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# The description of HIV- associated sensory neuropathy symptoms in individuals of African ancestry whose home-language is isiZulu

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# THE DESCRIPTION OF HIV-ASSOCIATED SENSORY NEUROPATHY SYMPTOMS IN INDIVIDUALS OF AFRICAN ANCESTRY WHOSE HOME-LANGUAGE IS isiZULU

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A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand Medical School, Johannesburg, in fulfilment of the requirements for the degree of Master of Science in Medicine.

Johannesburg, 2011

## DECLARATION

I, Asma Shaikh, declare that this dissertation is my own unaided work, unless otherwise specified. It is being submitted for the degree of Master of Science in Medicine at the University of the Witwatersrand, Johannesburg.

This work has not been submitted before for any degree or examination at this or any other university.



Signature

The 8th day of December 2011

## ABSTRACT

In South Africa, English-language versions of neuropathic pain screening tools typically are used to screen for and diagnose neuropathic pain in the clinical and research setting. It is assumed that most individuals understand the English-language symptom descriptors in these tools (e.g. burning, pins-and-needles, aching, tingling or itching) despite English being the first-language of less than 10% of South Africans. The objectives of this study was firstly to determine what isiZulu terms are used to describe the symptoms of neuropathic pain by individuals whose home-language is isiZulu, and secondly, to determine the level of understanding of typical English neuropathic pain descriptors by these isiZulu speakers. Fifty-four participants with symptomatic HIV-associated sensory neuropathy (HIV-SN) were recruited to participate in the study. Participants were firstly asked to describe, in isiZulu, the pain and/or abnormal sensations in their feet and lower legs. Thereafter, a list of common English neuropathic pain descriptors was read to participants and they were asked to identify which words and phrases described their sensory symptoms. If they identified a particular term as describing their symptoms, participants were asked to provide an isiZulu equivalent for that English term. Participants typically used the isiZulu words “ziyashisa” (hot-48%), “amajaqamba/amacramps” (cramping-35%), “ziyaluma/kuyaluma” (itching-22%), “ndikindiki” (numb-22%) or phrases indicating numbness in their feet and lower legs to spontaneously describe their symptoms. When prompted with English neuropathic pain descriptors, “cramping” (89%) was the most selected term followed by the terms “hot” (87%), “burning” (65%), “tight” (61%) and “itching” (59%). The English terms that were the least understood by participants included “throbbing” (96% of participants did not understand the term), “radiating” (83% did not understand the term), “tingling” (78% did not

understand the term), “pricking” (72% did not understand the term), “aching” (70% did not understand the term) and “numb” (63% did not understand the term). Overall, when isiZulu speakers with HIV-SN describe their neuropathic symptoms spontaneously, the descriptors used are similar to commonly-used English neuropathic pain descriptors (when prompted with the terms). However, the understanding of English terms can be poor, indicating the need for the development of neuropathic screening and assessment tools in languages more accessible for the patients who are being assessed. The results obtained contribute to a better understanding of the description of neuropathic pain in isiZulu speakers, which will aid in the diagnosis and management of neuropathy in individuals prone to neuropathy.

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*Conference oral presentations*

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## ABBREVIATIONS

| | |
|---|---|
| ACTG | AIDS Clinical Trials Group |
| BPNS | Brief Peripheral Neuropathy Screen |
| DN4 | neuropathic pain diagnostic questionnaire 4 |
| DSP | distal sensory polyneuropathy |
| EQ-5D | European Quality of Life 5-dimensions |
| HIV | Human Immunodeficiency Virus |
| HIV-SN | HIV-associated sensory neuropathy |
| ICC | Intraclass Correlation Coefficient |
| LANSS | Leeds Assessment of Neuropathic Symptoms and Signs |
| MPQ | McGill Pain Questionnaire |
| NPQ | Neuropathic Pain Questionnaire |
| NPS | Neuropathic Pain Scale |
| NPSI | Neuropathic Pain Symptom Inventory |
| PPI | Present Pain Intensity |
| PRI | Pain Rating Index |
| QST | quantitative sensory testing |
| ROC | receiver operating characteristic |
| S-LANSS | self-completed LANSS |
| SF-MPQ | short form-McGill Pain Questionnaire |
| SPNS | Subjective Peripheral Neuropathy Screen |
| VAS | visual analogue scale |

# CHAPTER 1

# LITERATURE REVIEW *

*A search strategy was performed using the PubMed, Scopus and Science Direct databases. Articles and reviews were sourced using the terms “neuropathic pain, neuropathic pain symptoms, pain scales, neuropathic pain screening tools and assessment questionnaires, neuropathic pain descriptors and HIV-neuropathic pain.” Relevant articles were those that focussed on the symptomatology of neuropathic pain and the development and reliability of existing neuropathic pain questionnaires. The reference lists of these papers were used to obtain related and relevant research articles and review papers.

## 1.1 INTRODUCTION

Neuropathic pain results when there is damage to the nervous system and is common in patients with cancer, diabetes and in individuals infected with the Human Immunodeficiency Virus (HIV) (Dworkin, 2002). The symptoms of neuropathic pain typically are described as “burning, stabbing, shooting, electric shock-like pain, tingling, pins-and-needles and numbness” (Jensen et al., 2001; Dworkin, 2002). These characteristic symptoms of neuropathic pain, together with a clinical examination form the mainstay of a neuropathy diagnosis (Bennett et al., 2007; Cruccu et al., 2010).

Most of the symptom assessments used to diagnose neuropathy were developed in English, French or German (Bennett et al., 2007) and then translated into other languages such as Turkish, English, Spanish, Italian and Portuguese (Yucel et al., 2004; Bouhassira et al., 2005; Perez et al., 2007; Padua et al., 2009; Santos et al., 2010). In South Africa, English neuropathic pain questionnaires are commonly used to assist the assessment and diagnoses of painful neuropathies in the clinical and research settings; however, this may pose a problem as the majority of the population does not speak English as a first-language (Census, 2001). The objectives of this dissertation were to determine the symptomatology of neuropathic pain in isiZulu-speaking patients with painful HIV-associated sensory neuropathy (HIV-SN), and to determine if English terms commonly used in English-language neuropathic pain questionnaires, are understood by isiZulu speakers who do not speak English as a first-language.

In this chapter, the background for understanding the basis of the study is presented, by reviewing pain assessment with a focus on the symptoms of neuropathic pain, and the impact culture and language may have on the assessment of pain.

## 1.2 MEASURING PAIN

Despite the anatomical structures involved in nociception being similar in all individuals, pain is a subjective experience and each individual experiences pain differently. The manner in which an individual expresses his or her pain is also a subjective phenomenon. Many factors including gender, ethnicity, race and age may influence how a person perceives, experiences and expresses pain (Zatzick and Dimsdale, 1990; Nayak et al., 2000; Sheffield et al., 2000).

Ehlich (1985) suggested three ways in which the pain experience may be expressed: i) crying or groaning, ii) pain interjections (e.g. saying “ow” or “ouch”) and iii) pain descriptions. Pain interjections and pain descriptions contribute to the language of pain: a language that allows communication between two individuals to take place so that the pain-free individual may sympathise with the sufferer, and possibly assert action to help the sufferer. For example, in the doctor’s consulting room, a patient presents the doctor with a series of symptoms and the doctor then, using the information, identifies the problem and treats the patient (Ehlich, 1985). This expression of pain by the patient leads to the measurement of pain by a health care provider and it is important that the verbal expression of pain be accurately understood to enhance diagnosis and treatment.

However, in countries rich in cultural and language diversity, the “accuracy” of pain assessment may become a problem because differences in cultural norms for expressing pain and linguistic barriers may lead to poor communication between patients and health care providers (Ferguson and Candib, 2002; Hsieh et al., 2011).

### *1.2.1 Cultural and racial differences to pain expression and the role of language and culture in the clinical setting*

Culture, race and ethnicity play a role in how an individual perceives, defines, and describes pain (Streltzer and Wade, 1981; Zatzick and Dimsdale, 1990; Lasch, 2000; Nayak et al., 2000; Edwards et al., 2001; Free, 2002). The literature describing these cultural and ethnic differences in pain perception and expression is extensive, thus in the remainder of this section, illustrative examples of these differences will be provided.

Streltzer and Wade (1981) looked at the treatment of pain following cholecystectomy surgery in patients from different ethnic groups (Caucasian, Hawaiian, Filipino, Japanese and Chinese) living in Honolulu. They found that Caucasian and Hawaiian patients required more analgesics to manage their postoperative pain as compared to patients with Chinese, Japanese and Filipino ethnicity (Streltzer and Wade, 1981). The results suggest differences in pain perception, pain tolerance and pain management across cultural groups.

Nayak and colleagues (2000) investigated cultural differences between university students in India and the United States of America, and found that despite the pain intensity of a cold pressor pain being rated similarly in both groups, pain tolerance, the ability to endure the pain, was higher for the Indian students. They also found that the two groups differed in their beliefs about pain expression. Indian students thought that it was less acceptable to show their pain on the outside or to make their pain known to others, whereas students from the United States approved of openly expressing their pain (Nayak et al., 2000). The authors suggested that Americans openly express pain in order to eliminate pain quickly and efficiently. Gender differences were also found in the study by Nayak and colleagues (2000), with males having higher pain tolerances than females in both groups, but Indian men had higher pain tolerances than did American men. Importantly, the authors cautioned that health care providers may interpret a patient's pain perception and experience based on their own cultural beliefs concerning pain expression, and not that of their patients, which may result in inefficient and ineffective pain management (Nayak et al., 2000). As health care providers have to rely on the patient's own verbal explanation and expression of pain, it is important that the linguistic, and in some cases cultural, barriers between patient and health care providers be resolved.

Nayak and colleagues (2000) only included the students in their study if they received at least 10 years of formal English education. In India, English is not the home-language for the majority of the population and to exclude those with less than 10 years English education may have been a limitation to their study in terms of cultural beliefs and pain perception. In South Africa, the majority of the population does not receive 12 years of education, let alone 10 years of formal

English education. According to the results of the 2001 census in South Africa, approximately 17.9% of the adult population received no education, 16% received some primary education, 6.4% completed primary school and approximately 30% of South African adults received some secondary education (Census, 2001). Health care professionals receive at least 15 to 18 years of formal education, depending on their profession, whereas most patients receive less than 12 years of education, thus creating vast differences in language skills in general.

Furthermore, there is great language diversity in South Africa and in sub-Saharan Africa. South Africa has 11 official languages: isiZulu, isiXhosa, Afrikaans, Sesotho sa Leboa, English, Setswana, Sesotho, Xitsonga, SiSwati, Tshivenda and isiNdebele, and according to the census in 2001, 23.82% of the South African population speak isiZulu as a home-language (Census, 2001). Approximately 17.6% speak isiXhosa as a home-language and less than 10% (8.2%) speak English as a home-language (Census, 2001). Other sub-Saharan languages include, Shona (Zimbabwe and Southeast Africa), Chichewa (Southeast Africa), and, Luhya and Tswana (Southern Africa). It is important to note the languages spoken in sub-Saharan Africa, as many people from these regions migrate to South Africa. With such a diverse range of languages spoken in South Africa by native South Africans and immigrants from sub-Saharan Africa, language barriers between health care providers and patients are inevitable, possibly resulting in a worsening of health care problems and inadequate pain treatment.

Ferguson and Candib (2002) conducted a literature review entitled “Culture, language, and the doctor patient relationship” and concluded that the relationship between the patient and physician were affected by race, ethnicity (culture) and language barriers. For example, patients who were not first-language English speakers were unlikely to prompt compassion from their doctors and were also unlikely to speak about their pain and thus create a bond with their doctors (Ferguson and Candib, 2002). As these patients did not speak about their pain to their doctors, the doctors were less likely to gain the necessary information regarding their patients’ condition and the patients’ were also not included in the medical decision-making or treatment process. In addition, patients who are not fluent in the language of the health care professional may not fully understand the value of their pain condition and may not understand the treatment prescribed to them, resulting in poor compliance or more visits to the physician to treat the pain (Ferguson and Candib, 2002). Adequate communication between doctor and patient requires the patient to spontaneously talk about their symptoms or the patient to respond to the doctor’s questions on symptoms. The doctor then uses the terms used by the patient to describe their condition to determine a differential diagnosis of the condition.

South Africa is rich in cultural diversity and it is important to inform those patients whose cultural teachings or language barriers with physicians, prevent them from seeking medical advice and help about the treatment strategies and options available to them. It is equally important for health care providers to make an early and correct diagnosis, based on verbal communication, of a possible pain condition. Early and correct diagnosis will lead to the initiation of correct treatment strategies and can only be achieved by effective communication

between patient and health care provider. In addition, effective communication will increase the patient's trust of the health care provider's decision regarding medical treatment and care.

Due to the subjective experience of pain and the differences in culture and education levels amongst different individuals, the need for screening and assessment questionnaires for pain conditions in languages other than English is required to cross these boundaries.

### *1.2.2 Pain scales*

Although there are different ways to assess pain, measuring pain is problematic due to the personal value of the pain experience. In general, there are two main types of pain measurements: uni-dimensional scales and multidimensional scales (Gracely, 1990). Uni-dimensional scales are simple measures of pain intensity and may be either numerical, (e.g. the Numerical Rating Scale where patients rate pain on a scale from 0 to 10, 0 being no pain and 10 being severe pain), verbal (e.g. the Verbal Descriptor Scale where patients choose one word to describe their pain intensity: mild, moderate or severe pain), or visual, (e.g. the visual analogue scale (VAS) where patients rate pain intensity on a horizontal line, with no markings, anchored at "no pain" and "worst pain imaginable") (McGuire, 1984; Jensen et al., 1986; Gracely, 1990). Uni-dimensional scales are appropriate for use in the clinical setting as sick patients may appreciate the ease of use and promptness of such scales when rating their pain intensity, and for patients who are poorly educated, these scales are easy to comprehend (Chapman et al., 1985). However, although these scales are simple, economical

and do not take much time to complete (usually less than 5-10 minutes, including explanation, administration and scoring of the scale), they only focus on pain intensity, thus simplifying the pain experience into one dimension. Uni-dimensional scales do not provide a total assessment of the pain experience, including the emotional, cognitive and sensory aspects of the pain experience which are important for assessing the nature of the pain and the impact the pain is having (McGuire, 1984; Chapman et al., 1985).

Multidimensional scales take into account the different qualities and dimensions of pain experience, for example, the sensory, spatial, emotive and affective dimensions of pain, as well as the location of pain, pain intensity and pain evaluation (McGuire, 1984; Gracely, 1990). Multidimensional scales may lead to better psychophysical, psychosocial and psychological assessments of pain than uni-dimensional scales, but they are usually time-consuming (taking approximately 15-30 minutes to explain to patients and to administer, and a further 10 minutes to score) and they are challenging to analyse (McGuire, 1984; Gracely, 1990). Furthermore, patients or subjects may find difficulty in understanding some of the terms used in these scales (Chapman et al., 1985).

Nociceptive pain is pain generated from stimulation of the primary afferents, is either somatic or visceral and is linked to inflammation, whereas neuropathic pain occurs when there is damage or trauma to the nervous system and can be peripheral or central in origin (Woolf and Mannion, 1999; Jensen et al., 2001; Dworkin, 2002; Urgellés-Lorié, 2008). As neuropathic pain is different from nociceptive pain in origin, one would expect differences in the sensations

experienced and therefore, the verbal description used to express neuropathic and nociceptive pain would also be different. There are no questionnaires specifically designed to diagnose nociceptive pain, but the unique symptom clusters that typically accompany neuropathic pain, irrespective of its possible cause, has led to several assessment and diagnostic tools being developed for neuropathic pain (Bennett et al., 2007; Cruccu et al., 2010).

The use of verbal pain descriptors has been shown to be effective when assessing the sensory and affective qualities of neuropathic pain and may also be used diagnostically in some pain conditions (Dubuisson and Melzack, 1976; Boureau et al., 1990). We will first discuss the development and validation of a pain questionnaire that was not designed for diagnosis of a specific pain condition, but for the assessment of pain in general: the McGill Pain Questionnaire. We will then focus on neuropathic pain and the questionnaires that were specifically designed to screen for and assess neuropathic pain conditions, their development and how they may differ from one another. We will focus mostly on the symptom component of the questionnaires.

### 1.2.3 The development of the McGill Pain Questionnaire (MPQ)

The McGill Pain Questionnaire (MPQ) originated from a wordlist created by Ronald Melzack and Warren Torgerson in 1971, and was the first multidimensional questionnaire to assess the quality of spontaneous pain (Melzack and Torgerson, 1971; Melzack, 1975). The need for a questionnaire such as the MPQ arose as, during that time, most of the tools used for pain measurement focussed on pain intensity only and failed to take into account the

“unique qualities” of different types of pain (Melzack, 1975). Accordingly, in 1971, Melzack and Torgerson created a wordlist focussing on multiple dimensions of the pain, to assist with the assessment and description of pain in humans (Melzack and Torgerson, 1971). The 102 terms on the list were sourced from the literature on clinical pain. The terms covered 3 classes of pain quality: sensory, affective and evaluative, and 13 subclasses for the sensory and affective classes: temporal, spatial, punctate pressure, incisive pressure, constrictive pressure, traction pressure, thermal, brightness, dullness, tension, autonomic, fear and punishment.

The wordlist was given to 20 subjects who were asked to identify if the descriptive words were placed in the correct subclass (Melzack and Torgerson, 1971). Eleven words, including “itching, tearing, taut, awful” and “wicked,” showed less than 65% concordance as belonging to a specific subclass and were then given to 20 different subjects who were asked to place these words in the appropriate subclass. Thereafter, all 102 words were presented to 140 university students, 20 doctors and 20 patients, who were asked to relate each word with a pain intensity rated on a numerical pain rating scale. All 3 groups of subjects showed strong agreement on the position of the words in each group. For example, in the thermal group, hot was associated with less pain than burning which was associated with less pain than scalding and the words in each group are thus placed in order of increasing pain intensity (Melzack and Torgerson, 1971). This wordlist, comprising 3 classes and 16 subclasses of pain descriptors was then used in the development of the MPQ.

In 1975, Melzack added a Present Pain Intensity (PPI) scale to the wordlist created by himself and Torgerson (Melzack, 1975). The PPI consists of five words; each associated with a number corresponding to pain intensity: 1=mild pain, 2=discomforting pain, 3=distressing pain, 4=horrible pain and 5=excruciating pain. The wordlist and PPI was then used in a pilot study where Melzack realised that certain important descriptors that patients wanted to use to describe their pain were not on the wordlist he and Torgerson had developed. He then added these missing words from wordlists that he and Torgerson used when creating their 102-wordlist. He also added another group of words to the list: cool, cold and freezing as these terms described a few pain conditions, even though they were not commonly used by patients (Melzack, 1975).

Melzack thus added 4 extra subclasses to the wordlist and the final list consisted of 3 classes with 20 subclasses (Melzack, 1975). The final version of this list is known as the MPQ and consists of 78 pain descriptors in total. A Pain Rating Index (PRI) is calculated once a patient completes the MPQ. For example, if a patient chose “hot” to describe the pain, he would get a rank value of 1 in that group. “Searing” would render a rank value of 4. When all the rank values from each group selected are added up, the total number represents the PRI. The higher the PRI, the greater the pain experience. The PRI has been validated and correlates well with the overall number of words chosen (Melzack, 1975).

The ability of the MPQ to differentiate between different types of pain has also been studied. Dubuisson and Melzack (1976) sought to determine if the MPQ could be used as a diagnostic tool. They recruited 95 patients who had already

been clinically diagnosed with differing pain conditions: menstrual pain, rheumatoid arthritis, labour pain, degenerative disc disease, toothache, metastic carcinoma, phantom limb pain and postherpatic neuralgia (Dubuisson and Melzack, 1976). All patients, in an interview format, were asked to choose words from the MPQ that accurately described their present pain and to complete the PPI. A stepwise multiple group discriminant analysis was used to analyse the data and the results showed that 77% of patients were correctly diagnosed based on the verbal descriptions they provided to describe their pain (Dubuisson and Melzack, 1976). The final version of the MPQ is shown in Appendix 1. While the MPQ is an invaluable tool for describing pain quality of a sensory, affective and cognitive level, it consists of many obscure English terms and it is lengthy and time consuming to complete and due to limited time available in clinical and research settings, the need for a shorter form of the MPQ became apparent.

#### *1.2.3.1 The short form MPQ (SF-MPQ)*

Lengthy questionnaires are a problem in the clinical setting as patients may be too ill or fatigued to fill out the questionnaire with ease. In the research setting, the lengthy version of the MPQ is a problem as time management is important for participants and they may be unwilling to spend a considerable amount of time filling out the MPQ, particularly if repeated measures are required. In 1987, the short form of the MPQ (SF-MPQ) was developed and validated by Melzack as it was more time efficient than its parent questionnaire (Melzack, 1987). The SF-MPQ consists of a VAS and PPI to rate pain intensity and 15 pain descriptors from the original MPQ: 11 sensory items and 4 affective items. Patients are

required to score each pain descriptor on the short form as 0-no pain, 1-mild pain, 2-moderate pain and 3-severe pain (Melzack, 1987).

To generate the items that would appear on the SF-MPQ, Melzack (1987) looked at those words that were commonly chosen by at least one third of patients, from previous studies, with a range of pain conditions including post-surgical pain, labour pain, dental pain, cancer, menstrual pain, arthritis and low back pain. The list consisted of 15 items that was validated against the standard MPQ (Melzack, 1987). The 15 items included in the SF-MPQ are:

- throbbing
- shooting
- stabbing
- sharp
- cramping
- gnawing
- hot-burning
- aching
- heavy
- tender
- splitting
- tiring-exhausting
- sickening
- fearful and
- punishing-cruel

*1.2.3.2 Validation of the SF-MPQ (Melzack, 1987)*

For the validation, both the SF-MPQ and the standard MPQ were read to patients with post-surgical, obstetrical or musculoskeletal pain before the patients received any pharmacological or other therapy and 30 minutes after therapy. The forms were administered in the following order: first the standard MPQ and then

the short form. Patients were asked to rate the pain intensity of the word or words that described their pain on a VAS. In addition, a similar intervention was carried out in patients with post surgical or dental pain. The need for the second intervention arose as the order in which the forms were given during the first intervention may have had an impact on the results. In the second intervention, the order of questionnaire administration was randomised. The results obtained from both interventions showed that all the descriptors on the short form were significantly correlated to those on the long form irrespective of the nature of the pain and the sequence in which the forms were given to patients.

Although the standard MPQ could correctly distinguish between the different types of pain, as shown by Dubuisson and Melzack in 1976, the most difficult pain to describe appears to be that of neuropathic pain.

### 1.3 NEUROPATHIC PAIN

Neuropathic pain is caused by damage or trauma to the peripheral or central nervous system and does not occur due to continuous tissue injury (Jensen et al., 2001; Dworkin, 2002). Examples of peripheral neuropathic pain syndromes include chemotherapy-induced neuropathy, painful diabetic neuropathy, phantom limb pain, trigeminal neuralgia and HIV-SN, while central neuropathic pain syndromes include central post-stroke pain, multiple sclerosis, Parkinson's disease and spinal cord injury pain (Jensen et al., 2001; Dworkin, 2002; Bouhassira et al., 2008). Chronic pain with neuropathic characteristics seems to be more prevalent in females (Bouhassira et al., 2008), and the risk of developing neuropathic pain increases with age (Bouhassira et al., 2008; Robinson-Papp et

al., 2010). Due to the vast number of causes of neuropathic pain, the prevalence of neuropathic pain in the general population may be relatively high as was found in the United Kingdom and in France, but there is shortage of epidemiological data concerning neuropathic pain (Torrance et al., 2006; Bouhassira et al., 2008). However, despite the various causes associated with neuropathic pain, neuropathic pain usually presents with similar symptoms and signs in patients (Jensen et al., 2001; Dworkin, 2002; Bouhassira et al., 2008; Robinson-Papp et al., 2010).

Pain associated with neuropathy can occur either spontaneously or may be caused by a stimulus (stimulus-dependent) (Jensen et al., 2001; Dworkin, 2002). Spontaneous pain may be continuous, often described as “aching, burning or cramping” (Woolf and Mannion, 1999; Jensen et al., 2001; Krause and Backonja, 2003), or may occur at intervals, frequently described as “stabbing, shooting or electric shock-like” (Bennett, 2001; Krause and Backonja, 2003; Bouhassira et al., 2004). Stimulus-dependent pain may be caused by a stimulus that is not usually perceived as painful (allodynia), or the patient may experience increased pain in response to a stimulus that is usually perceived as painful (hyperalgesia) (Woolf and Mannion, 1999; Jensen et al., 2001; Krause and Backonja, 2003; Bouhassira et al., 2004; Portenoy, 2006). Patients may also experience dysesthesias, abnormal sensations that are unpleasant, such as itching, tingling or numbness, as well as paresthesias, abnormal sensations that are not unpleasant, such as pins-and-needles (Dworkin, 2002; Krause and Backonja, 2003; Bouhassira et al., 2004; Bouhassira et al., 2005).

As the above-mentioned symptoms are fairly unique to neuropathic pain syndromes, a clinical diagnosis of neuropathy is usually made when a patient presents with symptoms (similar to what has been described) and signs of a neuronal deficit consistent with the anatomical location of the symptoms (Treede et al., 2008; Cruccu et al., 2010). Signs indicating a potential neuropathy include loss of function, a negative sensory sign that includes numbness, weakness, areflexia or hyper-reflexia, and positive sensory signs including hyperalgesia or allodynia (Rolke et al., 2002; Treede and Baron, 2008; Cruccu et al., 2010). These symptoms and signs are commonly found on assessment and diagnostic tools related to neuropathic pain and assist with the evaluation and diagnosis thereof.

### *1.3.1 The diagnostic property of the MPQ for neuropathic pain*

The MPQ has been tested as a diagnostic tool in patients with painful diabetic neuropathy (Masson et al., 1989). The descriptions from the MPQ of 42 patients with diabetic neuropathy were compared to the pain descriptions from the MPQ obtained from 49 patients with non-neuropathic pain in the feet and legs. A linear discriminant analysis showed that 79% of neuropathic pain patients and 86% of patients with non-neuropathic pain were correctly diagnosed based on descriptions from the MPQ (Masson et al., 1989). Similarly, Boureau and colleagues (1990) aimed to determine if the use of verbal pain descriptions could accurately diagnose neuropathic pain in neuropathic pain patients. One hundred patients with various causes of neuropathic pain (97 patients with chronic benign pain were in the control group), were assessed in the study and were asked to fill out a French reconstruction of the MPQ. The questionnaire consisted of 61 pain

descriptors and patients were asked to choose which of these words best described their pain (Boureau et al., 1990).

The most frequently chosen words by patients with neuropathic pain were “burning, electric shock, tingling, pricking, itching” and “cold” (Boureau et al., 1990). The term “shooting,” which is also commonly used to describe neuropathic pain, did not significantly differ from the non-neuropathic group. All words relating to the affective component of pain were not commonly chosen by patients with neuropathic pain. Seventeen out of the 61 descriptors were found to reach a significant intergroup difference and were included in further factor analysis and stepwise analysis. The factor analysis produced a 7-factor solution and the terms relating to the different aspects of neuropathic pain were placed in different factors, namely, intermittent pain (“electric shock”), permanent pain (“burning”) and dysesthesias (“tingling, pricking” and “itching”). The stepwise discriminant analysis showed that four terms (“electric shock, itching, tingling” and “burning”) could be used to correctly diagnose patients with neuropathic pain (Boureau et al., 1990). The authors also state that the therapeutic value associated with the correct identification of pain is important as it may encourage patients to recognize pain as an indication of an underlying problem and thus patients, by definition, are already seeking help.

However, the findings of Rasmussen and co-workers (2004) are in contrast to those of Boureau and colleagues (1990). Rasmussen and co-workers found that descriptive words could not separate patients with neuropathic and non-neuropathic pain. The authors used a Danish version of the SF-MPQ in their

study and found no differences in the selection of the typical neuropathic pain descriptors “burning/scalding, shooting and pricking” between patients with either definite or potential neuropathic pain, and patients with pain unlikely to be caused by a neuropathy (Rasmussen et al., 2004). The term “burning” differed between patients with central neuropathy and peripheral neuropathy, but could not distinguish between neuropathic pain patients and those less likely to have neuropathic pain. It is unclear whether their results are peculiar to the Danish language and culture, or whether they reflect the complexity in trying to diagnose neuropathic pain using only symptoms, as is the case when using the MPQ.

The MPQ and SF-MPQ are both non-specific questionnaires for neuropathic pain and include a range of pain descriptors that take into account all types of pain conditions. Although the items on the MPQ can assist in diagnosing neuropathic pain, there are too many items and using the MPQ for diagnosis of neuropathic pain may become a tedious task. In addition, no clinical signs of a neurological disease are assessed and the affective items on the MPQ are not frequently used to describe neuropathic pain as the description of neuropathic pain takes on a more sensory dimension (Boureau et al., 1990; Rasmussen et al., 2004). The short-comings of the MPQ and SF-MPQ for assessing neuropathic pain created demand for specific neuropathic pain assessment and diagnostic tools. These tools included pain descriptions common, but not necessarily unique, to neuropathic pain, included an assessment of signs where possible, and did not consume too much time to administer and score, thus making the new tools practical for clinical use. In the next sections, some of the more popular neuropathic pain assessment and diagnostic tools will be described.

### 1.3.2 Neuropathic Pain Scale (NPS)

The Neuropathic Pain Scale (NPS) is an assessment tool and was developed in 1997 by Galer and Jensen in the United States of America (Galer and Jensen, 1997). The NPS was developed specifically to evaluate the different symptoms of neuropathic pain as there were no other questionnaires developed for neuropathic pain conditions at that time, other than the non-specific MPQ and SF-MPQ. The NPS was developed in English and the aim of the development of the NPS was to create a pain measure that took into account all the pain qualities common in neuropathic pain patients (Galer and Jensen, 1997). The questionnaire assessed symptoms only, and not signs, and is therefore useful for the characteristics of the sensory aspects of neuropathic pain but not for the diagnosis of neuropathic pain when used alone.

#### *1.3.2.1 Development and validation of the NPS (Galer and Jensen, 1997)*

The authors' used their subjective clinical experience to select the terms used on the scale, selecting the most common words used by patients with neuropathy to describe their pain. The NPS includes eight items related to the symptoms of neuropathic pain, one item related to the intensity of neuropathic pain and one item related to how unpleasant the pain is. Patients rate whether they have a symptom listed on the scale and they rate the severity of the symptom on an 11-point pain rating numerical scale. The eight symptom items are:

- sharp
- hot
- dull
- cold
- sensitive
- itchy

- deep pain and
- surface pain

The scale was validated in two separate interventions. The first intervention consisted of 288 patients with neuropathic pain of mixed origin (post-hepatic neuralgia, reflex sympathetic dystrophy, traumatic peripheral nerve injury and painful diabetic neuropathy). Patients were asked to complete the questionnaire and rate the intensity of their symptoms. A Pearson's correlation coefficient between all 10 descriptors was used to determine if these terms truly assessed the symptoms of neuropathic pain. Thereafter, a chain of 10 Analysis of Variances was carried out to determine if the items on the NPS could distinguish between the different neuropathy diagnoses. The results showed that the items "sharp, cold, sensitive" and "itchy" were able to discriminate post-hepatic neuralgia from the other diagnostic groups, but the NPS could not distinguish between the remaining three neuropathic pain groups.

The second intervention consisted of 78 patients with neuropathic pain of mixed origin (traumatic peripheral nerve injury, reflex sympathetic dystrophy, diabetic neuropathy, causalgia and spinal cord injury) who received infusions of lidocaine and phentolamine to treat their pain (Galer and Jensen, 1997). The aim of the second intervention was to determine the sensitivity of items found on the NPS to neuropathic pain treatments. Patients were required to fill out the NPS before and after they received the treatments. The authors found that most of the symptoms of neuropathic pain on the NPS decreased after lidocaine administration and phentolamine infusion. They also found that lidocaine was more successful at improving "deep" pain and "unpleasant" sensations than phentolamine. Based on

their validation studies, they suggest using the NPS in studies focussing on neuropathic pain symptoms and the treatment thereof (Galer and Jensen, 1997).

The results from the two validity interventions proved that the NPS is effective when assessing the unique pain qualities associated with neuropathic pain and that the majority of the items on the scale are sensitive to the effects of neuropathic pain treatment (Galer and Jensen, 1997). However, as there are only 10 items on the NPS, the NPS does not cover the range of symptoms experienced by patients with neuropathic pain (Galer and Jensen, 1997). This may have encouraged the development of other neuropathic pain assessments. The NPS was also not assessed for use in nociceptive pain, and can therefore not distinguish between neuropathic and nociceptive pain.

### 1.3.3 Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale

The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale is a diagnostic tool that can differentiate between neuropathic and non-neuropathic pain and was developed and validated in 2001 in two separate interventions that are described in the same paper (Bennett, 2001). The LANSS was developed as the NPS could not distinguish between neuropathic and non-neuropathic pain conditions. The first intervention focussed on the construction of the pain scale and the second intervention tested the validity and reliability of the pain scale (Bennett, 2001).

*1.3.3.1 Development and validation of the LANSS (Bennett, 2001)*

The initial scale was constructed using pain descriptions that were sourced from published data and patient surveys, and consisted of six groups of terms related to neuropathic pain symptoms, and each symptom was phrased in a question format. The dimensions of pain in the six groups included stimulus-independent pain (ongoing superficial pain with thermal qualities, ongoing superficial pain with dysesthesias-like qualities, ongoing spontaneous deep pain and paroxysmal pain), stimulus-dependant pain and autonomic dysfunction.

In an interview with 60 patients (30 with neuropathic pain; 30 with nociceptive pain), the scale was read to patients and they were required to decide in a "yes/no" format, which questions described their pain. Patients were also exposed to two sensory functioning tests: pin-prick threshold and the presence or absence of allodynia. In addition, they were asked to rate their pain intensity over the past week and provide information on how frequently the pain had occurred in the last week. Logistic regression modelling analysis was used to determine which descriptive words and sensory tests could, together, predict whether a patient had a neuropathic pain condition. Both groups of patients were equal in pain intensity and pain frequency, but there were more patients with neuropathic pain who had a raised pin-prick threshold and the presence of allodynia. In addition, the question pertaining to ongoing deep pain was selected frequently by patients with neuropathic and those with nociceptive pain, and was thus eliminated from the construction of the final version of the scale.

The final version of the LANSS Pain Scale is divided into two components: a pain questionnaire and a sensory testing component (Bennett, 2001). Below are two examples of the pain questionnaire component of the LANSS:

> 1) Does your pain feel like strange, unpleasant sensations in your skin? Words like pricking, tingling, pins-and-needles might describe these sensations.
>
> a) NO-My pain doesn't really feel like this..... (0)
>
> b) YES-I get these sensations quite a lot..... (5)
>
> 5) Does your pain feel as if the skin temperature in the painful area has changed abnormally? Words like hot and burning describe these sensations.
>
> a) NO-I don't really get these sensations..... (0)
>
> b) YES-I get these sensations quite a lot..... (1)
>
> [Extracted from the LANSS Pain Scale by Michael Bennett (2001)].

The LANSS Pain Scale contains seven items in total and the pain questionnaire contains five symptom items assessing:

- pricking, tingling, pins-and-needles
- electric shocks, jumping or bursting
- hot or burning
- pain caused by light touching and
- autonomic changes

The sensory testing on the scale includes two clinical examination items:

- brush allodynia and a raised pin-prick threshold.

Each question with the related pain items is given a specific score on the scale. The score was obtained by using a scoring system that uses the odds ratio for each item on the scale (Bennett, 2001). The odds ratio was calculated for each of the following groups: thermal, dysesthesias, paroxysmal, evoked pain,

autonomic, allodynia and an altered pin-prick threshold. For example, the odds ratio for the thermal group was 1(1.41), therefore the question pertaining to hot or burning pain was given a score of 1 if those symptoms are present in the patient. The odds ratio for dysesthesias group was 5(5.24) so if the patient presents with pricking, tingling or pins-and-needles, the patient would be given a score of 5. The final overall maximum score obtainable using the scoring method was 24 and, with the value of 12 providing the lower threshold for classifying a patient as being more likely to have pain of neuropathic origin than nociceptive pain (Bennett, 2001).

The scale was then validated and its reliability was examined in a separate intervention consisting of 40 patients with neuropathic or nociceptive pain (20 patients in each group) (Bennett, 2001). Patients were required to complete the scale on two different occasions. On the first occasion, the investigator assisted the patient with completing the scale and on the second occasion, a clinician assisted the patient with completing the scale. The scores from the investigator and clinician were then compared to evaluate the validity and reliability of the scale between investigator and clinician.

There were no significant differences between patients with neuropathic pain and nociceptive pain in terms of pain intensity and pain frequency. There were also no significant differences between the investigator and clinician with regards to LANSS scores, pain classification and the items present on the LANSS Pain Scale. When compared, the clinician and investigator could correctly identify 33 out of the 40 patients as having neuropathic pain using the LANSS Pain Scale,

using a cut-off score of 12 or more (with a specificity of 80% and a sensitivity of 85%). The results from the second intervention also showed that each item on the scale was positively associated with neuropathic pain and, as no item was redundant, no other item was removed. The LANSS is thus a reliable tool for differentiating neuropathic pain from non-neuropathic pain and is used as a diagnostic tool (Bennett, 2001).

#### *1.3.3.2 Development and validation of the self-completed LANSS (S-LANSS) (Bennett et al., 2005)*

In 2005, the self-completed LANSS (S-LANSS) was developed to identify neuropathic pain in the clinical setting and in population surveys. S-LANSS was developed from the original LANSS questionnaire (Bennett, 2001). The two sensory test items were reworded so that the questions ask the patients to examine themselves as the S-LANSS is to be self-completed (Bennett et al., 2005). Other pain items were modified to make the words clearer and the scoring system for both, sensory test items and pain descriptions, remained the same as the scoring system on the original LANSS. Additional changes on the S-LANSS was the inclusion of a body chart and an 11-point numerical pain rating scale anchored at “no pain” and “pain as severe as it could be.” As with the original LANSS, a total score of 12 out of 24 suggests neuropathic pain (Bennett, 2001; Bennett et al., 2005). S-LANSS was validated in two independent studies: a clinic validation study and a postal survey validation study and is the only tool to have been validated against an existing neuropathic pain measurement, the NPS (Bennett et al., 2005).

In the clinic validation study, the sample size consisted of 200 patients (100=neuropathic pain, 100=nociceptive pain) who were asked to fill out the S-LANSS without aid from a researcher and, thereafter, in an interview format, a researcher read out the S-LANSS and NPS to patients (Bennett et al., 2005). This was done so that unaided data could be compared to interview data. In addition, clinicians who assisted with diagnosis were asked to rate the certainty of the diagnosis of neuropathic pain on a 10cm VAS. This was done to determine if the S-LANSS could predict neuropathic pain from non-neuropathic pain.

The results of a discriminant validity analysis showed that the S-LANSS could correctly distinguish between the two types of pain in the unaided and interview format when compared to the clinical diagnosis. A convergent validity analysis showed that five of the items on the NPS (sharp, hot, cold, sensitive and intensity of surface pain) were successful at determining neuropathic pain as these items were associated with a clinical diagnosis of neuropathic pain. These same 5 items were also associated with a score of 12 or more on the S-LANSS and an additional 3 items (intensity, itchy and unpleasantness) were also associated with a score of 12 or more on the S-LANSS. These results showed that the S-LANSS had similar psychometric properties to the NPS, a validated tool.

For the postal validation study, two patient populations were recruited to participate (Bennett et al., 2005). The first consisted of 160 patients from a general practice population and the second population consisted of 150 patients from a pain clinic. All 310 patients were posted the S-LANSS, NPS and a demographic questionnaire and 174 patients responded to the survey. The

responses from the 174 patients (general practice population and pain clinic) were combined for analysis. The five items on the NPS (from the clinical validation study) were used as an indicator for possible neuropathic pain as there was no clinical diagnosis in the postal survey study. From the 174 patients, 58 had an S-LANSS score of 12 or more and produced greater combined intensity scores on the NPS compared to patients with non-neuropathic pain. In addition, patients with neuropathic pain also produced greater scores on the five NPS items from the clinic validation study. The S-LANSS is thus validated in postal research as a diagnostic tool for neuropathic pain. The S-LANSS is an efficient and valid tool that can be used to identify neuropathic pain in clinical settings and in postal research.

### 1.3.4 Neuropathic Pain Questionnaire (NPQ)

The purpose of the Neuropathic Pain Questionnaire (NPQ), developed by Krause and Backonja in 2003, was to provide a universal evaluation of the symptoms related to neuropathic pain and to distinguish between pain that is neuropathic in nature and pain that is non-neuropathic (Krause and Backonja, 2003). The NPQ was developed as the NPS could not distinguish between neuropathic and non-neuropathic pain and, although the LANSS Pain Scale was developed for this very reason, it only focussed on four of the pain descriptor groups. The NPQ was developed as an assessment tool as well as a diagnostic tool, but only relies on symptoms for the diagnosis, which as already discussed for the MPQ, may be a limitation.

*1.3.4.1 Development and validation of the NPQ (Krause and Backonja, 2003)*

The initial NPQ consisted of 32 items that were obtained from patient charts at the University of Wisconsin Hospital and Clinics Pain Clinic and from reviewing literature on neuropathic pain. Initially, the study sample consisted of 532 patients with various pain aetiologies, but only data from those with neuropathic pain and non-neuropathic was used for further analysis. The 32-item questionnaire was given to patients from the remaining 382 patients (149 presented with pain of neuropathic origin and 233 had non-neuropathic pain) who were willing to answer the questionnaire. Patients were required to rate their pain on a numerical scale ranging from 0 to 100 for each item they chose.

Factor analysis yielded 6 factors and the 32-item questionnaire was reduced to 12 items loading on those factors: 10 items related to the sensations or sensory responses of neuropathic pain and 2 items related to affect. The 32 items were also subjected to *t*-tests and those items that could distinguish between neuropathic and nociceptive pain were further analysed. Those items that were significantly different from each other for nociceptive and neuropathic pain at a level of $p<0.001$, were analysed using a multiple discriminant analysis to find out the extent to which each term could distinguish between the two pain states. The final version of the questionnaire consists of 10 items related to sensations or sensory responses of neuropathic pain:

- burning
- overly sensitive to touch
- shooting
- numbness
- electric
- tingling

- squeezing
- freezing
- unpleasantness and
- overwhelming

The two items related to affect are: increased pain due to touch or pressure and increased pain due to changes in weather. Examples of the items “burning pain” and “numbness” are provided below:




[Extracted from the NPQ by Krause and Backonja (2003)].

A scoring sheet is provided on the NPQ and calculation of the score determines if the patient has pain of neuropathic origin or not (Krause and Backonja, 2003). For each term on the NPQ, a different coefficient (sourced from the discriminant analyses) is provided. In order to determine the final score, the rating provided by the patient is multiplied by the coefficient for each term. The product for all 12 items is then added up together with a constant provided on the NPQ and a score below 0 means that the patient has non-neuropathic pain whereas a score of 0 or above predicts a neuropathic pain state.

The NPQ is a diagnostic and assessment tool that can distinguish neuropathic pain from non-neuropathic pain and the authors also suggest that the NPQ can

be used to monitor treatment effects (Krause and Backonja, 2003). However, the scoring is complicated and it doesn't include assessment of signs. Moreover, the NPQ cannot distinguish between the different types of neuropathic pain. A short-form of the NPQ was developed in an attempt to find out what was the minimum number of words that were useful in predicting neuropathic pain conditions (Backonja and Krause, 2003). The subjects included in this study were those that had participated in the development of the long form of the NPQ. The final sample size consisted of 278 subjects with either neuropathic pain (n=110) or non-neuropathic pain (n=168) and who had completed the long form of the NPQ. A stepwise discriminant analysis was used to analyse the 12 items on the long form and the results produced 3 items; numbness, tingling and increased pain in response to touch, that could accurately distinguish neuropathic pain from non-neuropathic pain with a sensitivity of 64.5% and a specificity of 78.6% (Backonja and Krause, 2003).

Despite the now growing number of questionnaires validated for neuropathic pain conditions, more assessment tools and diagnostic tools were developed.

### 1.3.5 Neuropathic Pain Symptom Inventory (NPSI)

The Neuropathic Pain Symptom Inventory (NPSI) was developed by Bouhassira and colleagues in 2004 in French to evaluate the different symptoms of neuropathic pain with respect to the characteristics and intensity of neuropathic pain, and is an assessment tool, not a diagnostic tool, for neuropathic pain (Bouhassira et al., 2004). It was developed for use as a self-administered questionnaire, and, as such the questionnaire is practical to use in large cohorts

of patients in multicenter studies. The initial version of the NPSI was created using terms based on clinical experience and terms extracted from the literature. A group consisting of 7 French and Belgium pain experts discussed and approved these 18 items that were to be part of the initial NPSI (Bouhassira et al., 2004).

*1.3.5.1 Development and validation of the NPSI (Bouhassira et al., 2004)*

The use of the 18 items was validated in a pilot study consisting of 39 patients with neuropathic pain. Participants were asked to complete the initial 18-term questionnaire and for each item, participants had to report the clarity of the wording, understanding and significance of each term with respect to their pain symptoms. This questionnaire consisted of four dimensions relative to neuropathic pain, namely, spontaneous ongoing pain (six items), spontaneous paroxysmal pain (four items), evoked pain (four items) and items related to paresthesias or dysesthesias (four items). After analysis of the data obtained in the pilot study, the word “dull” was removed as majority of the participants considered the term to be unrelated to their neuropathic pain.

The 17-item scale was then presented to 176 patients, with either peripheral or central nerve damage, to test the validity of the final version of the NPSI. The scale was then reduced to 12 items after factor analysis was performed and Intraclass Correlation Coefficient (ICC) was determined. The factor analysis yielded a 5-factor solution. “Numbness, painful cold, cramp, lancinating” and “itching” were removed as they showed poor reliability with the ICC and did not fit into any of the 5 factors. “Shooting” and “electric shock” were both removed as

they both appeared to assess the same pain quality. “Pain evoked by contact with something warm” was also removed as less than 20% of participants chose the phrase. The final version of the NPSI consists of 12 items in total: 10 items are related to the descriptors of neuropathic pain symptoms (listed below) and 2 items assess how long spontaneous ongoing and paroxysmal pain lasts, for example, how many pain attacks the patient had in the past 24 hours. The 10 descriptor items are:

- burning
- squeezing
- pressure pain
- electric shocks
- stabbing
- evoked pain to brush
- evoked pain to pressure
- evoked pain to cold
- tingling and
- pins-and-needles

An example of a question with a descriptor appearing on the NPSI is provided below. The question and scale for each of the descriptor terms mentioned above follows the same format to the one shown in the example with the underlined term changed for the various symptoms.

**Q1: Does your pain feel like burning?**

No burning 0 1 2 3 4 5 6 7 8 9 10 Worst burning imaginable

**Q6: Does your pain feel like stabbing?**

No stabbing 0 1 2 3 4 5 6 7 8 9 10 Worst stabbing imaginable

[Extracted from the NPSI by Bouhassira and colleagues (2004)].

The NPSI is a general assessment tool for neuropathic pain intensity and after the NPSI is completed, a total intensity score out of 100 is calculated. The total pain intensity score is calculated by adding up the intensities for the seven neuropathic pain symptoms and the three items related to evoked pain. The greater the calculated score on the NPSI, the greater the severity of the pain experienced by patients.

This study showed that the NPSI is a valid and reliable tool for assessing neuropathic pain, and the validity of the NPSI was further supported by a factor analysis performed on data obtained from 111 patients who filled out the NPSI on a second visit, approximately 1 month later. The factor analysis produced 5 factors that were similar to the 5 factors obtained from the 176-patient data. The NPSI was translated from French into English using the forward-backward translation process; however, this version has not yet been validated in patients who speak English (Bouhassira et al., 2004).

### 1.3.6 Douleur Neuropathique en 4 questions/ neuropathic pain diagnostic questionnaire (DN4)

The neuropathic pain diagnostic questionnaire (DN4) was developed by Bouhassira and colleagues in 2005, and was developed in French (Bouhassira et al., 2005). The DN4 is a diagnostic tool for neuropathic pain and was developed as the other neuropathic pain diagnostic tools were not available in French. As a diagnostic tool, the DN4 assesses signs and symptoms of neuropathic pain.

*1.3.6.1 Development and validation of theDN4 (Bouhassira et al., 2005)*

The items on the questionnaire were extracted from the literature, and also based on clinical experience of the authors. The questionnaire assessed the symptoms (based on interviews with participants) and signs (based on clinical examination) of patients with neuropathic pain. The initial questionnaire consisted of nine symptom descriptors and eight items related to clinical examination. The nine symptom descriptors were “burning, squeezing, painful cold, electric shock, lancinating, pins-and-needles, tingling, numbness” and “itching.” The clinical examination items included hypoesthesia to touch, prick, heat and cold and pain evoked by brushing, pressure, contact with cold and contact with heat.

One-hundred and sixty patients, with central or peripheral neuropathic pain and non-neuropathic pain, participated in the validation study. Participants attended two screening sessions, separated by approximately three days. Two different investigators carried out the screenings on the separate days and no treatment was administered after the first visit. The first investigator diagnosed participants with neuropathic or non-neuropathic pain using standard clinical diagnostic criteria. Thereafter, in an interview, the DN4 questionnaire was read out to patients. During the second visit, the second investigator carried out the procedure in a similar manner. Treatment was administered to patients after the second visit.

Factor analysis was performed and yielded 9 factors. Hypoesthesia to touch, prick, heat and cold were included in factor 1, factor 2 included evoked pain due to brushing, contact with cold and contact with heat, factor 6 included tingling and

pins-and-needles and all other factors included a single remaining item. Logistic regression modelling was performed after factor analysis and seven items were not included in this analysis. “Squeezing, lancinating” and “pain increased by pressure” were removed as the prevalence of these was similar in patients with neuropathic pain and non-neuropathic pain. Hypoesthesia to heat, hypoesthesia to cold, pain increased by heat and pain increased by heat cold were removed as they had a high inter-relation coefficient with other items on the list as found in the factor analysis. Logistic regression modelling analysis and receiver operating characteristic (ROC) curves were performed to determine if the remaining 10 items were effective in distinguishing neuropathic pain from non-neuropathic pain.

A minimum score of 4 out of 10 was obtained from this analysis as the required score to distinguish between the pain states. In addition, the same tests were used to analyse the 7 items related to symptoms to determine if the items could differentiate neuropathic pain from non-neuropathic pain and a score of 3 out of 10 was obtained as the minimum score to distinguish between the two pain states. The final version of the DN4 thus has 10 items in total: 7 items are related to the symptoms of neuropathic pain and are shown below:

Question 1: Does the pain have 1 or more of the following characteristics?

| | YES | NO |
|---|---|---|
| 1. Burning | | |
| 2. Painful cold | | |
| 3. Electric shocks | | |

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

| | YES | NO |
|---|---|---|
| 4.Tingling | | |
| 5. Pins-and-needles | | |
| 6. Numbness | | |
| 7. Itching | | |

[Extracted from the DN4 Questionnaire by Bouhassira and colleagues (2005)].

The remaining three items are related to the clinical examination: hypoesthesia to touch, hypoesthesia to prick and pain evoked or increased by brushing (Bouhassira et al., 2005). For all 10 items, a “yes” response renders a score of 1 and a “no” response renders a score of 0. The total is then calculated and a score of equal to or greater than 4 out of 10 suggests pain of neuropathic origin. As with the NPSI, the DN4 was translated into English, but has not yet been validated in English-speaking patients (Bouhassira et al., 2005).

### 1.3.7 ID Pain

The ID Pain screening tool was developed in 2006 by the ID Pain Steering Committee and was developed to distinguish neuropathic pain from pain that is nociceptive in origin (Portenoy, 2006). ID Pain was developed as existing questionnaires (LANSS Pain Scale, S-LANSS, NPS, NPQ and DN4) were not being used in the primary care setting and the authors felt that there was a need for a simple, easily administered screening tool that could be used in the primary care setting.

The initial list of terms was sourced from existing neuropathic pain assessment questionnaires and from the experience of the clinicians present on the ID Pain Steering Committee. This initial list of 120 items relating to the characteristics and symptoms of neuropathic pain was reviewed for repetitive or unclear items. After elimination of these terms, a list of 89 items was used in the studies to follow (Portenoy, 2006).

The ID Pain screening tool consists of six items and was developed in two stages. The first stage comprised of the reduction and construction of the 89-item list into the ID Pain screening tool and the second stage tested the validity and reliability of the ID Pain screening tool (Portenoy, 2006).

*1.3.7.1 The development and validation of the ID Pain screening tool (Portenoy, 2006)*

The first stage consisted of 586 adult patients who had non-headache pain for at least 30 days. Patients filled out the 89-item list of words and approximately 2 weeks thereafter were referred to a pain specialist who classified the patients as having neuropathic pain, nociceptive pain or pain of mixed etiology. The data obtained from the 89-item questionnaire was subjected to a univariable logistic regression and from this analysis, 65 items were retained for further analysis while an exploratory factor analysis followed by a logistic regression also retained 65 items for further analysis (55 of these 65 items were the same for the univariable logistic regression and factor analysis). Both sets of 65 items were subject to a model building stage that produced 2 sets of items that could be used in the final scale. A stepwise analysis and best subsets analysis yielded 23 items that again underwent statistical analysis and re-examination of the steering committee to create the 6-item ID Pain scale. Items relating to numbness and touch were included as the steering committee felt that these items were expected to distinguish nociceptive pain from non-nociceptive pain.

The steering committee chose the scoring method of -1 to 5 on the ID Pain and the scores for each item on the tool were calculated using a ROC curve, with

scores of 3, 4 and 5 indicating pain of neuropathic origin. This screening tool does not take into account measures of pain intensity or other qualities of pain and is therefore not classified as a multidimensional screening tool for neuropathic pain. This tool is a simple, time-efficient tool for neuropathic pain diagnosis and can be self administered by patients but, it does not include an assessment of signs. In addition to the pain items on the tool, there is a body chart requesting patients to shade in the areas where pain is felt. The ID Pain screening tool is presented below:

| Question | Score | |
|---|---|---|
| | Yes | No |
| 1. Did the pain feel like pins-and-needles? | 1 | 0 |
| 2. Did the pain feel hot/burning? | 1 | 0 |
| 3. Did the pain feel numb? | 1 | 0 |
| 4. Did the pain feel like electric shocks? | 1 | 0 |
| 5. Is the pain made worse with the touch of clothing or bed sheets? | 1 | 0 |
| 6. Is the pain limited to your joints? | -1 | 0 |

[The ID Pain screening tool by Portenoy and colleagues (2006)].

Data from 308 patients (neuropathic, nociceptive and mixed pain), who did not participate in the first stage of the study, were used in the validity and reliability of the 6-item scale. Patients were asked to fill out a series of questionnaires: the 6-item scale, the modified Brief Pain Inventory, the Hospital Anxiety and Depression Scale and the global anxiety VAS. Approximately 5 to 10 days later, patients were asked to fill out the 6-item scale as well as the modified Brief Pain Inventory. The most frequent terms used to describe all three types of pain and the most common physical findings in this part of the study are shown in Table 1.1. Using data from the second stage of the study, an ICC and kappa statistic showed that the score indicating nociceptive pain was 1, a score indicating mixed pain was 2 and a score of 3 or more indicated pain of neuropathic origin.

**Table 1.1:** The most common terms used to describe neuropathic, mixed and nociceptive pain and the most common physical findings amongst all three pain groups in stage one of the validation study for the ID pain screening tool.

| | **Neuropathic pain patients (n=105)** | **Mixed pain patients (n=104)** | **Nociceptive pain patients (n=99)** |
|---|---|---|---|
| Burning/aching/ stabbing | 84% | 86% | 74% |
| Numbness | 71% | 63% | 42% |
| Tingling | 67% | 59% | 43% |
| Pain on motion | 45% | 67% | 76% |
| Sensitivity to pin-prick | 74% | 44% | 32% |

### 1.3.8 The Brief Peripheral Neuropathy Screen (BPNS)

Although the Brief Peripheral Neuropathy Screen (BPNS) (Cherry et al., 2005) is not a semantic tool for neuropathic pain, a short summary of the BPNS will be provided as the tool was used to screen participants for a neuropathy in the present study. The BPNS was derived from the Subjective Peripheral Neuropathy Screen (SPNS) (McArthur, 1998) and will therefore be briefly described first.

#### *1.3.8.1 The Subjective Peripheral Neuropathy Screen (SPNS) (McArthur, 1998)*

McArthur (1998) tested the validity of the Subjective Peripheral Neuropathy Screen (SPNS) as a tool that could correctly diagnose peripheral sensory neuropathies in HIV patients. She compared the SPNS to quantitative sensory testing (QST) methods as a means of detecting neuropathy in HIV positive patients with peripheral sensory neuropathy and in HIV patients without a peripheral neuropathy (McArthur, 1998). The SPNS consists of three symptom

items (pain/burning/aching, pins-and-needles and numbness) located in the hands and arms or in the feet and legs and patients were required to rate the severity of these symptoms. The results showed that the severity scores on the SPNS were significantly correlated to measures obtained from the vibratory component on the QST and, the SPNS was found to be a reliable and validated tool for detecting peripheral neuropathy in HIV patients. The study by McArthur also showed that the symptoms felt in the hands could not distinguish between patients with neuropathy and those without and the component relating to the symptoms in the hands could be removed (McArthur, 1998).

*1.3.8.2 Validation of the BPNS for use in HIV-associated sensory neuropathy*

The BPNS is very similar to the SPNS with additional components involving clinical examinations to detect possible neuropathy. The BPNS is commonly used in AIDS Clinical Trial Group (ACTG) studies and is also referred to as the ACTG neurological screening tool (Cherry et al., 2005). In its standard form, the symptom screen involves participants identifying whether symptoms in their feet and legs feel like: “burning or aching”, “pins-and-needles”, or ““numbness (lack of feeling)”. If the participant has one or more of the symptoms, they rate the intensity of each of the symptoms on an 11-point numerical symptom rating scale ranged from 0 (no symptoms) to 10 (severe). The clinical examinations include testing for a reduced or absent ankle reflex using a reflex hammer and a decreased vibration sense in the patient’s big toe. The bilateral presence of symptoms and signs of peripheral neuropathy is required for a diagnosis of HIV-SN to be made.

In 2005, Cherry and colleagues wanted to assess and validate the properties and practicality of the BPNS for use in diagnosing sensory neuropathies in HIV infected individuals (Cherry et al., 2005). They compared the BPNS against more time consuming methods for the diagnosis of HIV-SN, namely, QST and intraepidermal nerve fiber density measures. The participants' vibration and thermal thresholds were tested in the QST method using computer software. For the intraepidermal nerve fiber density measures, a skin biopsy of 3mm from the lateral side of the distal calf was collected and analysed according to standard methods (Cherry et al., 2005). The results showed that the tool has a specificity of 98% and a sensitivity of 84% for a reduced or absent ankle reflex. This clinical sign was related to a high sensory threshold from the QST and a lower intraepidermal nerve fiber density. The presence of numbness had a specificity of 81%, a sensitivity of 86% and the degree of severity was associated with high sensory threshold from the QST and a lower intraepidermal nerve fiber density in the distal calf (Cherry et al., 2005).

The tool has thus been validated for the diagnosis of HIV-SN, and is commonly used in South Africa for the clinical diagnosis of HIV-SN in research and medical practices. However, it remains unknown if South African patients, who do not speak English as a first-language, truly understand the symptom terms listed on the BPNS.

### *1.3.9 A summary of the questionnaires*

Table 1.2 shows a summary of all the questionnaires listed in this section. The development of the questionnaires has been ongoing for the last two decades

and the need for such questionnaires to assist clinicians with the assessment and correct diagnosis of neuropathic pain and early treatment of the condition cannot be stressed upon enough. These questionnaires are important in assisting researchers involved in epidemiological research and those who are interested in the symptom measures of neuropathic pain. The development and validation of such a vast range of assessment and diagnostic tools suggest that neuropathic pain is indeed difficult and problematic to diagnose and evaluate.

**Table 1.2:** A summary of the pain assessment and diagnostic questionnaires.

| | **MPQ (SF-MPQ)** | **NPS** | **LANSS** | **S-LANSS** |
|---|---|---|---|---|
| **Year of development** | 1975 (1987) | 1997 | 2001 | 2005 |
| **Language of development** | English (English) | English | English | English |
| **Number of symptom items** | 78 (15) | 10 | 7 | 7 |
| **Symptom items** | **Sensory items*<br>Throbbing<br>Shooting<br>Stabbing<br>Sharp<br>Cramping<br>Gnawing<br>Hot or burning<br>Aching<br>Heavy<br>Tender<br>Splitting<br>*Affective items*<br>Tiring/exhausting<br>Sickening<br>Fearful<br>Punishing/cruel | Sharp<br>Dull<br>Sensitive<br>Deep pain<br>Hot<br>Cold<br>Itchy<br>Surface pain | Pricking, tingling or pins-and-needles<br>Electric shocks, jumping or bursting<br>Hot or burning<br><br>Pain caused by light touching<br><br>+ 2 clinical examination items | Pricking, tingling or pins-and-needles<br>Electric shocks, jumping or bursting<br>Hot or burning<br><br>Pain caused by light touching<br><br>+ 2 clinical examination items |
| **Self-administered** | No | Yes | No | Yes |
| **Symptoms/ clinical examination** | Symptoms | Symptoms | Both | Both |
| **Diagnostic/ assessment tool** | Both | Assessment | Diagnostic | Diagnostic |

| | NPQ | NPSI | DN4 | ID-Pain | BPNS |
|---|---|---|---|---|---|
| **Year of development** | 2003 | 2004 | 2005 | 2006 | 2005 |
| **Language of development** | English | French | French | English | English |
| **Number of symptom Items** | 12 | 12 | 10 | 6 | 3 |
| **Symptom items** | Burning<br>Overly sensitive to touch<br>Shooting<br>Numbness<br>Electric<br>Tingling<br>Squeezing<br>Freezing<br><br>How unpleasant is the pain?<br><br>Increased pain due to touch<br><br>Increased pain due to weather changes | Burning<br>Squeezing<br>Pressure pain<br>Electric shocks<br>Stabbing<br><br>Evoked pain to brush<br><br>Evoked pain to pressure<br><br>Evoked pain to cold<br><br>Tingling<br>Pins-and-needles | Burning<br>Painful cold<br>Electric shocks<br>Tingling<br>Pins-and-needles<br>Numbness<br>Itching<br><br>+ 3 clinical examination items | Pins-and-needles<br>Hot or burning<br>Numb<br>Electrical shock<br>Is pain made worse with touch? | Burning/ aching<br>Numbness<br>Pins-and-needles<br><br>+2 clinical examination items |
| **Self-administered** | Yes | Yes | No | Yes | No |
| **Symptoms/ clinical examination** | Symptoms | Symptoms | Both | Symptoms | Both |
| **Diagnostic/ assessment tool** | Both | Assessment | Diagnostic | Diagnostic | Diagnostic |

*The pain symptoms found on the SF-MPQ.

**Note**: only terms used to describe pain symptoms or questions pertaining to the stimuli that may evoke pain are shown in Table 1.2. MPQ=McGill Pain Questionnaire; SF-MPQ=short form MPQ; LANSS=Leeds Assessment for Neuropathic Symptoms and Signs Pain Scale; S-LANSS=self-completed LANSS; NPQ=Neuropathic Pain Questionnaire; NPSI=Neuropathic Pain Symptom Inventory; DN4=neuropathic pain diagnostic questionnaire; BPNS=Brief Peripheral Neuropathy Screen.

Most of the above-mentioned questionnaires have been adapted and validated in other languages and were translated using either a forward-backward translation method only, while others were developed using a reconstruction-based method (Stein and Mendl, 1988; Boureau et al., 1992; Perez et al., 2007; Koc and Erdemoglu, 2010; Van Seventer et al., 2010). In the forward-backward translation procedure, terms are forward-translated into the language concerned and then back-translated into English by a different translator to ensure authenticity of the translation (Van Seventer et al., 2010). Briefly, a reconstruction-based method involves translating the terms and then reconstructing the questionnaire by excluding, including or rephrasing other items that are well understood by the population being studied, making it language and culturally specific. More detail on the forward-backward translation and reconstruction-based methods will be provided shortly, when the guidelines that should be followed when creating or translating questionnaires are mentioned.

The MPQ has been translated and validated in Portuguese (Varoli and Pedrazzi, 2006), German (Kiss et al., 1987; Stein and Mendl, 1988) and Italian (De Benedittis et al., 1988), amongst others. Assessments for neuropathic pain have also been translated into various languages: the NPS has been translated into at least 24 languages (Cruccu et al., 2010), the DN4 has been translated and validated in languages such as Portuguese (Santos et al., 2010) and Spanish (Perez et al., 2007), while the NPSI has been translated into 50 other languages (Cruccu et al., 2010) including Italian (Padua et al., 2009) and English (Bouhassira et al., 2004). The LANSS and S-LANSS have both been translated into Turkish (Yucel et al., 2004; Koc and Erdemoglu, 2010). Irrespective of language, a pain assessment or diagnostic tool should be valid and consistent

amongst various cultural groups and this can only be achieved if “equivalence” is present between the original and translated questionnaires (Herdman et al., 1997); however, the translation of questionnaires may be prone to a few problems.

### *1.3.10 The pitfalls of translating questionnaires into other languages*

Language-appropriate questionnaires should lead to improved and correct diagnosis of neuropathic pain and will provide data that is accurate for use in clinical and epidemiological studies. None of the questionnaires, specific and non-specific to neuropathic pain, have been translated or validated in languages that are spoken by majority of the South African population. A few questionnaires, such as the SF-MPQ, NPS and NPSI have been translated, but not validated, into Afrikaans (PROQOLID, 2009; PROQOLID, 2011a; PROQOLID, 2011b) and there are currently no questionnaires in an African language. Language is complex, and the differences in syntax, context and grammar play an essential role in translating questionnaires into a different language to ensure that it reads correctly and is well understood. The easiest way to translate existing questionnaires into a new language may be to directly translate it. However, many problems occur when questionnaires are translated into other languages as Mkoka and colleagues (2003) illustrate in their study.

Mkoka and colleagues (2003) tested the forward and back-translation of an isiXhosa version of the European Quality of Life 5-dimensions (EQ-5D) questionnaire. The questionnaire was forward-translated into isiXhosa by translators fluent in both isiXhosa and English (Mkoka et al., 2003). The back-

translation was carried out by a similar group of translators and a draft of the isiXhosa version was tested in nine isiXhosa-speaking subjects. In the translation process, it was found that a few words could not be directly translated into isiXhosa as the backward translation of these words proved. The word “mobility” on the EQ-5D was difficult to translate as the isiXhosa equivalents were back-translated as, for example, “movement of any object.” After much thought, the term “ukuhamba-hamba” was suggested but back-translation of this term emerged as “casual sex.” It was then decided that the isiXhosa equivalent to be used was “ukuhamba” which literally means “to walk.” Although “ukuhamba” does not sufficiently suggest mobility as such, it was the closest word that suggested a state of mobility (Mkoka et al., 2003).

Guillemin and colleagues (1993) mention two ways of creating questionnaires in a different language that will take into account cultural differences. The first method consists of creating a new questionnaire entirely or, the second method includes translating a questionnaire by following the correct guidelines to ensure that it is relevant and correct for different cultures. The second method is known as “cross-cultural adaptation” and is a reconstruction-based method for translating questionnaires (Guillemin et al., 1993). In their paper “Cross-cultural adaptation of Health-related Quality of Life Measures: literature review and proposed guidelines,” Guillemin and colleagues suggest guidelines that should be taken into account when translating existing questionnaires.

Their guidelines include five basic steps (Guillemin et al., 1993):

i) Forward-translation of the questionnaire. This step should be completed by at least two different translators, who are qualified in the field,

ii) Back-translation of the translated terms. This stage should be completed as many times as was completed in the forward-translation process. Appropriate translators should be used and should include those who are not only fluent in the language, but can also identify common colloquial and idiomatic phrases in the language,

iii) Review of the questionnaire by an expert committee. A group of experts should be recruited to create the final version of the questionnaire. The committee should review the terms and phrases on the translated list and should modify them, reject those that are irrelevant and create new ones if necessary. They should also ensure that the new questionnaire reaches complete equivalence with regards to language and culture. Generally the following four "equivalences" should be looked at: semantic, idiomatic, experiential and conceptual. Each of these "equivalences" will be discussed in detail in the paragraphs that follow.

*Semantic equivalence* is achieved when words in the different languages have the same meaning. In some instances achieving the same meaning may result in grammar and vocabulary discrepancies.

*Idiomatic equivalence* is sometimes hard to achieve as idioms and colloquialisms cannot be translated or are difficult to translate into a different language as they lose their essence.

*Experiential equivalence* refers to using sentences with examples that are common to the target population's everyday lifestyle and experiences. When Mkoka and colleagues (2003) aimed to translate the sentence "confined to bed" on the EQ-5D, they found it difficult as firstly, it assumed that all the participants slept on actual beds and thus experiential equivalence is not achieved in this instance. Secondly, the isiXhosa idiom "ukulala ngendlu" translated as "lying in the house," could not be used due to semantic differences (Mkoka et al., 2003).

*Conceptual equivalence* is based on the equality of concept. In other words, a word may have semantic equivalence but there may be differences with regards to concept. As an example, when Mkoka and colleagues (2003) attempted to translate the word "male" into isiXhosa, they found that there was a difference between boys and men that was not related to age groups but rather a cultural difference that was based on initiation. "Indoda" (male) could thus not be used in the questionnaire as a boy who was not initiated could not be called an "indoda." The authors then found a word that could aptly apply to a mature male and used this form instead (Mkoka et al., 2003).

iv) Pre-testing the questionnaire for equivalence involves asking participants to fill out the newly translated and adapted questionnaire to ensure that the above-mentioned equivalences are reached, and,

v) Re-examination of weighting scores. The final step uses statistical methods in order to determine the most appropriate manner of combining all the information on the new questionnaire.

Cross cultural adaptation of existing questionnaires thus requires two phases; the translation phase and the adaptation phase to ensure that it is reliable and validated, not only with regards to language, but in a cultural context as well. Although cross-cultural adaptation does not consume much time and is more cost effective than developing a new questionnaire, it still requires invaluable time, dedication and numerous people and stages of development (Guillemin et al., 1993). As none of the neuropathic pain assessment tools and diagnostic questionnaires have been translated in a South African population, the need for a study to do so is apparent due to the vast linguistic and cultural differences that exist between different individuals.

## 1.4 SIGNIFICANCE OF STUDY AND OBJECTIVES FOR CURRENT STUDY

### *1.4.1The need to measure neuropathy conditions in South Africa*

Is there a problem using English-based neuropathic pain questionnaires in South Africa? Firstly, South Africa has one of the largest populations of HIV infected individuals with a prevalence rate of approximately 10.5% (Census, 2001). From the 33 million people infected with HIV worldwide, approximately 5.4-5.8 million are South Africans (UNAIDS, 2010). At almost every stage of HIV infection, peripheral neuropathy remains the most frequent neurological disorder (Ferrari et al., 2006; Arasho et al., 2008). Patients with HIV-SN present with painful feet,

often described as “burning” or ”aching” and some patients may present with pins-and-needles or numbness and the management of HIV-SN is centred on treating these symptoms (Ferrari et al., 2006; Arasho et al., 2008; Wadley et al., 2011). In the South African population, the prevalence of symptomatic HIV-SN is approximately 57% (Wadley et al., 2011). Wadley and colleagues (2011) found, in their study, that pain was present in approximately 76% of South African participants with HIV-SN, pins-and-needles in 46% of participants and 48% of participants experienced numbness in their feet.

Secondly, neuropathic pain is not limited to individuals with HIV and in South Africa, diabetes affects approximately 3.9% of the population (the results are adjusted for age and based on the prevalence of diabetes in South Africans from a rural community of Zulu ancestry) (Motala et al., 2008). Diabetes can affect any part of the nervous system and the most frequent neuropathy in diabetic patients is distal symmetric polyneuropathy (DSP) (Boulton et al., 2005). DSP is a chronic condition, affects the lower limbs and feet more than it affects the hands and is present in approximately 50% of diabetic patients (Boulton et al., 2005). Pain and sensations described by patients with DSP include “burning, aching, sharp pain, electric-like or shooting pain”, and “numbness” (Bhadada et al., 2001; Boulton et al., 2004; Boulton et al., 2005).

### *1.4.2 Assessing neuropathic pain in South Africa*

With the numbers of HIV infected and diabetic individuals increasing in South Africa daily, it is important that health care practitioners are able to detect and diagnose peripheral neuropathy early to initiate treatment strategies immediately.

However, it may be challenging for practitioners to detect the early signs and symptoms of peripheral neuropathy and manage the pain if patients cannot fully express themselves or complete standardized questionnaires because of language barriers.

In addition, investigators who have previously carried out neuropathy studies in a South African population may have experienced problems when trying to communicate with participants who did not speak English as a home-language. A study testing the usage and understanding of neuropathic pain descriptors in individuals of African ancestry whose home-language is isiZulu and who are not fluent in English is needed to assist practitioners, health care providers, patients and researchers.

As cultural and racial differences exist in pain perception, experience and management, it is important to measure and assess neuropathic pain in South Africa, as such information will contribute to the understanding of neuropathic pain in individuals of African ancestry. To date, no such study has been conducted in South Africa. Therefore, the objectives of this study were to determine what terms are used by isiZulu speakers to describe their neuropathic pain symptoms and to determine the level of understanding of terms on English-based neuropathic pain questionnaires that are used to diagnose and assess neuropathic pain in South African patients whose home-language is not English.

The objectives of the present study were as follows:

i) to determine the words used by isiZulu speakers to spontaneously describe their neuropathic pain symptoms,

ii) to determine the understanding of English neuropathic pain descriptors found in commonly used neuropathic pain questionnaires,

# CHAPTER 2

# METHODOLOGY

The study was approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (clearance number: M090669), and written informed consent was obtained from all participants. An interpreter fluent in isiZulu facilitated the recruitment, consent and interview procedures.

## 2.1 PARTICPANTS

Sixty-nine participants (47 females and 22 males) were recruited from the Virology Clinic at Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa. Participants were invited to participate in the study if they currently were experiencing any pain or abnormal sensations in their feet and lower legs, they had been on stable antiretroviral therapy for at least one month, and they spoke isiZulu as their primary language. We defined primary language as the participant's preferred language of communication when conversing with family and friends. If participants met the inclusion criteria, they were screened for the presence of peripheral sensory neuropathy using the BPNS generally used in ACTG studies (Cherry et al., 2005). If peripheral neuropathy was present, participants were asked to partake in the interview component of the study.

### *2.1.1 Exclusion criteria*

From the 69 participants initially recruited, 15 were excluded from the study: 3 participants did not have peripheral neuropathy, and 12 did not meet the criteria of isiZulu being their primary language. Thus, the final cohort consisted of 54 (38 females and 16 males) South African participants with HIV-SN.

## 2.2 SCREENING FOR NEUROPATHY

The BPNS was used to diagnose the presence of HIV-SN. To avoid priming patients with English-language descriptors of neuropathic pain during the screening process, we changed the symptom screen of the tool to ask only whether the individual had pain or unusual feelings in their feet and lower legs, and if so, to rate their intensity of the symptom as mild, moderate or severe. The modified version of the screening tool is presented in Appendix 2.

No changes were made to the screening tool for the assessment of signs of neuropathy. Ankle reflexes were evaluated using a reflex hammer that was struck against the Achilles tendon while the examiner observed for the presence of a reflex movement of the foot. If no reflex could be elicited, the individual was asked to reinforce the reflex by clenching their fists while the tendon strike was repeated. The reflex was recorded as being absent only after failure to elicit a reinforced reflex. Vibration sense was assessed using a 128 Hertz tuning fork. Before assessing vibration sense in the feet, individuals were familiarized with the vibration sensation by striking the tuning fork and placing it on the individual's wrist. Once they were familiar with the sensation, the tuning fork was struck again and placed on the distal interphalangeal joint of the big toe and the time taken for the participant to cease perceiving the vibration was measured in seconds using a stopwatch. A deficit in vibration sense was recorded if the duration of sensation from the time the tuning fork was struck to when the individual reported they could no longer perceive the vibration was less than ten seconds. The ankle reflex and vibration sense testing procedures were repeated on both legs. Participants had to present with symptoms (pain and/or abnormal sensations)

and at least one sign in both legs to be diagnosed with HIV-SN. All neuropathy assessments were performed by the researcher, and to ensure quality control in the screening process, the researcher was trained in the procedure prior to commencing the study, and the trainer verified the researcher's diagnosis at random times during the study.

In participants diagnosed with HIV-SN, additional information on the participant's HIV disease (CD4 T-cell count, date of HIV diagnosis) and treatment (current and previous antiretroviral drug use) history, and whether they had additional risk factors for developing a peripheral neuropathy (e.g., diabetes mellitus, alcoholism and tuberculosis infection), was obtained from their medical records. The participant's age, gender, ancestry and highest level of schooling was obtained by asking the participants for the information.

**2.3 THE INTERVIEW**

After meeting the inclusion criteria for the study, participants had an interview which consisted of the following components: 1. A spontaneous description by participants, in isiZulu, of the pain and abnormal sensations in their lower legs and feet and what triggered the sensations. Participants were not prompted during this spontaneous description, but were encouraged to give a complete description of all the sensations and triggers for the sensations.

2. A list of commonly used English neuropathic symptom descriptors was read to participants and they were asked to identify which terms accurately described

their pain. Before the list was read, it was made clear to all participants that the descriptive words about to be read to them referred to the pain and sensations in their feet and lower legs only. Participants were required to answer “yes, I have the symptom,” “no, I do not have the symptom” or “I do not understand what the word means” after each term was read to them. For the words they selected, they were immediately asked to provide an equivalent isiZulu term for the English description.

An example of how this second component of the interview process proceeded is provided below:

**Interviewer**: “Does the pain in your feet and lower legs feel like an electric-shock or electric like?”

**Participant**: “No”

**Interviewer**: “Does the pain feel knife-like or stabbing?”

**Participant**: “Yes”

**Interviewer**: “And how would you describe the stabbing pain in isiZulu?”

**Participant**: “Ziyahlaba”

**Interviewer**: “Does your pain feel like pins-and-needles?”

**Participant**: “I don’t understand”

Each interview was recorded using a digital camcorder (Sony Handy-cam DCR-SX40E (PAL), Sony Corporation, South Africa). However, as most of the participants were uncomfortable with their faces being recorded, the lens of the camcorder was turned away from participants and only the audio component of the interview was recorded. The interview lasted approximately 20 minutes and participants were offered refreshments during the interview.

## 2.4 DEVELOPMENT OF THE ENGLISH WORDLIST OF NEUROPATHIC SYMPTOM DESCRIPTORS

The inventory of English terms we used to describe the symptoms of neuropathy was constructed from terms commonly used to describe neuropathy symptoms in the English-language versions of the McGill Pain Questionnaire (Melzack, 1975), Neuropathic Pain Scale (Galer and Jensen, 1997), the Leeds Assessment of Neuropathic Symptoms and Signs (Bennett, 2001), Neuropathic Pain Questionnaire (Krause and Backonja, 2003), Neuropathic Pain Symptom Inventory (Bouhassira et al., 2004), Neuropathic pain diagnostic questionnaire (Bouhassira et al., 2005) and the ID Pain screening tool (Portenoy, 2006). Other neuropathic symptom descriptors that were not found on the neuropathic pain assessments listed above, were obtained from research publications pertaining to neuropathic pain and were included in the list.

To determine if the primary wordlist was appropriate for the study, a pilot study was performed on the first three participants who were willing to partake in the interview. The methodology for the pilot study followed the procedure mentioned above (2.3 The Interview). The pilot interviews showed that the words “bursting, strange/unusual, squeezing, dull, intense, lancinating, gnawing, splitting, piercing, tender” and “sensitive” were not understood by any of these participants, and this caused the participants to becoming visibly embarrassed by their lack of understanding of so many terms. Thus, the initial wordlist of 33 words and phrases was reduced to 21 items as the certain terms that patients did not know the meaning to, were removed from the list (Table 2.1). The terms cold and freezing were combined after the first three interviews because the participants

could not distinguish between the two words. In addition, completing the list of 33 words was time consuming and participants became agitated towards the end of the lengthy interview as they needed to see their physician or collect their medication from the pharmacist.

**Table 2.1**: The development of the English-language neuropathic symptom wordlist read to participants during the interview.

| | Terms in initial list | Terms in final list | Source of terms (references) |
|---|---|---|---|
| 1 | Electric shock/electric | 1. Electric shock/electric | 2,3,4,5,7,8,10 |
| 2 | "Knife-like"/stabbing | 2. "Knife-like"/stabbing | 1,3,8,9 |
| 3 | Pins-and-needles | 3. Pins-and-needles | 3,4,5,7,8,9 |
| 4 | Bursting* | | 5 |
| 5 | Tight | 4. Tight | 1 |
| 6 | Strange/unusual* | | 6 |
| 7 | Hot | 5. Hot | 1,4,6 |
| 8 | Burning | 6. Burning | 1,2,3,4,5,7,8,9 |
| 9 | Cold | 7. Cold/Freezing | 1,6,7,10 |
| 10 | Freezing | | 1,2 |
| 11 | Tingling | 8. Tingling | 1,2,3,5,7,8,9 |
| 12 | Pricking | 9. Pricking | 1,5 |
| 13 | Jumping | 10. Jumping | 1,5 |
| 14 | Shooting | 11. Shooting | 2,8,9,10 |
| 15 | Numb | 12. Numb | 1,2,4,6,7,8,9 |
| 16 | Squeezing* | | 2, 3 |
| 17 | Itching | 13. Itching | 1,6,7,8 |
| 18 | Evoked by heat | 14.Caused by heat (e.g. A hot bath) | 2,8 |
| 19 | Evoked by cold | 15. Caused by cold (e.g. on a cold day or after a cold bath) | 2,8 |
| 20 | Evoked by pressure | 16. Caused by pressure/ touching the skin (e.g. blankets/socks) | 2,3,4,7,8,10 |
| 21 | Aching | 17. Aching | 1,9 |
| 22 | Dull* | | 1,6 |
| 23 | Intense* | | 1,6 |
| 24 | Throbbing | 18. Throbbing | 1,8 |
| 25 | Lancinating* | | 1,10 |
| 26 | Gnawing* | | 1 |
| 27 | Splitting* | | 1 |
| 28 | Piercing* | | 1 |
| 29 | Cramping | 19. Cramping | 1 |
| 30 | Sharp | 20. Sharp | 1,6,9 |
| 31 | Tender* | | 1,5 |
| 32 | Sensitive* | | 2 |
| 33 | Radiating | 21. Radiating | 1 |

*the terms from the initial list that were removed as they were the least understood terms.

The words in the first column are all the words initially chosen for the wordlist, the list of words in the second column are the words in the final version of the questionnaire that was read to participants during the interview. The citation numbers in the third column refer to the source from which the words were obtained: 1: Melzack, 1975 (McGill Pain Questionnaire), 2: Krause and Backonja, 2003 (Neuropathic Pain Questionnaire), 3: Bouhassira et al., 2004 (Neuropathic Pain Symptom Inventory), 4: Portenoy, 2006 (ID Pain), 5: Bennett, 2001 (Leeds Assessments for Neuropathic Pain Symptoms and Signs), 6: Galer and Jensen, 1997 (Neuropathic Pain Scale), 7: Bouhassira et al., 2005 (neuropathic pain diagnostic questionnaire), 8: Dworkin, 2002 9: Mendell and Sahenk, 2003, 10: Cruccu et al., 2004.

## 2.5 DATA ANALYSIS

All audio recordings were transcribed and all isiZulu sections of the transcriptions were translated into English by a professional translation service (Perfect Transcribers, Braamfontein, Johannesburg), as well as by the interpreter who assisted with data collection. In all cases, the two independent translations were compared, and where the translations differed, both translators were consulted and a consensus translation agreed on.

Descriptive statistics and content analysis were used to analyse the data. We analysed data in the following manner:

### *2.5.1 Spontaneous description of neuropathic symptoms in isiZulu*

We extracted all the descriptive terms and phrases used by participants to describe their symptoms, both in the English translation and original isiZulu, as well as the phrases that indicated what triggered the pain.

### *2.5.2 Selection and understanding of English neuropathic symptom descriptors by isiZulu speakers*

From the list of English terms read to participants, we calculated the percentage of participants who chose each term to describe their neuropathic symptoms, the percentage who did not choose the term to describe their symptoms, and the percentage that declared that they did not understand the English term.

*2.5.3 Understanding of English terms*

To confirm whether words chosen from the English list of terms were correctly understood by participants having the symptom, we compared the meaning of the English term to the meaning of the isiZulu term they gave us as being equivalent to the English term. If the back-translation of the isiZulu term matched the English term, then the participant was judged as having truly understood the English term. If the back-translation of the isiZulu term matched an English word that belongs to the same grouping of words on the MPQ, then too were participants judged as having truly understood the term. For example, in the punctate pressure group the terms “knife-like/stabbing” and “pricking” can be found. If the term “knife-like/stabbing” was read to a participant and they agreed that they had the symptom, but provided an isiZulu term that was back-translated as “pricking,” the participant was said to have a true understanding of the term “knife-like/stabbing.”

*2.5.4 Comparison of spontaneous terms versus prompted English terms*

The descriptive terms and phrases provided during the spontaneous description of neuropathic pain were compared to the prompted English terms. A percentage concordance was calculated for each term on the English wordlist.

*2.5.5 Impact of pain on daily activities*

Although the impact of neuropathic pain on everyday lives was not a primary objective to the study, participants willingly and spontaneously provided information regarding this topic. We thus extracted the isiZulu phrases and the

English translation of those phrases, from these spontaneous verbal responses, which showed the impact of neuropathic pain on the participants' lives.

# CHAPTER 3

# RESULTS

## 3.1 DEMOGRAPHICS

The mean age of participants was 42 yrs (SD 10yrs), and the percentage of females was 70%. All participants were on antiretroviral therapy for at least one month when interviewed, and at least 92% had been exposed to Stavudine (data available for 49 participants only). Ten percent of participants had a history of alcoholism, 37% of tuberculosis infection and 8% of diabetes mellitus. The median current CD4 T-cell count was 361cells/$mm^3$ (range 35-837cells/$mm^3$, data available for 42 participants only).

Fifty-nine percent (n=32) of participants identified themselves as being of Zulu ancestry; 11% were of Xhosa ancestry, 11% were of Sotho descent and 19% had identified themselves as being of other ancestry, typically Tswana, Shangaan, Pedi or Swati. Irrespective of their self-identified ancestry, all participants spoke isiZulu either as a home-language or as their primary language of communication with their friends. Seventy-six percent (n=38) of participants had received less than 12 years of formal education, with the median number of years of education being 10 years (inter-quartile range:8-12) (data available for 50 participants only). Eight-two percent (n=41) of participants had received some or completed secondary education (8-12 years education), 16% had received primary education (1-7 years education) and 2% had received no education.

## 3.2 PAIN INTENSITY

The intensity of foot and lower leg pain reported by participants with pain (n=51) is shown in Figure 3.1. The majority of participants (72%) reported experiencing moderate to severe pain. The remaining three participants who did not

expereince pain, experienced numbness and paresthesias only (not shown in figure 3.1).

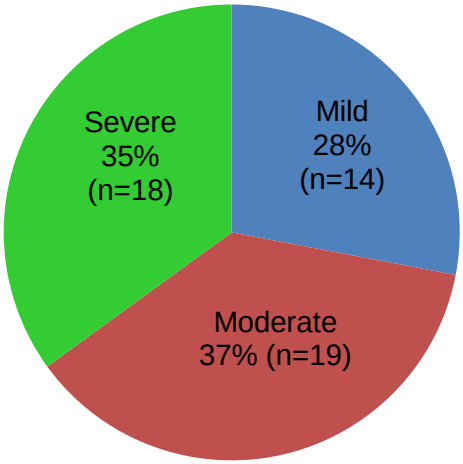



**Figure 3.1:** Pain intensity (mild pain, moderate pain and severe pain) reported by the 51 participants who had pain.

### 3.3 SPONTANEOUS DESCRIPTION OF NEUROPATHIC SYMPTOMS IN ISIZULU

The isiZulu terms spontaneously provided by participants when describing their neuropathic symptoms in their feet and lower legs are shown in Table 3.1. In addition, participants also provided examples of what triggered the sensations in their feet and lower legs.

The terms “hot,” “cramping,” “itching” and “numbness” were the most common terms spontaneously used to describe the symptoms of neuropathy. We included “numbness” even if participants did not use a term for it, but if they described the

sensation in such a way that it indicated lack of sensation in their feet or lower legs.

**Table 3.1:** isiZulu terms spontaneously used by participants to describe their neuropathic symptoms, and the percentage of participants who used each term.

| **isiZulu term used by paticipants** | **% participants who used the term*** | **English translation of spontaneous isiZulu term** |
|---|---|---|
| Ziyashisa, Ukushisa | 48 | Hot |
| Amajaqamba, Namacramps, Ama-cramps. Namajaqamba | 35 | Cramping |
| Phrase in text | 30 | Pain caused by walking |
| Buhlungu, Zibabuhlungu | 32 | Painful/Sore |
| Kuyaluma, Ziyaluma, | 22 | Itching |
| “Numb,” Ndikindiki | 22 | Numb |
| Kubanda, Ziyabanda | 17 | Cold |
| Phrase in text | 17 | Pain caused by pressure/touch |
| Ziyashisa, Zinokushisa | 7 | Burning |
| Ezihlabaya, Nziyahlaba | 6 | Stabbing |
| Kuyahlaba, ezihlabaya | 6 | Pricking |
| Phrase in text | 4 | Pain caused by cold |
| Phrase in text | 2 | Pain caused by heat |
| Kuyahlaba | 2 | Pins-and-needles |

*n=54

An example of an isiZulu phrase containing the symptom “hot” from the spontaneous verbal responses is shown below. The phrase is shown in isiZulu, just as the participant described the pain and sensations, with the English translation in bold letters after the isiZulu. The underlined term is one of the terms listed in Table 3.1.

...njengamanje izinyawo zami ziyashisa ngaphansi. **...like right now my feet are hot underneath.** *Participant 5*

Participants also provided examples stating how pain may be evoked by pressure, touch or a thermal stimulus. Approximately 30% (n=16) of participants reported pain when walking:

Ngathi manginyathela nginyathela ameva. **It feels like I am walking on thorns.** *Participant 8*

Seventeen percent of participants (n=9) reported pain caused by touching the feet (e.g.massaging the feet or when the feet were covered with blankets):

And uma mhlawumbe ziba nokuthintana neshidi uma ngilele ziba buhlungu. **When they get into contact with a sheet they get painful.** *Participant 5*

A total of 4% (n=2) said that the pain was caused by a cold stimulus:

Mangingahlala la kubanda khona like e cementini zibebuhlungu. **When I sit on a cold surface like cement, they get painful.** *Participant 61*

Only 2% (n=1) reported pain caused by heat:

Kodwa kuba isikhathi esincane, mangizifaka emanzini ashisayo zibabuhlungu nakhona imizuzu emihlanu. **But they are only painful if I**

**put them in hot water and even then it is just for 5 minutes.** *Participant 37*

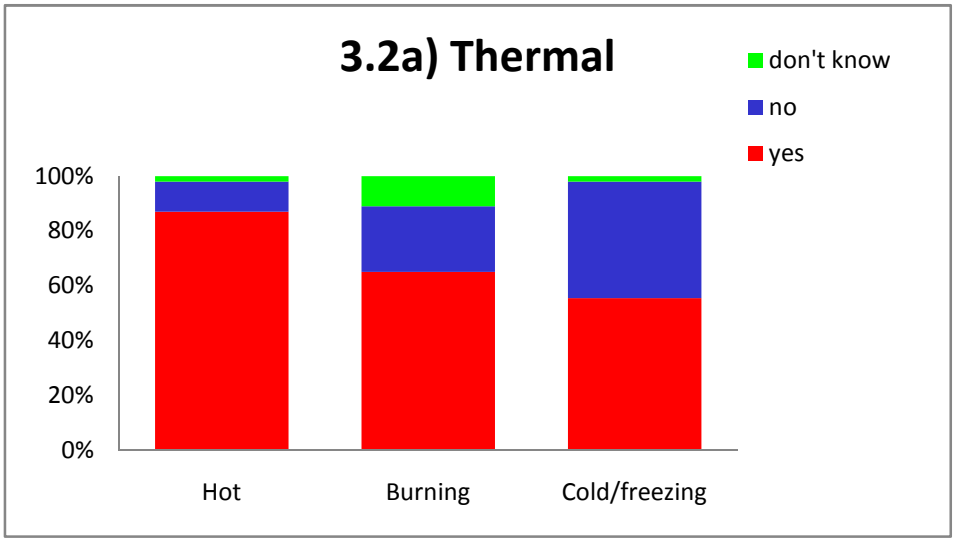
Additional phrases are presented in Appendix 3.

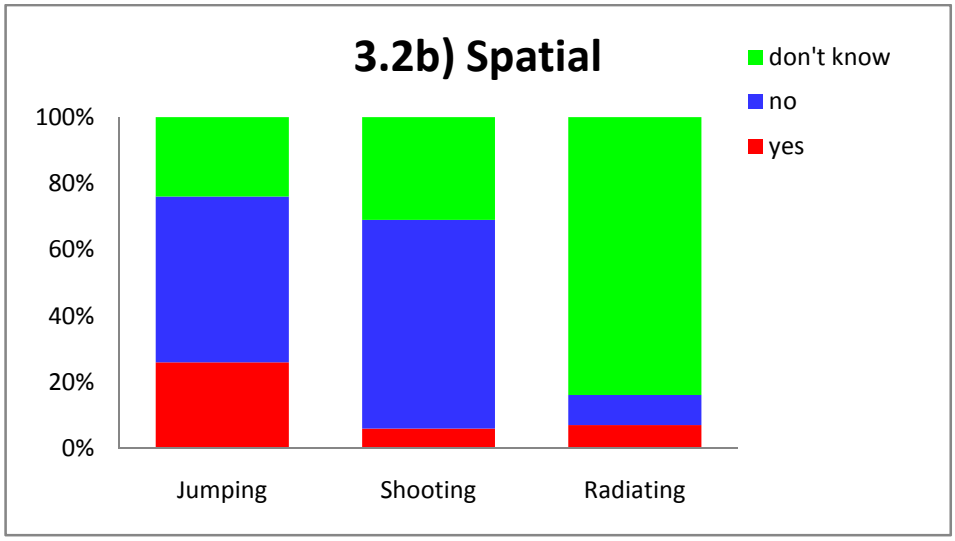
## 3.4 SELECTION AND UNDERSTANDING OF ENGLISH NEUROPATHIC SYMPTOM DESCRIPTORS BY ISIZULU SPEAKERS

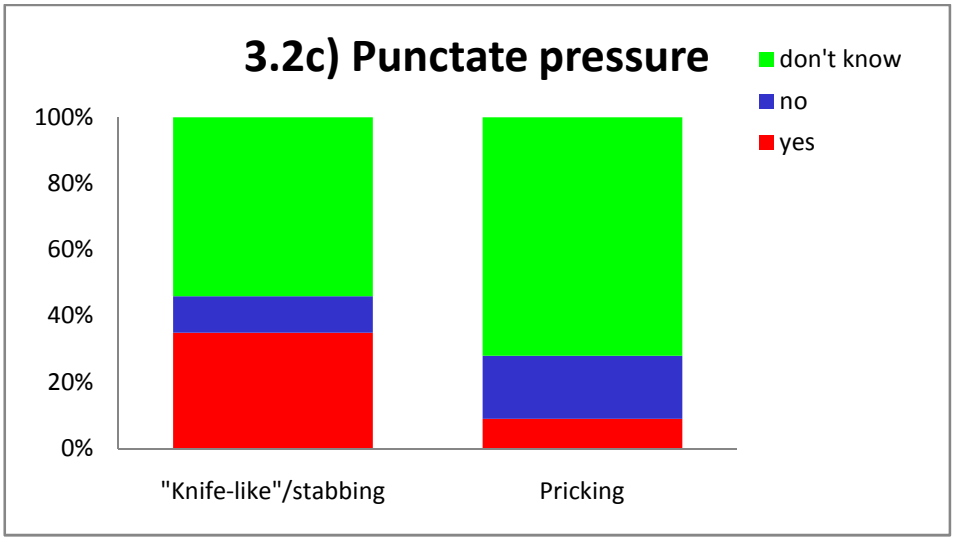
The percentage of patients who chose each word to describe their symptoms from the list of English terms is indicated in figures 3.2a-j. “Cramping” (89%; figure 3.2i) was the most common English term chosen by participants to describe their neuropathic symptoms when prompted with the English neuropathic pain descriptors, followed by the terms “hot” (87%; figure 3.2a), “burning” (65%; figure 3.2a), “tight” (61%; figure 3.2i) and “itching” (59%; figure 3.2d).

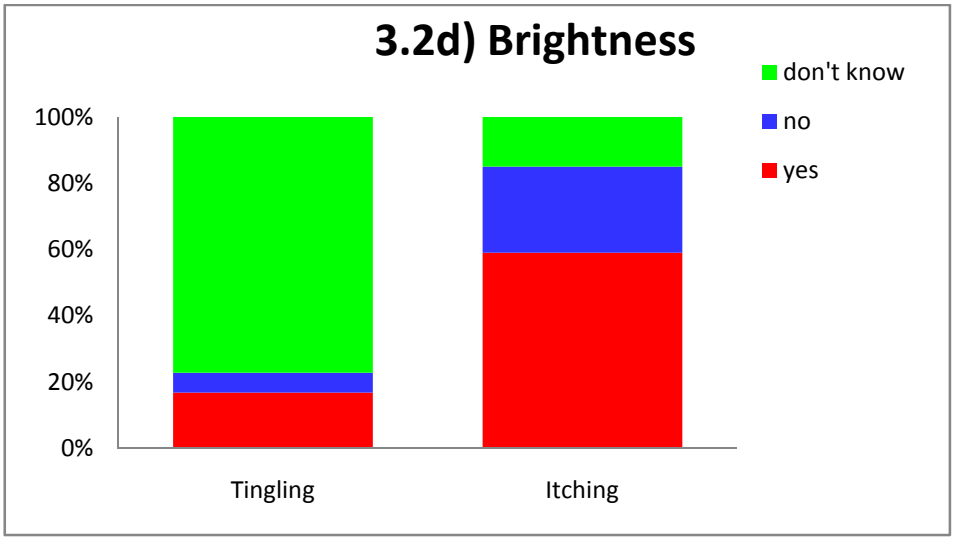
The least chosen English words were “shooting” (63% said “no” when asked if the term described their symptoms; figure 3.2b) and “jumping” (50% said “no” when asked if the term described their symptoms; figure 3.2b). The least understood English terms by participants were “throbbing” (96% did not understand the term; figure 3.2h), “radiating” (83% did not understand the term; figure 3.2b), “tingling” (78% did not understand the term; figure 3.2d), “pricking” (72% did not understand the term; figure 3.2c), “aching” (70% did not understand the term; figure 3.2j) and “numb” (63% did not understand the term; figure 3.2j).

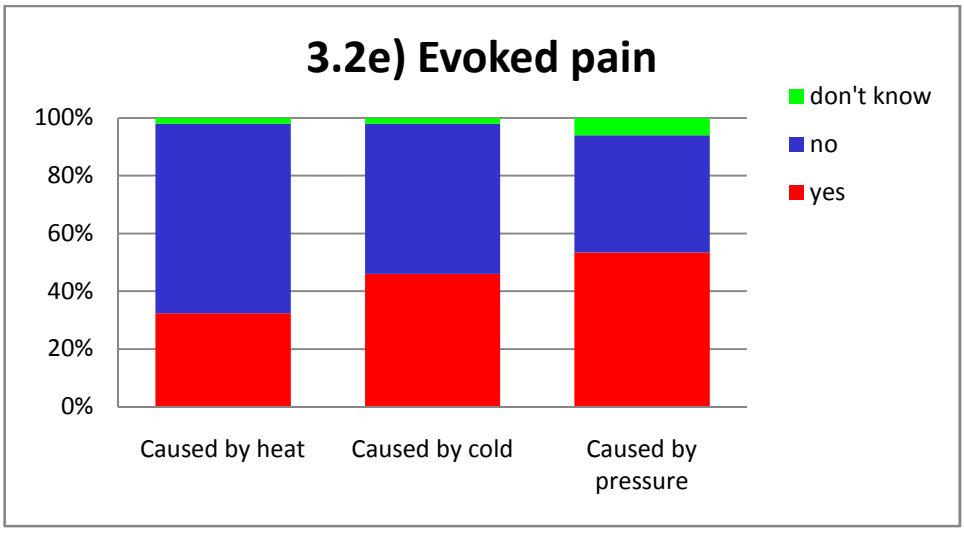
When prompted with the trigger for the pain, 32% (n=17) of participants reported that their symptoms were caused by heat, for example, a hot bath, and 46% (n=25) percent reported the symptoms of neuropathy caused by cold, for example, a cold day or a cold shower. Fifty four percent (n=29) said that the pain was caused by pressure to the feet and lower legs while standing, as well as skin contact when wearing socks, blankets or shoes.

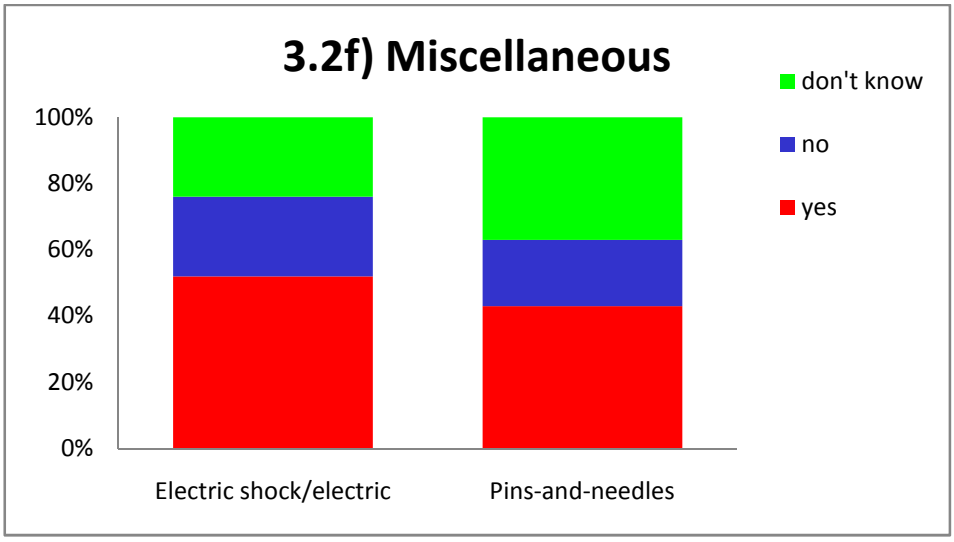


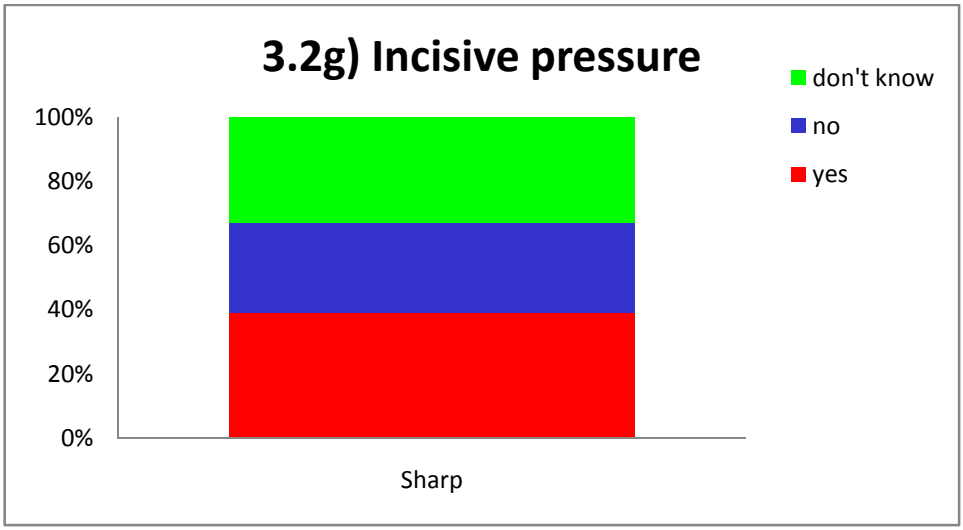



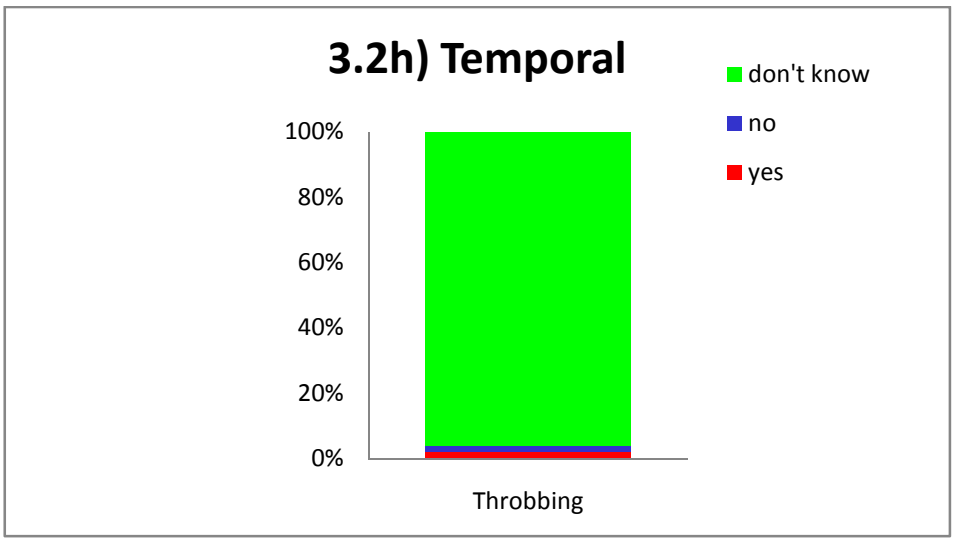

3.2c) Punctate pressure
don't know
no
yes
100%
80%
60%
40%
20%
0%
"Knife-like"/stabbing
Pricking

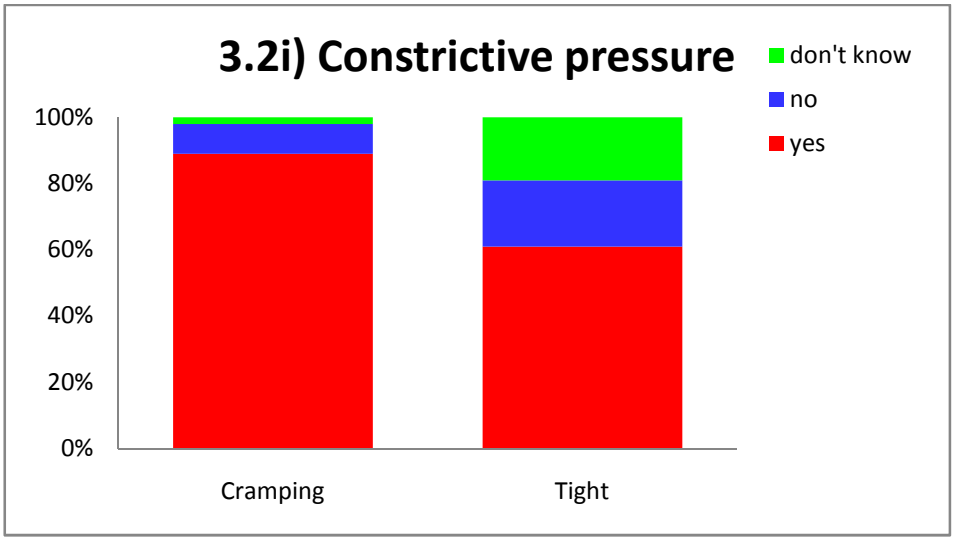

3.2d) Brightness
don't know
no
yes
100%
80%
60%
40%
20%
0%
Tingling
Itching

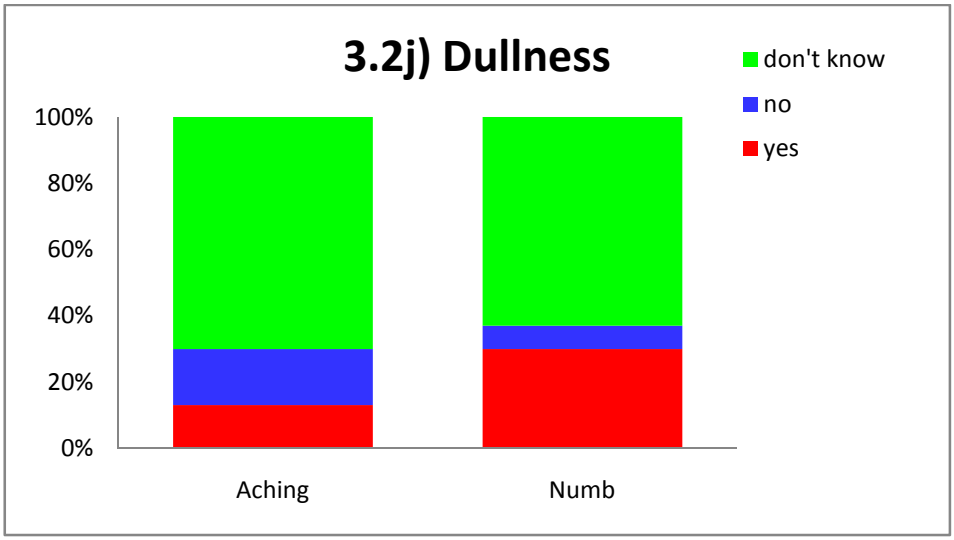

3.2e) Evoked pain
don't know
no
yes
100%
80%
60%
40%
20%
0%
Caused by heat
Caused by cold
Caused by pressure


3.2f) Miscellaneous
100%
80%
60%
40%
20%
0%
Electric shock/electric
Pins-and-needles
don't know
no
yes


3.2g) Incisive pressure
100%
80%
60%
40%
20%
0%
Sharp
don't know
no
yes


3.2h) Temporal
100%
80%
60%
40%
20%
0%
Throbbing
don't know
no
yes




Figures 3.2a-j: Percentage of participants (n=54) who chose each English neuropathic pain descriptor to describe their neuropathic symptoms (red), those who did not choose each term (blue) and those who did not understand each term (green). The words from the list are grouped according to their position on the McGill Pain Questionnaire grouping of words.

### 3.5 UNDERSTANDING OF ENGLISH TERMS

We determined if the words chosen by participants to describe their neuropathic symptoms were truly understood by the participant or not. For example, for the

term “itching,” 32 out of the 54 participants chose the term to describe their pain. From the 32 participants, 26 had a true understanding of what “itching” meant. This was determined by looking at the isiZulu equivalents they provided for the term “itching” and then back-translating this equivalent into English. If it matched the English term, then participants were judged as having a true understanding of the English term. Table 3.2 shows the 21 neuropathic pain descriptors, the number of participants who chose the term to describe their symptoms and the number of these participants who had a true understanding of the English descriptor.

**Table 3.2:** True and false understanding of the English-language neuropathic symptoms chosen by participants from the list of 21 English words to describe their neuropathic symptoms.

| English term | Number of participants who chose term* | Number of participants who had a true understanding of the term (%) | Number of participants who had a false understanding of the term (%) | isiZulu equivalents** |
|---|---|---|---|---|
| 1. Electric shock/electric | 28 | 17 (61) | 11 (39) | kudonseka imisipha (feels like an electric shock)<br>ugesi (electric shock)<br>Engathi kuyoshoka (electric shock) |
| 2. “Knife-like”/stabbing | 19 | 11 (58) | 8 (42) | Iyahlaba (stabbing/pricking)<br>Engihlaba (stabbing) |
| 3. Pins-and-needles | 23 | 17 (74) | 6 (26) | Ngihlatswa yinalithi (pins-and-needles) |
| 4. Tight | 33 | 19 (58) | 14 (42) | Ukuqina/ ziyaqina/ iyaqina (tight) |
| 5. Hot | 47 | 46 (98) | 1 (2) | Ziyashisa/ ukushisa<br>iyashisa/ kuyashisa (hot) |
| 6. Burning | 35 | 32 (91) | 3 (9) | Ziyashisa/ ukushisa<br>iyashisa/ kuyashisa (burning) |
| 7. Cold/ Freezing | 30 | 25 (83) | 5 (17) | Ukubanda/ ziyabanda<br>Ziyagodola<br>Ziyabanda kakhulu (very cold) |
| 8. Tingling | 9 | 3 (33) | 6 (67) | Ziyakitaza (tingling) |

| English term | Number of participants who chose term* | Number of participants who had a true understanding of the term (%) | Number of participants who had a false understanding of the term (%) | isiZulu equivalents** |
|---|---|---|---|---|
| 9. Pricking | 5 | 3 (60) | 2 (40) | Ziyahlaba (pricking)<br>Iyahlaba (pricking) |
| 10. Jumping | 14 | 4 (29) | 10 (71) | ama cramps iwo ajampayo (it is cramps that are jumping) |
| 11. Shooting | 3 | 1 (33) | 2 (67) | uzwa ngathi kukhona (It is pulling) |
| 12. Numb | 16 | 12 (75) | 4 (25) | Ndikindiki (numb)<br>Ziyalala (they are sleeping)<br>Ziyasinda (they become heavy) |
| 13. Itching | 32 | 26 (81) | 6 (19) | Ziyaluma (itching)<br>Ukuluma (itching)<br>Manginwaya (when I am scratching) |
| 14.Caused by heat | 17 | 11 (65) | 6 (35) | mangigeza ngamanzi ashisayo ziba buhlungu khakulu (when I have a hot bath, they get painful) |
| 15. Caused by cold | 25 | 14 (56) | 11 (44) | Uma kubanda (on a cold day) amanzi abandayo (cold water makes them more painful) |
| 16. Caused by pressure | 29 | 22 (76) | 7 (24) | Uma ngibeka ingubo (when I put blankets on my feet)<br>Uma ngifaka amasokisi noma izikathulo (when I put on socks or shoes) |
| 17. Aching | 7 | 5 (71) | 2 (29) | Ubuhlungu (painful/aching)<br>Ibabhuhlungu (painful/aching) |
| 18. Throbbing | 1 | 1 (100) | 0 (0) | Like a heartbeat going “doof doof” |
| 19. Cramping | 48 | 46 (95) | 2 (5) | Amakrempu/ Zibanamakrempu/ Amajaqamba/ namajaqamba/ Iyabambana (cramping/cramps)<br>Ziyabambeka (they get stiff) |
| 20. Sharp | 21 | 14 (67) | 7 (33) | Iyahlaba/ kuyahlaba/ bukhali (sharp) |
| 21. Radiating | 4 | 1 (25) | 3 (75) | ubi kuyanyakaza (like there is something radiating/moving) |

*n=54

**examples of the isiZulu equivalents for the English neuropathic symptom descriptors provided by participants if the English term described their symptoms.

The terms that majority of the participants had a true understanding of included “burning, hot, cramping, cold/freezing” and “itching”. The least understood terms chosen by participants to describe their symptoms were “radiating, jumping, shooting” and “tingling.”

## 3.6 COMPARISON OF SPONTANEOUS TERMS VERSUS PROMPTED ENGLISH TERMS

Table 3.3 shows the comparison of the spontaneous isiZulu terms used by participants to describe their symptoms to the English terms the same participants chose when prompted with the English symptom wordlist. The analysis was used to determine if participants used similar words when describing their neuropathic pain symptoms in both circumstances. A percentage concordance was calculated for each term. For example, 26 participants used the isiZulu term for “hot” to spontaneously describe their neuropathic pain symptoms and from the 26 participants, 24 (percentage concordance=92%) chose “hot” when prompted with the English term. Participants typically chose equivalent English words from the wordlist to those isiZulu words they spontaneously used to describe their symptoms. Participants chose many more additional words (median: 6 more words on average (interquartile range: 4-8 words)) to describe their symptoms when they were prompted with the terms. On average, there was an 80% level of agreement between the spontaneous and prompted terms.

**Table 3.3:** Comparison of the spontaneously used isiZulu terms to describe symptoms, to the prompted English terms chosen by participants when describing their symptoms. A percentage concordance was calculated for each term.

| | **Number of participants who spontaneously used the isiZulu term*** | **Number of participants who chose the term when prompted with the English term** | **% concordance** |
|---|---|---|---|
| Hot | 26 | 24 | 92 |
| Cramping | 19 | 18 | 95 |
| Itching | 12 | 9 | 75 |
| Numbness | 12 | 5 | 42 |
| Caused by pressure | 11 | 7 | 64 |
| Cold/ Freezing | 9 | 8 | 89 |
| Burning | 4 | 2 | 50 |
| Pricking | 3 | 0 | 0 |
| Knife-like/ Stabbing | 3 | 2 | 67 |
| Caused by cold | 2 | 2 | 100 |
| Pins-and-needles | 1 | 1 | 100 |
| Caused by heat | 1 | 0 | 0 |
| Tight | 1 | 1 | 100 |
| Electric shock | 0 | 0 | 0 |
| Sharp | 0 | 0 | 0 |
| Throbbing | 0 | 0 | 0 |
| Aching | 0 | 0 | 0 |
| Tingling | 0 | 0 | 0 |
| Radiating | 0 | 0 | 0 |
| Jumping | 0 | 0 | 0 |
| Shooting | 0 | 0 | 0 |

***n=54**

## 3.7 IMPACT OF PAIN ON PARTICIPANTS' DAILY ACTIVITIES

The statements reflecting the impact of pain on the participants' lifestyles are grouped by topic and the English translations are shown in bold lettering. Additional phrases are listed in Appendix 4.

### *3.7.1 Sleep and pain at night*

For some of the participants, the pain seemed to be more prominent at night and in the morning. Nineteen percent of participants (n=10) reported that sleep was affected by neuropathic pain:

> Ngalendlela zibuhlungu ngakhona, nginokuvhuka ebusuku ngi funa into yokuzenza ngcono. **The way they are painful they make me wake up at night to look for something to make them better.** *Participant 50*

Nine percent of participants (n=5) reported feeling more pain at night:

> Ebusuku zibabuhlunge ngaphansi ngathi umuntu angangishaya, it seems as if all i-weight yami goes down, bese aya-paina. **At night they get very painful, I wish someone could just hit me underneath; it seems as if all my weight has gone down to my feet and then they get painful.** *Participant 29*

### *3.7.2 Waking up in the morning*

Some participants (15%) also reported that the pain affected waking up in the morning or getting out of bed.

> Uthola mhlawumbe uma ngisembhedeni kuba nzima ukwehla ngobuhlungu. **You find that it becomes so difficult to get out of bed because of that pain.** *Participant 7*

*3.7.3 Daily activities affected by pain*

For some participants, walking and running (41%) was a painful experience:

> Ziba namajaqamba. **They get cramps.** Bese ngihluleka ukuhamba. Ngibambelele. **Then I am unable to walk, I hold on to something.** *Participant 62*

For some participants (9%) the pain affected the type of footwear that could be worn.

> …and then even isihlangu asingeni, mina ndisebenzisa amaphaca nje kunetha kubanda. **…and I can't even wear proper shoes; I always have to wear sandals even when it's cold.** *Participant 13*

*3.7.4 The functional impact of neuropathic pain*

Pain associated with neuropathy also affected some participants functionally. The manner in which an individual copes with the pain and how they allow pain to affect their lives is dependent on the individual. For example, one participant reported a sense of hopelessness:

> Mina sendizincamile vele iindaba zenyawo, andisenalo nje ithemba. Even uDoctor ndandibuza ukuthi zizobanjani, wathi izinyawo endizohlala ndinazo, mandizidlele nje ama-ARVs no kudla nje oku-healthy, otherwise iinyawo zona azizukuya ndawo. So, kulapho nje ngavele ngalahl' ithemba,

> ngavele ngazamukela nje. **I've given up on my feet ever getting better, I have no hope. I asked the Doctor once if my legs were going to get better, and he said no I should just focus on taking my ARVs and eating healthy, but my legs will always be sore. So, that is when I lost hope, and accepted the pain.** *Participant 13*

Another realised that the pain experience was something other people will not be able to empathise with:

> Kubuhlungu ngale ndlela ongayazi. **It is painful in a way that you would never understand.** *Participant 4*

One participant said that she would not allow the pain to have a negative influence on her lifestyle:

> But yona akusiyo i pain yokuthi angeke ngikwazi ukuhamba, ngeke ngikwazi ukwenza lutho("niks"). **But it is not the pain that will prevent me from walking or doing anything.** *Participant 5*

The above statements illustrate that neuropathic pain affected the participant's everyday living. Waking up in the morning, walking a short or long distance, running and sleep are a few of the daily activities affected. Activities that the rest of us find simple and effortless become a painful and uncomfortable experience for those with neuropathic pain.

# CHAPTER 4

# DISCUSSION

# AND

# CONCLUSION

*4.1 Summary of findings*

Our objectives were to determine what words are used by isiZulu speakers with HIV-SN, to spontaneously describe their symptoms and to determine their understanding of common English neuropathic pain descriptors. The participants in the present study spontaneously described their symptoms, in isiZulu, as hot ("ziyashisa/ukushisa"), cramping ("amacramps/amajaqamba"), itching ("ziyaluma/kuyaluma"), numb ("ndikindiki") or used phrases that indicated numbness in their feet and lower legs. When participants were prompted with English terms that are commonly found on existing assessment and diagnostic tools, participants chose the terms "cramping, hot, burning, itching" and "tight" to describe their symptoms of neuropathy. The present study shows that there are common terms used to describe the symptoms of neuropathy by European patients from previous studies and the South African participants in our study. Thus, neuropathic pain seems to display similar traits and characteristics in different racial and cultural groups. The few differences in descriptor choice could be due to the different causes of the neuropathies concerned.

In addition to the objectives, we serendipitously found that HIV-SN had an impact on the lives of those with the neuropathy. The symptoms of neuropathy and the severity of these symptoms may have a negative impact on the participants' everyday lifestyles, affecting their sleep patterns and daily activities and, in some participants the symptoms seemed to affect them in a functional manner. We can also conclude if using English-based questionnaires in the clinical and research settings in South Africa is appropriate or not as many individuals speak isiZulu as a home-language. We suggest the development of a neuropathic pain

questionnaire in a language that is appropriate and well understood by South African patients. The questionnaire should be developed from first principles as there are important terms that are essential in the diagnosis and assessment of neuropathic pain that were not understood or were misinterpreted by our participants.

*4.2 Discussion*

The terms “hot, burning and itching” emerged as the most frequent terms chosen by participants from the wordlist to describe the symptoms of neuropathic pain. In addition, the isiZulu words “ziyashisa/ukushisa” (hot/burning) and “ziyaluma/ukuluma” (itching) were amongst the most frequent terms spontaneously used by participants to describe their symptoms. Thus, the South African participants used terms that are commonly used to describe neuropathy symptoms by other populations and are commonly found on existing neuropathic pain questionnaires (Galer and Jensen, 1997; Bennett, 2001; Krause and Backonja, 2003; Bouhassira et al., 2004; Bouhassira et al., 2005; Portenoy, 2006). Terms such as “hot and/or burning” are found on the NPS, LANSS, NPQ, NPSI, S-LANSS, DN4 and ID-Pain. The term “itching” occurs on the DN4 and the NPS. Despite cultural and linguistic differences, the symptomatology of neuropathic pain is apparently highly conserved.

Throbbing, radiating, tingling, pricking, aching, and numb were the least understood and the least chosen terms to describe neuropathic pain. Although the term “throbbing” is usually associated with non-neuropathic pain (Rasmussen et al., 2004), our participants may have not chosen the term to describe their

symptoms simply because they did not understand what the term meant, with only 2% of participants understanding what “throbbing” meant.

A single word, the term “cramping” is not frequently found on common neuropathic pain questionnaires (Galer and Jensen, 1997; Bennett, 2001; Krause and Backonja, 2003; Bouhassira et al., 2005; Portenoy, 2006). However, in the present study, “cramping” was used when participants spontaneously described their neuropathic pain symptoms (35%) and when they were prompted with the term (89%). This is consistent with the results obtained by Dubuisson and Melzack (1976) and Masson et al., (1989), who both found that cramping was one of the common terms used to describe the symptoms of neuropathic pain in patients with phantom limb pain and painful diabetic neuropathy, respectively. In addition to using the isiZulu term “amajaqamba,” to describe the cramp-like pain, some participants used words such as “ama-cramps” or “namacramps’’ to describe their pain. The latter terms are simple isiZulu derivatives from the English word “cramp.”

The above information may prove to be vital when health care practitioners are assessing patients, who do not speak English as a first-language, with diabetes, HIV, cancer and patients with any other conditions who may be prone to developing a neuropathy. For example, if an HIV infected individual complains of “cramping” or “ama-cramps” in the lower legs, feet or toes, then the practitioner should not necessarily regard this as a muscle cramp, but should rather initiate further investigation or assessment for possible peripheral neuropathy. The early

detection of neuropathy will prevent further nerve damage by immediate provision of the correct treatment.

It remains unclear whether isiZulu speakers and native English speakers assume the same meaning for the term “cramp.” However, participants frequently clenched their fists when describing a “cramping” pain, illustrating tightness or constriction, which is similar to the English meaning of a “cramp.” Furthermore, participants seemed to constantly regard the terms “cramping” and “tight” as describing the same symptom. For many participants, these terms meant the same thing and this was noted in the back-translation of the isiZulu terms they provided. In the wordlist created by Melzack and Torgerson (1971), “cramping” and “tight” were grouped in the constrictive pressure group, thus, if participants provided the isiZulu equivalent for “tight” when asked if they had a cramping pain, they were judged as having truly understood the terms and vice versa.

Knife-like or stabbing was chosen by 19 participants and 29 participants did not know what these terms meant. “Iyahlaba, ziyahlaba, kuyahlaba” were the most common isiZulu equivalents given for the terms knife-like or stabbing. The same isiZulu equivalents were provided for the English terms “pricking” and “sharp”, suggesting that these three different symptoms are regarded as similar sensations to isiZulu speakers. “Stabbing” and “pricking” both belong to the punctate pressure group on the MPQ, whereas “sharp’ belongs to the “incisive pressure” group on the MPQ (Melzack, 1975). The subtlety of the words used to describe these different symptoms is thus lost in isiZulu and isiZulu speakers may possibly associate all four sensations with the same pain despite the terms being

associated with different pain intensities according to the MPQ. Alternatively, the context of how the word is used may indicate the magnitude of the stimulus.

A lack of understanding the terms found on assessments and diagnostic tools may compromise the diagnosis of neuropathic pain or the treatment of neuropathic pain. Some terms from the list of English terms that were not well understood by participants' if they chose the term to describe their symptoms included "tingling, jumping, shooting and radiating." For example, when asked if the term "tingling" described their symptoms, participants would provide isiZulu terms that, back-translated as "cramps," "itching" or "tight." When the term "jumping" was read to participants, they misinterpreted the term to imply physical jumping instead of a jumping pain sensation in the feet and lower legs. Although the terms "tight" and "itching" were well understood universally, one participant misheard "tight" as "tired" while another associated "itching" with "eating." This implies that using terms on English questionnaires for patients who are not first-language English speakers is challenging as they may misinterpret many terms, even though they believe they understand the terms, or they may associate the terms with other English words as these words do not form part of their everyday vocabulary. This lack of understanding or misinterpretation may possibly lead to a misdiagnosis or under-diagnosis of neuropathic pain as patients could insist they have a symptom when in fact they are symptom-free, or they may deny having a symptom allowing the condition to progress.

It may be beneficial to both health care providers and patients if the health care provider familiarised themselves with a few common terms that a patient may use

when describing his or her symptoms. For example, in the present study, “ziyashisa, ukushisa and iyashisa” were the isiZulu terms used spontaneously by participants to describe sensations of hotness and “ziyaluma, kuyaluma and ukuluma” were the isiZulu terms used to spontaneously describe itchiness. The common suffix in these terms is “-shisa” for hot and “-luma” for itchiness. As can be seen, there is no particular term that exists in the isiZulu language to describe a certain symptom and therefore, health care providers and researchers should take note of the suffix to determine what symptoms the patient or participant is presenting with when attempting to communicate with their patients.

Similarly, when participants were prompted with the term “electric shock” to describe neuropathic pain, 28 participants chose electric shock to describe their neuropathic pain symptoms and 17 of these participants had a true understanding of the term. The common isiZulu terms and phrases used to describe the electric shock-like pain was “iyashoka” or “kuyashoka”. We see that participants used the suffix “-shoka” which is derived from the English term “shock”.

The jargon term pins-and-needles, was also occasionally described as “ziyahlaba” while other descriptions included the isiZulu word “inalithi” or “izinalithi” (translated as “needles”). It is difficult to judge if patients truly understood the essence of a pins-and-needle-like sensation, even though they may have understood what the English terms “pins” and “needles” refer to. As Dubuisson and Melzack (1976) point out, an environmental reference may be associated with certain pain descriptors and they provide an example of a

burning pain resulting when a child burns on a hot stove. It remains questionable if participants in our study associated “pins-and-needles” with the environmental reference of an actual pricking pain of a needle as they provide the isiZulu equivalent for the word “needle” and further investigation is needed to determine this.

Furthermore, as the description of pain is purely subjective in nature, researchers have to rely on the participant’s description of their own pain. This becomes difficult when participants themselves cannot provide answers relevant to the research. For example, when asked if pain was caused by pressure, a participant replied “I do not know what causes the pain” or when asked if the pain is caused by cold, a participant replied “when it is cold, I cannot sleep.” In the latter case it is unsure if the participant cannot sleep due to the pain caused by cold or due to the cold itself.

Neuropathic pain also had an impact on the participants’ everyday lifestyles, as they spontaneously described to us. Although the various symptoms associated with neuropathic pain are a constant reminder of the condition, it may also have a negative influence on an individual’s everyday activities. For example, sleep is affected when an individual awakens during the night to either physically find some relief for the pain, or when an individual has to remove sheets or blankets as these evoke pain in the feet. Gray and Berger (2007) mention that sleep deprivation itself can cause worsened pain experience as the person is fatigued resulting in aggravated pain or the body’s response to pain may be impaired in HIV patients.

The impact of neuropathic pain on quality of life has been shown by Poliakov and Toth (2011). Findings from their study showed that patients with polyneuropathy and neuropathic pain were more likely to be unemployed compared to patients with polyneuropathy without neuropathic pain (Poliakov and Toth, 2011). Similarly to the present study, sleep was impaired by those patients with neuropathic pain and patients reported increased sleep disturbances and less hours of sleep. Furthermore, depression and anxiety symptoms seem to have s greater impact on quality of life in those individuals with neuropathic pain (Poliakov and Toth, 2011).

### *4.3 Conclusion and recommendations for further research studies*

In conclusion, the results from this study suggest that it is a better option to develop and validate a screening or assessment tool for neuropathy in South Africa from first principles, resulting in a new questionnaire. The mere forward and backward-translation of existing questionnaires should not be applied as the items on the questionnaire need to reach semantic, conceptual, experiential and idiomatic equivalence to guarantee that they are culturally acceptable for South African patients and participants. In the present study, participants provided different terms for the terms “hot, itching, pricking and cold/freezing” and so forth and an agreement on which terms to use should be made so that the questionnaire has semantic equivalence.

In terms of experiential equivalence, the items used to illustrate what may evoke pain should also be considered. For example, as poverty is rife in South Africa, patients may not relate to socks, blankets or hot water and more easily

accessible items should be used to illustrate evoked pain. The term “pins-and-needles” should be translated in such a way that it gets across the meaning of what the sensation actually feels like, hence reaching conceptual equivalence, instead of illustrating actual “pins” and “needles.” Furthermore, perhaps there is an idiomatic or colloquial expression that is easily understood by those who speak isiZulu to describe numbness or a knife-like pain and further language studies are proposed.

In addition, it would be beneficial to create a new language-appropriate neuropathic pain questionnaire for the South African population as the term “cramping,” used to describe the participants’ symptoms in our study, is not found on any other neuropathic pain questionnaires and will be lost if the existing tools are simply translated into isiZulu. Furthermore, terms commonly found on existing questionnaires, such as “tingling, electric-shock like, jumping, and sharp” were not chosen by participants to describe their symptoms as they did not experience the symptom or they did not understand the term and including these terms in an isiZulu questionnaire will thus be to no avail. Simply translating questionnaires into isiZulu could be problematic and may not adequately measure pain. This knowledge may also apply to other verbal pain scales that require translation into an African language.

Terms such as “hot,” “burning” and “itching,” that were used to describe neuropathy symptoms in South Africans who speak isiZulu as a home-language, are similar to the terms used by English speakers and European populations. The similar terms suggest that the symptoms of neuropathic pain do not discriminate

between individuals from various cultural and racial groups. From the present study we can conclude whether or not English neuropathic pain questionnaires that are used globally (in the United Kingdom, European countries and the United States of America), are appropriate for South African patients who speak isiZulu as a home-language. The results from our study show that certain key terms such as “numb,” “tingling,” and “pricking”, used in the assessment and diagnosis of neuropathic pain are not well understood by South Africans who speak isiZulu as a home-language, therefore, we propose the development of a neuropathic pain questionnaire that is language-appropriate for South African patients. A language-appropriate questionnaire will improve the diagnosis of neuropathy in South African patients, will result in more accurate data for epidemiological and clinical studies, and will add validation to cultural studies.

### *4.4. Limitations to the study*

The most important limitation to the study is the fact that the primary investigator does not speak isiZulu as a first or second-language. The language barrier between primary investigator and participant made it rather difficult to communicate, and the study purpose, as well as what was expected of participants, may not have been fully understood by participants. However, the advantage of the primary investigator’s lack of isiZulu knowledge may have prevented biased data and the results are thus objective in nature. There was a translator present at all times during the data collection period, who facilitated communication with the investigator.

Participants could have felt intimidated when the terms that were read to them were not fully understood and instead of responding with “I do not understand the term,” participants responded with “no,” despite being told that it was acceptable if they did not understand the term. It was thus difficult to judge if participants truly understood the term or not, and we based the results on the manner in which participants responded, for example, how hesitant or puzzled a participant was when responding to the question. The environment in which the interview was carried out and recorded was not the most suitable as it was prone to noise and there may have been interruptions when individuals, not part of the study design, would occasionally walk into the room where the interview was taking place. The above may have distracted participants and the recordings were occasionally unclear to the transcribing and translating company due to the noise. We suggest conducting interview research in rooms that are completely silent and prone to as little disturbance as possible. These limitations should be considered for future language studies based on interview nature, as improving the overall study design will result in improved and more accurate data for qualitative research.

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# APPENDICES

**APPENDIX 1: McGill Pain Questionnaire**

# McGILL PAIN QUESTIONNAIRE

| 1 | 2 | 3 | 4 |
|---|---|---|---|
| 1. Flickering | 1. Jumping | 1. Pricking | 1. Sharp |
| 2. Quivering | 2. Flashing | 2. Boring | 2. Cutting |
| 3. Pulsing | 3. Shooting | 3. Drilling | 3. Lacerating |
| 4. Throbbing | | 4. Stabbing | |
| 5. Beating | | 5. Lancinating | |
| 6. Pounding | | | |

| 5 | 6 | 7 | 8 |
|---|---|---|---|
| 1. Pinching | 1. Tugging | 1. Hot | 1. Tingling |
| 2. Pressing | 2. Pulling | 2. Burning | 2. Itching |
| 3. Gnawing | 3. Wrenching | 3. Scalding | 3. Smarting |
| 4. Cramping | | 4. Searing | 4. Stinging |
| 5. Crushing | | | |

| 9 | 10 | 11 | 12 |
|---|---|---|---|
| 1. Dull | 1. Tender | 1. Tiring | 1. Sickening |
| 2. Sore | 2. Taut | 2. Exhausting | 2. Suffocating |
| 3. Hurting | 3. Rasping | | |
| 4. Aching | 4. Splitting | | |
| 5. Heavy | | | |

| 13 | 14 | 15 | 16 |
|---|---|---|---|
| 1. Fearful | 1. Punishing | 1. Wretched | 1. Annoying |
| 2. Frightful | 2. Gruelling | 2. Blinding | 2. Troublesome |
| 3. Terrifying | 3. Cruel | | 3. Miserable |
| | 4. Vicious | | 4. Intense |
| | 5. Killing | | 5. Unbearable |

| 17 | 18 | 19 | 20 |
|---|---|---|---|
| 1. Spreading | 1. Tight | 1. Cool | 1. Nagging |
| 2. Radiating | 2. Numb | 2. Cold | 2. Nauseating |
| 3. Penetrating | 3. Drawing | 3. Freezing | 3. Agonising |
| 4. Piercing | 4. Squeezing | | 4. Dreadful |
| | | | 5. Torturing |

# Present Pain Intensity (PPI)

People agree that the following 5 words represent pain in increasing intensity. They are:

| 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| Mild | Discomforting | Distressing | Horrible | Excruciating |

Which would best describes your present pain? _____

## VAS PAIN RATING

In your experience, how would you rate he pain you are currently feeling:

No pain _____ The worst pain I have ever felt

**APPENDIX 2: Neurological Screening Tool**

# Neurological Screening Tool

1. Symptoms

Do you experience any pain or abnormal sensations in your feet or lower legs? ☐ YES ☐ NO

Please describe the intensity of you pain:

| Mild | Moderate | Severe |
|---|---|---|
| ☐ | ☐ | ☐ |

2. Signs

Instructions for evaluating perception of vibration

Strike the end of a 128 Hz tuning fork hard enough that the sides touch. Place the vibrating tuning fork on a bony prominence on the subject's wrist to be sure that they can recognize the vibration or "buzzing" quality of the tuning fork. Again, strike the ends of the tuning fork 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.

2.1 Vibration sense:

a. Great toe DIP joint perception of end of vibration in seconds R ☐ L ☐

b. Vibration perception score: R ☐ L ☐

Vibration perception
0=felt ≥ 10 seconds
1=felt < 10 seconds

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, if necessary, by having the subject clench fist.

2.2Ankle Reflexes: R ☐ L ☐

Ankle Reflexes
0= absent
1=present

**APPENDIX 3: Spontaneous verbal pain descriptions of neuropathic pain symptoms**

Additional examples of the spontaneous verbal descriptions used by participants to describe their symptoms are shown below. The phrases are in isiZulu, just as the participant had said, and the English translations are shown below it. The underlined terms are the terms found in Table 3.1 of Chapter 3: Results.

Uma ngilele ngizwa ngibanjwa ama-cramps.
I get a lot of cramps. *Participant 18*

So, sometimes ziba namajaqamba.
They also get cramps sometimes. *Participant 61*

Ziyaluma. They are itchy. *Participant 35*

Izinyawo nziyahlaba umangime isikhathi eside. **If I have been standing, they start stabbing.** *Participant 35*

…kodwa ngizwa kuthi noma **ngihamba** ngizwa ubuhlungu.
…and (they) got painful when I **walked**. *Participant 50*

…bese ziyabanda sometimes…
…and sometimes they feel cold… *Participant 12*

Uthole ukuthi sometimes ngibacela ukuthi bangirabhe, ababuhlungu kakhulu mabangibamba, inyawo libabuhlungu kakhulu.
I sometimes ask them to massage my feet, but they become more painful when they touch them. *Participant 30*

Nokuthi sometimes zinokuba-numb.

Sometimes they feel numb. *Participant 23*

Uma sengizwa lezizinhlungu, iminwe yezinyawo iba ndikindiki, angiyizwa.

My toes are numb, I cannot feel them. *Participant 58*

Kuyahlaba nje. It is pricking. *Participant 8*

...and then sometimes kuba sengathi kuyahlaba ngaphansi kwenyawo.

...and then sometimes I get pins-and-needles under my feet. *Participant 29*

**APPENDIX 4: Impact of pain on everyday lifestyles**

Listed below are the isiZulu phrases and English translations of the spontaneous verbal responses given by participants which show the impact pain has had on their lives. These additional phrases are an appendix to section 3.7 in Chapter 3: Results.

3.7.1 Sleep and pain at night

Ebusuku angifaki ingubo noma kubanda kanjani, ziyashisa. **I don't wear anything at night, no matter how cold they are hot.** *Participant 4*

And then ke nama-cramp mara hayi everyday. Ngize ngithathe i-ice ngiyibeke lapho kube ngathi kuya-stopa. Ngoba mangilele impela ngiyavuka ngilishaye phansi ukuthi yiyo nje into engingathi ingiphethe kakhulu. **I also have cramps sometimes but not all the time and I put ice on my leg to make it better. I get them even when I'm sleeping and then I have to get out of bed and jump up and down. That is my major problem.** *Participant 16*

Ja mangilele ziba buhlungu kakhulu. **Yes they are very painful when I am sleeping.** *Participant61*

3.7.2 Waking up in the morning

Uma ngivuka ekuseni angikhoni ukunyathela. **I can't even stand when I wake up in the morning.** *Participant 12*

Futhi uma ngivuka ekuseni, ngathi langaphansi kunento efana neqhwa. **And when I wake up in the morning it feels like my feet have ice underneath.** *Participant 47*

3.7.3 Daily activities affected by pain

And then mangihambe uthola kuthi isicathulo siyaphuma angizwa ukuthi isicathulo siphumile. **Sometimes my shoe would come out whilst I am walking but I would not feel that it is gone.** *Participant 59*

And kakhulu “ziyangiaffecta” uma ngigijima. **And also they affect me especially when I am running.** *Participant 5*

Kusho ukuthi le pain isuka la emadolweni bese yehla ngemilenze. Mayifika laphansi kwezinyawo, yenze engathi nginyathela amaqhwa. **This pain starts from the knees and it goes down my legs and when it get to my feet it makes me walk like I am walking on ice.** *Participant 7*

Uma ngihamba kunalento engidonsayo ngingakhoni ukushesha bese ngizwa engathi ngiyakhathala. **When I am walking it feels like there is something pulling me and I am not able walk fast and I feel like I am getting tired.** *Participant 3*

ADDITIONAL: Interesting and unique phrases to describe neuropathic pain

Participants also provided interesting and unique phrases indicating how they, as individuals, perceive pain and sensations associated with neuropathic pain:

Kwesinye isikhathi uthola ukuthi izinyawo ziyashisa uma uthi uzikhiphela phandle kwengubo nakhona zibande. Then awazi ukuthi wenzenjani manje. Ngihlale ngizihlikihla nakhona kushise. Sometimes ngithatha ama ice cubes ngithi ukuzipholisa. **Sometimes you find that my feet are hot but when I take them out of the blanket they get cold, and you just don't know what to do. I am always rubbing them but they also get hot from rubbing and I have to use the ice cubes to cool them off.** *Participant 58*

Kutholakale ukuthi lokuluma kungaphakathi. Akukho ngaphakathi esikhumbeni. **You find that the itch is inside the skin, not on the surface of the skin.** *Participant 10*

## APPENDIX 5: Ethical clearance certificate

**UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG**

Division of the Deputy Registrar (Research)

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**
R14/49 Asma Sheikh

| | |
|---|---|
| **CLEARANCE CERTIFICATE** | **M090669** |
| **PROJECT** | The Semantics of Human Immunodeficiency Virus-Associated Sensory Neuropathy Symptoms in Individuals of African Ancestry Whose First-Language is not English |
| **INVESTIGATORS** | Asma Sheikh. |
| **DEPARTMENT** | School of Physiology |
| **DATE CONSIDERED** | 09.06.26 |
| **DECISION OF THE COMMITTEE*** | Approved unconditionally |

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

**DATE** 09.06.26 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr A Bentley

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**DECLARATION OF INVESTIGATOR(S)**

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

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...
.....