad and Olsen (2010), concur with this viewpoint in their review on quality of life, and recommend that quality of life research must focus on economic evaluations. The possible reasons for differences may be similar in nature to the reasons alluded to in the discussion on the aspect of pain such as the socio-environmental issues affecting these participants. The baseline visual analogue scale score or state of health measure of 68.6 (95% CI

63.5, 73.8) reflect a moderate self-perception value which is consistent with the values in Jelsma, et al., (2005).

The health related quality of life profile shows that 42% (n=67) of the participants had some problems with mobility as well as completing usual activities. Washing or dressing presented as a problem in 9% (n=14) of the participants. Participants perceived themselves to be in a better state of health as shown by the state of health median score of one (1). Rusch, et al., (2004) and Miners, et al., (2001) found similar outcomes while using the ICF in a study in Canada, and the EQ5D in United Kingdom respectively for a sample of PLWHA. Myezwa, et al., (2009)'s study using the ICF and Jelsma, et al., (2005) using the EQ5D, both assessed for problems experienced by PLWHA in South Africa and found similar pattern of proportions of PLWHA who had these problems. Hence 56% (n=35) of participants in Myezwa, et al., (2009)'s study had mobility problems while 9% (n=8) of the participants had self-care problems in Jelsma, et al., (2005)'s study. Since quality of life is a personal matter, the clinical characteristics of the participants will now be discussed.

Clinical characteristics of the participants

The participants in this study showed similarities in the characteristics tested for including: age, gender, education level, period of diagnosis and period on ARVs, CD4+ count and the peripheral neuropathy scores for the experimental and control groups. HIV related information of the participants summarized in Table 4.2 shows that of the sample under study 45% (n=72) of the participants had known their HIV status for more than two years. The results show that 70% (n=112) of the participants had a CD4+ count of less than 300 cells per cubic mm. However 45% (n=72 of the CD4+ count results were stale, as they were more than a year old. An explanation is found in the National Drug and Therapeutics Policy Advisory Committee, NDTPAC (2010) protocol which provides for a repeat CD4+ count after one year. Combination antiretroviral therapy of stavudine, lamivudine and nevirapine, which comprises of the dideoxynucleosides , known for their neuro-toxic effects (Keswani, et al., 2002), was used by 59% (n=94) of the participants. This first line protocol is currently being phased out in Zimbabwe and a new protocol requires a change in the antiretroviral therapy used depending on the reporting of adverse clinical response (NDTPAC 2010). Menez, et al., (2011) in a South African study with 9040 participants on HAART showed that stavudine is associated with co-morbidities which seem to outweigh the drugs benefits, concurring with the WHO position. This is consistent

with the findings in Van Griensven, et al., (2010), where in a cohort in which 2190 participants who had used stavudine were re-assessed for a variety of toxic effects after its substitution.

The study also brought out a need for the policy makers to consider offering rehabilitation services in the same package as other services for a token fee to PLWHA. As a result of the preliminary results, the study team convinced the Department of Rehabilitation at the College of Health Sciences, University of Zimbabwe to approach the Municipal of Harare seeking to collaborate in setting up Rehabilitation departments at all municipal clinics. This was done and currently the two partners are working on a memorandum of agreement (at the time of writing), which entails a pilot will be trialed before a full implementation is accomplished.

5.3 Limitations of the findings of the study

The study findings may not be generalized to all individuals living with HIV/AIDS who have DSP as the participants were from a particular demographic setting. There was a high level of participant withdrawal, which reduces the actual sample size and compromises the quality of the study even when intention to treat analysis is the method used. Thus the high withdrawal rate discussed earlier certainly cannot be ignored as a limitation in that the actual effect of intervention becomes compromised by the reduced sample size. However the intention to treat analysis is realistic and approximates the results more for use in clinical practice where the behavior of the participants is unpredictable as it is practical. There was high staff turnover and newly qualified physiotherapist, who were therefore inexperienced with regards to HIV care, were recruited as the research assistants. While clinical reports indicate significant changes within groups, the low adherence to exercise does not rule out the effects of other variables like group support becoming a confounding variable.. Walking, which was used by the control group had a significant effect as shown by within group results, when compared with the effects of the exercise intervention done in the experimental group. However the study could not suspend the usual method as this was unethical. The timing of the staging of the study might have been made more appropriate to eliminate interference by participants' personal adjustment issues. The study setting made the study difficult to implement as the participants were experiencing a challenging socio-economic situation.

CHAPTER 6

6. CONCLUSION

This study asked what the effect of progressive resisted exercises was on the performance oriented mobility and health related quality of life of people living with HIV and AIDS related distal symmetrical poly-neuropathy (DSP), a common neurological condition associated with HIV complications (Nicholas, et al., 2007b). People with DSP commonly have problems with mobility, altered gait and balance affecting their quality of life (Ites, et al., 2011) and progressive resisted exercises have been reported to attenuate these impairments (O'Brien, et al., 2008).

This study was an assessor-blind randomized controlled trial design. It consisted of two studies because the initial study had a high dropout rate. For the analysis the results from the two studies that used the same method were pooled and the sample size was n=160. In Study 2 participants were sourced from ten family care clinics and antiretroviral therapy dispensing clinics in Harare. The experimental group (n=80) had an intervention program of PRE while the control group (n=80) had usual treatment. The results on gait and balance scores using the POMA did not show differences in effect between the intervention and the control group (95%CI 0.00-0.02 p = 0.8). Similarly there were no differences of effect for muscle strength (95%CI 0.00-0.08) p=0.13-0.8) and pain (95%CI 0.0-0.06 p>0.13). However the effect on quality of life changes were significantly different between the two groups (95%CI 0.00-0.12 p= 0.04). Quality of life was strongly and positively associated with gait, odds ratio 1.01 (95%CI 1.00 – 1.04), strongly negatively associated with pain odds ratio 0.98 (0.97 – 0.99), and peripheral neuropathy odds ratio 0.91 (0.82 – 1.01). There was significant relationship between the level of pain and level of balance and the, odds ratio 0.64 (0.46 – 0.83), and level of peripheral neuropathy, odds ratio 1.17 (1.04 – 1.13). Results of this study demonstrate consistence with the findings by previous studies which show that PRE improves muscle strength, gait and balance in peripheral neuropathy.

6.1 Recommendations for further research

The results of this study suggest the need to do a follow-up study on the participants who have had their drug regimen changed from stavudine to other new drugs as this would assist the community to determine the rate/and recovery of people who have been exposed to toxic antiretroviral drugs like stavudine. There is need to also analyse the results of the brief peripheral neuropathy so as to establish the implications of painless neuropathy or numbness. Walking may also be used as an management approach on its own or in combination with a simple exercise programme as the results of this study established.

Future studies may need to profile the participants' motivation levels with regards to predicting their compliance behavior. This may be made feasible if the programme utilises the recommendations based on Basta, Reece and Wilson (2008)'s study, where they used the trans-theoretical model to predict the stages of change on the path to compliance. Using such a model implies the factoring in of motivation as a crucial factor in behavior modifications to start and continue exercise. This approach would greatly enhance the use of intention to treat analysis for practical environments. The participants would then be invited to explain their self-care strategies to get an understanding of their coping mechanisms. Further studies could apply these findings on DSP to other co-morbidities like diabetes mellitus and alcoholic DSP where quality of life evaluations should focus on economic evaluations.

Carrying out this study under the 2009-2011 socioeconomic situations in the country (MoHCW, 2009) of the study was a challenging exercise on its own. Hence, although the ethical procedure systems were in place, it took longer, up to two months, to get clearance at each level as there were few reviewers available for this purpose following the brain-drain which had occurred in the preceding 2003- 2008 period. The financial system was recovering and accessing funds for implementing the trial was very difficult where most donor agencies had now limited their operations to what they considered as essentials only. Thus the research team was left with funds from the school and from the scholarship for reimbursing the research team and the participants for their time and for transport purposes. As it was a difficult time there was a high loss to follow up in Study 1 as participants could not afford transport

fares, as well as movements and relocations as the participants sought livelihood. The study also suffered a lot from expectations to provide food and money by the participants to reimburse for time lost away from their business and as the participants left the study. Having outlined the problems encountered as a consequence of the socioeconomic circumstance; the discussion will now attempt to recommend possible approaches to such scenarios. Firstly the responsibility of completing the study rests squarely with the research team and as such, the team must be aware of the reality and set a realistic plan of action with enough time to offset for unforeseen events. We recommend that when faced with such a situation it may be advisable to set the study nearer to the participant i.e. in the community. If possible a plan to reimburse the participants must be made within the ethical boundaries.

6.2 Conclusion

This research study established that progressive resisted exercises have positive effects on the health related quality of life in subjects with HIV/AIDS related distal symmetrical poly-neuropathy. However this study did not show a difference of the effects of progressive resisted exercises on performance oriented mobility, measured through the effect on gait, balance and gait and muscle strength in subjects with HIV/AIDS related distal symmetrical poly-neuropathy when compared to advice to exercise at home.

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APPENDICES

Appendix A: Brief Peripheral Neuropathy Screen

Appendix A1

Subjective Peripheral Neuropathy Screen Questionnaire (by the participant)

Code:_____ Date _____

Please take a few minutes to answer the following questions about the feeling in your legs and feet. Check yes or no based on how you usually feel. Thank you.

1. Do you ever have legs and/or feet that feel numb?	□ Yes □ No
2. Do you ever have any burning pain in your legs and/or feet?	□ Yes □ No
3. Are your feet too sensitive to touch?	□ Yes □ No
4. Do you get muscle cramps in your legs and/or feet?	□ Yes □ No
5. Do you ever have any prickling or tingling feelings in your legs or feet?	□ Yes □ No
6. Does it hurt at night or when the covers touch your skin?	□ Yes □ No
7. When you get into the tub or shower, are you unable able to tell the hot water from the cold water?	□ Yes □ No
8. Do you ever have any sharp, stabbing, shooting pain in your feet or legs?	□ Yes □ No
9. Have you experienced an asleep feeling or loss of sensation in your legs or feet?	□ Yes □ No
10. Do you feel weak when you walk?	□ Yes □ No
11. Are your symptoms worse at night?	□ Yes □ No
12. Do your legs and/or feet hurt when you walk?	□ Yes □ No
13. Are you unable to sense your feet when you walk?	□ Yes □ No
14. Is the skin on your feet so dry that it cracks open?	□ Yes □ No
15. Have you ever had electric shock-like pain in your feet or legs?	□ Yes □ No

Appendix A2

Physicians Checklist / Questionnaire for Screening of Peripheral Neuropathies related to HIV and ART (*To be assisted by nurse working at the ART clinic*)

Demographic characteristics and General health Status of the Patient

1. **Gender**: Female □ Male □

2. **Age** ----------years

3. Highest level of education

a) Tertiary education (University, Institution of higher learning --- ☐
b) Secondary school education (S4 – 6) ---------- ☐
c) Secondary school education (S1 – 3) ---------- ☐
d) Primary education ---------- ☐
e) Any other (please specify) ---------- ☐

4. Occupation ☐

a) Public (government) service ---------- ☐
b) Peasant (farmer, or livestock) ---------- ☐
c) Self – employed (business) ---------- ☐
d) Private organisation (NGO, bank, insurance etc) --------- ☐
e) Unemployed (do not have a job for the last 3 months)--- ☐
f) Any other (please specify) ---------- ☐

5. Marital status ☐

a) Single ---------- ☐
b) Married ---------- ☐
c) Divorced ---------- ☐
d) Separated ---------- ☐
e) Widow / widower ---------- ☐
f) Cohabitating (live together with a temporally male/female partner- ☐
g) Any other (please specify) ---------- ☐

6. **Place of residence** ----------(write it in here)

7. **When the patient's HIV was diagnosed**:

a) 1 – 6 months ago---------- ☐
b) 6 – 12 months ago---------- ☐
c) 1 – 3 years ago---------- ☐
d) 4 – 6 years ago---------- ☐
e) 7 – 9 years ago---------- ☐
f) 10 – 15 years ago---------- ☐
g) More than 15 years ago---------- ☐

8. Clinical HIV staging:

1. Clinical stage I ---------- ☐
2. Clinical stage II ---------- ☐
3. Clinical stage III ---------- ☐
4. Clinical stage IV ---------- ☐

9. Is the patient on Anti-retroviral treatment?

1. Yes ☐ 2. No ☐

10. **If yes, please specify the type (s) of ARVs** ----------
---
---

11. **For how long the patient has been on ARVs treatment**?

a) 1 – 6 months---- ---------- ☐
b) 6 – 12 months----- ---------- ☐
c) 1 – 3 years---- ---------- ☐
d) 4 – 6 years---- ---------- ☐
e) 7 – 9 years ---------- ☐
f) 10 – 15 years----- ---------- ☐
g) More than 15 years---------- ☐

12. **Please indicate if the patient has the following conditions: (Tick that apply)**

a) Diabetes mellitus ---------- □

b) Vitamin B deficiency ----------□

c) Cancer ----------□

d) Multiple sclerosis ----------□

e) Spinal cord disorders and cognitive problems ----------□

f) Hypothyroidism ----------□

g) Uraemia ----------□

h) Toxic exposure ----------□

i) Hereditary neuropathy----------□

j) A history of neoplasm ----------□

k) Any other (please specify) ----------□

13. **Please indicate if the patient present the following symptoms:(Tick all that apply**)

a) Pain: Hand and arms □ Feet and Legs □

b) Paraesthesia: Hand and arms □ Feet and Legs □

c) Numbness: Hand and arms □ Feet and Legs □

14. If the patient presents any of the above symptoms, when did the symptoms start? (If remember/recorded)

a) Before start ARVs □

b) After starting ARVs □

15. If after start ARVs, after how long on ARVs did the symptoms commence (if remember or recorded)

a) 1 – 6 months---- ---------- □

b) 6 – 12 months----- ---------- □

c) 1 – 3 years---- ---------- □

d) 4 – 6 years---- ---------- □

e) More than 6 years ---------- □

Appendix A3: ACTG Brief Peripheral Neuropathy Screening Tool

INSTRUCTIONS FOR RECORDING SUBJECTIVE ELICITED SYMPTOMS

Ask the subject to rate the severity of each symptom listed in question 1 on a scale of 01 (mild) to 10 (most severe) for right and left feet and legs. Enter the score for each symptom in the columns marked R (right lower limb) and L (left lower limb). If a symptom has been present in the past, but not since the last visit, enter '00-Currently Absent'. If the symptom has never been present, enter '11-Always Been Normal'

Always been normal	Currently absent	Mild_____Severe									
11	00	01	02	03	04	05	06	07	08	09	10

1. SYMPTOMS R L

a. Pain, aching, or burning in feet, legs …… ☐☐

b. "Pins and needles" in feet, legs …… ☐☐

c. Numbness (lack of feeling) in feet, legs …… ☐☐

INSTRUCTIONS FOR GRADING SUBJECTIVE ELICITED SYMPTOMS

Use the single highest severity score from question 1. above to obtain a subjective sensory neuropathy score. If all severity scores are '00' or '11', the subjective sensory neuropathy score will equal '0'

Presence/Severity Score of:
01 – 03 = Grade of 1
04 – 06 = Grade of 2
07 – 10 = Grade of 3
11 or 00 = Grade of 0

2. Subjective sensory neuropathy grade …….. R L ☐☐

3. Location of symptoms

Use Score of:
0 = None
1 = feet only
2 = extends to ankles
3 = extends above ankle but not to knee
4 = extends to knees
5 = extends above knees

R L

a. Pain, aching, or burning in feet, legs …… ☐☐

b. "Pins and needles" in feet, legs …… ☐☐

c. Numbness (lack of feeling) in feet, legs …… ☐☐

INSTRUCTIONS FOR EVALUATING PERCEPTION OF VIBRATION

Compress the ends of a 128 Hz tuning fork just hard enough that the sides touch. Place the vibrating tuning fork on a bony prominence on the subject's wrist or hand to be sure that they can recognize the vibration or "buzzing" quality of the tuning fork. Again, compress the ends of the tuning fork just hard enough so that the sides touch. Immediately place the vibrating tuning fork gently but firmly on the top of the distal interphalangeal (DIP) joint of one great toe and begin counting the seconds. Instruct the subject to tell you when the "buzzing" stops. Repeat for the other great toe.

4. Vibration Perception

R
L

a. Great toe DIP joint perception of vibration in seconds | | |

b. Vibration perception score R
L
0 = felt > 10 seconds
1 = felt 6-10 seconds | | |
2 = felt < 5 seconds
3 = not felt
8 = unable/did not evaluate

INSTRUCTIONS FOR EVALUATING DEEP TENDON REFLEXES

With the subject seated, the examiner uses one hand to press upward on the ball of the foot, dorsiflexing the subject's ankle to 90 degrees. Using a reflex hammer, the examiner then strikes the Achilles tendon. The tendon reflex is felt by the examiner's hand as a plantar flexion of the foot, appearing after a slight delay from the time the Achilles tendon was struck. Use reinforcement by having the subject clench his/her fist before classifying the reflex as absent.

<u>Ankle reflexes</u>
0 = absent
1 = Hypoactive
2 = Normal deep tendon reflexes
3 = Hyperactive
4 = Clonus
8 = unable/did not assess

R
L

5. Ankle reflexes …….. | | |

Appendix A4: Bepa rekukukokai

Shona version of the Subjective Peripheral Neuropathy Screen Questionnaire (by the participant)

Runhare rwenyu _____Code_____Date _____

_____

Tinokumbira kuti mutore nguva shomanana kupindura zvamunonzwa mumakumbo uye mutsoka dzenyu. Nyorai pana hongu kana kuti pana kwete zvichienderana nezvamunowanzo kunzwa. Tatenda.

-

1. Munombo nzwa chiveve mumakumbo nemutsoka here? □ Hongu □ Kwete
2. Munonzwa kupiswa here mutsoka kana mumakumbo? □ Hongu □ Kwete
3. Makumbo enyu anoteta kubatwa here? □ Hongu □ Kwete
4. Munomboita kuoma kwamarunda here mumakumbo kana mutsoka? □ Hongu □ Kwete
5. Munombonzwa kunenge kubayiwabayiwa mumakumbo enyu here kana mutsoka? □ Hongu □ Kwete
6. Munorwadziwa here usiku kana kuti kana magumwa ganda renyu nemachira? □ Hongu □ Kwete
7. Kana muchindogeza munotadza here kunzwa kuti mvura iri kupisa here kana kutonhora? □ Hongu □ Kwete
8. Munomboita here kunzwa kubaiwabayiwa mutsoka kana mumakumbo? □ Hongu □ Kwete
9. Munombonzwa here kunge makumbo kana tsoka dzenyu dzarara, kana kushaiwa kunzwa makumbo kana tsoka dzenyu? □ Hongu □ Kwete
10. Munonzwa kushaiwa simba here kana muchifamba ? □ Hongu □ Kwete
11. Zvamunonzwa zvinonyanya usiku here? □ Hongu □ Kwete
12. Makumbo kana tsoka dzenyu kana zvose zvinorwadza here kana mofamba? □ Hongu □ Kwete
13. Munotadza here kunzwa tsoka dzenyu kana muchifamba? □ Hongu □ Kwete
14. Ganda renyu remutsoka rakaomara here kana kuita man'a? □ Hongu □ Kwete
15. Munombonzwa here kurwadziwa kunge munogwinhwa nemagetsi mutsoka kana mumakumbo enyu? □ Hongu □ Kwete

Generic Screening Tools for Peripheral Neuropathy, (*Neurology Working Group of the National Centre in HIV Epidemiology and Clinical Research, 2004)*

Appendix B: Performance–Oriented Mobility Assessment

Balance Instructions: *The subject is seated on a hard, armless chair.* The following maneuvers are tested		**Gait** Instructions: *The subject stands with the examiner, walks down the hallway or room at the usual pace. The subject is asked to walk down the walkway' turn' and walk back after being instructed to go.(using the usual walking aids.)*	
1. Sitting balance		1. Initiation of gait (immediately after go)	
Leans or slides on the chair,	0	Any hesitancy or multiple attempts to start	
Steady, safe	1	No hesitancy to start	0
2. Arising		2. Step length and height	1
Unable to arise without help	0	Right swing foot does not pass left stance foot	
Able but uses arms to help	1	with step	
Able without using arms	2	Passes left stance foot	0
3. Immediate standing balance (first 5 seconds)		Left swing foot does not pass right stance foot with step	1
Unsteady, swaggers, moves feet, marked		Passes right stance foot	0
trunk sway,	0	Right foot does not clear floor completely with	1
Steady but uses walker or other support	1	step	
Steady without walker or other support	2	Right foot completely clears floor.	0
4. Standing balance (after 5 seconds		Left foot does not clear floor completely with	1
Unsteady		step	0
Steady but wide stance (heels 10 cm apart	0	Right foot completely clears floor	
and uses cane or other support		3. Step symmetry	1
Narrow stance without support	1	Right and left step lengths not equal	
5. Nudged (*Light push on the sternum, subject with feet as close together as possible)*	2	Right and left steps appear equal	0
		4. Step continuity	1
		Stopping or discontinuity between steps	
Begins to fall,		Steps appear continuous	0
Staggers, grabs, catches self	0	5. Path (*estimated in relation to floor*	1
Steady	1	*tiles 30cm in diameter observe*	
6. Eyes closed (*feet as close together as possible)*	2	*excursion of 1 foot over about 3 meters of the course)*	
Unsteady		Marked deviation	
Steady	0	Mild /moderate deviation or uses walking aid	0
7. Turning 360º	1	Straight without walking aid	
Discontinuous steps		6. Trunk	1
Continuous	0	Marked sway or uses walking aid	2
Unsteady (grabs staggers)	1	No sway but flexion of knees or back or	
Steady	0	spread arms	0
8. Sitting down	1	No sway no flexion, no use of arms, and no	
Unsafe (misjudged distance, falls onto chair)		use of walking aid	1
Uses arms or not a smooth motion		7. Walking stance	
Safe smooth motion	0	Heels apart	2
	1	Heels almost touching while walking	
Balance score	2	Gait score	0
			1
	/16		/12

Adapted from Kegelmeyer, et al., (2007) and Faber, et al., (2006).

Appendix C: South African English version of the EQ-5D

By placing a tick in one box in each group below, please indicate which statements best describe your own state of health TODAY.

Mobility

I have no problems in walking about	❑
I have some problems in walking about	❑
I am confined to bed	❑

Self-Care

I have no problems with self-care	❑
I have some problems washing or dressing myself	❑
I am unable to wash or dress myself	❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities	❑
I have some problems with performing my usual activities	❑
I am unable to perform my usual activities	❑

Pain/Discomfort

I have no pain or discomfort	❑
I have moderate pain or discomfort	❑
I have extreme pain or discomfort	❑

Anxiety/Depression

I am not anxious or depressed	❑
I am moderately anxious or depressed	❑
I am extremely anxious or depressed	❑

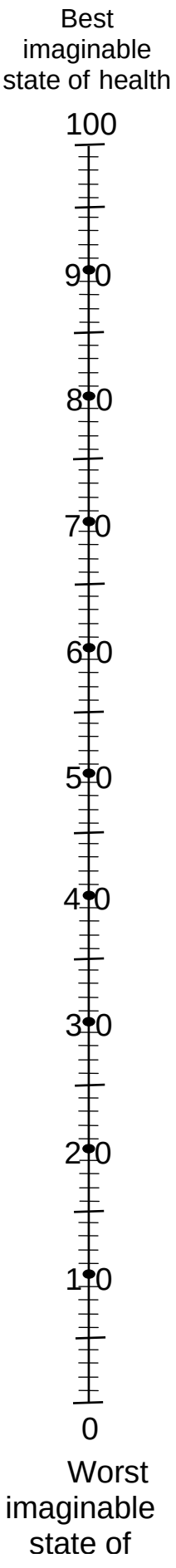
Compared with my general
level of health over the past 12 months,
my state of health today is:

Better	❑	PLEASE TICK
Much the same	❑	ONE
Worse	❑	BOX

To help people say how good or bad their state of health is, we have drawn a scale on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale, in your opinion, how good or bad your own health is today. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is today.

Your own state of health today



Because all replies are anonymous, it will help us to understand your answers better if we have a little background data from everyone, as covered in the following questions.

1. Have you experienced serious illness?

	Yes	No
yourself	❑	❑
in your family	❑	❑
while caring for others	❑	❑

PLEASE TICK APPROPRIATE BOXES

2. What is your age in years? [ ]

3. Are you male or female?

Male	Female
❑	❑

PLEASE TICK APPROPRIATE BOX

4.

I smoke	❑
I used to smoke	❑
I have never smoked	❑

PLEASE TICK APPROPRIATE BOX

5. Do you now, or did you ever, work in health services or social welfare?

Yes	No
❑	❑

PLEASE TICK APPROPRIATE BOX

If so, in what capacity? .....

6. Which of the following best describes your main activity?

self employed	❑
in formal employment	❑
retired	❑
homemaker/domestic worker	❑
student	❑
seeking work	❑
other (please specify)	❑ .....

7. What was the highest grade that you attained at school?

PLEASE TICK APPROPRIATE BOX

	Yes	No
8. Do you have a diploma or equivalent?	❑	❑

9. State the area/suburb in which you stay, Please write it here.....

Appendix D: Shona Version of the EQ-5D

Muchikwata chimwe nechimwe chemhinduro dzinotevera, isa mucherechedzo mukabhokisi kari kumucheto seizvi [✔] pamhinduro imwe chete yaunofunga kuti ndiyo inonyatsotsanangura utano hwako PARINHASI.

Kugona kufamba

Handinetseki kufamba ❑
Kufamba kunondinetsa ❑
Handigone kana nekufamba kose ❑

Kuzvishambidza

Ndinogona zvangu kuzvishambidza ❑
Handinyatsogona kuzvigezesa kana kuzvipfekedza ❑
Handigone kuzvigezesa kana kuzvipfedza ❑

Mabasa enguva dzose *(Akafanana ne: kushanda, kudziidza mabhuku, kuita basa remumba kana repamba, kutandara kana kuvaraidzana nemhuri)*

Handinetseki nokuita mabasa angu andinowanzoita nguva dzose ❑
Ndinonetseka kuita mabasa angu andinowanzoita mazuva ose ❑
Handichagoni kuita mabasa angu andaiwanzoita mazuva ose ❑

Kurwadziwa/ Kusagadzikana

Handisi kurwadziwa ❑
Ndinorwadziwa zwangu zvishoma ❑
Ndinorwadziwa zvakanyanya. ❑

Kunetsekana mupfungwa / Kuremerwa

Hapana zvinondinetsa mupfungwa ❑
Ndine zvinodinetsa zwakati kuti ❑
Ndirikushushikana zvakanyanya ❑

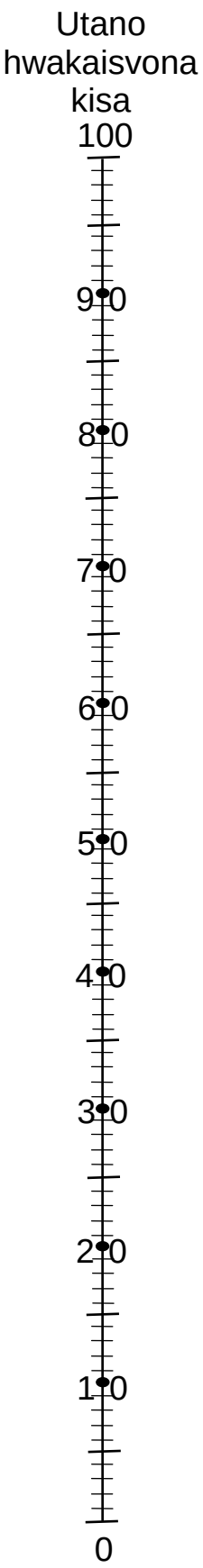
Kana ndichienzanisa utano hwangu pamwedzi gumi nemiviri yapfuura neparinhasi, ndingati zvangu nhasi:

Zvava nani ❑ SARUDZA
Zvakangofanana ❑ BHOKISI
Zvatonyanya ❑ RIMWE CHETE

Kuti tibatsire vanhu kuti vaone kunaka kana kushata kwakaita utano hwavo parinhasi, takupa chikero ichi chekupimisa nacho utano hwako. Chine nhamba dzinobvira pasi pana 0 kusvika kumusoro kuna 100. 0 anoratidza utano hwakadzikira hwemunhu anorwara zvakasvoipisa. 100 anoratidza utano hwakaisvonakisa hwemunhu asingarware.

Tinokumbira kuti unongedze nhamba pachikero apa yaunofunga kuti ndiyo inoratidza ipo chaipo pane utano hwako nhasi uno. Ita izvi nokunyora mutsetse unotangira kubva pachibhokisi chiri pazasi icho wakananga nechekurudyi uko kunechikero uchinoguma ipo chiapo pane nhamba yawasarudza yaunofungira kuti ndiyo chaiyo inoratidza pava neutano hwako nhasi.

Utano hwako nhasi uno.



Sezvo mhinduro dzako dzichange dzisina zita rako, tinokumbirawo kuti utiudzewo zvimwe zvemagariro aka neupenyu hwako kubva muneizvi zvinotevera. Isa mucherechedzo mukabhokisi seizvi ✔ pamhinduro yaunenge wasarudza .

1. Wakamboona here munhu achirwara zvakaipisisa? Hongu Kwete

Ndiwe here iwe pachako? ❑ ❑

Mumwewo here wemumhuri menyu? ❑ ❑ SARUDZAI BHOKISI RIMWE CHETE

Mumwewo here wawakaona mubasa reutano kana mukubatsira vanhu kwawaiita? ❑ ❑

2. Une makore mangani? ☐

3. Uri murume kana kuti mukadzi here? Murume Mukadzi

❑ ❑ SARUDZAI BHOKISI RIMWE CHETE

4. Unoputa fodya here?

Ndinoputa. ❑

Ndaimboputa ❑ SARUDZAI BHOKISI RIMWE CHETE

Handina kugara ndamboputa ❑

5. Unoshanda basa reutano kana rekubatsira vanhu here izvozvi, kana kuti wakamboshanda basa reutano kana rekubatsira vanhu here? Hongu ❑ Kwete ❑ SARUDZAI BHOKISI RIMWE CHETE

Kana zviriizvo, waishanda uri pachinzvimbo chipi? .....

6. Pane zvirikutevera izvi, tiudze chaungati ndicho chaicho chinhu chikuru chauri kuita**:**

basa rekuzvishandira ❑

basa rekubairwa chitupa ❑

pamudyandigere ❑

basa remumba kana pamba ❑

mwana wechikoro ❑ SARUDZAI BHOKISI RIMWE CHETE

kutswaka basa ❑

Chimwewo chatasiya (tiudze kuti chii) .....

7. Wakasvika pagwaro ripi nekufunda kwako kuchikoro? ☐

8. Une dhipuroma here kana kuti imwewo kosi zvayo yakafanana nedhipuroma? Hongu ❑ Kwete ❑ SARUDZAI BHOKISI RIMWE CHETE

9. Kana uchiziva nzvimbo/rukesheni raunogara tinyorerewo apa …….

Appendix E: Wong Baker Faces

Wong-Baker FACES Pain Rating Scale



Explain to the person that each face is for a person who feels happy because he has no pain (hurt) or sad because he has some or a lot of pain. Face 0 is very happy because he doesn't hurt at all. Face 1 hurts just a little bit. Face 2 hurts a little more. Face 3 hurts even more. Face 4 hurts a whole lot. Face 5 hurts as much as you can image, although you don't have to be crying to feel this bad. Ask the person to choose the face that best describes how he is feeling.

Rating scale is recommended for persons age 3 years and older.

Brief word instructions: Point to each face using the words to describe the pain intensity. Ask the child to choose face that best describes own pain and record the appropriate number.

From Wong DL., Hockenberry-Eaton M, Wilson D, Winkelstein ML., Schwartz P. **Wong's Essentials of Pediatric Nursing,** 6/e, St. Louis, 2001, P. 1301. Copyrighted by Mosby, Inc. Reprinted by permission.

Appendix F: Scoring EQ-5D health states

(Based on A1 TARIFF BASED ON UK SURVEY (1993))

Values for the 243 health states defined by the EuroQoL classification have been calculated using a regression model. The following worked example indicates how these coefficients are to be used so as to compute the estimated values for each state.

Calculating EQ-5D state scores - a worked example

EuroQoL dimension	Level 2	Level 3
Mobility	0.069	0.314
Self-care	0.104	0.214
Usual activity	0.036	0.094
Pain / discomfort	0.123	0.386
Anxiety / depression	0.071	0.236
	Constant = 0.081	N3 = 0.269

The arithmetic needed to recover the estimated value for any health state from this table of decrements is given by the following example:

Taking health state 1 1 2 2 3

Full health (1 1 1 1 1) = 1.0

Constant term (for any dysfunctional state) (subtract 0.081)

Mobility.. level 1(subtract 0)
Self-care.. level 1(subtract 0)
Usual activity.. level 2(subtract 0.036)
Pain / discomfort.. level 2(subtract 0.123)
Anxiety / depression.. level 3(subtract 0.236)

Level 3 occurs within at least 1 dimension (subtract N3 parameter 0.269)

Hence the estimated value for state 1 1 2 3 3 is given by

1.0 - 0.081 - 0.036 - 0.123 - 0.236 - 0.269 = .2

- 0.081 - 0.036 - 0.123 - 0.236 - 0.269 = .255

Appendix G: Per protocol analyses of post intervention results between the experimental group and the control group

Introduction

The results of the study were analysed to establish the effect of progressive resisted exercises on gait, balance and pain as outlined in the objectives using per protocol analysis. The analysis will establish if there was a difference in the muscle strength change between the control group and the experimental group post intervention and within the control group and within the experimental group post intervention.

Muscle strength difference between the combined control group and combined experimental group

The mean muscle strength difference between the combined control group and experimental group post intervention is summarized in Table 4.9 below.

Table 4.9 Mean muscle strength difference between the control group and experimental group after intervention (n=64)

Muscle	Mean muscle strength difference	Standard error	(CI)	p value
Right quadriceps	-0.01	1.15	-2.31- 2.28	1.0
Left quadriceps	0.89	1.14	-1.39- 3.16	0.44
Right hamstrings	-0.13	0.67	-1.47- 1.20	0.84
Left hamstrings	-0.35	0.67	-1.69- 0.98	0.60
Right gastrocnemius muscle	-0.38	1.07	-2.51- 1.76	0.72
Left gastrocnemius muscle	-0.10	1.11	-2.33- 2.13	0.93
Right tibialis anterior	1.01	1.01	-1.00- 3.01	0.32
Left tibialis anterior	0.87	0.94	-1.01- 2.76	0.36

There was no difference in the mean muscle strength change between the combined control group and the combined experimental group, p range of p =0.32 to p =1.0.

Gait, balance and pain differences between the combined control group and combined experimental group after intervention

These results answer the objectives 1, 2 and 3 on the effects of progressive resisted exercises. The differences in the gait score, balance score and pain score between the control group and the experimental group after intervention are summarized in Table 4.10.

Table 4.10 Difference in the gait score, balance score and pain score between the control group and the experimental group after intervention

Variable	z scores	p value
Gait	-0.60	0.55
Balance	-1.08	0.28
Pain scores	-2.38	0.02

There was no difference in the changes in the gait scores of the performance oriented mobility assessments between the experimental and control groups p=0.55. The balance scores of the performance oriented mobility between the experimental and control group after the intervention were similar p=0.28. There was a difference in the pain score change between the control group and the experimental group p=0.02.

Health related quality of quality differences between the combined groups after intervention

The difference in the quality of life score between the control group and the experimental group after intervention is shown in Table 4.11

Table 4.11 Difference in the quality of life score between the control group and the experimental group after intervention

	QOL utility score change	Standard Error	(Confidence Interval)	p value
QOL utility score	12	7.40	-2.76 - 26.81	0.11

The changes in the health related quality of life in the combined experimental group and combined control groups after the intervention were similar p=0.11.

The relationships between the changes in gait, balance, pain and quality of life

The fourth objective that sought to establish if there is a relationship between the levels of performance-oriented mobility and health related quality of life in participants with HIV/AIDS related DSP will be explored in this section based on the per protocol analysis.

Gait relationships

Gait relations with quality of life are presented in Table 4.12a, below. Gait was also related with the level of neuropathy, level of education and muscle strength of the right tibialis muscle as presented in Table 4.12a, Table 12b and Table 12c below.

Table 4.12a Univariate model showing the correlation between gait and quality of life, level of neuropathy, level of education and muscle strength of the right tibialis muscle

Variable	Odds ratio	Confidence interval	z	p value
Right tibialis anterior muscle strength	1.17	1.04-1.31	2.69	0.007
Quality of life	1.03	1.02- 1.05	1.03	0.00
Level of neuropathy	0.82	0.67- 1.0	-1.96	0.05
Level of education	0.70	0.50- 0.98	-2.08	0.05

The results of the models depicted in table 4.12a demonstrate significant association between the changes in gait and quality of life (p=0.001). There is also a significant association between gait and the level of neuropathy (p=0.03), level of education (p=0.02) and muscle strength of the right tibialis anterior muscle (p=0.02).

Table 4.12b Adjusted model showing the correlation between gait and the quality of life, level of neuropathy, level of education and muscle strength of the right tibialis muscle after adjusting for time and group

	Odds ratio	Confidence interval	z	p value
Right tibialis anterior muscle strength	1.28	1.1- 1.5	3.22	0.001
Quality of life	1.03	1.02- 1.06	3.76	0.00
Level of neuropathy	0.80	0.66- 0.98	-2.15	0.03
Level of education	0.69	0.49- 0.97	-2.16	0.03

Table 4.12c Multivariate model showing the relationship between gait and the quality of life, level of education and muscle strength of the right tibialis muscle

	Odds ratio	Confidence interval	z	p value
Right tibialis anterior muscle strength	1.22	1.03-1.45	2.27	0.02
Quality of life	1.03	1.01- 1.06	3.29	0.001
Level of education	0.60	0.39- 0.92	-2.16	0.02

The results of the models depicted in table 4.12a and table 4.12b demonstrate significant relation in the changes in gait and quality of life (p=0.001). There is also a correlation between gait and the level of neuropathy (p=0.03), level of education (p=0.02) and muscle strength of the right tibialis anterior muscle (p=0.02).

Balance relationships

The relationship between balance and the level of pain, and muscle strength of the right and left hamstring muscle are described in Table 4.13a and Table 4.13b.

Table 4.13a Univariate model showing the correlation between balance and the quality of life, level of pain, and muscle strength of the right hamstring muscle

	Odds ratio	Confidence interval	z	p value
Right hamstring muscle strength	1.20	1.04- 1.38	2.45	0.01
Left hamstring muscle strength	1.18	1.02- 1.38	2.20	0.03
Level of pain	0.51	0.37- 0.72	-3.83	0.00

There was significant correlation between the level of balance and the level of pain (p=0.00) muscle strength of the right hamstring muscle p=0.01, muscle strength of the left hamstring muscle p=0.03. There was no correlation between balance and quality of life.

Table 4.13b Adjusted model showing the correlation between balance, level of pain and the quality of life

	Odds ratio	Confidence interval	z-score	p value
Level of pain	0.54	0.37- 0.77	3.38	0.001

There was significant correlation between the change in balance and the level of pain, (p=0.001) as depicted by the adjusted model. The multivariate model showed a similar significant relationship between balance and the level of pain (p=0.002)

Pain relationships

The relationship between pain and the quality of life, level of neuropathy, and muscle strength of the left gastrocnemius muscle strength is shown in Table 4.14a and Table 4.14b.

Table 4.14a Univariate model showing the correlation between pain and the quality of life, level of neuropathy, and muscle strength of the left gastrocnemius muscle

	Odds ratio	Confidence interval	z-score	p value
Left gastrocnemius muscle strength	1.08	1.00- 1.17	1.95	0.051
Quality of life	1.02	1.01- 1.03	2.82	0.005
Level of neuropathy	0.88	0.76- 1.01	-1.81	0.07

The correlation between pain and the quality of life was significant (p= 0.005) using the univariate model. Pain was also trended to correlate with the level of peripheral neuropathy p=0.07.

Health related quality of life relationships.

The correlation between the quality of life and pain, the level of neuropathy, level of education level of health, muscle strength of the right and left quadriceps muscles is shown in Table 4.15a Table 4.15b and Table 4.15c below

Table 4.15a Univariate model showing the correlation between the quality of life and pain, the level of neuropathy, level of education level of health, muscle strength of the right and left quadriceps muscles

	Odds ratio	Confidence interval	z	p value
Muscle strength right quadriceps	1.08	1.0- 1.18	1.86	0.06
Muscle strength left quadriceps	1.11	1.01-1.21	2.19	0.03
Pain score	0.59	0.43- 0.81	-3.27	0.001
Level of health	0.41	0.22- 0.76	-2.85	0.004
Level of neuropathy	0.86	0.76 0.97	-2.42	0.015

The correlation between quality of life and pain were similar p=0.001, the level of neuropathy p=0.01, level of health p=0.004, muscle strength of the right and left quadriceps muscles p=0.06 and p=0.03 respectively.

Table 4.15b Temporal and group adjusted model showing the correlation between the quality of life, level of health, muscle strength of the right quadriceps muscle strength of the left quadriceps muscle and pain

	Odds ratio	Confidence interval	z	p value
Level of health	0.39	0.21-0.73	-2.92	0.004
Muscle strength right quadriceps	1.09	1.0-1.19	1.92	0.055
Muscle strength left quadriceps	1.13	1.02- 1.25	2.32	0.021
Pain	0.56	0.4- 0.79	3.35	0.01

The correlation between quality of life and pain was significant p=0.001, and with the level of health p=0.004, muscle strength of the right and left quadriceps muscles p=0.06 and p=0.03 respectively in the temporal and group adjusted and the multivariate model.

Appendix H: Post intervention results of Study 1 and Study 2

The combined results of the reassessments done post intervention at week 12 of in Study 1 and Study 2 will be presented below. The results showing individual study results are presented in Appendix H

Gait performance (Study 1 and Study 2 combined)

Gait performance post intervention assessed using the performance oriented mobility (POMA) in the participants in Study 1 and Study 2 combined is presented in Table 4.9

Table 4.9 Gait scores post intervention in the participants (Study 1 and Study 2) (n=64)

Gait score	Control group (n=29) n (%)	Experimental group (n=16) n (%)
Poor (<9)	0	0
Good (9-10)	3 (13.3)	6 (18.8)
Excellent (11-12)	26 (86.7)	29 (71.2)

Balance performance (Study 1 and Study 2 combined)

Table 4.10 below presents the level of balance performance post intervention measured using the performance oriented mobility (POMA) in the participants in Study 1 and Study 2.

Table 4.10 Balance scores post intervention in the participants (Study 1 and Study 2) (n=64)

Balance score	Control group 1 (n=15) n (%)	Experimental group 1 (n=35) n (%)
Poor (<10)	0	0
Good (11-14)	7(33.3)	14 (50)
Excellent(15-16)	22 (66.7)	21 (50)

Pain levels Study 1 and Study 2 combined

Table 4.11 shows the pain levels of the participants in combined Study 1 and Study 2 post intervention as assessed Wong baker faces.

Table 4.11 Pain levels at post intervention in participants in (Study 1 and Study 2 combined) (n=64)

Pain level	Control group 1 (n= 29) n (%)	Experimental group (n=33) n (%)
No hurt (0)	3 (10.3)	10 (6.2)
Hurts a little bit (1)	8 (20)	14 (43.7)
Hurts a little more (2)	8 (33.3)	4 (18.8)
Hurts even more (3)	7 (26.7)	6 (25)
Hurts whole lot (4)	3 (10.3)	1 (6.3)

There was no difference in the pain level between the experimental and the control group, after the intervention for both Study 1, p=0.12 and study 2 p=0.17.

Health related quality of life levels Study 1 and Study 2

Table 4.12 below presents the health related quality of life levels of the participants in study 1 and study 2 post -intervention, as assessed by EQ5D

Table 4.12 Health related quality of life levels post intervention of the participants in study 1 and study 2 (n=64)

EQ5D level of health	Control group (n=29) n (%)	Experimental group (n=35) n (%)
Better	25 (80)	29 (68.8)
Same	3 (13.3)	4 (18.7)
Worse	1 (6.7)	2 (12.5)
VAS		

The health related quality of life visual analogue scale showed no difference between the groups at post intervention point p=0.68.

Appendix I: Hand Held Dynamometer





Appendix J: Approval of Title and Ethical Clearance Letters from Committees.

Faculty of Health Sciences
Medical School, 7 York Road, Parktown, 2193
Fax: (011) 717-2119
Tel: (011) 717-2745

Reference: Ms Tania Van Leeve
E-mail: tania.vanleeve@wits.ac.za
25 March 2009
Person No: 327583
PAG

Mr K Mkandla
29 Bath Road
Avondale
Harare
Zimbabwe

Dear Mr Mkandla

Master of Science in Physiotherapy: Approval of Title

We have pleasure in advising that your proposal entitled "*The effects of progressive resisted exercises on performance oriented mobility in persons with HIV related poly-neuropathy*" has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Mr Khumbulu Mkandla

CLEARANCE CERTIFICATE	M090214
PROJECT	The Effects of Progressive Resisted Exercises on Performance Oriented Mobility in Persons with Human Immunodefieincy Virus Related ....
INVESTIGATORS	Mr Khumbulu Mkandla.
DEPARTMENT	Department of Physiotherapy
DATE CONSIDERED	09.02.27
DECISION OF THE COMMITTEE*	Approved unconditionally

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

DATE 09.03.25 CHAIRPERSON .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Ms H Myezwa

DECLARATION OF INVESTIGATOR(S)

CITY OF HARARE

Director of Health Services

All correspondence to be addressed to the
DIRECTOR OF HEALTH SERVICES

DIRECTOR OF HEALTH SERVICES Rowan Martin
Building, Civic Centre, Pennefather Avenue,
off Rotten Row, Harare, Zimbabwe.
P.O. Box 596 Telephone 753326 753330/1/2
Fax: (263-4) 752093

Ref: 12/9/14

Your Ref.. .....

14 October 2009

Khumbula Mkandla
7 York Road
Parktown 2193
SOUTH AFRICA

Dear Sir

Re: **REQUEST TO SOURCE FOR PARTICIPANTS OF CLINICAL TRIAL AT THE OPPORTUNISTIC INFECTIONS CLINIC AT WILKINS AND BEATRICE ROAD HOSPITALS**

I refer to the above.

Permission is hereby granted for you to carry out the above clinical trial at the two city hospitals. Could you kindly liaise with the sisters-in-charge for the hospitals for further information.

Yours faithfully

DIRECTOR OF HEALTH SERVICES
SM/gm

Cc - Sisters-in-charge - Wilkins Hospital
- BRIDH

1

Telephone: 621100-19
Fax: 621157

ZIMBABWE

Reference:

HARARE CENTRAL HOSPITAL
P. O. Box ST 14
SOUTHERTON
Harare
Zimbabwe

11th June 2009

TO WHOM IT MAY CONCERN

RE: **REQUEST TO SOURCE PARTICIPANTS AT OPPORTUNISTIC INFECTIONS CLINIC AT HARARE HOSPITAL FOR CLINICAL TRIAL**

This memo serves to introduce Mr. Khumbula Mkandla who is a student with School of Therapeutic Sciences - Faculty of Health Sciences in South Africa.

Permission has been granted and at the end of research a copy of research proposal is submitted to the hospital for record.

HARARE CENTRAL HOSPITAL
CHIEF EXECUTIVE OFFICER
11 JUN 2009
P.O. BOX ST 14, SOUTHERTON
ZIMBABWE

Mr. G.A.N. Vera
CLINICAL DIRECTOR

HARARE CENTRAL HOSPITAL
CLINICAL DIRECTOR
11 JUN 2009
P.O. BOX ST 14, SOUTHERTON
ZIMBABWE

Telephone: 791792/791193/792747
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E-mail: mrcz@mrczimshared.co.zw
Website:- www.mrcz.org.zw



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

MRCZ APPROVAL LETTER

Ref: MRCZ/B/62 **Date: 9 SEPTEMBER 2009**

Mr. K. Mkandla
University Of the Witwatersrand
Department Of Physiotherapy
South Africa

RE: The Effects of Progressive Resisted Exercise on Performance Oriented Mobility in Persons with HIV Related Poly-neuropathy

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:-

(a) Study Protocol
(b) Consent Forms (English And Shona)
(c) Study questionnaires

- **APPROVAL NUMBER** **:MRCZ/B/62**

The above details should be used on all correspondences, consent forms and documents as appropriate.

- **MRCZ MEETING DATE** **: N/A**
- **APPROVAL DATE** **: 9 September, 2009**
- **EXPIRATION DATE** **: 8 September 2010**
- **TYPE OF MEETING** **: Expedited review**

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 Offices should be submitted one month 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 3 working days using standard forms obtainable from the MRCZ Offices.
- **MODIFICATIONS**: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ Offices 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 Offices.
- **QUESTIONS**: Please contact the MRCZ on Telephone No. (04) 791792, 791193 or by e-mail on mrcz@mrczimshared.co.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.

Yours Faithfully

R. Gutsire
.....
MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

MEDICAL RESEARCH COUNCIL OF ZIMBABWE
09 SEP 2009
APPROVED
P. O. BOX CY 573
CAUSEWAY, HARARE

PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH
Registered with the USA Office for Human Research Protections (OHRP) as an International IRB
(IRB Number IRB00002409 IORG0001913)

UNIVERSITY OF ZIMBABWE

COLLEGE OF HEALTH SCIENCES

MEMORANDUM

FROM: Chairman, Joint Research Ethics Committee **DATE:** 15 Sept 2010

TO: Khumbula Mkandla, Department of Rehabilitation **EXT:** 2239/2242
c.c: Chairman, Department of Rehabilitation

RE: **THE EFFECTS OF PROGRESSIVE RESISTED EXERCISES ON PERFORMANCE ORIENTED MOBILITY IN PERSONS WITH HIV RELATED POLY-NEUROPATHY – JREC/23/09.**

Thank you for your application for an annual renewal of your protocol. The Joint Research Ethics Committee has reviewed and approved your application to continue conducting the abovenamed study.

Renewal Date: 15 September 2010

Expiry Date: 15 September 2011

Prof MM Chidzonga

JOINT PARIRENYATWA HOSPITAL
& COLLEGE OF HEALTH SCIENCES
RESEARCH ETHICS COMMITTEE
2010 -09- 15
APPROVED
P O BOX A178, AVONDALE, HARARE
mmchidzonga@med.sch.uz.ac.zw

CITY OF HARARE

HEALTH Depart

Received from K. MAKANDLA

Amount in words SEVENTY - DOLLARS ONLY

Vote	Item	$
3701	8116	70

Date 4-01-11 № 57558 for City Treas

Repro Printers

CITY OF HARARE

Director of Health Services
DR STANLEY MUNGOFA
MD (Cuba) MPH (Dm)

All correspondence to be addressed to the
DIRECTOR OF HEALTH SERVICES

Ref.....

Your Ref.....

DIRECTOR OF HEALTH SERVICES
Rowan Martin Building,
Civic Centre,
Pennefather Avenue,
off Robert Rew.
Harare, Zimbabwe.
P. O. Box 596
Telephone: 753320
753330/1/2
Fax: (263-4) 752093

15 December 2010

Mr Kumbulani Makandla
School of Therapeutic Sciences
Faculty of Human Sciences
7 York Road
Parktown 2198
South Africa

Dear Sir,

REQUEST TO SOURCE FOR PARTICIPANTS OF CLINICAL TRIAL AT THE ANTIRETROVIRAL THERAPY DISPENSING MUNICIPAL CLINIC.

I acknowledge receipt of your letter dated 18 September 2010. Permission is granted for you to source for participants at our municipal health facilities.

You will be required to pay R479 or its equivalent in USD administration fee prior to commencement of the study.

Once payment is made kindly liaise with the Assistant Director of Health Services (Nursing) for further assistance.

Please note that it is our institutional policy that written permission should be sought from this department prior any presentation or publication of research findings.

Yours faithfully

DIRECTOR OF HEALTH SERVICES
PC/cb

CITY OF HARARE
4/1/11
CITY HEALTH DEPARTMENT

Cc Assistant Director Nursing

S/C Kwadzanai Please allow him/her to undertake research as stipulated in his/her proposal. Gentleman. AD(HS&N) 10/01/11
Please assist
Cleared by the Director of Health Services
A.C. MUGOMBA Acting DHS(N) 4/1/11

Telephone: 791792/791193/792747
Telefax: (263) - 4 - 790715
E-mail: mrcz@mrczimshared.co.zw
Website:- www.mrcz.org.zw



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

MRCZ CONTINUING APPROVAL LETTER

Ref: MRCZ/B/62 **Date: 14 September, 2010**

Mr. K. Mkandla
University Of Witwatersrand
Department Of Physiotherapy
South Africa

RE: The Effects Progressive Resisted Exercise O Performance Oriented Mobility I persons With HIV Related Poly-neuropathy

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 continue conducting the above titled study. This is based on the following

(a) Study Protocol
(b) Consent Forms (English And Shona)
(c) Study questionnaires

- **APPROVAL NUMBER** **:MRCZ/B/62**

The above details should be used on all correspondences, consent forms and documents as appropriate.

- **MRCZ MEETING DATE** **: N/A**
- **APPROVAL DATE** **: 13 September, 2010**
- **EXPIRATION DATE** **: 13 September, 2011**
- **TYPE OF MEETING** **: Expedited review**

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 Offices should be submitted one month before the expiration date for continuing review.

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- **QUESTIONS**: Please contact the MRCZ on Telephone No. (04) 791792, 791193 or by e-mail on mrcz@mrczimshared.co.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.

Yours Faithfully

.....
MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE



PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH
Registered with the USA Office for Human Research Protections (OHRP) as an International IRB
(IRB Number IRB00002409 IORG0001913)

UNIVERSITY OF ZIMBABWE

COLLEGE OF HEALTH SCIENCES

MEMORANDUM

FROM: Chairman, Joint Research Ethics Committee **DATE:** 15 Sept 2011

TO: Mr Khumbula Mkandla, Department of Rehabilitation **EXT:** 2239/2242
c.c: Chairman, Department of Rehabilitation

RE: THE EFFECTS OF PROGRESSIVE RESISTED EXERCISES ON PERFORMANCE ORIENTED MOBILITY IN PERSONS WITH HIV RELATED POLY-NEUROPATHY : JREC/23/09.

Thank you for your application for an annual renewal of your protocol. The Joint Research Ethics Committee has reviewed and approved your application to continue conducting the above named study.

Renewal Date: 15th September 2011

Expiry Date: 14th September 2012

Professor MM Chidzonga

Telephone: (263) - 4 - 791792/791193
Telefax: (263) - 4 - 790715
E-mail: mrcz@mrczimshared.co.zw
Website: http://www.mrcz.org.zw

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

CONTINUINING REVIEW APPROVAL LETTER

Ref: **MRCZ/A/B62** **15 September 2011**

Khumbula Mkandla
University of The Witwatersrand
Johannesburg
South Africa

RE:The Effects of Progressive Resisted Exercise on Performance Oriented Mobility in Persons with HIV Related Poly-Neuropathy

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) Progress Report

- **APPROVAL NUMBER : MRCZ/A/B62**

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

(i) MRCZ MEETING DATE : 15 September 2011
(ii) EXPIRATION DATE : 14 September 2012
(iii) TYPE OF MEETING : EXPEDITED

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- **QUESTIONS:** Please contact the MRCZ on Telephone No. (04) 791792, 791193 or by e-mail on mrcz@mrczimshared.co.zw.

Other

- Please be reminded to send in copies of your research results for our records as well as for Health Research Database.
- You're 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 ZIMB
15 SEP 2011
APPROVED
P. O. BOX CY 573 CAUSEWA

OF ZIMBABWE
15 2011
AP D
P. O. BOX CY HARARE

Appendix K: Participant Consent Information Sheet

APPENDIX 23A: SUBJECT INFORMED CONSENT

PROTOCOL TITLE:

THE EFFECTS OF RESISTED EXERCISES ON PERFOMANCE ORIENTED MOBILITY IN PERSONS WITH HIV RELATED POLY-NEUROPATHY PROGRESSIVE

NAME OF RESEARCHER: Khumbula Mkandla, *BSc. Physiotherapy (Hons)*

PHONE: 011 874 996 *Tel: 263-4-797800*

PROJECT DESCRIPTION:

Hallo. I am a postgraduate student (MSc), in the Physiotherapy Department at the University of the Witwatersrand, Johannesburg, South Africa. I am conducting a study in Zimbabwe in the field of HIV/AIDS care. I am inviting you to take part in this study on the effects of exercises on mobility in persons with HIV related poly-neuropathy.

You are one of the 78 people whom we expect to participate in this study to be done in the Harare area in Zimbabwe. You were selected as a possible participant in this study because you are an adult living with HIV-related poly-neuropathy.

YOUR RIGHTS

Before you decide whether or not to volunteer for this, study you must understand purpose, how it may help you, the risk to you, and what is expected of you .This process is called information consent.

PURPOSE OF RESEARCH STUDY

The aim of this study is to find out the effects of exercise on mobility and health related quality of life in people living with HIV. As part of this study, I need to make sure I find what effect exercises have on gait, balance and pain levels in people with HIV/AIDS related poly neuropathy. The study also wishes to see if the effect on mobility changes the health related quality of life in people with poly neuropathy.

Initials _____

PROCEDURES INVOLVED IN THE STUDY

- Permission from you to look at your medical records to get information on your diagnosis and treatment?
- Permission from you to assess if you are having any problems with feeling and strength in your legs. I will test how well you move around and for strength a non-invasive dynamometer (a small machine to measure force exerted) will be used. I will also use a set of activities to test your balance and the will ask you how much pain you have because of your condition.
- You will be required to answer some questions for about 30 minutes to find out what other difficulties/troubles you have that may be caused by any disturbance in movement. There will be questions on how you feel about yourself and the quality of life you have now.
- Following this all names will be put in a hat and you may be chosen to be in a group which will do exercises or you may be chosen to be in a group that does what is normally done in Zimbabwe. The exercises will be done in a gym in Harare where the group will not be identified as a group of participants with HIV but an exercise group. You will exercise for 50 minutes twice a week. The reason of exercises is to strengthen the muscles so as to improve the way they work.
- At the beginning of the exercise programme and after four months your sensation, strength of leg muscles and balance will be tested

RISKS AND DISCOMFORTS

Except for working hard and getting body aches initially from exercising, we do not expect you to have any ill effects from this exercise. Normally in Zimbabwe the doctors and nurses offer you advice on home exercise. All potential participants will receive this standard care whether or not s/he participates in the research study.

BENEFITS AND/OR COMPENSATION

We expect that if you are in the group that does exercises you may become fitter, improve your gait and balance as well as reduce your pain and get a better quality of life. However we cannot and do not guarantee or promise that you that this will certainly happen from this study. Your transport costs will be covered but there are no costs involved in taking part in the exercise sessions.

CONFIDENTIALITY OF RECORDS

Care will be taken to ensure that no names are recorded. You will be given a code on the records and only I and the research assistants will have access to the list that links your name to the code. Under some circumstances, the ethics council and my examiners may need to look at patient records to check if the study is being done properly. However the information that is obtained in connection with this study that can be identified with you will remain confidential and will be made known only if you agree.

Initials _____

STUDY WITHDRAWAL

If you feel you do not want to take part in the study for any reason you are free to do so. The normal treatment and services that you would need will not be affected in any way. If you should choose to participate, please sign the attached consent form and be assured you are free to stop at any time.

IN THE EVENT OF INJURY

The risk of injury during this study is low. However should any injury occur during exercise such as a strain or sprain; treatment will be made available at Parirenyatwa Hospital. You should understand that we will not be able to pay for your treatment so the costs of such treatment will be paid by you.
In the case that you get an injury, contact Anne Butau 0912 831 018 who will assist you.

PROBLEMS/QUESTIONS

Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over.

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research subject or research-related injuries; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the Medical Research Council of Zimbabwe on telephone 791792 or 791193.

AUTHORIZATION

You are making a decision whether or not to participate in this study. Your signature indicates that you have read and understood the information provided above, have had all your questions answered, and have decided to participate.

The date you sign this document to enroll in this study, that is, today's date, MUST fall between the dates indicated on the approval stamp affixed to each page. These dates indicate that this form is valid when you enroll in the study but do not reflect how long you may participate in the study. Each page of this Informed Consent Form is stamped to indicate the form's validity as approved by the MRCZ.

Initials _____

AUTHORIZATION

I have read this paper about the study or it was read to me. I understand the possible risk and benefits of this study. I know being in this study is voluntary. I choose to be in this study: I know I can stop being in the study and will not lose any benefits entitled to me. I will get a copy of this consent form. (Initial all the previous pages of the consent form)

_____

Client Signature Date

_____

Client Name (Printed)

_____

Research Signature Date

_____

Witness Signature Date

Initials _____

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

APPENDIX 23B: GWARO REKUBVUMA KWAKAZIVISWA

MUSORO WECHIDZIDZO

THE EFFECTS OF RESISTED EXERCISES ON PERFOMANCE ORIENTED MOBILITY IN PERSONS WITH HIV RELATED POLY-NEUROPATHY PROGRESSIVE

ZITA REMUTSVAGIRIDZI: Khumbula Mkandla, *BSc. Physiotherapy (Hons)*

RUNHARE: 011 874 996 *Tel: 263-4-797800*

RONDEDZERO YECHIDZIDZO

Makadii Ini ndiri kuita dzidzo yepamusoro (MSc), muDepartment rePhysiotherapy paUniversity yeWitwatersrand, muJohannesburg, South Africa. Ndiri kuita chidzidzo chetsvagiridzo muZimbabwe maererano nezve kubatsirwa kweavo vaneutachiona hwe shuramatongo (HIV/AIDS). Ndinokukokai kuti mubatane nesu muchidzidzo ichi chinoongorora zvingaitika kumafambiro emunhu ane utachiona hweHIV uye achirwadziwa nemakumbo kana achinge aita zvekusimbisa muviri wake. Muri mumwe wevanhu makumi manomwe nesere avanhu vatiri kutarisira kuti vapinde muchidzidzo ichi chichaitwa munharaunda yeHarare muZimbabwe. Imi makasarudzwa semumwe angangopinda mutsvagiridzo iyi nekuti muri munhu abvazera anorarama neutachiona hwe HIV uye muchirwadziwa nemakumbo.

KODZERO DZENYU

Musati mafunga kuti mupinde here kana kuti kwete muchidzidzo ichi munofanira kunzwisisa chinangwa chechidzidzo, kuti munogona kubatsirika sei, zvinogona kukukuvadzai, uye zvinotarisirwa kwamuri. Maitire awa ndiwo anonzi kubvuma kwakaziviswa.

CHINANGWA CHECHIDZIDZO

Chinangwa chechidzidzo ichi ndechekutsvagiridza kuti chii chinoitika kana munhu aita urongwa hwekusimbisa muviri pakugona kwake kufamba uye magariro ane chekuita neutano muupenyu hweavo vari kurarama neHIV. Ndinoda kubata chokwadi maererano nezvinoitika kana munhu ane utachiona hweHIV uye achirwadziwa nemakumbo achinge aiita zvekusimbisa nyama maererano nemafambiro ake, mutsigo pakumira neudzamu hwemarwadzo. Chidzidzo ichi chinodawo kuwona zvinoitika kana mafambiro emunhu ane marwadzo emakumbo asanduka maererano nemanakiro ehupenyu hwake.

Initials_____

MATANHO EZVIITWA HWECHIDZIDZO

- Mvumo kubva kwamuri yekuti ndigone kutarisa mumagwaro akanyorwa nezveutano hwenyu kuti ndiwane ruzivo maererano nekuti munechirwere chipi uye kuti makamborapwa sei?
- Mvumo kubva kwamuri yekunyatsoongorora kana muine dambudziko maererano nekubatwa kana kushaya simba mumakumbo. Ndichaongorora kuti munofamba zvakanaka here uye ndichapima simba ririmumakumbo ndichishandisa kamuchina kadiki kano shandiswa kupima simba rinenge richishandiswa (dynamometer). Ndichazenge ndichishandisa zviitwa zvakasiyana siyana kuitirakuona kuti munomira makatsiga here uye ndichakubvunzai mushure mechiitiko chega chega kana pane kurwadziwa kwamunenge muchinzwa nekuda kwedambudzo ramuinaro.
- Muchange muchizotarisirwa kupindura mibvunzo kwenguva ingangoita maminitsi anokwana makumi matatu kuti titsvage kana paine mamwe matambudziko kana kunetseka kwamungadaro muinako kuchikonzerwa nenekukanganisika kwakaitika pamusoro pamafambiro enyu. Pachaitawo mibvunzo pamusoro pezvamunonzwa pamusoro penyu uye kunaka kweupenyu hwamuri kurarama parizvino.
- Mushure meizvi mazita ose achaiswa munguwani (hat) uye munozogona kuiswa muboka kana muchikwata chevachazo ita maexercise kana kuti muboka rinoita zvinosingoitwa muZimbabwe. Zviitwa zvekusimbisa muviri izvi zvichaitwa munzvimbo iri muHarare apo boka revanege vari muchirongwa ichi vanenge vachizivikanwa seboka rekuzvisimbisa muviri chete. Muchaita zvekusimbisa muviri izvi kwemaminitsi makumi mashanu kaviri pasvondo. Chikonzero chekusimbisa muviri kuti nyama dzemuviri dzivandudzwe mashandiro adzo.
- Pamavambo nepekupedzisira pechirongwa mushure memwedzi mina muchaongororwa manzwiro enyu, simba remakumbo nekutsiga pakumira.

MARWADZO KANA ZVINGANGOIPA

Kunze kwekushanda zvine simba nekungorwadziwa nenyama dzemuviri mushure mekushanda muzviitwa zvekusimbisa muviri hapana zvimwe zvakaipa zvatinotarisira kuti zvingakonzerwe nechirongwa ichi. Kazhinji muZimbabwe vana chiremba nevakoti vanokunyeurirai chete kuti munoita zvekusimbisa muviri muri kumba. Vose vangangopinda muchidzidzo ichi vachapihwa nyeuriro iyi zvisinei kuti vapinda kana kuti varegera kupinda muchidzidzo chetsvagiridzo iyi.

ZVAMUNGANGO BATSIRIKA NAZVO

Tinotarisira kuti kana muri muchikwata chichange chichiita zvekusimbisa muviri muchagwinya uye kufamba nemutsigo wenyu zvichiva nani ukuwo marwadzo enyu oderera imi muchivawo neraramo yeupenyu yakavandudzwa. Zvisinei hatigoni kuti tikuvimbisei kuti izvi ndizvo zvichaitika zvechokwadi nekuda kwechidzidzo ichi. Muchapihwa muripo wemari yamunenge mashandisa kufambisa iyo muchadzorerwa asi hapana dzimwe mari dzamunozoripiswa kuti muite zvekusimbisa muviri nevamwe.

Initials_____

KUBUDA MUCHIDZIDZO

Munogona kusarudza kuregera kupinda muchidzidzo kana kubuda muchidzidzo panguva ipi zvayo pasina kurasikirwa nezvamakakodzera kubatsirikana nazvo. Kurapwa kwenyu kwemazuva ose nezvimwe zvamunoitirwa zvamunoda hazvizokanganiswi nenzira ipi zvayo. Kana masarudza kuva mumwe wevari muchidzidzo, tapota isai runyorwa pabepa remvumo rakanamirirwa pamberi muine idi rekuti makasununguka kuregera chero ipi nguva zvayo.

KUCHENGETEDZWA KWERUZIVO PAMUSORO PENYU

Tichanyatso cherechedza kuti hapana mazita anonyorwa pasi. Muchapihwa imwe nzira yekucherechedza kuti ndimi (code) mune zvichanyorwa pamusoro penyu uye ini neve boka rangu ndisu tichange tichiziva kuti imi ndimi vapi. Pane dzimwe nhambo kanzuru inopa mitemo nemashandiro atinoita patsvagiridzo nevachaongorora basa rangu vanogona kutarisa magwaro atinonyora aneruzivo rwamunenge matipa vachida kuona kuti chidzidzo ichi chiri kuitwa nemazvo. Zvichakadaro, ruzivo rwamunenge matipa maererano nechidzidzo ichi rwunogona kukunongedzai kuti ndimi ani rwucharamba rwakachengetedzwa uye ruchabudiswa kanemi chete muchibvuma.
Zvisinei ruzivo urwu rwungango budiswa kana zvichidikanwa nemutemo.

KANA MUCHINGE MAKUVARA

Mukana wekukuvara muchidzidzo ichi mushoma. Zvisinei zvazvo, kana muchinge makuvara zvakaita sekuminyuka, kanawo kudhonzeka kwenyama, munokwanisa kuzorapiwa pachipatara che Parirenyatwa. Tinokumbira kuti munzwisise kuti hatikwanise kunge tichizokubhadharirai kuchipatara nekudaro imi muchazokumbirwa kuti mubhadhare mari yekurapwa mega. Kuri kuti makuvara chayayi nhare kuna Anne Butau panhamba dzinoti 0912 831 018 iye anozo kubatsirai.

MATAMBUDZIKO/MIBVUNZO

Tapota bvunzai zvenyu nyangwe ipi zvayo mibvunzo pamusoro pechidzidzo ichi kana gwaro remvumo iyi iye zvino.
Kana muine imwe mibvunzo mune ramangwana munogona kuzondifonera panhare dzinoti 011 874 996 / 263-4-797800

Kana muine mibvunzo pamusoro pechidzidzo ichi kana kuti gwaro rekupamvumo iri pamusoro peiyo yapindurwa, nemusori ,kusanganisira mibvunzo ine chekuita netsvagiridzo iyi kana pekodzero dzenyu semunhu achange arimuchirongwa kana kukuvara kunechekuita nechidzidzo ichi. Kana kuti kana maona sekuti mabatwa zvisina kururama uye muchida kutaura nemumwe munhu asiri muboka revatsvagiridzi sununguka kuona ve Medical Research Council of Zimbabwe panhare idzi 791792 or 791193

Initials_____

MVUMO YENYU

Mavakuita sarudzo yekuti munoda here kana kuti hamudi kubatidzana nesu muchidzidzo ichi. Kuisa runyorwa kwenyu kucharatidza kuti maverenga mukanzwisisa tsananguro yatakupai pamusoro pechidzidzo uye kuti mibvunzo yenyu yose yapindurwa uye kuti mafunga kubatidzana nesu.

Zuva ramunoisa runyorwa rwenyu pagwaro iri rekupinda muchidzidzo ichi rinova zuva ranhasi, RINOFANIRA kuwira pakati pemazuva akaratidzwa pachitambi chemvumo chakaiswa pabepa regarega. Mazuva awa anoratidza kuti bepa iri ndere chokwadi apo munopinda muchidzidzo asi izvi hazviratidzi kuti muchange muri muchidzidzo kwenguva yakadii. Rimwe nerimwe remapepa awa emvumo akadhindwa kuratidza kuti zvechokwadi bepa iri rakabvumidzwa neve MRCZ.

MVUMO YENYU

Ndaverenga bepa iri pamusoro pechidzidzo ichi kana kuti ndaverengerwa nemumwe munhu. Ndanzwisisa zvingangoipa nekubatsirikana kungaitika muchidzidzo ichi. Ndinoziva kuti kuva muchidzidzo ichi kuda changu. Ndinoda kuva muchidzidzo ichi: Ndinoziva kuti ndinogona kuregera kuva muchidzidzo ichi pasina kurasikirwa ne izvo ndinofanira kubatsirikana nazvo. Ndichawana mapepa akafanana neandapa mvumo yangu awa. (Nyorai mavara ekutanga pamazita renyu pamapepa ose egwaro remvumo iri)

_____

Runyorwa rwenyu Date

_____

Zita renyu (nyorai zvinoverengeka)

_____

Runyorwa rwemutsvagiridzi Date

_____

Runyorwa rwemufakazi Date

Initials _____

MUCHAPIWA RIMWE BEPA REKUBVUMA KWENYU KUTI MUCHENGETE.