THE TEST-RETEST RELIABILITY OF THE LOWER EXTREMITY FUNCTIONAL SCALE IN HIV-RELATED DISTAL SENSORY PERIPHERAL NEUROPATHY

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DECLARATION

I, Abraham C Munemo, declare that this research report is my own work. It is being 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.

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.....04th.....day of .....DECEMBER.....2017.

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DEDICATION

To my wife,

Sandra,

for all her support, love and long suffering without murmuring;

To my children,

Esther, Emmanuel, and Michael,

for your support, encouragement, prayers, and inspiration.

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DEFINITION OF TERMS

People Living with HIV (PLWHIV). : This is defined as people living with HIV. Acquiring HIV no longer means certain death. It has been changed to a chronic illness under treatment medication.

People living with AIDS. (PLWA). : This is defined as people living with an acquired immune deficiency syndrome (AIDS). These could be infants, children or adults. This is the recommended term due to the fact that it shows that individuals who are infected may continue to live longer and productively (UNAIDS, 2007).

Test-retest Reliability. : This is defined as the quality of being trustworthy or of performing consistently well over an interval of time.

Construct Validity (CV). : This is the degree to which an outcome tool measures what it claims, or purports, to be measuring.

Lower Extremity Functional Scale (LEFS). : This is an outcome measure that is used to measure the lower limb functional activities and movements.

Distal Sensory Peripheral Neuropathy ; damage to or disease affecting nerves, which may impair sensation, movement, or other aspects of health, depending on the type of nerve affected. In this study we are looking to causes by the use of the antiretroviral medication.

LIST OF ABBREVIATIONS

ADL	-	Activities of Daily living
AIDS	-	Acquired Immunodeficiency Syndrome
CD4	-	Cluster Definition 4
CDC	-	Centres for Disease Control
CNS	-	Central Nervous System
CT	-	Computer Tomography Scans
CVA	-	Cardio Vascular Accident
DNA	-	Deoxy Ribonucleic Acid
DSPN	-	Distal Sensory Peripheral Neuropathy
EFV	-	Efavirenz
FIM	-	Functional Independence Measure
GBS	-	Guillain Barre Syndrome
HAART	-	Highly Active Antiretroviral Therapy
HIV	-	Human Immunodeficiency Virus
HIV/AIDS	-	Human Immunodeficiency Virus/Acquired immunodeficiency Syndrome
HRQOL	-	Health-related quality of life
ICF	-	International Classification of Function
ICU	-	Intensive Care Unit
LEFS	-	Lower Extremity Functional Scale
LLFI	-	Lower Limb Functional Index
NNRTIs	-	None Nucleoside Reverse Transcriptase Inhibitors
NRTIs	-	Nucleoside Reverse Transcriptase Inhibitors
PCP	-	Pneumocystics Jiroveci/Carinii Pneumonia
PLWA	-	People living with AIDS
PLWH	-	People living with HIV
QOL	-	Quality of Life
RNA	-	Ribonucleic Acid
RVD	-	Retro Viral Disease
SEM	-	Standard Error Measurement
SF-36	-	Short Form 36-item questionnaire
STI	-	Sexually Transmitted Infection
TB	-	Tuberculosis.
TENS	-	Transcutaneous Electrical Stimulation.
UNAIDS	-	The Joint United Nations Programme on HIV/AIDS.

WHO	-	World Health Organization
WOMAC-PF	-	Western Ontario and MacMaster Universities Osteoarthritis Physical Function

ABSTRACT

Background: The Human Immunodeficiency Virus (HIV) and the Acquired Immune Deficiency Syndrome (AIDS) have posed a serious disease burden on society. The side effects issuing from the anti`-retroviral drugs (ARVs) include Distal Sensory Peripheral Neuropathy (DSPN), a common neurological complication. The Lower Extremity Functional Scale (LLFS) is a reliable and valid tool that has been used for measuring the lower limb functional capacity of patients presenting with DSPN in countries other than Botswana. As such, it is necessary to test its test-retest reliability in Botswana.

Aim: The aim of this study was to determine the test-retest reliability of the Lower Extremity Functional Scale (LEFS) among HIV-related DSPN patients in Botswana.

Methodology: This study involved a test-retest reliability study based on a time interval of seven to 10 days. A total of 320 HIV patients from six hospitals in Gaborone, Botswana, were screened for DSPN according to the relevant inclusion and exclusion criteria .The percentage of the total patients who were diagnosed with DSPN was 26.3% (84). The lower extremity functional scale LEFS questionnaire was administered twice with a seven to 10-day period interval and the results of the assessment were recorded and analysed.

Measurements of central tendencies were used to summarize the demographic data and the clinical information for the lower extremity functional scale information obtained. Because the data sets were categorical, Spearman's correlation analysis was conducted to determine the efficacy of the test-retest reliability.

Furthermore, the Intraclass correlation (ICC) was used for measuring the internal consistency of the LEFS questionnaire. Demographic data such as age, gender, education and marital status, and clinical information pertaining to the participants were used to describe them.

Results: A total of 84 HIV patients from six hospitals who were on anti-retroviral therapy (ART) and presenting with DSPN participated in the study. The test-retest reliability was found to range from r_s=0.74-0.99, ICC = 0.96. SEM=4.88

Conclusion: The study results showed strong test-retest reliability and good internal consistency. Hence, the LEFS questionnaire can be considered reliable as a standard from which to monitor lower limb functionality in HIV-related Distal Sensory Peripheral Neuropathy among patients in Botswana.

CHAPTER ONE: INTRODUCTION

1.1. BACKGROUND

Both the Human Immunodeficiency Virus (HIV) and the Acquired Immune Deficiency Syndrome (AIDS) have been prevalent in the human population for over three decades. In the ensuing years, interest in the measurement of self-reported functioning and wellbeing, or health-related quality of life (HRQOL), in HIV-infected individuals has been extensive (Gabel et al., 2012). Although there is still no cure for HIV, the increased use of anti-retroviral therapy (ART) has led to substantial improvements in AIDS-free survival and also the decline in mortality in HIV-infected individuals (Murphy et al., 2001, Krentz et al., 2005, Cettomai et al., 2010). Modifications to the natural progress of the HIV disease through the use of anti-retroviral drugs have in fact had diverse effects, both beneficial and toxic, on patients since these drugs have significantly improved the quality of life in the patient population but also have significant side effects (Brinley Jr et al., 2001).

HIV, recognised as a chronic disease, has been reported to have a long-term effect on the mental, sensory and perceptive functions and the genitourinary, cardiovascular and respiratory systems of human beings (Hanass-Hancock et al., 2013). In fact, Distal Sensory Peripheral Neuropathy (DSPN) is the most common neurological complication issuing from the use of anti-retroviral drugs (ARVs) by HIV patients (Manji and Miller, 2004, Gonzalez-Duarte et al., 2007, Nicholas et al., 2010, Wadley et al., 2011).

The prevalence of peripheral neuropathy among people living with HIV (PLHIV) patients receiving ARV treatment in South Africa has been reported to be as high as 49% (Maritz et al., 2010). DSPN is widely undiagnosed and undertreated in most

medical institutions, and more especially in resource-limited settings (Cettomai et al., 2010).

The long-term use of ARVs has been associated with peripheral neuropathies (Ellis et al., 2008, Cettomai et al., 2010). The ARVs most commonly used in developing countries were Isoniazid and Stavudine (Robertson et al., 2008). It has been reported in the literature that these drugs predispose patients who have been diagnosed with HIV to symptoms of peripheral neuropathy (Cettomai et al., 2010). The specific pathophysiology of DSPN, although a common complication of the HIV disease, is not well understood. However, there has been evidence to suggest that the long-term use of ARVs results in mitochondrial toxicity, which subsequently results in tissue damage (Gardner et al., 2014).

In rehabilitation, there is a dearth of knowledge concerning the optimal interventions to improve lower extremity function and to manage such symptoms. In sub-Saharan Africa, only two studies from Kenya and Rwanda have used the lower limb functional scale as an outcome measure to evaluate lower limb function in HIV patients diagnosed with DSPN (Cettomai et al., 2010, Tumusiime, 2014).

The Lower Extremity Functional Scale (LEFS) is a reliable tool that has been used to detect the functioning of the lower limbs (Binkley et al., 1999). Hence, it enables the assessor to determine the functionality and the quality of life of the patient. The LEFS has been found to be both reliable and valid in evaluating lower limb function on account of the musculoskeletal problems that are so prevalent in the lower limbs of the elderly and the middle aged (Watson et al., 2005, Στασή et al., 2015).

Hoogeboom et al. (2012) evaluated the reliability and validity of the LEFS in evaluating lower limb function in patients with osteoarthritis of the hip and knee. It has been shown that the LEFS tool, in conjunction with other outcome measures

associated with hip and knee arthritis, such as the Hip Osteoarthritis Outcome Score and the Knee Osteoarthritis Outcome Score, is reliable and valid. The study by Hoogeboom et al. (2012) showed that the LEFS obtained higher specificity and sensitivity levels in the evaluation of lower limb impairment as opposed to those obtained by the Western Ontario and McMaster Universities Osteoarthritis Physical Function (WOMAC PF) Scale.

The LEFS questionnaire has been reported to have good measurement properties, namely test-retest reliability and cross-sectional construct validity. As such, it could be an alternative to the WOMAC-PF Scale (Cettomai et al., 2010).

An Italian version of the LEFS has been found to be reliable, valid and responsive in measuring lower limb impairment in people suffering from musculoskeletal problems (Cacchio et al., 2010). In sub-Saharan Africa, in Kenya and Rwanda specifically, the LEFS questionnaire has been used to effectively evaluate lower limb function and has been found to be reliable and valid (Cettomai et al., 2010, Tumusiime, 2014).

Since individuals with HIV are surviving longer, often in fact living for decades with the disease, chronic comorbidity such as DSPN must be addressed (Keswani et al., 2002). It is important, therefore, to include the management of peripheral neuropathy which is a common problem recognised among HIV patients when the holistic intervention approach is applied (Myezwa et al., 2009, Nicholas et al., 2010). Furthermore, the characterization of lower extremity function in HIV patients and their quality of life (QOL) must also be addressed in order to provide clinicians with optimal outcome assessments to measure DSPN changes with treatment over time (Ellis et al., 2008, Nicholas et al., 2010).

Evidence on the test-retest reliability of the LEFS in the evaluation of lower limb impairment among HIV patients is scanty. Because only two studies in sub-Saharan Africa have used the LEFS as an outcome measure among HIV patients (Cettomai et al., 2010, Tumusiime, 2014). A similar study in Botswana, also in sub-Saharan Africa, would, according to the UNAIDS report in 2015 (UNAIDS, 2015) be welcomed in that Botswana has a high prevalence of HIV with an estimated 350 000 people living with HIV/AIDS.

There is much evidence of long-term comorbidity of HIV in Botswana's HIV population (Ansari et al., 2002, Gupta et al., 2010). There is thus a need for the Lower Extremity Functional Scale (LEFS) to be used in this country since this outcomes measure is easy to administer and also to score (Binkley et al., 1999). This study therefore set out to test the reliability of the LEFS questionnaire as an outcome measure in the identification of lower limb impairment among PLHIV patients in Botswana.

1.2. RESEARCH PROBLEM

The test-retest reliability of the Lower Extremity Functional Scale (LEFS) in the measurement of lower extremity function in HIV patients who are on ART (anti-retroviral therapy) treatment was unknown in Botswana prior to the initiation of this study.

1.3. AIM OF THE STUDY

The aim of this study was therefore to determine the test–retest reliability of the LEFS as an outcome measurement tool to establish lower limb function in patients with HIV related DSPN in the case of Botswana.

1.4. OBJECTIVES OF THE STUDY

- To establish the test-retest reliability of the LEFS in the measurement of lower limb function in HIV-related DSPN in Botswana
- To determine the internal consistency of the LEFS for lower limb function in HIV-related DSPN in Botswana
- To describe the demographic and clinical characteristics of HIV patients with DSPN in Botswana
- To determine the construct validity of the LEFS in participants with DSPN in Botswana.

1.5. SIGNIFICANCE OF STUDY

By establishing the test-retest reliability of the LEFS for patients with HIV related DSPN, through identification tools which are both valid and reliable, rehabilitation professionals and other medical practitioners will acquire more information about DSPN patients' problems The LEFS is recommended as a measure to determine the challenges that the patients in the sample are experiencing. The test-retest reliability of the LEFS will provide better understanding of DSPN in Botswana.

Peripheral neuropathy is one of the most common musculoskeletal problems among HIV patients and is associated with functional limitations. The extent of these limitations needs to be comprehensively assessed. Therefore, this study sets out to provide information that will inform health professionals about rehabilitation outcome measures and provide a clearer picture of the lower limb functional outcomes of peripheral neuropathy in PLHIV patients in Botswana.

1.6. GENERAL OUTLINE OF THE STUDY

Chapter One

Chapter one is focused on the background to this study and the necessity for undertaking this research. A statement of the problem and the aims and objectives of this study are also presented in this chapter.

Chapter Two

Chapter Two focuses on a review of the relevant literature justifying the necessity for undertaking this project and the steps in the process of this study.

Chapter Three

Chapter Three focuses on the methodology of the study and includes the pilot study and the main study.

Chapter Four

This chapter is focused on presenting the results emanating from the statistical analysis of the data.

Chapter Five

Chapter Five focuses on a discussion and interpretation of the results of the study

Chapter Six

This is the final chapter in the thesis and it focuses on summarizing the study.

1.7. SUMMARY OF CHAPTER ONE

This chapter explains the background and the need for the test-retest reliability of the LEFS in HIV-related DSPN. The problem statement and the aims and objectives of the study are explained in this chapter.

2. CHAPTER TWO: LITERATURE REVIEW

2.1. INTRODUCTION

The literature review focuses on peripheral neuropathy as one of the most common side-effects of anti-retroviral therapy in people living with HIV. This chapter reviews the literature on the presentation and the limitations associated with peripheral neuropathy in people infected with HIV, with the main focus being on the test-retest reliability of the LEFS in HIV-related DSPN.

The search engines used in this research included Google Scholar, the Google Search Website, Pubmed, and various physiotherapy journal publications, EBSCO, Cochrane Collaboration and Science Direct. Key words used were Lower Limb Functional Scale (LEFS), Human-immunodeficiency Virus/Auto-immune Deficiency Syndrome (HIV/AIDS), validity, test-retest reliability, Distal Sensory Peripheral Neuropathy (DSPN), quality of life (QOL) and Anti-retroviral Therapy (ART). Physiotherapy articles pertaining to the Lower Extremity Functional Scale, and published between 1995 and 2016 were included in this review.

2.2. EPIDEMIOLOGY OF THE PANDEMIC OF HIV/AIDS GLOBALLY

There are approximately 36.7 million people in the world who are infected with HIV and the epicentre of the disease is in sub-Saharan Africa, especially in southern Africa (UNAIDS, 2011). As a result of effective pharmacological management, as well as other policies and strategies, there has been a significant reduction in the prevalence of the pandemic in most southern African countries (Deanna Cettomai, 2010). In the face of the high death rate of approximately two million people in the 2010 decade, an intensified dispensation of highly aggressive anti-retroviral

therapy was rolled out to raise the life expectancy among people suffering from HIV and AIDS (Samji et al., 2013).

Unfortunately, there are a number of related side effects of the anti-retroviral drugs. These are due to their neuro-toxic nature and the complications arising from the HIV infection. Apart from, but also together with them, these opportunistic infections have presented a major medical challenge in the management of HIV (Nicholas et al., 2010). One of the complications of anti-retroviral drugs is Distal Sensory Peripheral Neuropathy. A summary of the impacts of HIV on the body systems is presented below.

2.2.1. HIV Impacts on the Body Systems

Systems affected by the HIV disease include the musculo-skeletal (Joseph and Habib, 2009), the nervous (Smurzynski et al., 2011), the respiratory (Ghezzi, 2011), the gastro-intestinal (Deeks et al., 2013) and the immune systems (McMichael et al., 2010).

2.2.2. The Musculo-Skeletal System

In the past, prior to the administration of ART, gross muscle atrophy or muscle mass loss tended to be the major clinical symptom signalling the occurrence of HIV (Dubé et al., 2007). This was attributed to elevated levels of glucocorticoids and cytokines in the body which tended to slow down the process of protein synthesis and to increase the rate at which the muscle structure is broken down. The elevated glucocorticoids and cytokine, levels have their source largely in the recurrent and consecutive opportunistic infections that HIV-infected patients are vulnerable to. The afore-mentioned eventually lead to energy consumption in periods of resting and also to poor appetite, the final result being the emaciation of the individual. In fact, general

body wasting still remains a major impact that the HIV has on the body (Dubé et al., 2007).

2.2.3. The Central Nervous System

Serious consequences for the nervous system also occur in HIV-infected patients. The final result when the human-immunodeficiency virus gains access to the brain is the destruction of the neurological cells of the central nervous system. This is complicated by the fact that there is reduced accessibility of the anti-retroviral drugs to penetrate the blood-brain barrier (Namanja et al., 2011).

It was therefore not unexpected for a large proportion (two-thirds) of the participants in a study conducted in Gauteng to report that they were presenting with cognitive impairments (Hanass-Hancock et al., 2013). Dementia is one of the more commonly reported cognitive impairments resulting from the HIV virus (Hanass-Hancock et al., 2015).

The most common neurological complication experienced by patients with the HIV is DSPN (Tumusiime, 2014). It brings with it comorbidity too. Studies have shown that the prevalence of neuropathy in HIV patients ranges from 38% to 53% (Nicholas et al., 2010). Individuals with HIV–related DSPN experience pain, paraesthesia, numbness, and more especially the impairment of their lower limbs. As a result, they suffer episodic disability (Phillips et al., 2010). Their functionality is impaired, and they experience a decline in their quality of life (Galantino et al., 2014). The use of ARVs aggravates the severity of peripheral neuropathy (Phillips et al., 2010). Some other risk factors compounding the problem of impaired lower limb function include advancing age and prior exposure to various kinds of anti-retroviral therapy regimens, as well as a longstanding history of HIV infection (Ances et al., 2012).

2.3. COMPLICATING FACTORS

In the event of advanced HIV disease and the use of substances and drugs other than the anti-retrovirals such as alcohol, marijuana or cocaine, the patient places himself at great risk of contracting DSPN and could also suffer a reduction in his/her CD4 count (Robinson-Papp et al., 2012).

Other adverse consequences in patients with HIV/AIDS on anti-retroviral therapy and resulting from unhealthy lifestyle practices in the form of substance and drug abuse do occasionally occur in conjunction with peripheral neuropathy. They include conditions such as lipodystrophy (Guaraldi et al., 2011) which occurs in patients on the Stavudine regimen. Their condition has been noted to be significantly different from those on the Zidovudine antiretroviral regimen (Guaraldi et al., 2011).

Other published literature sources point to instances where distal sensory neuropathy presents in patients that have not yet commenced the antiretroviral therapy regimen (Robertson et al., 2008). Important to note is the fact that the occurrence of DSNP shows a significant association with the destruction of the myelin sheath surrounding the peripheral nerves which can generally be attributed to infection due to the human-immuno virus (Robertson et al., 2008).

2.4. CLINICAL STAGES OF HIV/AIDS

According to the World Health Organisation (WHO) classification, the progression of HIV is classified into four stages, as outlined in Table 2.1 below.

Table 2.1: WHO Clinical Stages of HIV/AIDS (World Health Organisation, 2007)

HIV Stages	Description of the Stages
Stage 1 *	▪ Asymptomatic persistent generalized lymphadenopathy ▪ Moderate unexplained weight loss (<10% of the individual's usual body weight) ▪ Recurrent acute respiratory infections (ARIs), Occurrence of the Herpes Zoster Complex
Stage 2 **	▪ Angular cheilitis, recurrent oral ulceration, popular pruritic eruptions ▪ Seborrheic dermatitis, fungal infections of the nails ▪ More than 10% unexplained body weight loss as opposed to the measured body weight ▪ >one month of unexplained chronic diarrhoea and intermittent or constant unexplained fever ▪ Chronic oral thrush- candidiasis, oral hairy leucoplakia, current TB (tuberculosis).
Stage 3 ***	▪ Intense bacterial infections such as empyema, pneumonia, joint or bone infection, pyomyositis , bacteraemia and meningitis ▪ Periodontitis, gingivitis or acute necrotizing ulcerative stomatitis ▪ Insidious anaemia (Hb <8g/dL), Neutropenia (neutrophils<500 cells/uL) ▪ Thrombocytopenia which is chronic (platelets < 50,000 cells/uL) ▪ HIV wasting syndrome, pneumocystic pneumonia ▪ Bacterial pneumonia which is severe and recurrent ▪ Herpes simplex infection which is chronic in areas; oesophageal candidiasis ▪ Extra pulmonary TB, cancers such as Kaposi sarcoma ▪ CMV cytomegalovirus infection (infections of other organs or renitis) ▪ Central nervous system toxoplasmosis, encephalopathy due to HIV ▪ Extra pulmonary cryptococcosis (inclusive of meningitis)
Stage 4	▪ Disseminated non TB mycobacterial infections ▪ Progressive multifocal leukoencephalopathy ▪ Lungs, bronchi and tracheal candida ▪ Diarrhoea infection, chronic cryptosporidiosis ▪ Disseminated mycosis (such as penicilliosis, histoplasmosis, coccidioidomycosis) ▪ Chronic isosporiasis ▪ Recurrent non-typhoidal Salmonella bacteria ▪ Cerebral as well as B-cell non-Hodgkins lymphoma ▪ Invasive cervical carcinoma ▪ Disseminated leishmaniasis, which is atypical ▪ Symptomatic HIV–associated nephropathy and cardiomyopathy ▪ Reactivation of the American trypanosomiasis (such as myocarditis or meningoencephalitis)

DSPN is commonly diagnosed in the third and fourth stages of the HIV disease (World Health Organisation, 2007).

2.5. DISTAL SENSORY PERIPHERAL NEUROPATHY IN HIV PATIENTS

HIV affects the nervous system directly and indirectly in that it affects the nerves, nervous tissue and exacerbates opportunistic infections .Table 2.2 outlines the aetiology and signs and symptoms of some of the common conditions presenting in HIV and AIDS patients. Included are the pathologies, signs and symptoms that are associated with the corresponding disease.

Table 2.2: Summary of Peripheral Neuropathies Associated with HIV

Condition	Pathology	Signs and symptoms	References
Guillain–Barré syndrome (Polyradiculopathy)	This is an acute inflammatory demyelination that occurs. Both intracellular, as well as hormonal, pathways occur. There will be the crossing of the ganglioside surface by the foreign antigens.	There is numbness, paraesthesia, weakness, pain of the limbs and on some occasions there will be a combination of the symptoms. Mostly there is progressive bilateral weakness of both limbs and the weakness progresses over a period of 12 hours to a period of 28 days before a plateau is reached. It ultimately leads to respiratory complications.	Yuki and Hartung (2012), Quinn (1997)
Sensory neuropathy and related or unrelated peripheral nerve dysfunction.	Neurotoxins produced by the mycobacterium avium complex and cytomegalovirus. They are the cause of loss of distal sensory nerves (axonal degeneration) and the unmyelinated nerves (Gale, 2003). ARVs are also causative agents of sensory peripheral neuropathy through the chemical destruction of the nerve myelin sheaths and this leads to disrupted nerve conduction (Manji and Miller, 2004). Injury occurs due to removal of the nerve myelin which facilitates the salutatory propagation of impulses and its insulation properties. Loss of the myelin results in nerve axonal degeneration and deterioration of nerve conduction (Gale, 2003). Worsened sensation is experienced when the posterior root ganglia are affected (White et al., 2004)	Changes in the perception of sensation, including pain, touch and temperature. Additionally patients experience hyperesthesia, paraesthesia and loss of proprioception.	Gale (2003), Manji and Miller (2004), White et al. (2004)
Progressive multifocal leuco-encephalopathy.	Infection of lymphocytes in the CNS may result in the multifocal cell lysis and demyelination. It can be due to the James Canyon virus (Brew et al., 2010).	Progressive hemiparesis Cognitive dysfunction Heminopia or ataxia Dysphagia and seizures Focal intracranial lesions (Manji and Miller, 2004).	Manji and Miller (2004), Brew et al. (2010)
Cytomelomegalo virus	CMV cause focal necrosis with necrotising ventriculo-encephalitis imbroglio nodules.	CMV renitis Rapid deliriumAltered mental status. Nystagmus Cranial neuropathies	Kenneson and Cannon (2007)

As outlined in Table 2.2 above, DSPN presents in several forms. Distal sensory peripheral neuropathy is one of the more common conditions that have emerged in the HIV disease trajectory. Clinical presentations of Distal Sensory Peripheral Neuropathy range from bilateral symmetrical polyneuropathy to monoradiculopathy

(seen on the unilateral side), to lumbar and brachial plexopathy, a syndrome that presents as diffuse infiltrative lymphocytosis (Sohal et al., 2009).

Peripheral neuropathy can manifest as the Gullaine Barre syndrome (GBS) in the form of inflammatory demyelinating polyradiculoneuropathy (Sohal et al., 2009). This type of neuropathy can be autonomic and can present in different forms at the different stages in the trajectory of progressive polyradiculopathy (Kaku and Simpson, 2014).

The occurrence of Distal Sensory Peripheral Neuropathy can be classified as a largely sensory dysfunction when there has primarily been injury to a sensory nerve (Hahn et al., 2008). DSPN is classified mainly as a sensory problem that manifests when the dorsal root ganglion is affected. However, circumstances do arise when the anterior horn is affected, which results in motor dysfunction. Motor activity dysfunction may manifest as a weakness in and a twitching of the lower limb muscles (Hwang et al., 2009).

A diagnosis of DSPN can be concluded by conducting a number of tests. Testing the patella reflex, ankle and the Achilles tendon reflex forms an important part of these diagnostic tests (Hahn et al., 2008). Other diagnostic tests include the two-point discriminatory test for vibration and thermal sensation. These reflex checks and sensory tests confirm the diagnosis of the condition, DSPN, in HIV-infected patients and therefore explain how the HIV and the related management strategies impact on the nervous system (Phillips, 2013). The specific mechanism by which DSPN occurs has been described in the literature (Robinson-Papp et al., 2012, Cherry et al., 2014).

2.5.1. Distal Sensory Peripheral Neuropathy Pathogenesis

The pathogenesis of the disease process can occur when macrophages are infected by the virus. The virus destroys the posterior root nerve ganglia by producing antigens and inflammatory cytokines (Hahn et al., 2008). Macrophages exist as facilitators of the nervous system that help in controlling movement and in signalling the leukocytes into the nervous system and its tissue whenever there is inflammation (Bhangoo et al., 2009). If the inflammatory process is lengthy or excessive, the clearing-up process to remove any infective pathogens eventually proves to be ineffective. The chances of infection and further pathology are then enhanced (Cherry et al., 2014).

As described above, the HI virus acts independently and exerts a direct effect on the nervous system, eventually resulting in DSPN. Yet another mechanism that acts on the central nervous system has its source in the HIV medication, which causes side effects to the body of the HIV patient and includes, amongst others, DSPN (Cherry et al., 2014).

2.5.2. Distal Sensory Neuropathy as a Side Effect of the HIV Drugs

The main aim behind the administration of the anti-retroviral drugs and treatment is to control the viral load and raise the CD4+ count to facilitate the immune-boosting process. Some of the well-known anti-retroviral medication that causes peripheral neuropathy includes Didanosine (ddl), Zalcitabine (ddC) and Stavudine (d4T). These drugs fall into the category, nucleoside reverse transcriptase inhibitors (NRTI) (National Drug and Therapeutics Policy Advisory Committee, 2010).

These anti-retroviral regimens are divided into various categories including the following: protease inhibitors, non-nucleoside reverse transcriptors and nucleoside reverse transcriptase inhibitors. The nucleoside reverse transcriptase inhibitors inhibit

the HIV enzymes that facilitate the reverse transcriptase process, thus preventing the copying of the RNA to become the DNA of the infected cells through the formulation of deceptive deoxyribonucleic acid chains. This leads to an incomplete DNA strand which is not able to assist in the development of a mature virus (National Drug and Therapeutics Policy Advisory Committee, 2010).

Most of the nucleoside reverse transcriptase inhibitors that are frequently used in Third World countries are permitted by the World Health Organisation (Bartlett and Gallant, 2000). Stavudine is one of the well-known nucleoside reverse transcriptase inhibiting drugs with familiar side-effects that are easily recognised. In contrast, the protease inhibitors are of little risk to Distal Sensory Neuropathy (Evans et al., 2007).

One of the more commonly known side-effects of anti-retroviral drugs is the increased occurrence of neuronal damage which makes potentially dormant peripheral neuropathy more evident (Keswani et al., 2002).

2.5.2.1. Mitochondrial toxicity and peripheral neuropathy caused by HIV drugs

On account of their toxic effects, nucleoside inhibitors, such as Stavudine, interfere with the mitochondrial oxidation in neuronal metabolic activities(Amanambu, 2013). The toxic effects of the Nucleoside Reverse Transcriptase Inhibitors (NRTIs) occur when intracellular tri-phosphorylation of the Nucleoside Reverse Transcriptase Inhibitors forms nucleotides which subsequently lead to the incorporation of the nucleotides into growing Deoxyribonucleic Acid (DNA) chains. This occurs through the viral enzyme reverse transcriptase process, which terminates the continued formation of DNA (Amanambu, 2013).

Tri-phosphorylation of the Nucleoside Reverse Transcriptase Inhibitors (NRTIs) in the cells results in two types of pharmacokinetic dispositions, one being a biologically inactive drug in the cell plasma and the second being the active NRTIs phosphate in cells (Stretcher et al., 1994). Most clinical symptoms of NRTI toxicities are exhibited as mitochondrial disease, and microscopic investigations show abnormal mitochondria and/or the depletion of mitochondrial DNA (mtDNA) in the cells and tissues that would have been affected (Dykens and Will, 2007).

NRTI triphosphates competitively inhibit the mtDNA polymerase y *in vitro* (Lewis, 2003), which will lead to a reduction in the mitochondrial respiratory chain proteins and thus facilitate anaerobic respiration, induce oxidative stress, and elevate mutations in the mtDNA, finally culminating in mitochondrial and, on occasion, tissue failure (Lewis, 2003). However, despite the fact that the NRTIs are able to alter the mitochondrial genes (Desai et al., 2008) the possible link between HIV drugs and the roxicities which they cause, including lactic acidosis, and peripheral neuropathy, is mitochondrial toxicity (Côté et al., 2002).

2.6. IMPAIRMENTS CAUSED BY HIIV-RELATED DISTAL SENSORY PERIPHERAL NEUROPATHY

Complications and impairments that present as a result of the HIV disease condition include muscular weakness, fatigue, lethargy, impaired sensory function, paraesthesia, imbalances in terms of the limbs, impairment of the activities of daily living, muscle dysfunction and issues related to the quality of life (Nicholas., 2012).

According to the International Classification of Function (ICF), functional human dimensions are categorised into domains which facilitate complete intervention after a functional assessment. Impairments are problems that are found in the bodily functions and structures such as significant deviation from normal body functions. or loss of functional activities of daily living (World Health Organization, 2001). Severe bodily impairments occur in the movement-related functions of the body, and the mental and neuro-muscular dimensions of the body (Myezwa et al., 2009).

Disability is currently defined as an umbrella term for impairments, limitations on activity, and restrictions on participation in activities. The term disability denotes the negative aspects of the interaction that occurs between an individual's health condition(s) and that person's contextual factors that include the personal and environmental factors (World Health Organization, 2001).

Sensory disruptions and impairments are some of the more common problems facing patients suffering from HIV/AIDS and have an impact on their neuro-musculoskeletal functions (White et al., 2004). Sensory axonal and neuronal damage leads to limitations on functionality and activities because of the ensuing clinical symptoms such as pain, numbness, paraesthesia and poor proprioception (Cettomai et al., 2013). Some patients face challenges such as those of not being able to discriminate between contrasting properties (e.g. between hot and cold), whereas others could be hypersensitivity on the skin to garments or textiles (Cettomai et al., 2013).

2.6.1. Neuropathic Pain in HIV-Related DSPN

According to the study by Verma et al. (2005), the other notable problem with HIV-related DSPN is pain of a neuropathic origin. Pain is common in patients with symptomatic HIV-related DSPN and there are a number of factors that contribute to

the intensity of the pain experienced and that concomitantly magnify the burden to be carried by the victims of this disease (Verma et al., 2005).

The pathophysiology of the disease can be explained in terms of the fact that, despite its cause, injury to the peripheral nerves will lead to a chain of molecular, anatomical and physiological changes (Mendell and Sahenk, 2003). Injury to the peripheral nerve fibres will result in abnormal stimulation being experienced by the victim in the vicinity of the place on the body where the injury occurred (Zimmermann, 2001).

Once there is neuro-inflammation of the nerves, the neuro-immune system is activated. This in turn cascades down to the production of chemokines, cytokines and surface antigens, especially in the dorsal/posterior root ganglion (DRG) (DeLeo and Yezierski, 2001, Liu et al., 2007). The upward regulation of membrane channels in the posterior root ganglion and the distal peripheral nerves surrounding the place of injury will lower the activation threshold and result in persistent pain This will facilitate the stimulation of the sensory fibres of the injured nerve (DeLeo and Yezierski, 2001). Injury to the nerve will cause the sympathetic axonal sprout surrounding the cell bodies and lead to an intensified response to the stimulation (Verma et al., 2005).

2.6.2. Peripheral Neuropathy Leading to Muscular Dysfunction

Peripheral neuropathy can lead to muscular dysfunction. The muscular dysfunction could include muscular twitching and cramps, as in the tightening of the muscles, as well as in a weakness being experienced in the intrinsic musculature of the foot, all as a result of neuronal impairment (Nicholas., 2012). The result of lactic acid accumulation as a by-product of the metabolism of the body, especially as a result of

anti-retroviral drugs, can also be regarded as one of the effects that disturbs muscle function (Phillips and Walker, 2004).

There are instances involving limitations on the activity levels of a patient, resulting in a concomitant reduction in the patient's participation in daily activities such as grooming, and community activities such as his/her attendance at weddings and funerals (Gabel et al., 2012). Limitations on daily activities will lead to compromises having to be made in terms of the attainment of health-related quality of life. Such limitations would represent a relevant outcome for the various functional activities that are important to patients when the efficacy of any management modality that has to be implemented is considered and evaluated. The objective would be to enhance the functionality of the patients in their daily living activities (Bril et al., 2011).

Some of the major areas that are of paramount importance to patients in their daily living include mobility, occupational and domestic activities, self-care, as well as recreational activities. Without a doubt, people suffering from HIV/AIDS would experience at least some of these limitations.

Factors associated with limitations on participation in activities in the case of patients suffering from DSPN would include lethargy, pain, paraesthesia, impaired proprioception, and depression (White et al., 2004). These compounding factors tend to present clinically as an impaired gait, reduced mobility and an elevated propensity to falling.

Such findings are also supported by Myezwa et al. (2009) who highlight the fact that most of the limitations on activity in HIV patients includes bathing, mobility, sleeping, as well as other common activities of daily living. The main areas that might restrict

participation include those associated with family life as a parent or spouse, of self-actualisation, and of pleasure in conducting occupational activities (Johnson., 2001).

2.7. MEDICAL TREATMENT OF DISTAL SENSORY PERIPHERAL NEUROPATHY

DSPN is currently managed through the self- care approach and through therapeutic interventions, in the form of both non-pharmaceutical and drug therapies (Gale, 2003). Such approaches correspond to those presented in the clinical context and to the preferred treatment plans prescribed and made available by medical practitioners (Nicholas., 2012).

Drug therapies include the administration of analgesics and other anti-retroviral medication to alleviate the clinical symptoms of DSPN. There are some drugs such as anti-convulsants that are used to reduce pain. They include gabapentin, carbazapine and pregabalin, as well as sodium valproate (Bril et al., 2011).

As a complement to drug therapies, there are alternative therapies such as physiotherapy modalities which are also applied to alleviate pain in the case of DSPN (Gale, 2003) The physiotherapy modalities that are used include therapeutic exercises (i.e. aerobic exercises, progressive resistance exercises) and generalised home exercise programmes such as walking (Nicholas et al., 2007).

Other modalities include acupuncture, massage and electrotherapy (e.g.TENS and IFT) (Verma and Simpson, 2007). Electrotherapy has been used as a non-drug therapy for neuropathies and includes interferential therapy, procedures such as transcutaneous electrical nerve stimulation and functional electrical nerve stimulation (Pieber et al., 2010).

In addition to electrotherapy, massage is effective in relieving pain. Massage and its variations, ranging from kneading, effleurage, petrissage, rhythmic stroking and rapid stroking, could all be collectively termed as Swedish massage (Ashton and Cassel, 2006). The effect that massaging has is to inhibit the pain pathways from stretch or pain receptors and to improve the quality of life. Massaging could be used in conjunction with the other modalities such as relaxation, acupuncture and the other oriental treatments (Galantino et al., 2006). Oriental practices such as Tai Chi, in combination with aerobic exercises, improve endurance, flexibility and balance in candidates suffering from DSPN (Nicholas et al., 2007).

Some of the strategies that have been shown to work as self-care strategies include hot and cold contrasting baths, pedal massage, humour, the elevation of the feet, rest, exercise, the use of herbs (including cannabis), prayer, a change of diet, environmental change, ambulation for long periods and some therapeutic exercises (Ownby and Dune, 2007).

Any practical physical activity that mitigates the symptoms of an illness, a disease or a condition, or improves the condition of the patient, thus promoting his/her physical health and slowing down the deterioration of his/her condition, is known as therapeutic exercise. However, most of the medical personnel are reluctant to prescribe exercise for patients for fear of exhaustion, which is believed to tend towards the suppression of the immune system and fatigue (Taylor et al., 2007). The numerous programmes to improve muscle strength, as well as endurance, include cycling, jogging, running, and a fast as well as a normal walking pace (White et al., 2004).

Prescribed exercises can be defined as prescribed physical activities as laid out in a protocol for an individual to conduct voluntarily in order to improve his/her good

health status or delay the deterioration thereof (Taylor et al., 2007). Therapeutic exercises performed at a sub-maximal level are used to predict maximal heart rate levels. Combined with resistance exercises, they have a significantly beneficial effect on the cardio-vascular and immune systems, on viral control and on fitness levels (O'Brien et al., 2008).

The various body-strengthening modalities include static exercises, supervised aerobic exercises and resistance exercises. They have a significant effect on the recovery of HIV patients and the rate at which the recovery takes place, and also improve the muscle strength of the individual (White et al., 2004).

2.8. OUTCOME MEASURES

'Outcome measures' is the term for the results of a test or an investigation that is used in an objective manner to monitor or determine the initial baseline level of function of a participant at the commencement of an investigation or treatment. Once the investigation or treatment has started, the same tool or measure can be used to determine any change that has occurred since the beginning of the investigation (Benbow et al., 1998).

2.9. PSYCHOMETRIC PROPERTIES OF OUTCOME MEASURES

"Psychometric properties" refers to the statistical properties of an instrument that is used to collect data for study purposes. This includes validity and reliability. Reliability refers to the consistency of the tool when used on two or more occasions, whilst validity refers to the accuracy of the tool when used on each occasion. The reliability of an instrument helps the researcher to make a valid assessment and it is the validity of the instrument that enables the researcher to be confident in making statistical predictions (Tesch, 2013).

2.9.1. Validity

Validity implies that the outcome measures selected really do measure that which they are purposed to measure. This concept encompasses answers to meaningful questions that are posed for obtaining meaningful answers and therefore meaningful information (Faber et al., 2006).

Face validity can be defined as logical validity, which is a simple form of validity which can be achieved by subjectively and superficially assessing whether or not the test outcome measures result from a meaningful investigation into what they are required to measure (Barnett et al., 2015). The term “face value” is appropriate in that the questions posed merely skim the surface in order for the researcher to form an opinion. This is the easiest form of validity that is sought in research. Since no objective measures are applied, it is the weakest form of validity (Lynn, 1986).

Construct validity refers to an independent variable or construct that is accurately defined. An example of an independent variable would be the leadership style of a school principal with the sub-scales of that construct being the various types of leadership style (e.g. authoritative, delegative and participatory leadership) (Keenan et al., 2008). Construct validity would reflect whether the items under investigation in the test are sound and valid, by employing the statistical technique of factor analysis. Each sub-scale should then have a good inter-item correlation which would be measured using the bivariate correlation method (Keenan., 2008).

Criterion validity could also be called concrete validity. It refers to the extent to which a study tool or measure is related to an outcome. Criterion validity can be divided into two categories, namely concurrent and predictive validity (Voepel-Lewis et al., 2010).

Concurrent validity can be defined as a valid comparison between the measure in the study and an outcome that is being assessed at the same time, and is appropriate when the researcher uses them the outcome measures in tool development and adaptation) (Atkinson et al., 2004).

2.9.2. Reliability

Reliability in terms of research implies that the results of an investigation would be found to be similar if the investigation were to be conducted more than once – at various times (repetitively). The term “test-retest reliability” would be appropriate in this context. Reliability could also apply to the extent to which the outcome measure can be determined but still retain its objective value. The term “inter-rater reliability” would be appropriate in this context (Bruton et al., 2000).

A tool or instrument used in an investigation is considered to be reliable when the researcher considers the internal constancy of the tool. This can be determined by statistically calculating Cronbach’s Alpha or the Intra-class correlation (Binkley et al., 1999). The inter correlation enables the researcher to assess the items of the instrument and to determine whether they are measuring the same construct.

There are various types of reliability that should be considered. These include the following:

- **Inter-rater reliability,** also called concordance, is the degree of agreement that is found among raters. Inter-rater reliability gives a score indicating the extent of homogeneity, as well as the consensus between the raters that is noted by the researcher. This measure has been shown to be useful when refining tools given to assessors who are deciding whether a particular tool is appropriate for measuring a particular variable. The different statistical measures used include Cohen’s Kappa and Fleiss‘s Kappa (Gwet, 2014).

- **Test-retest reliability** is the measure of reliability that is calculated and determined when a researcher administers the same outcome measuring tool twice over a period of time using the inputs (information) from the same participants in the study. The scores from the first and second data collection times can be statistically correlated in order to assess the outcome measure for stability over the period of time between the two data collection times (Kizlik, 2012).
- **Intra-rater reliability** is the degree of agreement found among repeated administrations of an investigative or diagnostic test conducted by a single person or rater (Bennell et al., 1998).
- **Internal consistency** is a measure that notes how a test addresses different constructs and comes up with reliable scores. The test-retest method involves administering the same outcome measure over a period of time and then comparing the results obtained from the first and second data collection times (Binkley et al., 1999)

2.10. HIV-RELATED DISTAL SENSORY PERIPHERAL NEUROPATHY OUTCOME MEASURES

Peripheral neuropathy is one of the common complications of patients with PLHIV who are on anti-retroviral drugs (ARVs). The literature has reported on several tools that have been used to measure the functional outcomes of such patients who are suffering from the associated peripheral neuropathy (Tumusiime et al., 2014).

The Lower Limb Functional Scale (LLFS) and the Lower Extremity Functional Scale (LEFS) are the two most commonly used outcome measures for lower extremity

function (Gabel.,1999). Outcome measures are the scales or indices that are presented to the patients in the sample for them to indicate their assessment of their condition. The completed scales are then interpreted by the researcher in order to accurately measure the various areas of interest from which the therapist is expecting a response (Hammond, 2000).

The selection of an outcome measure depends on the requirements of the therapist and the type of outcome information that the therapist is interested in measuring (Hammond, 2000). Of paramount importance is the fact that these outcome measures must have sound clinometric as well as psychometric properties to ensure the validity and reliability of the instrument being used. Furthermore, the outcome measures in question should cause no pain or discomfort to the patient or participant (Hammond, 2000). The LEFS questionnaire used in this study has previously been shown to be reliable, valid and responsive to change (Galantino et al., 2014).

Because the LEFS is a tool used in investigating musculoskeletal conditions such as hip arthritis (Pua et al., 2009) and in joint replacements (Yeung et al., 2009), it was used in this study to determine the test–retest reliability of the LEFS outcome measure in HIV–related DSPN,

Some screening using other screening tools had been undertaken prior to the main test-retest study to select participants for this research project. The screening tools used in the initial study included the Brief Peripheral Neuropathy Screening (BPNS), as well as the Brief Peripheral Neuropathy Tool. These tools are discussed in the sections below.

2.11. THE SUITABILITY OF THE BRIEF PERIPHERAL NEUROPATHY SCREEN (BPNS) FOR DIAGNOSING DSPN IN HIV/AIDS PATIENTS

The Brief Peripheral Neuropathy Screen (BPNS) was used as the initial screening tool to select the participants for this study. Having proved itself to be both reliable and valid, and facilitative of self-reporting, it was the tool of choice for this study for specifically diagnosing Distal Sensory Peripheral Neuropathy (Cherry et al., 2005). Furthermore, this screening tool is able to monitor both objective and subjective outcomes which are consistent with peripheral neuropathy, the disease focused on in this study.

BPNS has established a reputation for itself in that it has been extensively used in research and clinical trial protocols such as in projects undertaken by the AIDS Clinical Trial Group (ACTG) (Cherry et al., 2005). The study undertaken by Cherry et al. (2005) conclusively pointed out that the BSPN is useful because it includes both the signs and symptoms of DSPN and therefore it can be used specifically for screening DSPN, which is HIV-related.

Mehta et al. (2011) also used the BPNS in a study of participants receiving ARVs in Mombasa, Kenya. The study recommended that doctors should find it easily able to integrate BPNS when reviewing HIV patients, especially in resource-limited areas. Tumusiime et al. (2014) in their study in Rwanda showed that the BPNS had proved to be an easy and reliable tool in a resource-limited environment where participants could not afford specialized expensive clinical tests. It was for these reasons that this researcher decided to use the BPNS in this study of Botswana. It was also used in both the pilot study and the main study.

Lower Extremity Functional Scale (LEFS)

The LEFS questionnaire is an outcome measure developed by Binkley et al. (1999) and measures lower extremity function in the following areas, namely ambulation, activities of daily living, functional activities and activities that measure strength, which include squatting and standing. The LEFS can be used by clinicians to measure patients' initial functionality, their ongoing progress and their outcomes, as well as to set functional goals for the patient.

The LEFS is efficient to administer (five minutes) and to score (one minute), and can be applied for research purposes and for clinical decision-making in respect of individual patients with musculo-skeletal dysfunction (Binkley et al., 1999). The LEFS is a reliable tool and its construct validity is supported by the fact that it compares favourably with the SF-36 (Binkley et al., 1999). The sensitivity of the LEFS to detect change in function is high (Binkley., 1999). Furthermore, the LEFS demonstrates comparable reliability in terms of scale width and maintains high criterion validity. Research by Binkley et al. (1999) found that the LEFS demonstrates sound clinometric properties.

Binkley et al. (1999) developed the LEFS tool to measure various lower extremity conditions. With the international classification of function ICF model as the initial guideline, the development of the tool followed the WHO model, which in itself covers components such as impairment, disability and handicap (World Health Organisation, 2005) particularly in the elderly.

The LEFS tool consists of 20 items which measure the level of difficulty in conducting the activities of daily living (ADLS). The scores of the instrument are shown as follows: 4 =”no difficulty”, 3 = “a little difficulty”, 2 = “moderate difficulty”, 1 = “quite a bit of difficulty”, 0 = “unable to perform activity”.

The participant is required to rank the scores, with the highest score of 80 being the normal function and the lowest of 0 being no functional activity at all (Binkley et al., 1999) . These functional scores are categorised as follows, “no difficulty” (80 points),”a little bit of difficulty” (79-60 points), “moderate difficulty” (59-40 points), “quite a bit of difficulty” (39-20), “unable to perform activity” or “extremely difficult” (19-0) (Schep et al., 2009).

The two most important reasons or investigating the functional status of the participants in the research are listed below:

- To document the physiotherapeutic outcomes in patients for the purposes of research, quality assurance and to establish the appropriate clinical standards; and
- To document the functional outcomes in order to plan and set the treatment goals for the successive functional levels for progress and outcomes in respect of individual patients (Gabel et al., 2006) .

The LEFS questionnaire is an effective scale for documenting the lower extremity function in terms of the reasons mentioned above, as well as the fact that this tool is easily administered. Furthermore, the LEFS tends to overcome the barriers that are identified when a health status measure is implemented in a clinical practice setting (Gabel et al., 2006). Because of a better understanding in terms of the interpretation of the LEFS measurement error and good detection in the case of the score changes, the measures of validity and reliability of this tool, as well as its sensitivity to change, are sufficient to justify its use at an individual level (Gabel et al., 2006).

Comparison between the outcome measure tool, Lower Extremity Functional Scale (LEFS) and the other tools

The LEFS is a reliable tool for assessing patients with musculoskeletal disorders. W A comparison of this scale with the Health Survey Questionnaire and the Medical Outcomes Study 36-item revealed that the construct validity of this tool is good. Furthermore, the LEFS compares favourably with the Lower Extremity Functional Index (LEFI) in terms of its scale width and its high level of criterion validity. A comparison of the LEFI and the LEFS showed that the LEFI performs better than the LEFS. It was also found that the response of the LEFI to change is better, that it reveals a low minimal detectable change score (MDC), that it is far superior in terms of internal consistency and readability, that it has a lower response error as well as a faster scoring and completion time (Gabel et al., 2006). Furthermore, the LEFS is more widely used as a tool than the LEFI, but, apart from the fact that the LEFI has better clinometric properties, this researcher chose to use the LEFS.

The LEFS is a tool that has been used to assess and diagnose different medical conditions and its test-retest reliability has been shown to be strong. A number of studies have been reviewed to assess the results of tests for the LEFS's reliability, validity and internal consistency. Table 2.3, for instance, is a comparison of the test-retest reliability of the LEFS under the respective medical conditions. Table 2.3 in its turn, outlines the studies in terms of the author, year of study, the aims and results of the study, and the reliability, validity and internal consistency of this tool and the data that were applicable at the time of this research.

Table 2.3: Comparison of the Test-Retest Reliability of the LEFS in Terms of the Respective Medical Conditions

Reference	Population	Study design	Aim	Key results	Reliability	Validity	Internal consistency
Alcock et al. (2012)	Patients with Acute Cruciate Ligament (ACL) reconstructive surgery Mean age: 29.4±10.6(M) 29.0(9.6)(F) N=45 Country: Canada	The repeat test measures observational study design	To describe the pattern of change in patients' lower extremity physical function after ACL reconstructive surgery and also to estimate the test-retest reliability of the LEFs	Improvement in LEFS scores within the 7th and 8th week of surgery. High correlation coefficient with test-retest reliability within four days	Test retest: ICC: 0.90 SEM: 3.7	n/a	n/a
Binkley et al. (1999)	Patients with lower extremity musculoskeletal problems Mean age: 44±16.2 Gender: Female=58 N=107	The repeat test measures observational study design	To report the development process, validation, reliability and the internal consistency of the LEFS	LEFS is valid and reliable for measuring physical function.	Test retest: R (entire sample)=0.94(95% lower limit CI=0.89) R(Chronic conditions)= 0.86 (95% lower limit CI=.80)	Construct validity: Correlations between SF-36 (Physical function) and LEFS, r=0.80 (95% lower limit CI=.73)	α=0.96
Kennedy et al. (2008)	Patients after one year of total knee arthroplasty (TKA) N=84	The repeat test measures observational study design	To describe the pattern of change in the lower-extremity functional status of patients after total knee arthroplasty (TKA)	LEFS scores improved in the first 26 weeks after which improvement was limited.	Test retest: ICC=0.85 SEM: 3.7	n/a	n/a

Yeung et al. (2009)	Patients with lower extremity musculoskeletal problems Gender: 65.5% female N=150	The longitudinal repeat test measures design	To determine the test-retest reliability, construct validity, and responsiveness in patients with lower extremity musculoskeletal problems	The LEFS showed good reliability and it is valid for measuring changes in function in patients with lower extremity musculoskeletal problems	ICC= 0.88 (95% CI: 0.74, 0.95). SEM =3.5 points	There was a significant difference between the LEFS scores of the respondents and non-respondents. w= 653.5, P=0.01	n/a

Table 2.3(b): Comparison of the Test-Retest Reliability of the LEFS in Terms of the Respective Medical Conditions

Reference	Population	Study design	Aim	Key results	Reliability	Validity	Internal consistency
Hoogeboom et al. (2012)	Patients diagnosed with hip or knee Osteoarthritis (OA) Mean age: 61±11 Gender: 63% Female N=106	Prospective study	To evaluate the psychometric qualities of the Dutch LEFS in patients with hip or knee OA	The Dutch version of the LEFS has good reliability, validity and internal consistency	Test retest: ICC = 0.86	Construct validity: Correlations between LEFs and the physical function Hip, r95%CI: 0.78(0.69-0.84) Knee, r95%CI: 0.78(0.73-0.83)	α=0.96
Lin et al. (2009)	Patients with ankle fracture N=306 Mean age=45.1 ±15.7 Gender: N=154 female	Randomized controlled trial	To measure clinometric properties of LEFS	The LEFs is useful for measuring and monitoring function in patients with ankle fracture.	n/a	Concurrent validity with Olerud Molander Ankle Score Short term: r=0.80 Medium: r=0.87 Correlation with walking (r=0.61) and stepping (r=0.63)	Baseline: α=0.92 Short-term follow up: 0.94 Medium-term follow up: 0.90
Cacchio et al. (2010)	Patients with one-sided lower extremity dysfunction	Prospective methodo- logical study of repeated	To determine the measurement properties of the Italian version of the LEFs.	The Italian version of the LEFs showed good reliability and internal consistency.	Test retest: Intra-rater: ICC=0.91, 95%CI=0.86-0.91	Construct validity: Correlation with the physical component of SF-36	α=0.94, 95%CI=0.91-0.96

	Gender: n=136 Mean age: 46.7±12.3 N=250	measures			Inter-rater: ICC=0.89 95% CI: 0.83- 0.91	R=0.61	
Pua et al. (2009)	Patients with hip OA Mean age: 62±10 Female: 60% Country: Australia N=100	Test-retest reliability	To measure correlates of physical function in patients with hip OA.	The LEFs showed better point estimates in measuring physical function in adults with hip OA.	Test retest: ICC (95%CI): 0.92 (0.85-0.96) Standardized SEM: 4.5	Discriminant validity: Stronger correlation with the physical function component of the SF-36 ICC=0.75(0.65-0.85), $p<0.05$	n/a

The studies presented in Table 2.3 above all show that the tool LEFS has a high test-retest reliability in terms of other medical conditions, including hip osteoarthritis and musculoskeletal dysfunction.

2.12. CONCLUSIONS EMANATING FROM THE LITERATURE REVIEW

The literature to show that HIV-related Distal Sensory Neuropathy is a major neurological complication that has a significant prevalence in patients on ARVs is substantial. The neurological impacts that DSPN has on the body include a wide range of impairments to the body systems. However, the major focus of this study is on the neurological system. The side effects of the ante-retroviral drugs tend to significantly aggravate the condition of DSPN. There are, however, treatment modalities that include drug therapies and non- drug therapies to manage one of these side effects, namely, the pain.

The Lower Extremity Functional Scale has proved to be one of the more successful and more commonly used a clinical outcome measures for measuring the functional capacity of patients with DSPN. The reason for this is that it has been shown to be reliable and valid in the case of certain medical conditions such as arthritis, hip and knee replacements; and hence the need to validate them in HIV-related DSPN.

3. CHAPTER THREE: METHODOLOGY

3.1. INTRODUCTION

Chapter Three explains the research study design, details of the participants, the instruments used, the nature of the procedures conducted, and the statistical analysis of the data. The instruments and procedures used both in the pilot study and the main study are outlined in this chapter.

3.2. STUDY DESIGN

This is a test-retest study design with a seven-to-ten-day interval between the two testing times.

3.3. POPULATION AND SAMPLING

3.3.1. Source of the Participants

Six clinics in Gaborone were used from which to collect data. The patients attending these clinics were employed in both the public and private sector. They were recruited for this research project when they came for their consultations with the infectious disease specialists, neurologists, HIV physicians, or when they came to collect their anti-retroviral medication.

All of the patients selected for this study had already been diagnosed as HIV-positive and were on anti-retroviral therapy. Furthermore, the patients who were included in the study were already presenting with symptoms of DSPN in the lower limb areas which had been confirmed by the HIV physicians (Cherry et al., 2014). The data collection was conducted on two separate occasions, the interval between the two being a period of seven months.

3.3.2. Sample Size

The sample size was calculated on the basis of the EPI information version 6 stat for population surveys or descriptive study random calculation. An HIV population estimated at 3500 with an expected 30% prevalence of DSPN, and a worst acceptable prevalence of 40%, was drawn for calculation. Using a 95% level of confidence, a sample size of 79 participants was finally obtained (Mohamad., et al 2013).

3.3.3. Eligibility Criteria

Inclusion criteria

- HIV patients on ART with DSPN
- The male and female participants who attended the clinics selected for this study were from both rural and urban areas.
- The patients were from 18 to 75 years of age.
- The participants were able to read or undergo a structured clinical interview to provide details of their use of ART and to understand the measurement tool used in the study.
- Patients on different types of ARVs
- Patients with DSPN, which had been confirmed by the Brief Peripheral Neuropathy Screening (BPNS) tool.

Exclusion criteria

- HIV patients on ART with no symptoms of DSPN
- Diabetic patients with DSPN issuing from the diabetes rather than from the ARV medication
- Those who had known injuries to the lower limbs such as fractures and burns
- Patients who could not understand the questions owing to mental impairment
- Patients who were HIV but who were not on ARVs

- Patients who were not from Botswana
- Patients with severe exposed wounds or Kaposi Sarcoma

3.4. ETHICAL CONSIDERATIONS

Ethical approval was sought from the University of the Witwatersrand's Human Research Ethics Committee (Medical), the ethical clearance number awarded being M140496 (See Appendix 6). Additionally, permission to undertake the study was sought and obtained from the respective HIV clinics. The ethical approval reference number for the hospitals was PMH 5/79 (155) (See Appendix 7). Written informed consent from the study participants was obtained before they participated. All participants were above the age of 18 years.

3.5. STUDY INSTRUMENTS

This section describes the instruments used in this study. They were BPNS, BPNST and the LEFS.

3.5.1. Translation of the Language on the Questionnaire

Some patients could not understand the English language version of the questionnaires. As such, the questionnaires were translated into Setswana in a manner similar to the presentation by (Tumusiime, 2014). Two independent Setswana professional language translators from the University of Botswana were commissioned to do this task. The questionnaires were translated and back translated to ensure content validity. A focus group comprising of the translators three rehabilitation specialists, and this researcher, met to ensure that the translated version was in fact a correct interpretation of the original questionnaire and that the meaning was the same. No major modifications to suit the cultural background of the

participants were needed. (The Setswana translation of the LEFS is presented in Appendix 1).

3.5.2. Administration of the Questionnaire

Brief Peripheral Neuropathy screening (BPNS)

As explained in Table 3,1 the Brief Peripheral Neuropathy Screening (BPNS) questionnaire, presented in both English and Setswana, was given to the participants to complete, (It is presented in Appendix 3 and described in the literature review).

Table 3.1: Brief Peripheral Neuropathy Screening Questionnaire (BPNS) Completed by the Participants

Instrument of study	Outcome variables to be tested	Procedure
Brief Peripheral Neuropathy Screen Questionnaire (BPNS) (Appendix 3)	Indications that the participants have at least three of the signs and symptoms of peripheral neuropathy	Participants were invited to fill in the questionnaire in order to voluntarily participate in the study. The participants needed to answer “yes” to at least three questions in the screening questionnaire before they were included in the study.

Brief Neuropathy Screening Tool (BPNST)

The brief neuropathy screening tool was also given to patients to ensure that only those with sensory neuropathy were identified for the study. Table 3.1 outlines the outcome variables and procedure for the BPNST.

Table 3.2: Brief Neuropathy Screening Tool (BPNST)

Instrument of study	Outcome variables to be tested	Procedure
(BPNS) Brief Peripheral Neuropathy Screen Tool (BPNST). (Appendix 5) .	Intensity of the symptoms of peripheral neuropathy recorded from the research candidates. The purpose of the Brief Peripheral Neuropathy Screening Tool was to verify the existence, if any, of symptoms such as pain which could be burning, sharp, pins and needles, stabbing or aching, muscular tightness due to cramps, tingling sensations and numbness. The Brief Peripheral Neuropathy Screening Tool was used when screening for Distal Sensory Peripheral Neuropathy by the physician.	Confirmation of the diagnosis of peripheral neuropathy was made possible through the physical assessment by the physician of symptoms such as pain and vibration sensation. The severity of the pain was noted through the usage of the visual analogue scale for pain severity. The physician used the 128 Hz tuning fork to determine vibration sensation and the duration of the tuning fork vibration was noted. Tendon-Achilles tapping was used to assess the reflexes of the ankle joint.

The Lower Extremity Functional Scale (LEFS)

The LEFS was used to assess the level of lower limb function in patients that were HIV positive and presenting with DSPN. Functionality was measured by assessing the difficulty experienced in a range of activities such as doing housework, involvement in hobbies, walking, standing, running, and activities of daily living (Binkley et al., 1999). Each of the activities was assessed using a Likert scale of 0-4.

The Lower Extremity Functional Scale (LEFS) (in Appendix 1, and described in the literature review), in both English and Setswana, was given to the participants (Appendix 1) to complete. Those patients who could not read and write were assisted by a trained interpreter.

The LEFS was used to establish the functional ability of the patients with Distal Sensory Peripheral Neuropathy (DSPN). The procedure involved offering the LEFS tool to patients after they had been screened for DSPN symptoms by the Brief Peripheral Neuropathy Screen Questionnaire (BPNS) while they were in the waiting area.

Thereafter each patient was offered a private room to complete the questionnaire. This procedure was maintained for every patient to ensure that the conditions were consistent and to reduce the possibility of random errors slipping in. This same procedure was followed when they came in to the clinic seven days later, the only exception being that they did not again fill in the Brief Sensory Neuropathy Screening questionnaire. Most patients were given a date for the retest whereas the remainder would routinely return for physiotherapy or a doctor's appointment.

3.6. PILOT STUDY

A pilot study was conducted on HIV patients with DSPN. The objective of the pilot study was:

- to determine the feasibility of conducting the study
- to determine any unforeseen challenges that might arise in the course of the main study
- to familiarize the researcher with the translated questionnaires and the study process, and to estimate the time by which the testing sessions would have been completed.

3.6.1. Pilot Study Procedure

The pilot study was conducted over a period of three weeks. Fifteen participants were recruited as the sample population to participate in the pilot study. It was decided that a sample size of at least 10% of the estimated sample would be sufficient to conduct a pilot study (Leedy and Ormrod, 2012).

The participants were screened on the basis of the BPNS questionnaire and confirmed as having DPSN. Five participants were recruited from the neurology unit of one clinic, and ten participants from an HIV infectious disease unit. The neurologist then confirmed the peripheral neuropathy diagnosis in each case.

The participants were then given the LEFS to complete on their own and were invited back for the second data collection time conducted using the LEFS tool after seven to ten days. The test-retest reliability value was subsequently calculated, an analysis made of the duration of the time taken, and any problems were identified, assessed and noted. The results and the discussion of the pilot study are discussed below.

Results of the pilot study

Fifteen patients participated in the pilot study.

Feasibility

It was possible and efficient to recruit the participants after screening with the Brief Peripheral Neuropathy Screening Questionnaire. The Setswana (translated version) and the English version of the LEFS were used. The language used was simple and easy to understand so that there was no need to alter any language terminology in either of the versions. The process of translating and back translating reduced the possibility of any errors creeping in. As such, the participants were able to answer the questions on the LEFS without any difficulty.

They reported that they understood the translated version and were able to answer all the questions without difficulty. None of the participants requested further explanation. During the course of the pilot study, this researcher managed to adjust punctuation and logistical issues that had not been foreseen before the study commenced.

Once the questionnaire had been completed by the patients and the relevant data collected, descriptive statistical analysis could be carried out to outline the patients' responses in terms of frequencies and the mode for each Likert score. Test-retest reliability using the Spearman's rank order correlation test (rho) was calculated to

assess the use of this tool (questionnaire) for testing for reliability, and a correlation of r_s = 0.7-1.00, $p<0.05$ was obtained.

The detailed results for each of the items listed in the questionnaire are outlined in Appendix 6.

One of the difficulties was that some participants could not afford to come for the second session owing to financial issues. As such, their data could not be used. Measures were taken in the main study, to ensure that the participants completed their assessments on both occasions. (The measures taken are explained below.) There was no significant change between the respective procedures adopted for the pilot study and the main study. Therefore, the results were included in the main study.

3.7. MAIN STUDY

This entire study was conducted over a period of seven months. Both the pilot study and the main study were completed over this period. This researcher used six clinics in Gaborone's urban hospitals, a combination of both private and government institutions, to select a sample population.

The initial number of the HIV patients invited for the study was 320. They were all HIV patients who had arrived at the clinics for consultations and to collect their ART medications during the time period in which the study was conducted and had accepted the invitation to participate in the study.

They were given the BPNS questionnaire to complete but only 84 managed to qualify as participants for the entire duration of the research process. Once the BPNS

questionnaires had been completed by the participants, they were referred to the physician for his BPNS tool assessment of the efficacy of the BPNS questionnaire as a diagnostic tool.

Once the neurologist/physician had confirmed the DSPN diagnosis for each of the participants , the demographic and clinical information for each patient was collected from the neurologist's/physician's checklist[1] for peripheral neuropathies The neurologist/physician then recorded the severity of the DSPN using the Brief Peripheral Neuropathy Screening tool in Appendix 5.

3.7.1. Objectives

The objectives of this study were as follows:

- To establish the test-retest reliability of the LEFS in the measurement of lower limb function in HIV-related DSPN in Botswana.
- To determine the internal consistency of the LEFS for lower limb function in HIV-related DSPN in Botswana.
- To determine the construct validity of the LEFS in participants with DSPN
- To describe the demographic and clinical characteristics of HIV patients with DSPN in Botswana.

3.7.2. Procedure

An invitation to participate was extended to the participants in this study. Those who answered "yes" to three or more questions in the BPNS questionnaire qualified to see the physician for subsequent screening. Those who were selected were requested to complete the LEFS questionnaire for the first time on their own. Finally,

they were requested to once again complete the same LEFS questionnaire when it was administered seven to 10 days after the initial administration.

Individuals who had challenges with reading and writing were assisted by a trained translator who helped them to use the translated questionnaire to complete the BPNS questionnaires. The translator played an important role in explaining and clarifying any possible misconceptions that the participants might have had. In order to ensure that the participants' information remained private and confidential, the process of collecting all the data for the study and of recording all the study procedures took place in a secluded room.

The same procedure used in the pilot study was repeated in the main study. To ensure that the participants returned for the second measurement and to minimise financial difficulties, patients were:

- Given a return date
- Contacted telephonically for follow-ups, and where necessary, visited in their homes.

3.7.3. Demographic Information

The demographic data and clinical information were collected from the physician's checklist for peripheral neuropathies (Appendix 4). The demographic information collected included details pertaining to marital status, sex, the age of the participants, the level of education attained, the type of job that they held, other HIV-related issues such as the CD4+ count, the duration of time on treatment, the HIV- stage in which they found themselves, and other comorbidities.

One of the critical components considered when recording the personal information was to take note of the types of antiretroviral medication administered to the participants.

3.7.4. Data Analysis

To ensure confidentiality, each research participant was awarded a different but unique anonymous code. The initial information pertaining to the participant was recorded on an Excel spreadsheet. The information was then converted and transferred into the Statistical Software Programme for Data Analysis (SPSS version 20). Table 3.3 below outlines the statistical tests used and the rationale for the tests.

Table 3.3: Outcome Measure, Statistical Test and Rationale

Outcome	Outcome Measure	Statistical Test	Rationale
Demographics	Age, gender, level of education attained, marital status, occupation and HIV clinical information	Descriptive statistics of means, standard deviation, frequencies and percentages	Measurements of central tendencies were used to summarize the data (Daniel, 1995).
DSPN	Prevalence and severity	Descriptive statistics of frequencies and percentages	Measurements of central tendencies were used to summarize the data (Daniel, 1995).
Measure of association between the diagnosis of DSPN and socio-demographic attributes	Age, gender, level of education attained, marital status, occupation and HIV clinical information	Fischer's Exact Test	Fischer's Exact Test was used to measure the association between categorical variables (Upton, 1992).
LEFS	Mean scores and specific scores for Tests 1 and 2.	Descriptive statistics of means, standard deviations, frequencies and percentages	Measurement of central tendencies were used to summarize the data (Daniel, 1995).
	Test-retest reliability	Spearman's rank order correlation coefficient	Spearman's rank order coefficient was used to measure the reliability of ordinal categorical variables (Binkley, 1999).
	Standard error of measurement (SEM).	SEM = SDdifference/√2 (SDdifference is the standard deviation of the mean change score between Tests 1 and 2) Measurement bias (Bland Altman Test, One sample T-Test, linear regression)	Determination of the type of error (random or systematic) (Watson, 2005).
	Internal consistency	Intra-class coefficient (ICC)	ICC was used to measure internal consistency of categorical variables (Watson, 2005).
	Construct validity	Factor analysis (Unrotated and varimax rotated)	To assess the construct of the different components of the tool (Binkley, 1999).

Descriptive statistics, namely frequencies, means, modes, standard deviations and percentages were used to summarise the demographic data. The level of sensory neuropathy was described in terms of three categories. These categories were obtained by using the Visual Analogue Scale (VAS) and were classified as mild (grade 1) when VAS =1-3, as moderate (grade 2) when VAS = 4-6 and as severe (grade 3) when Vas= 7-10. These three categories were descriptively calculated and tests for the respective associations between these three categories and the demographic variables such as age, gender, marital status, and HIV clinical stage,

duration of the HIV infection and of the administration of anti-retroviral drugs were conducted using Fischer's Exact Test.

As the variables were categorical and ordinal, Spearman's rank order correlation coefficients and the intra-class correlations were used to establish the test-retest reliability value and the internal consistency of the LEFS, The Spearman's correlation coefficients were classified according to their significance levels so that a strong correlation was assessed as rho ≥ 0.7, moderate at rho < 0.7 ≥ 0.5, and a weak correlation was assessed as rho ≤ 0.5 (Tumusiime et al., 2014).

The alpha level was set at $p < 0.05$. Intra-class correlations were calculated on SPSS version 20 to assess the internal consistency of the LEFS when used among participants with HIV-related DSPN. The factor analysis and the measurement error were calculated using the Bland Altman test and the SEM was calculated.

3.8. CONCLUSION

The participants were selected from the six clinics in Gaborone. The tools that were used in the study were the BPNS, the physician's checklist for peripheral neuropathy - also containing demographic and clinical information, the BPNST recording the severity of DSPN, and the LEFS.

Important information relating to the participants' demographics was obtained and recorded by the physician, neurologist or HIV doctor. The scores obtained for the LEFS were recorded and the test–retest reliability of the LEFS among HIV positive patients on ART and with DSPN was calculated.

Spearman's rank order correlation coefficient and the Intra-class coefficients (ICC) were used to determine the test-retest reliability level and for internal consistency respectively. The Fischer Exact Test was used for measuring the level of association between the demographic variables pertaining to the patients and the three categories in terms of the severity of the DSPN that they were experiencing. The varimax, determined by factor analysis, and the measurement error were calculated using the Bland Altman test and the SEM was calculated.

4. CHAPTER FOUR: RESULTS

4.1. INTRODUCTION

This chapter presents the results of the main study. The main aim in this research study was to determine the test-retest reliability of the LEFS in HIV-diagnosed patients with DSPN who were on ARVs. The results in this chapter are presented under the following headings and in the following order:

a. Participants recruited
b. Demographic and clinical information pertaining to the participants
    - Severity grading of Distal Sensory Peripheral Neuropathy
    - Association between LEFS measures and the severity grading of DSPN
    - Association between socio-demographic variables and severity grading of DSPN
c. Test-retest reliability of the LEFS
    - Frequencies of the first response and the second response.
    - Spearman's correlation coefficients for the means of LEFS between Test One and Test Two respectively
    - Measurement of error
d. Internal consistency of the LEFS in HIV-related DSPN participants
e. Construct validity of the LEFS
f. Conclusions

4.2. PARTICIPANT RECRUITMENT

A total of 320 patients were screened for potential recruitment for the study, but only 84 (26.3%) of the overall screened patients met the inclusion criteria to determine the sample size. Figure 4.1 below illustrates the process for recruiting participants.

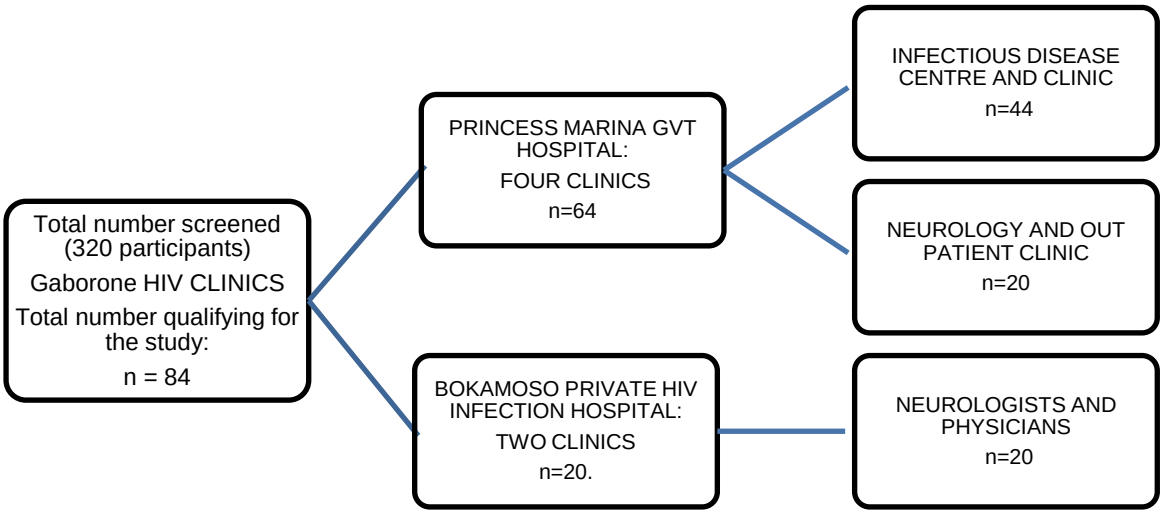

Figure 4.1: Source of the Patients from the Six Clinics and the Centres

A total of 320 patients were screened and 84 met the criteria of the BPNS test and completed the testing on both occasions.

4.2.1. Demographic Information Pertaining to the Participants

Table 4.1 below outlines the demographic data pertaining to the participants in the study.

Table 4.1: Demographic Attributes of the Patients in the Study (n=84)

Attribute	**n (%)**
Gender	
Females	59 (70.2%)
Males	25 (29.8%)
Age group	
<30 years	8(9.5%)
31 – 40 years	27 (32.1%)
41 – 50 years	24 (28.6%)
<51 years	25 (29.8%)
Mean age, (SD)	38(±13.0)
Marital status	
Single	56 (66.7%).
Married	12 (14.3%).
Divorced	2 (2.4%).
Separated	2 (2.4%).
Widow/Widower	4 (4.8%)
Cohabitation.	8 (9.5%)
Level of Education	
Tertiary education	13 (15.5%)
Secondary education (Form 3-6).	13 (15.5%)
Secondary education (Form 1-3)	27 (32.1%)
Primary education	25 (29.8%)
Nil (did not attend school)	6 (7.1%)
Occupation	
Public (Government) service	12 (14.3%)
Peasant (farmer or livestock farmer)	3 (3.6%)
Self-employed (businessman)	13 (15.5%)
Private organisation (NGO, bank, insurance company, etc.)	26 (31.0%)
Unemployed. (have not had a job for the past three months)	20 (23.8%)
Any other piece jobs (i.e temporary jobs)	10 (11.9%)

The mean age of the participants was 38 ± (13.0) years and 70.2% (59) were females. The majority of the participants were single (66.7%), had at least some form of secondary education (63.1%) and were employed (64.4%).

4.2.2. HIV-Related Information

This section shows the results of the HIV information of the participants with respect to the year of diagnosis and the duration of the ARV therapy. Table 4.2 outlines the HIV- related information pertaining to the participants.

Table 4.2: HIV-related Information Pertaining to the Participants (n=84)

HIV information	n (%)
Duration of time since diagnosis of HIV	
1-6 months	2 (2.4%)
6-12 months	2 (2.4%)
1-3 years	5 (6.0%)
4-6 years	9 (10.7%)
7-9 years	20 (23.8%)
10-15 years	40 (47.6%)
>15 years	6 (7.1%)
Length of time the patient has been on ART	
1-6 months	4 (4.8%)
6-12 months	2 (2.4%)
1-3 years	11 (13.1%)
4-6 years	7 (8.3%)
7-9 years	20 (23.8%)
10-15 years	32 (38.1%)
>15 years	8 (9.5%)
Type of ARV treatment	
Travuda.	6 (7.1%)
Alluvia.	3 (3.6%)
Nevirapin.	1 (1.2%)
Combined treatment(two to three different drugs)	62 (73.8%)
Atripla.	11 (13.1%)
Teevir.	1 (1.2%)
Clinical stage of HIV infection	
Stage 1*	5 (6.0%)
Stage 2**	5 (6.0%)
Stage 3***	39 (46.4%)
Stage 4****	35 (41.7%)

More than half of the participants (53.7%) were diagnosed with HIV more than 10 years ago and 47.6% had been on ARVs for at least 10 years. Most of the participants were in Clinical Stage 3 (46.4%) and Stage 4 (41.7%) of the disease. All the participants in this study reported sensory neuropathy, and the frequency of DSPN and the severity grades for DSPN for this sample are reported in Table 4.3.

Table 4.3: Diagnosis and the Grade of Severity of Distal Sensory Peripheral Neuropathy

Grading of DSPN	**n**	**%**
Mild (grade 1)	25	29.8
Moderate (grade 2)	45	53.6
Severe (grade 3)	14	16.7
Total	84	100

The results of the DSPN assessment showed that more than half (53.6%) of the participants were in the moderate range of sensory neuropathy (grade 2). The grade of sensory neuropathy was tested for its association with socio-demographic factors to obtain a better understanding of the participants presenting with this condition.

Table 4.4: LEFS Measures and the Grade of Severity of DSPN

	Measure 1 LEFS		**Measure 2 LEFS**	
DSPN severity	**Mean**	**SD**	**Mean**	**SD**
Grade 1	65.60	16.59	64.4	17.35
Grade 2	62.62	19.95	61.22	20.77
Grade 3	60.71	20.00	51.00	19.87

The correlation between the LEFS and the severity of DSPN was established on the basis of Spearman's correlation test and showed an inverse relationship ($r=-0.22$, $p<0.05$).

Table 4.5 shows the association between the socio-demographic variables and the grade of severity of sensory neuropathy.

Table 4.5: Association between Socio-Demographic Variables and the Grade of Severity of Sensory Neuropathy

Variable	Fischer's Exact Test
Age	0.68
Gender	0.28
Marital status	0.37
HIV: clinical stage	0.26
ART: duration	0.42
HIV infection: duration from the time of diagnosis	0.04

The duration of the HIV infection from the time of diagnosis was found to be the only socio-demographic variable that showed a significant association with the grade of severity of sensory neuropathy ($p<0.05$).

4.2.3. Frequency of the LEFS Response: Test 1 and Test 2

Tables 4.6 and 4.7 below outline the results of the response of the participants to specific questions relating to the LEFS.

Table 4.6: LEFS Frequencies for Test 1

Item	Functional activities, n (%)	Extremely difficult	Considerably difficult	Moderate	Slightly difficult	No difficulty
a	Any of the usual work, housework or school activities	4(4.8)	5(6.0)	8(9.5)	15(17.9)	52(61.9)
b	Your usual hobbies, recreational or sporting activities	8(9.5)	4(4.8)	8(9.5)	12(14.3)	52(61.9)
c	Getting in and out of the bath	2(2.4)	4(4.8)	6(7.1)	8(9.5)	64(76.2)
d	Walking between rooms	2(2.4)	3(3.6)	4(4.8)	4(4.8)	71(84.5)
e	Putting on shoes or socks	1(1.2)	3(3.6)	8(9.5)	5(6.0)	67(79.8)
f	Squatting	12(14.3)	6(7.1)	6(7.1)	9(10.7)	51(60.7)
g	Lifting an object, like a bag of groceries, from the floor	1(1.2)	6(7.1)	8(9.5)	6(7.1)	63(75.0)
h	Performing light activities around your home	2(2.4)	1(1.2)	7(8.3)	10(11.9)	64(76.2)
i	Performing heavy duties around your home	12(14.3)	6(7.1)	9(10.7)	14(16.7)	43(51.2)
j	Getting in and out of the car	2(2.4)	4(4.8)	5(6.0)	7(8.3)	66(78.6)
k	Walking for two blocks	3(3.6)	3(3.6)	7(8.3)	9(10.7)	62(73.8)
l	Walking for a mile.	10(11.9)	4(4.8)	11(13.1)	13(15.5)	46(54.8)
m	Going up or down 10 stairs (about one flight of stairs).	9(10.7)	5(6.0)	11(13.1)	17(20.2)	42(50.0)
n	Standing for one hour.	16(19.0)	2(2.4)	21(25.0)	8(9.5)	37(44.0)
o	Sitting for one hour.	6(7.1)	4(4.8)	6(7.1)	9(10.7)	59(70.2)
p	Running on even ground.	15(18.1)	4(4.8)	18(21.7)	7(8.4)	39(47.0)
q	Running on uneven ground.	19(22.6)	2(2.4)	21(25.0)	11(13.1)	31(36.9)
r	Making sharp turns while running fast.	18(21.4)	3(3.6)	15(17.9)	10(11.9)	38(45.2)
s	Hopping.	14(16.7)	4(4.8)	10(11.9)	11(13.1)	45(53.6)
t	Rolling over in bed.	-	-	-	2(2.4)	82(97.6)

(Extremely difficult 0 – Not difficult 4)

As shown in Table 4.6 above, more than half of the participants had no difficulty in performing each of the following activities in Test 1:- getting in and out of the bath, walking between rooms, putting on shoes or socks.

Table 4.7: LEFS frequencies for Test 2

Item	Functional activities, n (%)	Extremely difficult	Considerably difficult	Moderate	Slightly difficult	No difficulty
a	Any of the usual work, housework or school activities	4(4.8)	5(6.0)	11(13.1)	21(25.0)	43(51.2)
b	Your usual hobbies, recreational or sporting activities	7(8.3)	6(7.1)	7(8.3)	14(16.7)	50(59.5)
c	Getting in and out of the bath	2(2.4)	7(8.3)	5(6.0)	11(13.1)	59(70.2)
d	Walking between rooms	2(2.4)	4(4.8)	10(11.9)	6(7.1)	62(73.8)
e	Putting on shoes or socks	1(1.2)	5(6.0)	9(10.7)	7(8.3)	62(73.8)
f	Squatting	11(13.1)	6(7.1)	7(8.3)	15(17.9)	45(53.6)
g	Lifting an object, like a bag of groceries, from the floor	1(1.2)	9(10.7)	9(10.7)	8(9.5)	57(67.9)
h	Performing light activities around your home	2(2.4)	3(3.6)	8(9.5)	16(19.0)	55(65.5)
i	Performing heavy duties around your home	12(14.3)	6(7.1)	12(14.3)	18(21.4)	36(42.9)
j	Getting in and out of the car	3(3.6)	4(4.8)	8(9.5)	13(15.5)	56(66.7)
k	Walking for two blocks	4(4.8)	4(4.8)	9(10.7)	13(15.5)	54(64.3)
l	Walking for a mile.	10(11.9)	7(8.3)	14(16.7)	18(21.4)	35(41.7)
m	Going up or down 10 stairs (about one flight of stairs).	9(10.7)	7(8.3)	13(15.5)	20(23.8)	35(41.7)
n	Standing for one hour.	18(21.4)	4(4.8)	18(21.4)	10(11.9)	34(40.5)
o	Sitting for one hour.	7(8.3)	7(8.3)	5(6.0)	15(17.9)	50(59.5)
p	Running on even ground.	15(17.9)	5(6.0)	18(21.4)	7(8.3)	39(46.4)
q	Running on uneven ground.	18(21.4)	2(2.4)	21(25.0)	12(14.3)	31(36.9)
r	Making sharp turns while running fast.	18(21.4)	3(3.6)	15(17.9)	12(14.3)	36(42.9)
s	Hopping.	14(16.7)	5(6.0)	10(11.9)	12(14.3)	43(51.2)
t	Rolling over in bed.	2(2.4)	7(8.3)	7(8.3)	3(3.6)	65(77.4)

As outlined in Table4.7 above, more than half of the participants had no difficulty in performing each of the activities in Test 2: getting in and out of the bath, walking between rooms, putting on shoes or socks, etc.

4.2.4. Test–Retest Reliability of the LEFS

The total mean score for the LEFS was calculated as per the instructions given by Binkley et al (1999). The results are shown in Table 4.8.

Table 4.8: Total Mean Scores for the First and Second Data Collection Times of the LEFS

	N	Minimum	Maximum	Mean	SD	SEM
Mean1	84	11	80	63.19	18.86	4.88
Mean2	84	8	80	60.46	19.94	

Table 4.9 below shows the results of the Spearman's rank order correlation test to determine the test-retest reliability of the LEFS.

The overall total mean score for Test 1 and Test 2 of the LEFS shows a mean value ranging from 60.46 to 63.19, with a standard deviation of 18.86 to 19.94. The correlation coefficient of the LEFS for the first and second data collection times is high, namely an rs value of 0.92 and a p value of <0.001.

Table 4.9: Spearman's Correlation Coefficients for the First and Second Data Collection Times for the LEFS

Item	Functional activities	First data set (Mean ± SD)	Second data set (Mean± SD)	Spearman (rs)	p-value
A	Any of the usual work, housework or school activities	3.26 ± 1.15	3.12 ± 1.15	0.80	<0.001
B	Your usual hobbies, recreational or sporting activities	3.14 ± 1.33	3.12±1.31	0.95	<0.001
C	Getting in and out of the bath	3.52 ± 0.99	3.4±1.08	0.89	<0.001
D	Walking between rooms	3.65 ± 0.91	3.45±1.03	0.74	<0.001
e	Putting on shoes or socks	3.6 ± 0.89	3.48±0.99	0.86	<0.001
f	Squatting	2.96 ±1.51	2.92±1.45	0.94	<0.001
g	Lifting an object, like a bag of groceries, from the floor	3.48 ±1.01	3.32±1.11	0.84	<0.001
h	Performing light activities around your home	3.58 ±0.88	3.42±0.97	0.79	<0.001
i	Performing heavy duties around your home	2.83 ±1.48	2.71±1.44	0.91	<0.001
j	Getting in and out of the car	3.56 ±0.97	3.37±1.07	0.73	<0.001
k	Walking for two blocks	3.48 ±1.04	3.3±1.14	0.82	<0.001
l	Walking for a mile.	2.96 ±1.40	2.73±1.39	0.77	<0.001
m	Going up or down 10 stairs (about one flight of stairs).	2.93 ±1.36	2.77±1.36	0.84	<0.001
n	Standing for one hour.	2.57±1.53	2.45±1.57	0.92	<0.001
o	Sitting for one hour.	3.32 ±1.23	3.12±1.32	0.80	<0.001
p	Running on even ground.	2.61±1.55	2.6±1.55	0.99	<0.001
q	Running on uneven ground.	2.39±1.55	2.43±1.53	0.98	<0.001
r	Making sharp turns while running fast	2.56±1.59	2.54±1.58	0.97	<0.001
s	Hopping	2.82±1.53	2.77±1.53	0.97	<0.001
t	Rolling over in bed	3.98±0.15	3.45±1.10	0.36	<0.001
	Total Mean	**63.19±18.86**	**60.46±19.94**	**0.92**	**<0.001**

The results of the test-retest reliability using the Spearman's rank order correlation coefficient to show the association between the data for the first and second collection times was found to be strong (rs=0.74-0.99). All functional activities showed strong and significant correlations between the first and second data collection times with the exception of item 't' (Rolling over in bed), which showed a

weak correlation between the first and second collection times (rs = 036, p<0.001), as shown in Table 4.10 above.

4.2.5. Internal Consistency of the LEFS in HIV Patients with Distal Sensory Peripheral Neuropathy

Table 4.10 below outlines the results pertaining to the internal consistency using the intra- class coefficient of the LEFS for Tests 1 and 2.

Table 4.10: Internal Consistency of Measures 1 and 2

	ICC	95%CI	Significance
Measure 1	0.96	0.95-0.97	0.00
Measure 2	0.96	0.95-0.97	0.00

The LEFS showed a high internal consistency, ICC=0.96 for both Tests 1 and 2, and a 95% consistency Index (CI) of 0.95 - 0.97.

4.2.6. Construct Validity

The construct validity variance values are presented in Tables 4.11 and 4.12 below:

Table 4.11: Factor Loading for LEFS in Test 1

	Questions/Items	Initial eigenvalues %variance	Sums of squared loadings %variance	Rotated sums of squared loadings %variance
Q1	Any of the usual work, housework or school activities	58.70	58.70	35.24
Q2	Your usual hobbies, recreational or sporting activities	7.80	7.80	30.75
Q3	Getting in and out of the bath	5.11	5.11	5.62
Q4	Walking between rooms	4.22		
Q5	Putting on shoes or socks	3.37		
Q6	Squatting	3.04		
Q7	Lifting an object, like a bag of groceries, from the floor	2.74		
Q8	Performing light activities around your home	2.48		
Q9	Performing heavy duties around your home	2.14		
Q10	Getting in and out of the car	1.80		
Q11	Walking for two blocks	1.52		
Q12	Walking for a mile	1.48		
Q13	Going up or down 10 stairs (about one flight of stairs)	1.34		
Q14	Standing for one hour	0.93		
Q15	Sitting for one hour	0.86		
Q16	Running on even ground	0.76		
Q17	Running on uneven ground	0.65		
Q18	Making sharp turns while running fast.	0.48		
Q19	Hopping.	0.32		
Q20	Rolling over in bed.	0.27		

Table 4.12: Factor Loading for LEFS in Test 2

	Questions/Items	Initial eigenvalues %variance	Sums of squared loadings %variance	Rotated sums of squared loadings %variance
Q1	Any of the usual work, housework or school activities	60.05	60.05	37.47
Q2	Your usual hobbies, recreational or sporting activities	8.38	8.38	30.97
Q3	Getting in and out of the bath	4.52		
Q4	Walking between rooms	3.47		
Q5	Putting on shoes or socks	3.18		
Q6	Squatting	2.93		
Q7	Lifting an object, like a bag of groceries, from the floor	2.65		
Q8	Performing light activities around your home	2.35		
Q9	Performing heavy duties around your home	2.09		
Q10	Getting in and out of the car	1.64		
Q11	Walking for two blocks	1.59		
Q12	Walking a mile	1.47		
Q13	Going up or down 10 stairs (about one flight of stairs)	1.26		
Q14	Standing for one hour	1.10		
Q15	Sitting for one hour	0.89		
Q16	Running on even ground	0.76		
Q17	Running on uneven ground	0.66		
Q18	Making sharp turns while running fast	0.41		
Q19	Hopping.	0.35		
Q20	Rolling over in bed.	0.26		

Tables 4.11 and 4.12 above are outlines of the results of the factor analysis for Tests 1 and 2. The factor analysis results show that the items for both the rotated and the unrotated components for Test 1 are loaded on Questions 1 to 3. The factor analysis results for Test 2 show that the items for both the rotated and the unrotated components are loaded on Questions 1 to 2.

Tables 4.13 and 4.14 below show the rotated and unrotated extracted components of the factor analysis respectively.

Table 4.13: Factor Analysis Coefficient for the Specific Items within the Split Components (Rotated)

		Factor analysis coefficient				
		Test 1			Test 2	
	Questions/Items	**1**	**2**	**3**	**1**	**2**
Q1	Any of the usual work, housework or school activities	**0.77**	0.43	-0.06	**0.76**	0.40
Q2	Your usual hobbies, recreational or sporting activities	**0.67**	0.43	0.05	**0.53**	0.45
Q3	Getting in and out of the bath	**0.84**	0.28	0.06	**0.81**	0.30
Q4	Walking between rooms	**0.86**	0.18	0.12	**0.81**	0.19
Q5	Putting on shoes or socks	**0.61**	0.21	0.22	**0.75**	0.12
Q6	Squatting	0.40	**0.75**	-0.01	0.37	**0.75**
Q7	Lifting an object, like a bag of groceries, from the floor	**0.63**	0.39	0.03	**0.73**	0.34
Q8	Performing light activities around your home	**0.76**	0.28	-0.01	**0.68**	0.42
Q9	Performing heavy duties around your home	**0.67**	0.47	0.02	**0.59**	0.50
Q10	Getting in and out of the car	**0.80**	0.32	0.05	**0.76**	0.39
Q11	Walking for two blocks	**0.54**	0.49	0.17	**0.57**	0.51
Q12	Walking for a mile	**0.63**	0.43	0.03	**0.70**	0.36
Q13	Going up or down 10 stairs (about one flight of stairs)	0.55	**0.63**	-0.09	0.51	**0.63**
Q14	Standing for one hour	0.48	**0.68**	0.17	0.57	**0.61**
Q15	Sitting for one hour	**0.59**	0.51	0.14	**0.71**	0.41
Q16	Running on even ground	0.24	**0.90**	0.05	0.22	**0.89**
Q17	Running on uneven ground	0.28	**0.87**	0.03	0.28	**0.87**
Q18	Making sharp turns while running fast	0.32	**0.85**	0.17	0.31	**0.86**
Q19	Hopping	0.39	**0.82**	0.08	0.32	**0.85**
Q20	Rolling over in bed	0.10	0.10	**0.96**	**0.69**	0.30

Table 4.14: Factor Analysis Coefficient of the Specific Items within the Split Components (Unrotated)

		Factor analysis coefficient				
		Test 1			Test 2	
	Questions/Items	**1**	**2**	**3**	**1**	**2**
Q1	Any of the usual work, housework or school activities	**0.85**	0.21	-0.14	**0.84**	0.20
Q2	Your usual hobbies, recreational or sporting activities	**0.78**	0.14	-0.03	**0.69**	0.01
Q3	Getting in and out of the bath	**0.81**	0.36	-0.02	**0.81**	0.31
Q4	Walking between rooms	**0.76**	0.45	0.05	**0.73**	0.39
Q5	Putting on shoes or socks	**0.61**	0.25	0.17	**0.64**	0.40
Q6	Squatting	**0.80**	-0.28	-0.09	**0.78**	-0.32
Q7	Lifting an object, like a bag of groceries, from the floor	**0.73**	0.13	-0.04	**0.77**	0.22
Q8	Performing light activities around your home	**0.75**	0.31	-0.07	**0.79**	0.13
Q9	Performing heavy duties around your home	**0.81**	0.11	-0.06	**0.78**	0.02
Q10	Getting in and out of the car	**0.81**	0.31	-0.02	**0.83**	0.21
Q11	Walking for two blocks	**0.75**	0.00	0.10	**0.76**	-0.01
Q12	Walking for a mile	**0.75**	0.11	-0.04	**0.76**	0.20
Q13	Going up or down 10 stairs (about one flight of stairs)	**0.82**	-0.09	-0.17	**0.80**	-0.13
Q14	Standing for one hour	**0.83**	-0.18	0.08	**0.83**	-0.08
Q15	Sitting for one hour	**0.79**	0.02	0.06	**0.81**	0.16
Q16	Running on even ground	**0.78**	-0.50	-0.04	**0.76**	-0.52
Q17	Running on uneven ground	**0.80**	-0.45	-0.06	**0.78**	-0.47
Q18	Making sharp turns while running fast	**0.82**	-0.42	0.09	**0.80**	-0.44
Q19	Hopping.	**0.84**	-0.34	-0.01	**0.80**	-0.42
Q20	Rolling over in bed	0.23	-0.03	**0.94**	**0.72**	0.23

The factor analysis results extracted for the rotated items divided the LEFS into two constructs (regular and strenuous), as shown in Table 4.15 below.

Table 4.15: Psychometric Sub-Constructs of the LEFS (Rotated)

	Construct 1 (Regular activities)		Construct 2 (Strenuous activities)
Q1	Any of the usual work, housework or school activities	Q6	Squatting
Q2	Your usual hobbies, recreational or sporting activities	Q13	Going up or down 10 stairs (about one flight of stairs)
Q3	Getting in and out of the bath	Q14	Standing for one hour
Q4	Walking between rooms	Q16	Running on even ground
Q5	Putting on shoes or socks	Q17	Running on uneven ground
Q7	Lifting an object, like a bag of groceries, from the floor	Q18	Making sharp turns while running fast
Q8	Performing light activities around your home	Q19	Hopping
Q9	Performing heavy duties around your home		
Q10	Getting in and out of the car		
Q11	Walking for two blocks		
Q12	Walking a mile		
Q15	Sitting for one hour		
Q20	Rolling over in bed		

The results showed that the LEFS items could be classified into regular activities and strenuous activities, as shown in Table 4.15.

The internal consistency of the respective components was further tested. This was necessary because factor analysis revealed a split in constructs.

Table 4.16: Internal Consistency of the Rotated Constructs

	Test 1				Test 2			
Components	**N**	**ICC**	**95%CI**	**p-value**	**N**	**ICC**	**95%CI**	**p-value**
1	12	0.94	0.92-0.96	0.00	13	0.95	0.93-0.96	0.00
2	7	0.95	0.93-0.97	0.00	7	0.95	0.92-0.96	0.00
3	1	-	-	**-**	**-**	**-**	**-**	**-**

The ICC showed strong internal consistency which proved to be significant in measuring the specific constructs (regular and strenuous activities). Further testing was carried out to determine the correlation of each component with the LEFS. This was necessary to test which sub-construct contributed to lower extremity function.

Table 4.17: Spearman's Rank Order Correlation of the Constructs with the LEFS

		Mean 1		Mean 2	
Rotated	**1**	0.29	0.00	0.47	0.00
	2	**0.83**	0.00	**0.73**	0.00
	3	-0.46	<0.001	-	-

4.3. CONCLUSION

This study measured the test-retest reliability of the LEFS in identifying lower limb functional impairment in HIV patients presenting with DSPN. The LEFS showed strong test-retest reliability for all activities except for Item 2, namely rolling over in bed. The standard error of measurement was 4.88. Factor analysis of the LEFS revealed two sub constructs – regular activities and strenuous activities. Furthermore, the study showed a high internal consistency and that the duration of the HIV infection from date of diagnosis was associated with the severity of the DSPN. The mean age of the participants was 38 years and they were mostly females.

The highest number of participants had a secondary education and was employed. The majority of participants were in Stage 3 of the clinical HIV stages, had been on ARVs for 10 to15 years and were taking a combination of ARVs.

The next chapter focuses on a discussion of the implications issuing from the results of this study.

5. CHAPTER FIVE: DISCUSSION

5.1. INTRODUCTION

This chapter discusses the results of the data analysis as presented in Chapter Four. The aim of the study was to determine the test-retest reliability and internal consistency of the LEFS questionnaire as an outcome measure in establishing lower limb functioning in patients with HIV-related DSPN.

The results are discussed in line with the following objectives:

- To establish the test-retest reliability of the LEFS in the measurement of lower limb function in HIV-related DSPN in Botswana.
- To determine the internal consistency of the LEFS for lower limb function in HIV-related DSPN in Botswana.
- To describe the demographic and clinical characteristics of HIV patients with DSPN in Botswana
- To determine the construct validity of the LEFS in participants with DSPN in Botswana.

5.2. TEST-RETEST RELIABILITY OF THE LEFS IN THE MEASUREMENT OF LOWER LIMB FUNCTION IN HIV-RELATED DSPN

The test–retest reliability of the tool, the LEFS questionnaire, in this sample of HIV-related DSPN patients was very good. The Spearman's rank order correlation coefficients (rs) were found to range from rs= 0.74 to 0.99. In this study, all questions showed strong reliability in patients diagnosed with DSPN, with the exception of one item , namely "rolling over in bed", which showed a weak correlation between the first and second recordings within the seven-day period.

One of the reasons for this anomaly is the possibility that the question around rolling over in bed was unclear and in this population may not have been particularly relevant - given that most of the participants were ambulant. In spite of this one aspect, one can conclude from the results that the LEF tool is reliable for measuring lower limb function in patients with DSPN.

As with Tumusiime (2014), our study aimed at determining the test–retest reliability of the LEFS in HIV-related DSPN and its internal consistency. The test-retest reliability results are comparable to those presented in Tumusiime (2014) study in Rwanda that reported a strong test-retest reliability among HIV-infected patients with DSPN ($rs \geq 0.70$). The afore-mentioned is but one of the studies that have tested LEFS in an HIV group with sensory neuropathy, the results of which can be compared with those of this study since the patient group is the same. Lower limb function is important to the overall quality of life, and a study by Galantino et al. (2014), showed that HIV-related DSPN diminishes the quality of life and the functionality of PLHIV patients on ARVs.

The LEFS has been used in the past to measure function mainly in the lower limb and in many different medical scenarios, including cases where patients have undergone anterior cruciate ligament (ACL) reconstruction surgery, and where patients have presented with musculoskeletal dysfunction, total knee arthroplasty, ankle fractures (Lin, 2009), diabetes and arthritis (Hoogeboom et al., 2012). Under such conditions, the reliability scores were found to range between 0.74 and 0.96.

Yeung et al. (2009) used the test-retest reliability of the LEFS for in-patients in an orthopaedic rehabilitation ward with fractures, where the coefficient showed a strong reliability of $r = 0.88$. Binkley et al. (1999) showed that the test-retest reliability of the LEFS is extremely sound in musculoskeletal disorders and reported a high r value of 0.94 (Binkley, 1999). Similarly, Stratford et al. (2009) found exactly the same level of

reliability in a study of patients who had undergone total knee arthroplasty. Alcock et al. (2012) revealed that the test-retest reliability of the LEFS in anterior cruciate ligament (ACL) reconstruction was high (r = 0.90).

It is encouraging to note that, according to the literature, reliability is attained in all conditions, thus making the LEFS a trustworthy tool. For example, in patients who had undergone total joint arthroplasty, the r-value reported was r=0.85 (Stratford et al., 2009).

In our study, this researcher translated the English version of the LEFS into Setswana and back translated it again into English. In a similar manner, Hou et al. (2014) translated the English version of the LEFS into Taiwanese and obtained a good test-retest reliability result (Hou et al., 2014). Other translated versions of the LEFS tool into Italian and Dutch have also shown good reliability (Cacchio et al., 2010, Negahban et al., 2014).

As noted before, one activity (item) in our study that did not obtain a high correlation between Test 1 and Test 2 was rolling over in bed. This is comparable to the study by Tumusiime et al. (2014) in which he reported a weak test–retest reliability level for “walking across from one building to another” (r=0.47) and for “putting on shoes and socks” (r= 0.44).

The implication of this result is that future research should examine the performance of the LEFS in a more heterogeneous HIV population. Part of the reason for this is congruent with previous research that has shown that most HIV patients experience a phenomenon known as episodic disability (O'Brien et al., 2008). In such a situation, patients could experience complete wellness and manage all activities until they experience opportunistic infections and periods of illness when they could be completely incapacitated (Myezwa et al., 2009). Perhaps further study into the

validity of the activities, listed as items in the tables and that affect the responses of a population that is ambulant should be undertaken. This was beyond the scope of this study and future research should consider this.

In using the LEFS questionnaire in the future, it might be necessary to consider the social and environmental context of the activities (items listed in the LEFS) and to modify them accordingly. Another reason for considering such adaptations could be the differing perceptions that respondents hold in respect of activities, as was noted in Rwanda where the population would not normally undertake such activities (Tumusiime, 2014). Such modifications to the activities or items in the LEFS questionnaire might also be necessary in the case of studies similar to this one.

Another recommendation in the case of this group of Botswana patients infected with HIV could be for the concept of rolling over in bed to be reconsidered and reviewed for clarity and understanding in the local language.

5.3. INTERNAL CONSISTENCY OF THE LEFS FOR LOWER LIMB FUNCTION IN HIV-RELATED DSPN

The internal consistency of the LEFS was tested during both Measurement 1 Time and Measurement 2 time and found to be high, thus indicating a good internal consistency in this study group. This implies that when the LEFS is applied for measuring consistency between the respective activities or items within the same test, but at different times, the scores are found to be similar and the results are therefore consistent.

The results obtained in this study are similar to those reported by (Binkley et al., 1999a) who, when using Cronbach's Alpha index, and testing patients with

musculoskeletal disorders, reported a result of α=0.96, indicative of a high level of internal consistency. Similarly, the LEFS demonstrated a high level of internal consistency (α>0.90) in a study were this scale was being applied for its clinometric properties to people with ankle fractures (Lin et al., 2009) and to individuals that had undergone ACL reconstruction (ICC=0.90).

Alcock et al. (2012) reported strong internal consistency (ICC =0.90) in their study, while the study by Kennedy et al. (2008) showed an intra-class correlation on the LEFS, indicative of a strong internal consistency. Similar results were shown by Thomas et al. (2012), who conducted a validation study on the Dutch LEFS to investigate participants with hip/knee osteoarthritis. With an ICC value of 0.96, the Dutch LEFS showed good internal consistency.

In another study, Cacchio et al. (2010) measured the properties of the Italian LEFS version in participants who were presenting with lower limb musculoskeletal dysfunction. Having calculated Cronbach's Alpha Index to be α= 0.94 in this case, the researchers concluded that the internal consistency of the LEFS was excellent.

With an ICC of 0.92, a good LEFS internal consistency level was shown when Pua et al. (2009) undertook a cross-sectional study of community-dwelling adults with hip osteoarthritis. These researchers used both the LEFS and the WOMAC-PF scale for assessing their sample population.

The calculated ICC for internal consistency of the LEFS in HIV-related DSPN is important in that it shows that the stability of the tool is good when it is used on separate occasions. In other words, there is limited variation between the respective results (data sets) for two tests of the same items which are conducted at different times. The literature reviewed in this study has revealed that the LEFS can be used

reliably in researching different disease conditions but that there is a dearth of literature to support its use in HIV-related neuropathy.

For the purposes of this study, the LEFS was translated into Setswana and tested for its usability and reliability among patients living with HIV and experiencing DSPN. Factor analysis was conducted to determine the construct validity of the scale. The results for the first data set show that the variables were differentiated into three components. When these components were analysed further, they could be categorised into separate components, namely difficult activities that are strenuous and regular activities that are not so strenuous. The only activity listed in the LEFS that did not reflect similar results to the other activities was Item t, namely rolling over in bed.

For the second data set, only two components emerged, namely the regular and the strenuous activities. These results show that the LEFS measures the construct of lower limb function based on different activities that present different levels of challenge to patients at different stages in their illness.

It was interesting and not surprising to note that the analysis for standard error measurement revealed that random error was present but that systematic error was minimal. The researcher had undertaken the necessary measures in the form of training, presenting detailed explanations to patients, translation and back translation, and finally ensuring that confidentiality was kept, to ensure that systematic error would be kept to a minimum.

An explanation for the random error that emerged from the statistical analysis of the data could be that individual decision-making by the participants cannot be avoided when a self-reporting tool such as the LEFS questionnaire is used (Schaeffer, 1996).

The demographic and clinical attributes of the participants in this study group proved to be interesting in that they revealed, in their collective form, comparable data sets and results that could contribute to a better understanding of the epidemiology of HIV-related DSPN.

5.4. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF HIV PATIENTS WITH DSPN IN BOTSWANA

In our study, we invited a total of 320 participants for potential inclusion into the study, but only 84 were screened as qualifying to go to the next stage of the study. Out of the HIV population in the six clinics, 26.3% reported symptoms of sensory neuropathy. The prevalence of DSPN within Sub-Saharan Africa that was found in other studies was higher than that for our study (Biraguma and Rhoda, 2012, Luma et al., 2012, Tumusiime, 2014). In Rwanda, Tumusiime (2014) and Biraguma and Rhoda (2012), found a prevalence of 59% and 40% DSPN respectively among HIV patients.

A lower percentage in Botswana is surprising considering that Botswana has been reported to have one of the highest HIV prevalence rates in the world and introduced the use of ART quite early on in the pandemic (Bennell et al., 1998). With our study, Botswana was found to have a higher number of females with DSPN and this is comparable to other sub-Saharan African studies (Biraguma and Rhoda, 2012, Tumusiime, 2014). The larger number of females is not surprising as generally, the prevalence of HIV is higher among females than males in Sub-Saharan Africa (Glynn et al., 2001, Ansari et al., 2002). A recent study by Keetile (2014) reported that a third of the females in Botswana are living with HIV whereas the men living with HIV amount to a quarter of the males population of Botswana..

The age group, 31-40 years, was found to be the one most seriously affected by HIV since 32.1% of the participants in the sample population of our study were HIV-infected. It was followed by the age group 41-51 years or more. Similar patterns relating to age distribution have been reported in other studies. For example, in a study conducted on HIV-related DSPN in Tanzania, the population had a mean age of 37 years (Mullin et al., 2011). Furthermore, a study conducted in Gabon which investigated the frequency of DSPN in people living with HIV also established that the participants' ages ranged from 17-74 years, with a mean age of 42.1 ± 11 years. However, unlike the results of our study, the majority were males (Philomène et al., 2015).

Even in a better-resourced population in the USA, the reported mean age for HIV-infected patients was found to be similar to a study by Anziska et al. (2012) on HIV DSPN where a mean age of 35 years was reported and which was mainly applicable to the female gender.

Another demographic variable that seems consistent in most studies and that applies to HIV patients is that of marital status. Many of the patients were single and this result was supported by studies on HIV conducted in South Africa (Shisana et al., 2009). In our study, the participants' level of education was predominantly found to be in primary and secondary education and less in tertiary education. The distribution of people infected with HIV in South Africa is not limited to those with no or lower education and spans across all levels of education (Myezwa et al., 2009, Hanass-Hancock et al., 2016). Most studies on HIV and disability-related studies also reported fewer people with tertiary and more with secondary and primary education. In fact, the distribution of participants is often commensurate with the country's educational status.

According to a study of HIV in Rwanda (Biraguma and Rhoda, 2012), socio-economic and educational factors were reported to be a risk factor for the development of HIV-related DSPN in this country. Low socio-economic status and poor education were reported to predispose women to a higher risk of being infected with HIV (Gregson et al., 2005, Shisana et al., 2009, Amuri et al., 2011).

A study of HIV in Gabon showed that 33.5% of the participants were unemployed. This figure is higher than the figure (23.8%) for the unemployed HIV-infected participants in our study. The majority (63.1%) of the participants in our study had reached the secondary educational level. This percentage is higher than the 51.9% reported in the Gabon study (Philomène et al., 2015).

The majority of patients in our cohort had lived with HIV for more than 10 years (54.7%) from the time of diagnosis and had also been on ART. Philomène et al. (2015) considered the stage of the disease and its treatment with medication to be very significant in terms of the severity of the presentation of HIV.

In our study, the severity of DSPN was worse within the sample population for patients who had lived with the virus for a minimum of 10 years after they had been diagnosed with HIV. Thus, a possible explanation that could be offered is that, logically, the longer one has lived with the HIV and has been treated with ARV drugs, the more likely the damage to the nerve tissue.

Several factors or mechanisms are listed below to explain this:

a) The direct effect of HIV on nerve tissue (Merrill and Chen, 1991).
b) The effect of ARV medication. The overall treatment for HIV consists of a number of treatments where a number of ARV drugs are administered. Such a regimen

increases the risk of mitochondrial toxicity and eventually damages the nervous tissue, thus leading to peripheral neuropathy (Smyth et al., 2007).

c) The aging process being compounded by HIV It was interesting to note that a high percentage (73.8%) of DSPN was recorded in the participants taking a combination of two to three drugs (O'Brien et al., 2008). This confirms the negative effect of ARV medication through its known side effects.

Interestingly, the duration of anti-retroviral therapies and the CD4 cell count were not found to be associated with DSPN in Tumusiime (2014). This is contrary to results from the Luma et al. (2012) which was conducted to determine adverse drug reactions experienced by HIV patients on ARVs. Luma et al. (2012) reported that 21.2% of all the adverse drug reactions experienced through the administration of ARVs were peripheral neuropathy cases.

In our study, all of the HIV patients with DSPN in the sample were in their third and fourth clinical stage of the disease, and a large proportion is likely to have been on ART for at least six years. The results of our study and those of the study by Luma et al. (2012) support the hypothesis that peripheral neuropathy is a prevalent adverse reaction to the long-term use of ART .

A common symptom of DSPN is pain and numbness. In our study, pain was the only clinical symptom that was measured to assess the severity of the DSPN and on the basis of the Visual Analogue Scale. 53.6% of the participants showed moderate severity in terms of the pain they were experiencing.

In a study conducted between 1993 and 2001 in Australia, pain (using the VAS for measurement) was found in 56% of the sample population, while 40% and 20% of

the participants respectively reported experiencing numbness and a vibratory sensation (Smyth et al., 2007).

A limitation of our study was the omission of numbness and vibratory sensation as symptoms justifying measurement. We regarded them as separate from the BPNS and recommend that they should be included in future studies of this kind. However, in defence of this omission, we wish to state that the purpose of our study was not to primarily diagnose DSPN, but to test the reliability and consistency of the questionnaire (tool) among the participants, namely Setswana- and English-speaking patients, once it had been translated into Setswana.

However it is important to note that one of the clinical findings of our study was that the severity of DSPN was found to be moderate in 53.6% of this cohort of patients, the results showed an inverse relationship between LEFS measures and the severity of the DSPN. This is not surprising since the functional status of a patient, as measured on the LEFS, is affected by the severity of the DSPN. The more severe the DSPN, the less functional the patient participating in our study would be (Ellis et al., 2008).

When the associations between the respective socio-demographic attributes and the severity of the DSPN were tested, the duration of the HIV infection from the time of having been diagnosed was the only factor that showed a significant association with the severity of the sensory neuropathy. Again this result was not unexpected because of the very nature of the pathological processes presenting in the HIV-ART interaction (White et al., 2004).

5.5. CONCLUSION

As the study has shown, the Intra-class correlation (ICC) of the LEFS in HIV-related DSPN patients in Botswana confirmed strong test-retest reliability in respect of the LEFS questionnaire and the level of performance in the respective activities. The results of this study also show that the LEFS tool has good internal consistency and is appropriate for monitoring the functionality of the lower limbs in patients with HIV-related DSPN in Botswana. Since the important task of identifying functional limitation in the lower limbs in HIV-related DSPN is an important aspect of rehabilitation, it is hoped that the results of this research will have contributed to the body of knowledge. Effective tools for facilitating more accurate and easier diagnoses would also assist the clinicians in their holistic management of the HIV disease.

The influence of the socio-demographic attributes of gender, age, marital status, level of education and occupation on HIV-related DSPN in respect of our study group proved to be consistent with the findings of other studies, with the exception of gender, where some studies showed a larger proportion of males than females suffering from HIV DSPN.

Clinical factors such as the duration of the HIV infection in each of the participants in our study from the time of diagnosis, the duration of the administration of the ARTs to each of the participants in our study, and the clinical stage into which each of the HIV-infected patients could be placed, were analysed to investigate their association with DSPN. The most significant clinical factor that was found when testing for the association between demographic data and DSPN was found to be the duration of the HIV infection in the patient from the time at which it was first diagnosed.

The results of this study contribute to a better understanding of HIV-related DSPN and the performance of the Lower Extremity Function Scale in terms of test-retest reliability, internal consistency, construct validity variance, and the level of measurement error. The LEFS can be used with reliability to assess functional activity among people living with HIV and DSPN.

CHAPTER SIX: CONCLUSION

The LEFS has been used widely in many studies for assessing the effectiveness of a tool that is both efficient and fairly quick to use, and able to facilitate comparisons with other conditions in the clinical setting. The literature also shows that the LEFS is reliable when used in different settings, and that DSPN is common among HIV patients who have been on ARV medication for a long time.

The main aim of this study was to establish the test-retest reliability of the Lower Limb Functional Scale in HIV-related Distal Sensory Peripheral Neuropathy for patients on anti-retroviral treatment. On the basis of high correlation coefficients calculated in the respective Spearman's statistical tests on the relevant data, high values, pointing to high levels of test–retest reliability, were found using this tool when it was administered at two points in time 7-10 days apart among people living with HIV and on ART and experiencing Distal Sensory Peripheral Neuropathy. All the activities (items listed in Table 4.8) had strong correlations except the functional activity of rolling over in bed, which had a weak correlation.

It is recommended that further studies be conducted in different settings and reflecting greater heterogeneity among patients to test the reliability and validity of the tool in investigating HIV patients' perceptions in respect of their performance levels (activities listed as items in Table 4.8). These would be useful to ensure that the weak correlation mentioned above was not just an outlier and occurring quite by chance. One of the reasons for suggesting additional investigations into this matter is that episodic disability is often experienced in HIV patients and therefore results in variations in their functional levels.

The Intraclass correlation (ICC) statistics were used to measure the internal consistency of the tool in the two measurements which were taken a week apart. Internal consistency was

also maintained in the translated version of the LEFS that was used in this study. Therefore, the use of the LEFS in different clinical settings in the country of Botswana should be possible since good test-retest reliability and internal consistency respectively were demonstrated. Furthermore, no major difficulties were experienced in using the LEFS in this study.

Construct validity was assessed using factor analysis with Varimax rotation and the un-rotated model to test whether the specific sub-constructs within the tool contribute to the overall construct of lower limb function. The constructs in the first permutation using the rotated model were divided into two components which we categorised as regular activities and more strenuous activities. In the un-rotated model, the constructs remained in one category. The constructs that contributed to the two components were further tested for internal consistency and showed that they do in fact contribute to the components of regular and strenuous activity.

Therefore the construct validity of the LEFS used in this Botswana population sample is intact. An interesting observation is that the participants under study were presenting with mild to moderate levels of DSPN, and this may account for the split in the sub-constructs. Further analysis would be required again in a more heterogeneous population and additional less-strenuous activities included for groups with more severe lower extremity functioning levels.

Testing for measurement error revealed that random error was present. This could be associated with independent decision-making by individual patients since the LEFS is a self-reporting tool.

The demographic data showed that the majority of participants were female and living alone, thus reflecting a similar gender distribution to those featured in studies conducted in Africa and abroad.

6.1. LIMITATIONS OF THE STUDY

There was significant resistance from both doctors and patients in private clinics to their participation in this study. On investigation, it became evident that both health-care staff and patients feared being stigmatised in the event of their information being published. This may have skewed the number of patients who agreed to participate from the private clinics. This was in spite of the researcher's assurance that their responses to the questionnaire would be treated confidentially through a method of encoding the data-collecting tools.

Government medical facilities were more forthcoming and cooperative but the participants admitted to the Infectious Disease Centre as referrals from other remote centres, participated initially only. Their second participation fell by the way owing to the problems they experienced in terms of distance and affordability. As such, these patients were not considered in the study. In some cases, doctors were too busy to assist, thus making recruitment very difficult and slow.

One of the main limitations of our study was the fact that it involved a sample of convenience. We could not include patients from the rural areas who had limited access to the medical facilities and thus obtain a rural set-up of activities relating to functional limitations of patients with HIV-related Distal Sensory Neuropathy.

6.2. FURTHER RECOMMENDATIONS EMANATING FROM THIS STUDY

This study consisted of a sample of HIV patients suffering from DSPN in an urban setting. As such, a similar study investigating a purely rural population sample of participants suffering from HIV-related DSPN might be useful to ensure its reliability

across all population groups. Furthermore, there is a need to increase the size of the population sample, which could probably be more representative of the larger population visiting the available medical facilities in Botswana.

There is a need to do extensive research concerning the construct and concordant validity in order to test these aspects against other tools such as the LEFI, the Health Status Questionnaire (SF-36), the Health-related Quality of Life (HRQOL) Questionnaire and the WOMAC-PF Questionnaire. This will facilitate a wide comparison of the functional testing of such individuals suffering from HIV-related DSPN and enable them to be monitored in areas where there are no specialists or doctors. The rural areas are where we find nurses and other specialised health workers conducting health services normally undertaken by better qualified professionals such as medical doctors, etc. As such, these self-reporting tools can be validated and used to good effect. The reason is that although measures of functionality are determined through self-reporting tools such as questionnaires, the afore-mentioned are considered valid and can be used to measure functionality across different populations with HIV.

This study has established the good test-retest reliability of the LEFS in a population of participants with HIV/ART-related DSPN. This study also showed that the LEFS has good internal consistency as a tool for investigating a sample population of patients with HIV and DSPN. Furthermore, It also has good construct validity but revealed the need to distinguish between strenuous and less strenuous activities among patients with HIV-related DSPN in Botswana.

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APPENDIX 1: LOWER EXTREMITY FUNCTIONAL SCALE (LEFS)

We are interested in knowing whether you are having any difficulty at all with the activities listed below **on account of your lower limb problem** for which you are currently seeking attention. Please provide an answer for **each** activity.

Activities Today, *do you* or *would you* have any difficulty at all with the following :	**Extreme difficulty or unable to perform activity**	**Considerable difficulty**	**Moderate difficulty**	**Limited difficulty**	**No difficulty**
1. Any of your usual work, housework or school activities	0	1	2	3	4
2. Your usual hobbies, recreational or sporting activities	0	1	2	3	4
3. Getting into or out of the bath	0	1	2	3	4
4. Walking between rooms	0	1	2	3	4
5. Putting on your shoes or socks	0	1	2	3	4
6. Squatting	0	1	2	3	4
7. Lifting an object, like a bag of groceries, from the floor	0	1	2	3	4
8. Performing light activities around your home	0	1	2	3	4
9. Performing heavy activities around your home	0	1	2	3	4
10. Getting into or out of a car	0	1	2	3	4
11. Walking for two blocks	0	1	2	3	4
12. Walking for a mile	0	1	2	3	4
13. Going up or down 10 stairs (about one flight of stairs)	0	1	2	3	4
14. Standing for one hour	0	1	2	3	4
15. Sitting for one hour	0	1	2	3	4
16. Running on even ground	0	1	2	3	4
17. Running on uneven ground	0	1	2	3	4
18. Making sharp turns while running fast	0	1	2	3	4
19. Hopping	0	1	2	3	4
20. Rolling over in bed	0	1	2	3	4

SETSWANA VERSION OF THE LOWER LIMB FUNCTIONAL SCALE

DITAELO

Re nale kgatlhego ya go itse gore a o nale bothata le go dira ditiri tse di mo mokwalong o o fa tlase mo go bakwang ke botsogo jwa maoto a gago.**Tsweetswee araba potso nngwe le nngwe e fa tlase**

Gompieno a o nale kgotsa o tlaa nna le bothata go dira tse difa tlase	**Bothata jo bofeteletseng kana go sa kgone gotlhelele**	**Bothata jo bo tseneletseng thata**	**Bothata jo bo fagare mme eseng thata**	**Bothata bo bo seng kae**	**Ga gona bothata**
1.Sepe sa tiro,lapeng kgotsa ko sekolong	0	1	2	3	4
2.Sepe se o seratng,motshameko kapo enele ele ithuthuntsho	0	1	2	3	4
3.go tsena le go tswa mo bateng ya botlhapelo	0	1	2	3	4
4.go tsamaya ka dinao magareng ga iphaposo	0	1	2	3	4
5.go rwala ditlhako le dikausu	0	1	2	3	4
6.go kotama	0	1	2	3	4
7.go kuka sepe hela jaaka mophuthelo wa dijo o di tsaya fa fatshe	0	1	2	3	4
8.go tsaya karolo ka go dira ditiro tse di motlhofo tsa mo gae	0	1	2	3	4
9.go tsaya karolo ka go dira ditiro tse di bokete mo gae	0	1	2	3	4
10.go tsena le go tswa mo koloing	0	1	2	3	4
11.go tsamaya sekgele sa dikago tse pedi	0	1	2	3	4
12.go tsamaya lobaka lo le leele(sekgala)	0	1	2	3	4
13.go ya godimo le ko tlase o pagamela ko ntlong e ko godimo(matlhatlhaganyane)	0	1	2	3	4
14. go ema oura	0	1	2	3	4
15. go nna oura	0	1	2	3	4
16. go tsamaya mo lefatsheng le le lekanetseng go sena dikhuti	0	1	2	3	4
17. go tsamaya mo tseleng e nang le dikhuti	0	1	2	3	4
18.go sheba ntse o tabogile ka boheho	0	1	2	3	4
19.go tlolatlola	0	1	2	3	4
20.go iphetsola mo bolaong	0	1	2	3	4

APPENDIX 2: SPEARMAN'S CORRELATION COEFFICIENTS FOR THE PILOT FIRST AND SECOND DATA COLLECTION TIMES FOR THE LEFS

Item	Functional activities	Spearman (rs)	p-value
1.	Any of the usual work, housework or school activities	0.80	<0.001
2.	Your usual hobbies, recreational or sporting activities	0.68	<0.001
3.	Getting in and out of the bath	0.97	<0.001
4.	Walking between rooms	0.97	<0.001
5.	Putting on shoes or socks	0.91	<0.001
6.	Squatting	0.96	<0.001
7.	Lifting an object, like a bag of groceries, from the floor	0.71	<0.001
8.	Performing light activities around your home	0.89	<0.001
9.	Performing heavy duties around your home	0.86	<0.001
10.	Getting in and out of the car	0.85	<0.001
11.	Walking for two blocks	0.95	<0.001
12.	Walking for a mile.	0.96	<0.001
13.	Going up or down 10 stairs (about one flight of stairs).	0.86	<0.001
14.	Standing for one hour.	0.94	<0.001
15.	Sitting for one hour.	0.99	<0.001
16.	Running on even ground.	1.00	
17.	Running on uneven ground.	0.95	<0.001
18.	Making sharp turns while running fast	0.96	<0.001
19.	Hopping	0.85	<0.001
20.	Rolling over in bed	0.86	<0.001
	Total Mean	**0.89**	**<0.001**

APPENDIX 3: BRIEF PERIPHERAL NEUROPATHY SCREEN (ENGLISH AND SETSWANA)

ENGLISH

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 /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 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 ☐

SETSWANA.

Tshekatsheko tsa batsaya karolo mo (Peripheral Neuropathy screen)

Code…….. Letsatsi……

Tsaya metsotso o arabe dipotso tse di latelang mabapi le ka fa o ikutlwang ka teng mo maotong a gago, tshwaya mo lebokosong le le latelang ka fa o ikutlwang ka teng.

Ka leboga.

1. A o atle utlwe o sa ikutlwi mo maotong a gago a le bosisi?

   Ee ☐ Nnya ☐

2. A o atle o utlwe o na le maoto a botlhoko jo bo fisang?

   Ee ☐ Nnya ☐

3. A maoto a gago a utlwa ka bonako fa o a tshwara kana o gata?

   Ee ☐ Nnya ☐

4. A ditsheka tsa gago tsa maoto di tshwarwa ke bogatsu?

   Ee ☐ Nnya ☐

5. A maoto a gago a na le go tlhabatlhaba fa o tsamaya?

   Ee ☐ Nnya ☐

6. A go botlhoko fa dikobo di kgoma letlalo la gago bosigo?

   Ee ☐ Nnya ☐

7. A o kgona go utlwa maoto a gago fa o tsamaya?

   Ee ☐ Nnya ☐

8. A o na le maoto a botlhoko jo bo bogale?

   Ee ☐ Nnya ☐

9. A o kile wa tshabelelwa ke go sa utlwa maoto a gago le fa o le mo borokong?

   Ee ☐ Nnya ☐

10. A o nna bokoa fa o tsamaya?

    Ee ☐ Nnya ☐

11. A dikai tse tsa botlhoko di a oketsega bosigo?

Ee ☐ Nnya ☐

12. A go botlhoko fa o tsamaya?

Ee ☐ Nnya ☐

13. O kgona go utlwa maoto a gago?

Ee ☐ Nnya ☐

14. A letlalo la maoto a gago le omeletse mo le phatogang?

Ee ☐ Nnya ☐

15. A o atle o nne le go sisimoga mo go tlang le botlhoko mo maotong a gago?

Ee ☐ Nnya ☐

APPENDIX 4: PHYSICIAN'S CHECKLIST FOR PERIPHERAL NEUROPATHIES

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 three 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) 1 – 15 years ago ☐
   g) More than 15 years ago ☐

8. **Clinical HIV staging:**
   a) Clinical stage I ☐
   b) Clinical stage II ☐

c) Clinical stage III ☐
d) Clinical stage IV ☐

9. **Is the patient on Anti-retroviral treatment?**
Yes ☐ No ☐

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

11**.** **For how long the patient has been on ARVs treatment**?
e) 1 – 6 months ☐
a) 6 – 12 months ☐
b) 1 – 3 years ☐
c) 4 – 6 years ☐
d) 7 – 9 years ☐
e) 10 – 15 years ☐
f) 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 presents 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 ☐

SESTWANA

Dipotso tsa bongaka mabapi le go sekwasekwa ga go tlhola bolwetse jwa (Peripheral Neuropathies) jo bo amanang le mogare le (ART) (Ka thuso ya tsa booki ba ba berekelang ko kokelong ya (ART)

Seemo sa molwetse go tswa mo go tsa botsogo le gore o dirang mo botshelong
Bong: Mme ☐ Rre ☐
Dingwaga……

3. **Dithuto tsa maemo a kwa godimo**
   a) Dithuto tsa maemo a kwagodimo (Mmadikolo) ☐
   b) Sekolo se segolwane sa lokwalo lwa (form 4-5) ☐
   c) Sekolo sa lokwalo lwa (form 1-3) ☐
   d) Sekolo se sebotlana sa (primary) ☐

4. **Tiro**
   a) Modiredi wa puso ☐
   b) Molemi morui ☐
   c) Go ipereka (o na le kgwebo) ☐
   d) Go ikemela ka nosi (kompone) ☐
   e) Ga o bereke (a o na le kgwedi tse tharo o sa bereke) ☐
   f) Go na le tse dingwe di nopole fa di le teng ☐

5. Sesupo sa gore a o tserwe/ga wa tsewa
   a) Ga wa nyalwa ☐
   b) O nyetswe ☐
   c) Le tlhalane le mokapelo ☐
   d) Kgaogane le mokapelo ☐
   e) Motlholagadi ☐
   f) Go nna le moratiwa wa gago le sa nyalana ☐
   g) Nopola tse dingwe fa di le teng ☐

6. **Lefelo la bodulo** (Kwala mo teng)

7. Molwetse o ne a itse seemo sa gagwe sa mogare go tswa leng fa a sena go tlhatlhobiwa

   a) Kgwedi ya ntlha go ya go tse di borataro ☐
   b) Kgwedi tse borataro- go ya go tse di lesome le bobedi ☐
   c) Ngwaga wa ntlha-go ya ngwageng tse tharo ☐
   d) Ngwaga tse nne –go ya ngwageng tse di borataro ☐
   e) Ngwaga tse supa-go ya ngwageng tse di bofera bongwe ☐
   f) Ngwaga tse di lesome-go ya ngwageng tse di lesome le botlhano ☐
   g) Ngwaga tse di lesome le botlhano le go feta ☐

8. Kalafi ya mogare go tsamaya kafa e thulagantsweng ka teng ka tatelano
   a) Thulaganyo (stage 1) ya ntlha ☐
   b) Thulaganyo ya bobed ☐
   c) Thulaganyo ya boraro ☐
   d) Thulaganyo ya bone ☐

9. A molwetse o tsaya diritibatse tsa mogare?
   1. Ee ☐ 2.Nnya ☐

10. Fa e le Ee rurifatsa ka go nopola mofuta wa diritibatsi tsa mogare (ARVs) tse o di tsayang
……
……
……

11. Ke lobaka le lekae molwetse a tsaya kalafi ya diritibatsi tsa mogare?
a) Kgwedi ya ntlha go ya go tse borataro ☐
b) Kgwedi tse borataro -go ya go tse di lesome le bobedi ☐
c) Ngwaga wa ntlha –go ya dingwageng tse tharo ☐
d) Ngwaga tse nne –go ya dingwageng tse di borataro ☐
e) Ngwaga tse supa-go ya dingwageng tse di bofera bongwe ☐
f) Ngwaga tse di lesome-go ya dingwageng tse di lesome le botlhano ☐
g) Ngwaga tse di lesome le botlhano le go feta ☐

12. Kopa o supe fa molwetse a na le diemo tsa malwetse a latelang ka go tshwaya mo lebokosong:

a) Bolwetse jwa sukiri ☐
b) Thaelo ya dikotla ya (vit B) ☐
c) Kankiri ☐
d) Multiple Sclerosis ☐
e) Malwetse /makoa a monyetsane le go tlhaloganya le go itse ☐
f) (Hypothyroidism) ☐
g) (Uraemia) ☐
h) Go tsenwa ke tšhefi ☐
i) Bolwetse jwa (neuropathy) jo bo neelwanang ka losika ☐
j) Ditso tsa (neoplasm) ☐
k) A mangwe fa a le teng a nopole……

13. Kopa o supe fa molwetse a supa dikai tsa malwetse a latelang ka go tshwaya mo lebokosong:

a) Botlhoko : Mo matsogong ☐ Mo maotong ☐
b) (Paraesthesia) : Mo matsogong ☐ Mo maotong ☐
c) Bosisi : Mo matsogong ☐ Mo maotong ☐

14. Fa e le gore molwetse o supa dikai tse di fa godimo, di simolotse leng dikai tseo? (Fa o gakologelwa)

a) Fa o ese o simolole diritibatsi tsa mogare (**ARV**s) ☐
b) Fa o simolola diritibatsi tsa mogare (**ARV**s) ☐

15. Fa o sena go simolola diritibatsi, dikai tsa bolwetse ga o bona di simolotse mo lobakeng lo lo kafe?(fa o gakologelwa supa ka go tshwaya mo lebokosong)

a) Kgwedi ya ntlha go ya borataro ☐
b) Kgwedi tse borataro- go ya ko go tse di lesome le bobedi ☐
c) Ngwaga wa ntlha –go ya go tse tharo ☐
d) Ngwaga tse nne-go ya go tse di borataro ☐

APPENDIX 5: ACTG BRIEF PERIPHERAL NEUROPATHY SCREENING TOOL (ENGLISH AND SESTWANA)

ENGLISH VERSION
INSTRUCTIONS FOR RECORDING SUBJECTIVE ELICITED SYMPTOMS

Ask the subject to rate the severity of each symptom listed in questions 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 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 system 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

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 SYMTOMPS

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

	R	**L**
Subjective Sensory neuropathy grade	☐	☐

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.

Vibration Perception

	R	**L**
Great toe DIP joint perception of vibration in seconds	☐	☐
(a) Vibration perception score		
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 clenches his/her fist before classifying the reflex as absent.

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

	R	**L**
Ankle reflexes	☐	☐

SESTWANA: ACTG (Brief Peripheral Neuropathy Screening Tool)
Ditaelo tsa go supa kgatiso ka dikai tsa botlhoko jwa bolwetse mo maotong le mo matsogo:

Kopa kana botsa ka seemo sa bogale jwa dikai tse di boditsweng mo karolong ya ntlha mo sekaleng sa (01 botlhoko jo bo fagare)mo leotong la moja le la ko molemeng.Tsenya letshwao mo temaneng e tshwailweng (R) le (L).Fa dikai tsa botlhoko di ne di le teng mo bogologolong,mme eseng la bofelo o tla o bona ngaka.Tsenya (00)---mo bošheng fa ne go sena botlhoko.Fa ne go sena botlhoko tsenya (11)--go supa gore botlhoko ke jo bo tlwaelesegileng ka nako tsotlhe.

Botlhoko jo bo tlwaelesegileng ka nako tsotlhe (normal)	Go tlhoka botlhoko mo bošheng(currently) absent	Mild_____severe									
11	00	01	02	03	04	05	06	07	08	09	10

		R	**L**
1.	Dikai tsa bolwetse (symptoms)		
	a) Botlhoko, le go fisa ga maoto	☐	☐
	b) Ditlhabi mo maotong	☐	☐
	c) Bosisi mo maotong	☐	☐

DITAELO TSA GO SUPA MATSHWAO A MAIKUTLO LE DIKAI TSA BOTLHOKO JWA BOLWETSE JWA MAOTO:

Dirisa letshwao lengwe le le kwa godimo le le supang botlhoko jo bo feteletseng mo karolong ya ntlha e ko godimo go tsaya matshwao a maikutlo ka bolwetse jwa (neuropathy).Fa tsotlhe di supa matshwao a (00) or 11 go raya gore maikutlo otlhe a botlhoko ke lefela (0).

Maduo a le teng a bogale jwa botlhoko
01-03=letshwao la ntlha
04-06=letshwao la bobedi
07-10=letshwao la boraro
11-00=letshwao la lefela

		R	**L**
2.	Matshwao a maikutlo a letshwao la (neuropathy)		
	Dikai tsa bolwetse fa di leng teng	☐	☐

Dirisa matshwao a latelang:
0 = Ga gona sepe
1 = Mo leotong fela
2 = Thapologela ko lenyenana
3 = Thapologela godimo ga lenyenana mme eseng ko lengoleng
4 = Thapologela ko mangoleng
5 = Thapologela ga godimo ga mangole

	R	**L**
a) Botlhoko jo bo fisang mo maotong	☐	☐
b) Setlhabi mo maotong.	☐	☐
c) Bogatsu/Bosisi mo maotong	☐	☐

DITAELO TSA GO SEKASEKA MAIKUTLO A GO UTLWA GO RURUMELA

Pataganya bofelo jwa (128 Hz tuning fork)thata mo go lekaneng mo eleng gore la tshwara mo ditlhakoreng.Baya motšhini(tuning fork)e rurumang mo lerapong la go iponatsa mo letsogong go tlhomamisa gore le kgona go lemoga go ruruma ga boleng jwa motšhini wa (tuning fork).Gape,pataganya bofelelo jwa (tuning fork)fela thata mo go lekaneng mo go tshwarang mo di tlhakoreng.Gone fela foo baya (tuning fork)e rurumelang ka bonolo mme e gateleditswe godimo ga “distal interphalangeal (DIP) mo makopanelong a nngwe ya monwana o mogolo o bo simolola go bala metsotswana.Go tla nna le kaetso ya gore go rurumela ga motšhini go ema leng.Boeletsa monwana o mongwe yo mogolo.

	R	**L**
Maikutlo a go utlwa ga go rurumela		
a) Maikutlo a go rurumela mo monwaneng o motona (DIP) fa bokopanelong ka metsotswana	☐	☐
b) Matshwao a maikutlo a go rurumela ka metsotswana	☐	☐
Lefela=La metsotswana >Lesome	☐	☐
Bongwe=Metsotswana-borataro-lesome	☐	☐
Bobedi=metsotso<b otlhano	☐	☐
Boraro=Go sa utlwale sepe	☐	☐
Bofera bobedi=Go sena tshekatsheko	☐	☐

Ditaelo tsa go sekaseka boteng jwa mosifa wa motsamao
Fa o dutse fatshe,motlhatlhobi o dirisa seatla sele sengwe go tobetsa go ya kwa godimo mo bolong ya leoto,(dorgiflexing the subjects ankle)go ya selekanyong sa 90(degrees).O dirisa sekokotelo sa(reflex hammer),Go tswa fong motlhatlhobi o itaya mosifa ba go bitsang bare (Achilles Tendon).Go tswa fa mosifa o utlwiwa ke motlhatlhobi ka letsogo jaaka(plantar flexion)ya leoto,e be go iponatsa morago go sena go diega go sekaenyana go tswa mo nakong e go iteilweng ka sekokotelo sa(reflex hammer)mo (Achilles Tendon).Dirisa thatafatso o tsentse huparela mo feising pele ga o kgaoganya motsamao jaaka o sena sepe.

Motsamao wa Lenyenana
0 = ga gona sepe
1 = Hypoactive
2 = Boteng jwa mosifa jo bo siameng
3 = Go le matlhagatlhaga
4 = Clonus
8 = Ga ke kgone go sekaseka

	R	**L**
Motsamao wa lenyenana (reflexes)	☐	☐

APPENDIX 6: ETHICAL CLEARANCE UNIVERSITY OF THE WITWATERSRAND

R14/49 Mr Abraham C Munemo et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140496

NAME: (Principal Investigator)	Mr Abraham C Munemo et al
DEPARTMENT:	Physiotherapy Botswana Bokamoso Private Clinic
PROJECT TITLE:	The Validity and Reliability of the Lower Extremity Functional Scale and the Lower Limb Functional Index in HIV-Related Distal Sensory Peripheral Neuropathy
DATE CONSIDERED:	25/04/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Hellen Myezwa
APPROVED BY:	Professor P Cleaton-Jones, Co-Chairperson, HREC (Medical)
DATE OF APPROVAL:	02/07/2014

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX 7: ETHICAL CLEARANCE: PRINCESS MARINA HOSPITAL

PLOT 1836 HOSPITAL WAY
TELEPHONE: 3621400
FAX: 3973776

RE PUBLIC OF BOTSWANA

PRINCESS MARINA HOSPITAL
P. O. BOX 258
GABORONE
BOTSWANA

REF: PMH 5/79(155)

5 May 2015

Mr. Abraham C Munemo
University of Botswana

Dear Mr Munemo

RE: The Utility of the Lower Functional Scale and the Lower Limb Functional Index in HIV-Related Distal Sensory Peripheral Neuropathy

The Research and Ethics Committee (REC) of Princess Marina Hospital met and discussed your request to do the study with the aforementioned title and full approval was given. You are asked to observe the following:

1. Always ask for permission from the head of unit/department that you will collect data from
2. You will not change any aspect of the study without permission from REC
3. Always ask for informed consent from people that you will use as your subjects
4. Please report any unforeseen circumstances including termination of this research
5. Allow REC access to the study at anytime for the purposes of auditing
6. This permission is valid for one year from 5 May 2015 to 4 May 2016
7. At the end of the study you are requested to give the REC a hard copy and soft copy of your report

Wishing you the best in your research

Thank you

Sincerely,

Gladness O. Tlhomelang
Secretary Research and Ethics Committee

APPENDIX 8: TURN-IT-IN REPORT

Mr

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