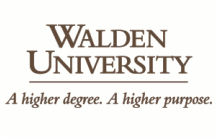

2017

A Comparison of Neuropathic Pain in HIV Disease and Diabetes Mellitus

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This is to certify that the doctoral dissertation by

Mary Catherine George

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

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Walden University
2017

Abstract

A Comparison of Neuropathic Pain in HIV Disease and Diabetes Mellitus

by

Mary Catherine George

MM, Florida State University, 1984

BM, Valdosta State University, 1980

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Health Psychology

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August 2017

Abstract

Neuropathy is a nerve disorder found in HIV disease and diabetes mellitus that indicates damage in the peripheral nervous system. Burning, tingling, stabbing, shooting, and painful sensations in the hands and feet are common symptoms of this chronic disorder, and no treatments are available that repair the nerves. The approved pain treatments are few and only available for the diabetic neuropathy population. A mixed-methods study of archival data was performed to compare patients with painful neuropathy (PN) associated with 2 diseases: HIV (HIV-PN) and diabetes mellitus (DPN). This study examined the similarities and differences of the pain narratives and common pain questionnaires from 12 HIV-PN and 11 DPN subjects. An independent *t* test of the Visual Analog Scale, Numeric Rating Scale, Brief Pain Intensity subscale, and the Short Form McGill Pain questionnaire failed to reject the null hypothesis that HIV-PN and DPN have equal pain levels. The qualitative analysis revealed 8 shared themes in both groups, with footwear challenges reported as the primary theme. This finding supports the many shared themes between these groups, yet education addressing these themes is minimal. One contrasting theme, privacy, was detected in the HIV-PN group, correlating statistically with the Beck Depression Inventory findings of guilt feelings. The theme of exercise was unique for the DPN group. Both groups had paralinguistic and nonverbal elements discovered in the recordings demonstrating the need for future research to explore these components. Results of education and research themes of privacy in the HIV-PN group and pain communication strategies for both groups will increase understanding of etiology, intervention, and patterns of pain for those diagnosed with neuropathy.

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Dedication

I would like to dedicate this study to all of those individuals I have known during the past 20-plus years diagnosed with HIV/AIDS and diabetes. My awareness of the complex challenges these individuals face could not have happened without the stories of so many patients who live with a chronic illness with great courage and persistence. I have been humbled by my opportunities to listen and witness the moments of life these individuals have shared. I have learned the healing power that can be found in being present and listening.

Acknowledgments

Embarking on the journey of accomplishing a dissertation would not have been possible without the loving support of my family and friends. I am so grateful for their constant encouragement, support, and unending patience and motivation that have given me the persistence to make progress. I don't think I would know what to do without my amazing family. I want to thank all of those whom I work with at the Icahn School of Medicine at Mount Sinai and the many volunteers, especially William Mau, Donna Koo, and Jackie Wu, who have assisted in the process of organizing research information. An amazing group of dedicated family, colleagues, and friends have inspired me to keep making progress: Noel and Roberta Haas George; Noel George, Jr.; Sister Angela Abood; George Davidson, PhD; David Simpson, MD; and Jessica Robinson-Papp, MD. I especially want to thank David Dorfman, PhD, and Linda Hamilton, PhD, who have been mentors and inspired me to pursue this degree. I would like to thank Dr. Anthony Napoli for a deeper understanding of conceptualizing methodology. Finally, I am deeply grateful for Dr. Jay Greiner, chairman of my committee. The amazing patience, motivation, encouragement, and gentle demeanor he provided were ever present during the many ups and downs of this process; I am ever grateful.

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Chapter 1: Introduction to the Study

Background

Human immunodeficiency virus (HIV) has infected approximately 36.7 million people worldwide, with close to 2.1 million individuals newly infected each year (World Health Organization [WHO], 2016). Access to combination therapy with antiretrovirals (cART) has increased the life expectancy of people living with HIV/AIDS (PLWHA) to an almost normal life span (Walensky, Auerbach, & Office of AIDS Research Advisory Council [OARAC], 2015). Many HIV patients experience multiple comorbidities (e.g., hepatitis C, heart disease, and diabetes), coupled with the progression of HIV disease. Physicians providing care for the HIV population are challenged when patients report symptoms of painful neuropathy. Neuropathic painful sensations in the feet and hands or balance and gait disturbances can be overlooked and underdiagnosed until these symptoms progress to a critical stage of chronic constant pain (Ellis et al., 2010; Gonzalez-Duarte, Robinson-Papp & Simpson, 2008).

Neurological complications in HIV disease involve both the central and peripheral nervous systems. The virus acts as a secret invader, using the cells of the immune system to enter the brain, spine, and peripheral nerves, destroying nerve cells with neurotoxins, which are created during the cell death of the immune cells used by the virus to propagate (Sacktor et al., 2010). Treatments for HIV disease have neurotoxic side effects, increasing the damage to the nervous system by potentially destroying the mitochondria of the neurons (Bennett, Doyle, & Salvemini, 2014).

HIV-associated distal symmetrical polyneuropathy (peripheral neuropathy, HIV-PN) is one of the leading neurologic complications in HIV disease. Approximately 70% of the HIV population will develop HIV-PN, with 30% to 50% reporting symptoms of burning, tingling, "pins and needles," stabbing sensations, and numbness (Ellis et al., 2010; Gonzalez-Duarte et al., 2008). The different symptoms of neuropathic pain experienced by patients diagnosed with HIV-PN prevent these individuals from living high-quality, functional lives. Scientists do not clearly understand the pathogenesis of HIV-PN, nor are there sufficient pain treatments to manage these patients' symptoms (Ellis et al., 2010). The lack of adequate pain relief for HIV-PN can cause increased levels of anxiety and depression, limit social interaction, and increase disability in these patients (Gonzalez-Duarte et al., 2008).

Diabetes mellitus (DM) affects approximately 382 million worldwide, with about 60% of these individuals suffering from symptomatic diabetic neuropathy (Guariquata et al., 2014). The number of diabetic diagnoses will almost double by the year 2035, making it an urgent issue in this population to reduce the burden of neuropathy that is associated with pain, blisters, infections, and related amputations. Diabetes, like HIV disease, has an unclear pathogenesis of neuropathy. The type of diabetes, and the complexities of comorbidities could be a contributing cause for peripheral nerve death that leads to the painful neuropathic sensations in people living with diabetes (Duby, Campbell, White, & Rasmussen, 2004). Type 1 diabetes is caused by either genetics or a viral disorder that causes the body's inability to produce insulin and manage glucose. Type 2 diabetes, while not entirely understood, is theorized to be a disease that occurs over time when the

insulin made by the body becomes unable to process glucose. Due to a complex combination of behavioral and genetic causes, 90% to 95% of those diagnosed with diabetes are Type 2 (Edwards, Vincent, Cheng, & Feldman, 2008).

Painful diabetic neuropathy (DPN) may be diagnosed when an individual is presenting with prediabetic symptoms such as impaired fasting glucose or glucose tolerance as an indication of a high risk of becoming a type 2 diabetic (Papanas & Ziegler, 2011; Ziegler, Papanas, Vinik, & Shaw, 2014). Similar to HIV disease, the most prevalent form of neuropathy is distal symmetrical polyneuropathy (DPN). Patients presenting with burning, tingling, and shooting pain with pins and needles who are aware of the risk due to diabetes seek the help of a neurologist or pain specialist to manage these painful symptoms. A small subgroup of patients who experience these symptoms are not diagnosed with diabetes, but when seen by a neurologist learn of their prediabetic status using the diagnostic tool of a glucose tolerance test (a test that examines how the body metabolizes sugar over a 2-hour period). Diabetes and prediabetic disorders are near epidemic proportions because of the rate of obesity in the United States and other countries that have an increased national gross domestic product and have adopted a western-influenced diet (Danaei et al., 2014). The increased rate of patients diagnosed with diabetes and prediabetes makes understanding and treating DPN an urgent need within the scientific community.

The cause of DPN is not well understood, but it is theorized that fluctuations of glucose and inadequate blood supply damage the nerves in the hands and feet, causing painful sensations, numbness, loss of balance, and change in the hair and skin. Over time,

amputations and hospitalizations can be attributed to the diagnosis of DPN (Daousi, Benbow, Woodward, & MacFarlane, 2006; Watkins & Thomas, 1998). While several drugs (e.g., pregabalin and duloxetine) have been approved by the Food and Drug Administration (FDA) to help manage the painful symptoms of DPN, these treatments offer only 30-50% improvement in pain symptoms (Bril et al., 2011; Dworkin et al., 2011).

Many people living with diabetes and PLWHA are on fixed incomes, struggle to afford behavioral pain relief options, and suffer from sleeplessness, depression, and social isolation, in addition to the complexities of managing diabetes or HIV disease (Almeida, Seal, & Clark, 2014; Salanitro et al., 2011). These pateints experience various comorbidities, and can be faced with provider mistrust, and often are undertreated for their chronic neuropathic pain (Martin, Daniel, & de C Williams, 2014). The complexities of providing pain treatments for these populations are challenged by the perception of the primary providers for those patients who report chronic pain. In a study conducted by De Ruddere et al., (2014), when patients reported pain incongruent with physiological medical evidence, there was an underlying mistrust of the patient's pain experience. In their study, vignettes of pain experiences were shown that included "medical evidence" based pain experiences that included both medical evidence and psychosocial behaviorally based descriptions with and without medical evidence descriptors (i.e., x-rays and magnetic resonance imaging). Those patients who demonstrated pain without medical evidence but with psychosocial behaviors were less likely to be believed by the health care providers. Understanding the complexity faced by

patients with chronic pain may provide a pain treatment model that can address those patients for whom the pain perception is multifaceted and appears to be unrelated to medical evidence. The need to provide sufficient pain treatments to these populations continues to go unmet. The potential to increase awareness about diverse treatment options for these patients could have the ability to improve quality of life in the context of this pain condition.

Statement of the Problem

Over 44 clinical trials have been conducted to investigate treatments for painful HIV-PN, with none of these studies resulting in a Food and Drug Administration (FDA) approval for pain treatment (Chetty et al., 2012; Ellis et al., 2010). The only treatments available for painful HIV-PN are off-label medications, which are approved by the FDA for other conditions (e.g., DPN and postherpetic neuralgia). Off-label treatments for HIV-PN have not shown to significantly alleviate the pain symptoms of HIV-PN (Attal et al., 2011), or improve the quality of life, or ability to function (Ellis et al., 2010). Other over-the-counter treatments such as acetaminophen and ibuprofen show no benefit as well yet are often provided as rescue medications in the clinical trial setting (Vo, Rice, & Dworkin, 2009). Opioids (e.g., Vicodin®, Percocet®, and oxycodone) have significant risks, and medical providers are hesitant to prescribe them due to the complexities of government regulations and the potential for abuse and, recently, the issue of accidental death. These controlled medications require stringent monitoring and patient contracts, placing the physician in a position of policing the patients' usage (Chetty et al., 2012). With no FDA-approved pain treatments available for HIV-PN, there is an increasing need

to understand the psychological or social factors of patients who suffer from painful HIV-PN. The implication that a significant percentage of the HIV population may be diagnosed with HIV-PN places urgency upon the scientific community to design better systems of treatment for painful symptoms of HIV-PN until prevention or nerve regeneration is a possibility.

Through this study, I sought to understand the pain perception of patients diagnosed with HIV-PN as compared to patients diagnosed with DPN. Awareness of how these two groups differ or are similar in the pain experience may increase understanding of why treatments have failed for pain relief of HIV-PN and help in the design of unique patient educational tools for coping and assessments for reporting pain. Measuring pain is subjective; comparing these two groups could aid in understanding pain outcome measures that are used for research and clinical assessments. Information about how painful HIV-PN differs from the DPN pain experience may lead to the development of biopsychosocial treatments or approaches that help patients holistically.

Pain medications are the focus when treating patients diagnosed with painful HIV-PN and DPN. A recent study using self-hypnosis reported benefit in reducing pain perception in HIV-PN for 17 weeks post-hypnosis induction (Dorfman et al., 2013). This study using behavioral modification is an indication that treatments incorporating integrative, biopsychosocial components can provide adjuvant treatment for pain relief and for those HIV-PN and DPN patients who desire non-pharmacological approaches as first-line treatment. Awareness of patient perceptions of pain and relief may reveal behavioral treatments that can offer greater pain relief than oral medications for those

suffering with HIV-PN or DPN. Increased understanding of how patients report and discuss pain may add to the development of comprehensive approaches to pain treatments in these two patient populations.

Study Rationale

There is interconnection among the nervous system, the immune system, and cognitive awareness. The theory of psychoneuroimmunology embraces the chemical pathways that are ever-present to maintain homeostasis (Ader, Cohen, & Felten, 1995) and optimize the ability of an organism to survive and thrive. Recognizing this interrelatedness between the physiological factors (nervous and immune systems) as well as the manner in which the human experience is influenced by psychological, environmental, and social interactions can inform medical practices and treatments. No studies are in the literature comparing the pain experience in the HIV-PN and DPN populations. The ability to measure and understand the perception of pain within the HIV-PN and DPN populations may provide increased knowledge as to psychological, behavioral, or environmental components that play a role in how individuals perceive and react to a chronic pain experience. Patient outcome measures (i.e., numeric pain rate scale, 0-10) are used in the research arena to determine a drug's effectiveness. Pain outcome measures are the primary deciding elements for medications that are eventually reviewed and approved by the FDA. This study provided an opportunity to begin to address the gap of knowledge as it relates to the neuropathic pain experience, using standard pain outcome measures and narratives in patients diagnosed with painful neuropathy due HIV disease or diabetes.

Purpose of the Study

The study was designed to investigate the differences and similarities in the pain experience of individuals diagnosed with painful HIV-PN or DPN. How an individual perceives chronic pain in HIV-PN and DPN is not an entirely unknown concept (Griswold, Evans, Spielman, & Fishman, 2005; Lucey et al., 2011). Patients who catastrophize and make poor adjustments due to a diagnosis of a chronic pain condition show that there is a relationship between pain experiences and biopsychosocial concepts. The biopsychosocial context of patients' pain perceptions is not typically incorporated or measured in the process of developing clinical trials for pain treatments. Nor are physicians who provide care for these patients inquiring into the multidimensionalexperience of patient pain perception. These patients are asked to measure pain by indicating a number on an 11-point scale. With the Numeric Rating Scale (NRS; Farrar, Young, LaMoreaux, Werth, & Poole, 2001), the patient selects a number that best represents the average pain experience within the past 24 hours. The patient is asked to choose a number on this scale, where 0 represents "no pain" and 10 represents the "worst pain." Many patients question what an average number would be or whether the worst level of pain is someone else's experience or their own (Robinson-Papp, George, Dorfman, & Simpson, 2015; Williamson & Hoggart, 2005). For this study, HIV-PN patients were compared to a group of patients diagnosed with DPN using standard pain scales that are used in many of the clinical trials for treatments with neuropathic pain (Dworkin et al., 2005).

As the HIV population experience a normal life span and diabetes becomes prevalent in the population; the ability of the medical community to understand and treat chronic neuropathic pain conditions is critical for reduced medical costs and improved patient quality of life. Knowledge of how painful HIV-PN differs from painful DPN can open the door to the development of comprehensive biopsychosocial treatments and educational models. Merlin et al. (2014) discussed the elements of the biopsychosocial model for chronic pain in HIV disease. The elements of stigma and social isolation, the biological comorbidities of substance abuse and psychiatric illnesses, and the chronicity of life stressors may reveal a distinct biopsychosocial treatment approach for the HIV population as compared to the diabetic population. Treatment models developed addressing the contributing components of the biopsychosocial model have the potential to reduce the pain experience and may prevent the development of or lessen the experience of chronic pain. The relationship between a patient's negative coping style and catastrophizing can be an indicator of poor pain relief and diminished quality of life, despite the use of pain treatments. There have been no studies exploring differences in the pain experienced by HIV-PN and DPN. Understanding these differences in the pain experience could be an opportunity for understanding why pain treatments have been developed and approved for the diabetic population but pain treatments continue to elude FDA approval to treat those patients diagnosed with painful HIV-PN. To better understand how individuals with painful HIV-PN compare to those diagnosed with DPN, a study that examines pain-rating outcome measures (i.e., Visual Analog Scale, NRS, and

Brief Pain Intensity Scale) and pain narratives could begin to define the essential differences and similarities of the chronic pain experience between these two populations.

Data for this study were gathered from a larger study entitled "The Experience of Chronic Pain in Neuropathic Pain and Back Pain: A Focus Group Approach" conducted at the Icahn School of Medicine at Mount Sinai from 2009-2012 (see Appendix A). The original study enrolled three chronic pain groups: HIV-PN, DPN, and chronic low back pain. The primary objective of the initial study was to examine the cognitive processes of the perception of pain when patients completed chronic pain questionnaires to assess the pain experience using focus group methodology. Within the context of this study, as a coinvestigator, I initiated an element of inquiry that included capturing each of the participant's narrative of his or her chronic pain journey. At Visit 2, each participant completed a packet of pain questionnaires duplicating what occurs within the context of a research study (Dworkin et al., 2008). Once the package was completed, the participants were recorded speaking freely about their pain history and experience. As a coinvestigator, I believed that capturing the recorded data would provide the ability to document the participant's pain experience before any study activities. Evaluating these data provides an opportunity to compare how people with diabetes and PLWHA, both diagnosed with painful neuropathy report pain, use standardized pain outcome measures and describe in their words the perception of their pain experience.

Although painful HIV-PN and DPN are potentially quite different physiologically, the clinical presentation can be quite similar: numbness, tingling, burning, shooting, and stabbing pains in the feet and hands; absent or diminished

reflexes; and absent or diminished sensations (e.g., vibration and pinprick). People living with diabetes may report more pain in addition to numbness, whereas those with HIV-PN report more pain that feels like tingling or "pins and needles" and numbness (Freeman, Baron, Bouhassira, Cabrera, & Emir, 2014). Treatments for both disorders are managed with a similar approach, with the HIV-PN population treated with off-label medications. The ability to understand how patients with this disorder differ in pain perception, prescribed treatments, and reported pain could be an opportunity to modify the clinical trial design or pain outcome measures or investigate different pain treatment approaches.

Research Questions

This study investigated differences between the pain experience of patients diagnosed with painful HIV-PN and those diagnosed with painful DPN. The primary issues addressed were those related to pain perception within the context of neuropathy as a disorder. The study sought to answer the following questions: What are the differences in the language of pain perception between HIV-PN and DPN? What are the pain perception themes described as they relate both to HIV-PN and DPN? How does pain perception differ when measured by standard pain questionnaires as compared to pain narratives?

Neuropathy is a disorder that occurs within the context of a primary illness for both diabetes and HIV disease. People with diabetes are educated about the possible development of neuropathy and foot care, and referrals to podiatrists are incorporated into primary care and diabetic education (Leese, Stang, Pearson, & Scottish Diabetes Foot Action Group, 2011). Neurological complications occur in approximately 70% of

PLWHA, and the risk for developing neuropathy is well known among primary care physicians, but it is unclear how well patients understand the potential of developing HIV-PN or how these patients are educated. This study examined the question of whether patients are aware of developing neuropathy in both HIV and diabetes. Are these patients educated about neuropathy as a risk factor, and what is understood by these patients when experiencing sensations in the feet?

Hypotheses

The primary question this study addressed that involved the use of the quantitative data: Are there differences in how patients suffering from painful HIV-PN and painful DPN report pain? The following were the hypotheses that I intended to address:

1. Research H1: There are differences between painful HIV-PN and DPN as measured by the short-form McGill Pain Questionnaire (SFMPQ; Melzack, 1987).
2. Research H2: There is a difference in HIV-PN pain as compared to DPN as measured by the Visual Analog Scale (VAS; Gallagher, Liebman, & Bijur, 2001).
3. Research H3: There is a difference in HIV-PN pain as compared to DPN as measured by the Numeric Rating Scale (NRS; Farrar et al., 2001).
4. Research H4: There is a difference in HIV-PN pain as compared to DPN as measured by a subscale of the Brief Pain Intensity scale (scBPI; Keller et al., 2004).

5. Research H5: There are differences in levels of depression between painful HIV-PN and DPN as measured by the Beck Depression Inventory (BDI; Geisser, Roth, & Robinson, 1997).

Study Design

For this study, I performed posthoc analyses of data from a larger research study to determine whether differences exist between the chronic pain perception of patients with HIV-PN versus DPN. The study data were collected in an original study (Appendix A) entitled "The Experience of Chronic Pain in Neuropathic Pain and Back Pain: A Focus Group Approach." The original study examined the perception of pain measures between these two groups and a group with chronic low back pain during focus group sessions. This study used data collected during Visit 1 (screening) and Visit 2 (baseline) from a total of 23 participants (12 HIV-PN and 11 DSP).

Research Population

This study consisted of participants representing East Harlem in New York City. Every effort was made to represent the ethnicity and diversity of East Harlem, including Caucasian, African American, and Latino populations. The original study was an exploratory study, with a maximum of 36 participants from three chronic pain groups, but this study examined the two groups of participants (n = 23) who consented to participation in the HIV-PN group and the DPN group.

This study consisted of a random sample of patients drawn from a group of well-characterized HIV and diabetic patients who attended the clinics at Mount Sinai Hospital. Participants were selected based on specific inclusion/exclusion criteria that included the

definition of HIV disease with distal symmetrical polyneuropathy (e.g., peripheral neuropathy with pain) and type 1 and 2 diabetes with painful distal symmetrical polyneuropathy. All data have been deidentified and stored at the Icahn School of Medicine at Mount Sinai. Institutional Review Board approval (Icahn School of Medicine and Walden University) was provided before any analysis of these data sets for the study.

The participants had confirmed diagnoses of the presence of HIV-PN or DPN, as well as confirmation of HIV disease status (current CD4 counts, viral load copies, and pain medication usage). The diabetic participants had a confirmation of disease status (hemoglobin A1C levels, glucose, body mass index, and pain medication usage). A review of medical records supported the participant's medical status. The data are currently stored in an encrypted database at the Icahn School of Medicine at Mount Sinai (ISMMS), located in New York City, New York. These data can only be accessed by the study team, of which I am a member.

All participants met the study inclusion/exclusion criteria and had a diagnosis of HIV disease or diabetes and painful peripheral neuropathy with confirmation by a neurologist. Males and females were included, in addition to individuals of diverse ethnicities and educational levels. Participants needed to be able to read and speak English in order to take part in the interviews.

Sampling Procedure

All participants were randomly selected from the HIV and diabetic populations of East Harlem. IRB-approved advertisements were placed in the clinical areas of Mount Sinai, and participants were screened on the phone for major descriptors of neuropathic

pain disorder. Each participant consented with an IRB-approved consent form and was examined by a neurologist to confirm the diagnosis of painful peripheral neuropathy. The study consisted of the following assessments for each participant at the visits:

- All participants consented as part of the original project with an approved consent form by the IRB of the Icahn School of Medicine at Mount Sinai;
- Medical history and medications were documented, and a neurological exam was performed;
- The VAS, NRS, short-form McGill Pain Questionnaire (SF-MPQ; Huskisson, 1974; McCormack, Horne, Sheather, 1988; Melzack, 1987) and the Brief Pain Intensity scale (BPI; Cleeland, 1989)—all established and reliable scales in pain for varied populations including HIV-PN and DPN studies (Melzack, 1975, 1987; Dworkin et al., 2008)—were used to record the pain experience of the participants;
- Demographics, education, pain medications, HIV status (t-cell counts and viral loads), and diabetes status (hemoglobin A1c, and BMI) were obtained from each participant in the two groups;
- Transcripts of participant interviews were audio recorded to capture the participants' narratives about the pain history and experience of HIV-PN and DPN participants within the context of an observational study (Lekas, Siegel, & Leider, 2011; Rodjkaer, Soderman, Ostergaard, & Lomborg, 2011).

- The Beck Depression Inventory (BDI), a well-established tool for determining depression (Geisser, Roth, & Robinson, 1997), was used to determine levels of depression between the HIV-PN and DPN groups.

Conceptual Framework

This study adopted the process of using an interpretive phenomenological analysis approach (IPS; Smith, 2004). IPS, in the context of this study, examined the meaning of chronic pain as experienced by participants who had either diabetes or HIV disease and how these individuals managed and viewed life. IPS is a common qualitative research approach and is well suited for examining the chronic pain experience within the setting of two complex diseases. IPS has been used successfully to investigate chronic pain as it relates to resilience, overactivity, and opioid use (Andrews, Strong, Meredith, Gordon, & Bagraith, 2015; Blake, Ruel, Seamark, & Seamark, 2007; West, Stewart, Foster, & Usher, 2012). IPS encompasses the practice of merging psychological, interpretative, and idiographic elements to uncover the meaning of a phenomenon (Smith, 2004). This study examined the narratives (audio and transcripts) of these clinically well-characterized participants diagnosed with HIV-PN and DPN as they freely discussed the pain experience during Visit 2 of the original study. The study team decided to collect the narratives of each participant of his or her pain perception and history. The study team made this decision based on my suggestion because very little is known of the dialog that occurs when a patient describes the pain experience to the physician for treatment within the context of HIV and Diabetes. The opportunity to examine the phenomenology of the pain narrative experience within the context of HIV and diabetes could help in

understanding how these participants complete pain questionnaires or barriers that are related to an unknown factor. The purpose of this study was to explore these narratives to uncover themes of how patients with HIV are similar or different when describing pain from those patients who have diabetes. This study revealed how stigma or emotions play a role in chronic pain perception for HIV-PN and DPN patients. In DPN, patients are educated about neuropathy as a possible risk of being diabetic and are provided treatments and referrals to podiatrists on a regular basis (Sumpio, Armstrong, Lavery, & Andros, 2010). Diabetic patients are educated about how to examine their feet and how to speak to clinicians when having issues that are related to numbness, foot sores, or other foot problems. There is no evidence that the same type of education occurs in the HIV population despite the risk of developing HIV-PN. Education about the risk of HIV-PN is missing from the primary care physician and HIV patient dialogue. The incidence of HIV-PN is at a high level, yet it is unclear why patients are not informed about the risks and consequences of being diagnosed with painful HIV-PN. My study team determined that by enrolling 12 participants, given our awareness of a typical 20-25% no-show rate for this population, we would have enough participants that would afford an opportunity for saturation to occur on any theme or concept that was revealed. For this study, the participants provided individual narratives; whether a concept or theme would reach saturation within the confines of this study was unknown.

The narratives were examined to determine how these two groups of participants were diagnosed with neuropathy and what the signs and symptoms were prior to the neuropathy diagnosis and how these patients perceived and managed their chronic pain

symptoms. This study had potential to reveal a fundamental belief in these two populations about the diagnosis of neuropathy and the chronic pain state that might uncover elements of why treatments have limited pain relief. Furthermore, this study might reveal the emotions that patients experience when allowed an opportunity to freely discuss their pain with no preconceived agenda. Participants in this study were provided monetary compensation for their time and travel, but there was no perception of benefit that could be attributed, as in other pain studies where the patient received a pain treatment or placebo. The only benefit in this study was the opportunity to speak freely about the pain experience and have someone listen. The examination of the narratives in this study could demonstrate what is called "narratological distress," which Lavie-Ajayi, Almog, and Krumer-Nevo (2012) described as a struggle between two unwanted narratives of chronic illness and societal skepticism of the chronic pain condition. The process of using IPS as the framework to uncover the meaning represented by the narratives of these two groups had potential to reveal new possibilities for social change.

Finally, this study, through the narratives of these participants, provided an examination of language and descriptors as they relate to pain experiences and where there are possible gaps and differences from the pain history when compared to the story the pain outcome measures reveal. The IPS process of examining these narratives with an idiographic focus may offer unknown elements about these two populations that could help in measuring pain that has meaning versus providing a number or drawing a line on a scale. As medicine moves toward a model of "patient-centeredness" empowering the patient, patients' perceptions, culture, and socioeconomic status are of equal concern to

the physician as the clinical diagnosis (Mead & Bower, 2000). This study may increase understanding of what is not captured when using pain outcome measures and how to address and measure the chronic pain experience of these two groups more effectively.

Assumptions and Limitations

The potential limitations of this study included the following:

1. The comparison of the pain outcome measures might not reveal any new information that is not already reported in the literature.
2. Due to the nature of this study, the data collected might not be sufficient to provide generalizable data in relation to the pain experience of these two populations.
3. The narratives of participants sharing their pain history story might be incomplete or insufficient in descriptors of the pain experience due to the nature of this study.
4. The number of participants completing the pain outcome measures might not be sufficient to provide a significant representation that is generalizable to larger populations.
5. Because the study used pre-existing data, the narratives of this urban population might not be generalizable to participants in other regions.
6. The study compared these two groups, with data initially collected for understanding the cognitive process of how these patient populations complete pain questionnaires; therefore, there may be unanswered questions due to the limitations of the dataset.

This study relied on a convenience sample of participants who were enrolled in a larger study that examined the cognitive processes used when making selections on standard pain outcome measures. The study enrolled participants who were members of the local HIV and diabetes clinics who were familiar with participating in research. The data for this study was obtained during screening and the baseline visit. The screening visit captured eligibility, demographics, and health status. During the baseline visit, average pain levels were collected using a packet of standardized pain outcome measures. After each participant had completed the pain measures, he or she engaged in the recording of a narrative about the pain experience, with minimum interaction or probing by the interviewer. These dialogues were recorded and transcribed. The transcriptions of the focus group for this study have been analyzed and published (Robinson-Papp et al., 2015). The narratives collected during the baseline visit have not been analyzed, nor does the study team anticipate analyzing these data. These narratives provide an opportunity for this study because they are unique narratives of these two pain groups allowing the language and story to be examined to determine if there are similarities or differences that are unique in what the participants shared about the chronic pain experience of neuropathy.

Generalizability

In the original study, every effort was made to include participants who were from the general population of the clinics for HIV and diabetes, but the original study team went a step further in confirming the diagnosis during the screening visit. One factor that may limit the generalizability of this study is the lack of a requirement for a specific

amount of pain for a participant to be included. In pain treatment clinical trials, a standard requirement is that subjects have a pain score equal to or greater than 4 on the Numeric Pain Scale for a minimum of 4 days within a 7-day period. The original study did not define a required, standard amount of chronic pain that would serve as a criterion for individuals to be included. While this study may not be able to address the clinical trial practices of including subjects with a specific amount of pain, this study may serve as the basis for inferences concerning the population of patients who attend urban clinics and have chronic pain. Clinical trial practices may be informed by this study when defining the inclusion/exclusion criteria for these populations for future studies on pain treatments.

Definition of Terms

The following are terms used throughout this study:

*Neuropathy (PN)***:** Damage to the nerves that causes a misfiring of communication from either peripheral or central systems or both to the brain, causing sensations of burning, tingling, shooting pain, or numbness. PN can be the result of a disease state (HIV or diabetes), exposure to toxic chemicals, or an unknown cause. Other symptoms related to neuropathic pain are sensitivity to light touch, balance disturbances, and leg or foot weakness (Treede et al., 2008).

Chronic pain: Pain that persists beyond 6 months or more; it can be constant or intermittent, but it is always present (Furlan, Sandoval, Mailis-Gagno, & Tunks, 2006).

Hermeneutics: The study of written, verbal, or nonverbal meaning. In the context of this study, there was an examination of participants' pain stories to understand the

verbal communication of the pain experience in these two populations (Boden & Eatough, 2014).

Narrative: The exchange between the clinician/researcher and patient/participant where the patient/participant is telling the story of his or her specific circumstances. The story includes culture, language, body language, and emotions for the clinician/researcher who is listening/recording within the context of the illness and life experience being shared (Charon, 2001).

*Polypharmacy***:** The process of having prescriptions for more than one medication at a time to treat chronic conditions. Typically, a patient is taking more than 6 medications for a variety of illnesses (Jongen, Hans, Benzon, Huygen, & Hartrick, 2014; Koberlein et al., 2013).

Psychoneuroimmunology (PNI): The study of how the systems of psychology, neurology, and immunology communicate within the human body (Uhlig & Kallus, 2005).

Phenomenology: The philosophy of the components of the human experience from the perspective of the individual. In the context of chronic pain, it involves the selection of language and story of the pain experience from the person's perception (Boden & Eatough, 2014).

Qualitative research: A process of collecting data through interviews, patient written documents, focus groups, narratives, stories, and researcher observations in order to capture the complex perceptions of patients within the context of health and medicine (Tong, Sainsbury, & Craig, 2007).

Social Change Implications

Social change may develop through revealing the similarities and differences in pain perception between HIV-PN and DPN, and such change is needed for these patients. Treatments and education not yet developed could be identified. Pain disorders are infrequently compared within the context of pain research. This study offers a comparison not only of pain outcome measures, but also of pain narratives of these two populations. The study findings may provide initial indicators of psychological, behavioral, or environmental elements that may contribute to the pain experience in HIV-PN as compared to DPN. Understanding the differences in pain perception between these two groups of patients could help in efforts to improve clinical practices, to inform the patient population of these factors, and to develop comprehensive treatment approaches for symptom relief. Furthermore, the study may reveal issues about how pain is measured between these groups and what issues may contribute to the challenges related to using pain scales. Understanding the differences between HIV-PN symptoms and those experienced by the DPN population could provide a biopsychosocial model for treatments of HIV-PN, which would lead to educating patients on focused coping skills, and possibly increased understanding of what contributes to the ineffectiveness of current pain treatments. Ultimately, the ability to raise the awareness of what these two populations perceive when experiencing chronic pain would lead to improved quality of life for these individuals and decrease their levels of isolation and depression.

Reducing the burden of painful HIV-PN and DPN specifically for those individuals who live in underdeveloped countries or those populations that are

educationally, socially, and economically challenged would be an immense opportunity for social change, as HIV and diabetes continue to be leading global medical problems. The underdeveloped areas of the world where HIV disease is highly prevalent have the least amount of resources yet have the greatest risk of developing painful HIV-PN due to the use of the antiretrovirals that have shown to have increased incidence of HIV-PN due to neurotoxicity (Ortblad, Lozano, & Murray, 2013). There is ever-increasing urgency to find therapies that reduce the painful symptoms of HIV-PN and DPN. Increased knowledge of how these individuals experience and perceive pain may be of help to improve quality of life for those infected with HIV or diagnosed with diabetes and provide symptom relief through the development of holistic treatments that address elements revealed by this study.

Role of the Researcher

Removing potential bias from a study that is qualitative in design is critical in assuring that the researcher maintains a neutral viewpoint in the interpretation of the narratives that are part of the qualitative data. The original narratives were captured by other researchers; I was only involved in several of the initial interviews. The capturing of the narratives of the participants' pain history was my original intent and not one that the investigational team felt strongly about including. It was my idea to explore the pain narrative that a participant might give at an initial encounter with a clinician when seeking treatment as compared to completing a pain questionnaire. The original purpose of the study was to uncover cognitive processing when comparing how a participant

selects a pain measure on a standard pain scale versus when sharing a narrative of the pain experience.

During the analysis process, it was my intent to redirect my observation to seek in an open and unbiased approach to uncover the themes and common terms that the participants used to explore areas that were both shared and uncommon to the population. I had access to medical student volunteers from the Icahn School of Medicine at Mount Sinai, who could, in a blinded fashion, review the narratives and confirm the themes and/or common language that was identified. Additionally, Dr. David Dorfman from the initial study was available to review and confirm the findings of the narratives that were reviewed. Every effort was made to approach the examination of these data from a neutral point of view, one that has become part of my expertise as I have engaged in several studies in which I have conducted patient interviews and focus groups, providing a neutral and open process so that the participants have an opportunity to share without prejudice. I have experience in the practice of mindfulness and improvisation techniques from my work in music and theater with the director Rhoda Levine (Levine, n.d.). As a researcher, I seek to engage patients in an open unbiased conversation. This process opened an ongoing dialogue with patients about self-harm, substance use, and the issue of trust when seeking pain treatments (George, Wongmek, Kaku, Nmashie, & Robinson-Papp, 2017; Robinson-Papp et al., 2015; Robinson-Papp & George, 2015). Finally, my chair, Dr. Jay Greiner, and the committee were available to offer assistance and guidance during the qualitative review process to further reduce bias during the process of analysis.

Ethical Considerations

The Institutional Review Board (IRB) of the Icahn School of Medicine at Mount Sinai provided an ethical review that expired on March 29, 2017, when the initial study and analysis for this study was complete. Ethical review was submitted to the Walden University IRB, and approval was received on January 22, 2016. All the data that were available from the original study were deidentified, which decreased the risk for loss of privacy and confidentiality. The risk-benefit consideration was extremely low because the study used preexisting deidentified data, yet risk of loss of privacy was always possible due to the uniqueness of the narratives. Every effort was made to maintain the privacy of these participants, and references to names or specific identifying elements of the narratives were not used within the context of this study.

Chapter 1 Summary

This study has the potential to increase knowledge of how HIV-PN and DPN differ in how pain is perceived. Pain outcome measures (VAS, NRS, BPI, & SF-MPQ), demographics, medical history, medications, and patient pain narratives were analyzed and comprised the elements of data for this study. Awareness of how chronic neuropathic pain contributes as a risk factor for increased isolation, diminished quality of life, and depression in these two populations may provide insight into a holistic medical model for pain treatment. Examining the differences and similarities in how patients with HIV-PN and DPN report and describe pain could lead to a shift in how treatments are developed and measured and could be used as an educational model for comprehensive approaches to pain treatments for HIV-PN and DPN. This study might also broaden awareness of

how pain perception can be elicited from patients who are experiencing chronic neuropathic pain to have a deeper understanding of patients' suffering. Expanding how the medical community grasps the chronic pain experience may shift how practitioners discuss pain and select pain treatments. The ability to maintain quality of life for individuals diagnosed with HIV-PN or DPN may aid them in finding the ability to engage in useful lives. The impact of social change may be even greater for those individuals with painful HIV-PN or DPN in creating a dynamic wherein patients with chronic pain are empowered by a practitioner-patient alliance that fosters the promotion of increased self-care and ability to preserve the lifestyle that a patient had before being diagnosed with painful neuropathy.

Chapter 2: Literature Review

Introduction

HIV and diabetes mellitus are two major illnesses that have the neurological disorder of painful peripheral neuropathy in common. There are no approved treatments for HIV-PN or DSP, despite numerous clinical trials. There are FDA-approved medications for pain relief in DPN, whereas HIV-PN has had multiple clinical trials with similar agents, and no approved therapies have shown to be better than placebo for pain relief. This situation poses the following question: Are there unique differences or similarities between these two populations that suffer from pain due to neuropathy? In this chapter, the goal is to review the situation whereby the physiology is not well understood in both of these diseases, yet the clinical presentations are very similar. This study was intended to compare these two groups in terms of painful peripheral neuropathy. It is unclear whether there is literature that describes the differences and similarities of neuropathy in these two disorders. As patient-centered care is the new paradigm in healthcare, understanding the distinct features as well as the similarities of these two populations from the patient's perspective can provide powerful information for future research, education, and clinical care.

HIV and Diabetes Mellitus

HIV disease is a global illness that has moved into its third decade of existence. While new infections have diminished, concern for providing health care and preserving quality of life while PLWHA live normal lifespans has defined the direction of healthcare for this population. In countries where PLWHA have access to antiretroviral medications

and consistent care, HIV disease has become a chronic illness. In other countries where care is inconsistent and medications are scarce or unavailable, the incidence of HIV continues to increase, placing additional burdens on available resources (Ortblad, Lozano, & Murray, 2013). Approximately 2.5 million individuals are infected with HIV, with larger percentages of new infections occurring in African and Latino communities and among those over the age of 55 (Centers for Disease Control and Prevention.[CDC], 2013; WHO, 2015).

The burden of HIV disease is complicated by the comorbidities that develop because of the viral infection, combination antiretroviral (cARV) treatments, aging, or a combination of these elements, or for reasons yet unknown. The nervous system acts as a compartment in the body, with the blood-brain barrier acting as a natural system of cells that protect the brain. Immune system cells can pass through the blood-brain barrier but can block some of the cARV treatments. The blood-brain barrier creates the possibility for a discordance of viral activity existing in the nervous system versus the activity in the blood (Calcagno et al., 2014). Neurological complications exist in approximately 70% or more of the HIV population. The most common of the neurological complications is known as *distal symmetric polyneuropathy* (DSP) or *HIV-associated distal polyneuropathy* (HIV-PN; Ellis et al., 2010; Estanislao, Morgello, & Simpson, 2005; Gonzalez-Duarte, Cikurel, & Simpson, 2007; Wullf, Wang, & Simpson, 2000). HIV-PN occurs in approximately 50-70% of the HIV population, with approximately 30-50% experiencing painful, debilitating symptoms (McArthur, Steiner, Sacktor, & Nath, 2010).

Diabetes mellitus (DM) is a chronic illness that is caused by metabolic disorders. These metabolic disorders create an inability for the body to metabolize or produce insulin due to the malfunction of the islet cells found in the pancreas (type 1) or inability of the cells of the body to metabolize insulin (type 2; CDC, 2014). DM is of global concern, with projections of 592 million cases worldwide by 2035. The burden of diabetes and its associated complications increases health care use, reduces quality of life, and increases loss of employment (Mehra, Merchant, Gupta, & Potluri, 2014). DM, similar to HIV, has many complications and comorbidities (vasculopathy and retinopathy), but peripheral neuropathy is the leading neurological disorder that contributes to nontraumatic amputations, depression, and foot ulcers in approximately 50%, with painful DPN occurring in 20-30% (Kaku, Vinik, & Simpson, 2015).

In this chapter, I look at the disorders of HIV-PN and DPN, exploring symptoms, and pain treatments. Understanding the similarities and differences between these two populations could contribute to increased awareness of why there are approved treatments for painful DPN while pain relief treatments for HIV-PN elude FDA approval, as well as why neither disorder has a treatment that repairs the resulting nerve damage and loss. Understanding the complexities of pain perception in individuals with HIV-PN and DPN can help in the development of future pain outcome measures, clinical trial designs, behavioral treatments, clinical care, and education.

Literature Review

Literature Search Process

The resources used for the review of the literature described in this chapter included PubMed, PsycINFO, the Walden University Library, and the Icahn School of Medicine at Mount Sinai Library. Other sources of information included the CDC website, WHO website, and textbooks on peripheral neuropathy and pain. The process of reviewing the literature began with selecting keywords that would potentially offer the most recent peer-reviewed research in the field. These keyword search terms were *HIV peripheral neuropathy, HIV-distal symmetric polyneuropathy, diabetes mellitus, diabetic neuropathy,* and *chronic neuropathic pain, pain perception, and chronic pain.* The search was centralized on the combination of HIV disease and DM, with keywords to access as broad a reach of literature as was available on these topics in the field. When combinations of terms were not successful in revealing any relevant literature, they were broadened (e.g., *HIV disease* and *diabetes;* or *HIV, diabetes*, *neuropathy,* and *chronic pain; chronic illness* and *pain*) to expand further what would be relevant literature available on these topics.

Neuropathic Pain

Neuropathic pain has recently been redefined by the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain (NeuPSIG; (Haanpaa et al., 2011) as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory nervous system" (p. 14). The definition is broad and can include many clinical presentations, but both HIV disease and DM include the

complexity of developing this common neurologic disorder called *neuropathy*. In many patients, the clinical evidence can be present upon exam, but the patient lacks any awareness of this disorder due to a lack of or misinterpretation of symptoms (Ang, Jaiswal, Martin, & Pop-Busui, 2014; Kaku, Vinik, & Simpson, 2015; Schütz & Robinson-Papp, 2013). Clinical presentations of these patients demonstrate diminished reflexes of the ankles and knees, with reduced sensory responses in the legs to cold, heat, and vibration. Often, a clinical exam is supported by abnormal objective tests such as electromyography and nerve conduction tests. Small percentages (5-10%) of patients are not clinically diagnosed with HIV or DM but present with neuropathy symptoms to a clinician. They discover the primary diagnosis (HIV or DM) of learning the source of injury to their nervous system (Chiles et al., 2014; Nicholas et al., 2007).

The pathophysiology of both illnesses is not well understood. DPN is thought to be caused by lack of stable glucose levels coupled with malfunction of the vascular system that impacts limbs, causing injury to the nerve fibers (Ang et al., 2014; Edwards, Vincent, Cheng, & Feldman, 2008). HIV disease also has complicated processes that cause nerve damage. HIV potentially destroys neurons by causing the mitochondria to malfunction in the peripheral nerves. The second process that injures the nervous system relates to treatments for HIV disease, specifically stavudine, didanosine, and zalcitabine. These drugs are from an older class of drugs called *nucleoside reverse transcriptase inhibitors* (NRTIs). This class of drug is known to have side effects that injure the nervous system by creating neurotoxic byproducts that are thought to damage the neuron mitochondria. NRTIs are not used in areas of the world where newer classes of drugs are

available for HIV disease treatments unless an individual has no other option for viremic control. These NRTIs are used in less developed countries because these drugs can be provided as generics and are more affordable. These medications have created an enormous burden in countries where developing neuropathy can bring about an inability for individuals to farm, travel by foot, or perform manual labor due to pain, gait disturbance, or numbness as a result of developing neuropathy (Makinson, Moing, Kouanfack, Laurent, & Delaporte, 2008).

Advances have been made in understanding neuropathy and potential areas to target for future treatments, but there are still no drugs available to prevent or reverse neuropathy. Pain relief medications are available to treat the symptoms of neuropathy. These treatments are varied and include anticonvulsants, tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and opiates. The only drugs FDA approved for DPN are pregabalin (Lyrica®), duloxetine (Cymbalta®), and tapentadol (Nucynta® ER), yet many drugs are used in an off-label fashion to aid DM patients for pain relief. HIV-PN has no approved pain relief treatments despite many clinical trials to investigate potential medications. Behavioral treatments have shown to be effective in the HIV-PN population, with a recent study of hypnosis showing a benefit after a 17-week period post self-hypnosis training (Dorfman et al., 2013). Past studies of acupuncture showed no benefit in HIV-PN as compared to sham acupuncture (Schlay et al., 1998) and a study of the supplement acetyl-L-carnitine was also shown to be no better than placebo (Valcour et al., 2009).

Only three agents have had positive results in treating painful HIV-PN in randomized placebo-controlled studies: recombinant nerve growth factor (rNGH), 8% capsaicin patch, and cannabis. None of these agents have been FDA approved, and PLWHA who have neuropathy are only capable of accessing treatments that are "off-label" and lack FDA approval. There is an urgent need to provide pain treatments or regenerative nerve treatments to increase the quality of life for those suffering from neuropathy in these two diseases.

HIV Distal Symmetrical Polyneuropathy

HIV-distal symmetrical polyneuropathy (HIV-PN) has been a recognized disorder since the beginning of the HIV/AIDS epidemic (William et al., 1983). The pathogenesis of HIV-PN is not well understood. Scientists believe that HIV or the cARVs damage neurons, which leads to a diagnosis of HIV-PN and requires a comprehensive neurological exam to determine the presence of this disorder. Neurologists as compared to primary care providers are better equipped for recognizing and diagnosing PN (Skopelitis et al., 2006). The signs and symptoms are often missed by a primary care provider or an infectious disease practitioner. The clinical signs of HIV-PN include absent or decreased ankle and/or knee reflexes, reduced or absent sensory perception (vibration, pinprick, and temperature), and symptoms of burning, tingling, and numbness (Gonzalez-Duarte et al., 2008; Kaku, Vinik, & Simpson, 2015; Verma, Estanislao, & Simpson, 2005). Positive symptoms are typically described as burning, "pins and needles," and sharp pain, while negative symptoms are numbness, awkwardness in walking, or heaviness or squeezing sensations (Elliott & Simpson, 2012; Kaku, 2015).

HIV-PN is often underdiagnosed because of lack of awareness of these symptoms; patients may believe that these symptoms are related to their HIV disease and not a separate disorder.

Primary care providers seldom check a patient's reflexes or gait, or perhaps they misunderstand the signs of HIV-PN (Gonzalez-Duarte et al., 2008; Kaku & Simpson, 2014; Skopelitis et al., 2006) until a patient begins complaining of pain in his or her feet or difficulty with walking. The primary care provider for the HIV population is focused on monitoring the course of HIV disease and the side effects of cARV therapy or other comorbidities that are prevalent in the HIV population (coinfection with hepatitis C). HIV-PN is not a disorder causing death, but when not properly diagnosed or untreated in a patient, it can lead to poor quality of life, social isolation, and difficulty in functioning with an increase in medication usage (Davis, Robinson, Le, & Xie, 2011; Stavros & Simpson, 2014).

HIV-PN Clinical Trials

The three agents that have shown positive results in clinical trials for treating painful HIV-PN are 8% capsaicin patch (Qutenza®), cannabis, and recombinant nerve growth factor (rNGF). None of these treatments have been approved by the FDA for painful HIV-PN in the United States, and the only treatments available are symptomatic treatments accepted for other types of neuropathic pain disorders (e.g., diabetic neuropathy, postherpetic neuralgia; Attal et al., 2011).

In Europe, the capsaicin 8% patch is approved for nondiabetic neuropathic pain (Wagner, Roth-Daniek, Sell, England, & Kern, 2012). Treatments with the capsaicin 8%

patch require trained physicians to administer and can be time consuming, and some individuals do not respond to this treatment, which presents a limitation for the use of this medication. The capsaicin 8% patch is only available in the United States for individuals diagnosed with postherpetic neuralgia. Treatment with this agent would only be available as an "off-label" treatment for people with HIV-PN (Mou et al., 2014). Very few insurance policies approve this agent in the United States, and the cost of the patch can be prohibitive.

The second treatment to show benefit in clinical trials for the treatment of HIV-PN is cannabis. Smoked cannabis was shown to have benefit for the treatment of neuropathic pain, with a reduction in pain of >30% as compared to a placebo-cigarette, with few side effects (Abrams et al., 2007). The use of marijuana in the HIV population has been well known to help with appetite, anxiety, depression, and pain relief, specifically pain relief from HIV-PN (Cinti, 2009; Woolridge et al., 2005). Prescribing and managing marijuana for a patient with HIV-PN is controversial given current drug enforcement laws. The use of marijuana is illegal from a federal perspective. Twenty-eight states have approved the use of medical marijuana within specific guidelines (specific medical conditions, number of ounces, and plants), but the side effects that occur with marijuana use (e.g., greater exposure to carcinogens than with cigarettes and possible cognitive and immune dysfunction, drug interactions) make prescribing a risk-benefit consideration.

The third drug that has shown benefits in treating painful HIV-PN in clinical trials is recombinant nerve growth factor (rNGF; McArthur et al., 2000). A double-blind

placebo-controlled study of 270 participants with two doses of a subcutaneous injection of rHGF given twice weekly showed pain relief for 18 weeks. rNGF was studied for the potential to regenerate damaged nerve fibers, in contrast to other studies that were done to determine whether a study drug would modify the pain experience. A 48-week open-label study that followed the double-blind study involved 200 participants and showed similar results to the earlier study (Schifitto et al., 2001). Due to negative results from a diabetic phase III clinical trial, the sponsor (Genentech, Inc.) decided to discontinue any further development of this agent (Apfel, 2002). The reasons for stopping further development of this agent may have been related to the placebo effect in the earlier trials, formulation issues, and profitability. A final issue was related to evidence of whether changes were occurring within the peripheral nerves to stimulate repair. HIV clinical trials showed improvement in pain, but no changes were seen in objective findings for neuroregeneration.

Lack of treatments for painful HIV-PN poses an urgent need in the HIV population because aging increases the risk of developing PN (Simpson et al., 2006). Biopsychosocial treatments need to be investigated in parallel with agents that either relieve painful symptoms or will repair nerve damage. On May 4, 2012, Pfizer announced the stopping of a Phase 3 multicentered global study of pregabalin in the HIV-PN population. The study had enrolled 246 of the targeted 416 participants. The reason for stopping the study was an interim analysis that showed that improvements in symptoms were no better than with placebo. This was the second attempt for Pfizer to conduct an HIV-PN clinical trial of pregabalin (Simpson et al., 2010; Simpson et al., 2014). The

challenge and financial burden of clinical trials for an investigative agent to treat the HIV-PN population have become less attractive to the pharmaceutical industry. Multiple past studies have been unable to demonstrate a drug that could be approved by the FDA (McDermott & Dworkin, 2014). In personal conversations with individuals in the pharmaceutical industry and contract research organizations (CROs), I have understood that there is a lack of recognition of HIV-PN as a problem. Several CROs and pharmaceutical companies have a poor understanding of the overall status of HIV-PN as a chronic problem and as a result have targeted other potential pain disorders (small fiber neuropathy or postherpetic neuralgia). These circumstances place urgency upon the scientific community to increase the understanding of why painful HIV-PN is such a complex and challenging disorder to treat and to continue to investigate why no treatments are available for this population.

HIV-PN Pain Treatments

All treatments available for painful HIV-PN are "off-label" medications, which are approved by the FDA for other pain conditions (e.g., diabetic neuropathy and postherpetic neuralgia). Off-label treatments for HIV-PN have not shown to significantly alleviate patients' pain (Attal et al., 2011) or improve the quality of life or ability to function (Ellis et al., 2010). The initial assessment for pain relief is to determine whether the patient is on any neurotoxic treatments (i.e., antiretrovirals; Gonzalez-Duarte et al., 2008), and whether there are any behavioral or nutritional components that may contribute to peripheral nerve damage (e.g., consumption of alcohol, or low vitamin B12, and D levels; Turner, 2008).

Alternative and complementary therapies can be a first approach to treament because of the many drugs that are used to treat HIV disease, but little has been substantiated in the literature of the effectiveness of these therapies (Liu, Manheimer, & Yang, 2005). Acupuncture, massage, biofeedback, hypnosis, and lifestyle modifications can provide some pain relief (Dorfman, 2008; Gonzalez-Duarte et al., 2007; Nicholas et al., 2007), but very little is known about the combination of alternative treatments and oral pain medications. Off-label pain treatments often used are antidepressants (amitriptyline and Cymbalta), antiepileptic drugs (gabapentin and pregabalin), and topical agents (lidocaine and capsaicin). Non-steroidal agents (NSAIDS; acetaminophen and ibuprofen) have no proven benefit, but can provide some pain relief. The many drug regimens that the HIV population make taking NSAIDS a challenge for the liver to process, therefore the use of NSAIDS is an unappealing alternative (Liss, Rattan, & Lewis, 2010).

Opioids (e.g., Vicodin, Percocet, and Oxycodone) have significant risks. Onen and colleagues (2012) performed a study of an HIV outpatient clinic to evaluate the use of opioids for treatments related to HIV-PN. The authors intended to characterize the use of opioids and to determine what clinical predictors correlated to opioid use. The study included 659 participants, which showed opportunistic infections (current and past), HIV-PN, depression, and coinfection with Hepatitis C as predictors of repeat opioid use. A subgroup was analyzed to determine opioid prescribing practices. The study revealed that 63% of the participants in the subgroup reported no pain relief and the random particpants selected to be screened for illicit drug were all positive. The challenge of

managing opioid use by medical providers in the HIV population is less than optimal. Krashin, Merrill, and Trescot, (2012) conducted a literature review looking at the use of opioids in HIV population for pain. The study raised the following issues related to prescribing opiates: (a) issues of drug-drug interaction between cARVs and opioids; (b) the complexity of capturing a patient's medical history including substance use or psychiatric diagnoses; and (c) the complication of the necessary documentation of an agreement between the clinician and patient. Using opioids in the HIV population is not a common practice and may be due to the primary clinician's limited time to accommodate a risk-benefit assessment; therefore, many of these patients are referred to pain management clinics, where access to available appointments can be weeks in the future, often patients go untreated. The rationale for a combination of drugs or polypharmacy is a possible alternative (Finnerup, 2010; Gilron, 2005). Polypharmacy has shown to be useful in the treatment of diabetic neuropathy or postherpetic neuralgia. The use of polypharmacy in the HIV-PN population should be considered with caution for PLWHA who are refractory to other pain treatments. The complexity of antiretrovirals and drug-drug interactions can make polypharmacy an undesirable approach due to the potential side effects and increased clinician oversight.

Risk Factors of HIV-PN

Aging, lower t-cell measures (nadir t-cells), older anti-retroviral treatments (d-drugs; didanosine, stavudine, and zalcitabine), and physical height are the leading risk factors for the development of HIV-PN (Anziska, 2012; Cherry et al., 2009; Simpson et al., 2006). A key risk factor in developing HIV-PN has shown to be exposure to

neurotoxic drugs (cART or d-drugs, or anti-tuberculosis medications, and pneumocystis pneumonia prophylaxis). The HIV-PN clinical presentation cannot be distinguished between HIV-PN caused by the virus or by exposure to neurotoxic drugs. Simpson (2006) and colleagues, performed a study designed to create a predictive model to understand the potential risk of developing painful HIV-PN. The two specific risks presented were: 1) The use of neurotoxic antiretrovirals. 2) A diagnosis of non-painful HIV-PN. Individuals with these two specific risks were 20% more likely to develop painful HIV-PN over time. The CDC (2013) predicts by the year 2020, 50% of the HIV population will be over the age of 55 due to the increased effectiveness and accessibility of antiretrovirals. Subsequently, the use of neurotoxic antiretrovirals in third world countries increases the risk of PLWHA who will suffer from neuropathy with little to no options for treatments or the ability to discontinue the neurotoxic antiretrovirals. The possibility for scores of the aging HIV population to be suffering from painful HIV-PN could become a present reality. A better understanding of how to diagnosis and provide pain relief needs to be found.

Understanding the pathology of neuropathic pain, coupled with the subjectivity of pain outcome measures reported by PLWHA, continues to make PN in the context of HIV disease a challenge to effectively diagnose and treat (Dworkin et al., 2005; Ellis et al., 2010). PLWHA are incapable of living a quality life in the context of neuropathic pain, making HIV/AIDS a global concern for the loss of productive years. HIV/AIDS is the sixth leading cause of loss of productive years, and neuropathy contributes heavily to depression, anxiety, and isolation. The scientific community must make finding

treatments for pain relief or nerve repair for PLWHA an important priority (Lucey et al., 2011).

Diabetic Distal Symmetrical Polyneuropathy

The neurological disorder of distal symmetrical polyneuropathy is the most prevalent disorder diagnosed in approximately 50% of individuals diagnosed with DM with the incidence occurring higher in Type 2 disease than Type 1 (Ang et al., 2014; Kasznicki, 2014). Approximately 20%-30% of these individuals have painful DSP. Scientists are still unraveling the process of how the nerve fibers are damaged in the presence of this disease; the theory centers on the fluctuations of glucose and the lack of vascularity as the contributing factors to the peripheral nerve damage. (Ang et al., 2014). DM patient's feet are regularly examined by the treating physicians to make sure that there are no foot ulcers or injuries that are not healing. Amputations are well known potential risk in diabetics. Patients can have either reduced vascularity caused by the DM or numbness caused by DSP both increasing the risk of infection and wounds that are not healing, both problems could result in an amputation. Patients can have other physical symptoms (itching and tingling) that could lead a patient to engage in self-injury creating an increased risk of amputation (Dorfman, et al., 2014).

People with diabetes are aware of the risk of developing DPN and are encouraged to include a podiatrist as a component of clinical care for DM. Patients are educated about glycemic control and foot care once diagnosed with DM. The risk of amputation is significant in this population and therefore increased awareness of neuropathy and the potential risks of foot ulcers, infections, and injuries are taken very seriously because

they can lead to depression, loss of function, and morbidity. Close to 4.6 million deaths occurred in 2011 due to diabetes (Armstrong & Andros, 2012). Amputations have increased the mortality rate for people living with diabetes within five years post amputation. Neuropathy is the first step in the potential development of foot ulcers, infections, and amputations (Mehra et al., 2014). Neuropathy is a major risk for the development of a diabetic foot ulcer (DFU) and can be an indicator of future decline. DPN is a major indicator of increased risk for depression, decreased mobility, and a major risk for DFUs. The price of diabetic foot care increases healthcare costs by approximately 1.5 billion US dollars annually (Hicks et al., 2014). Educating and understanding how patients perceive the diagnosis of DPN and symptoms in the feet and foot care could add to the increased awareness of future complications. Patients who maintain glycemic control and proactively engage in preventive foot care can help reduce the cost of healthcare utilization.

DPN Pain Treatments

Many of the same treatments that are used for painful DPN are used as "off-label" treatments for painful HIV-PN and DPN. FDA approval for the treatment of DPN has also been challenged by failed studies. Pain treatment is one of the primary goals because treatments haven't shown to be effective in regenerating or repairing the damaged nerves. Known drugs are non-steroidal anti-inflammatories (NSAIDs), anti-epileptics, antidepressants (tricyclics, SSRIs and SNRIs) and opiate based treatments (tramadol, oxycodone, and morphine). Three drugs have shown an improvement in pain, pregabalin (Lyrica®), duloxetine (Cymbalta®), and tapentadol (Nyucenta®). All are FDA approved

for the treatment of DPN (Albers & Pop-Busui, 2014; Vadivelu et al., 2015). In the United States, there are many more individuals suffering from DPN than have access to private insurance or can afford other types of treatment (i.e., vitamin supplements and acupuncture). The DPN population has commonly tried alternative treatments like HIV-PN, yet there is limited clinical evidence of effectiveness in some of these alternative therapies (Galuppo, Giacoppo, Bramanti, & Mazzon, 2014). These treatments include over-the-counter supplements (B vitamins, alpha-lipoic acid, and primrose oil; Gomes & Negrato, 2014; Khalil, 2013), capsaicin creams, lidocaine patches or transcutaneous electrical stimulation (T.E.N.S) unit (Vorobeychik, Gordin, Mao, & Chen, 2011; Shaqura, et al., 2014). The TENS unit uses the concept of disrupting the pain pathway to the dorsal root ganglia in the spine and creates an interrupted electrical path for the pain response and therefore decreases pain perception. The pain relief is relatively short-lived therefore, TENS units are being developed to stay at low levels in the body and provide a continuous electrical disrupt in the pain pathway. These units are not always available or affordable, nor are they easily applied, and maintained, but for some individuals with intractable pain without any relief from oral medications, the TENS unit offers possible relief (Pieber, Herceg, & Paternostro-Sluga, 2010).

Another device that is in development is monochromatic infrared photo energy (MIRE; Harkless, DeLellis, Carnegie, & and Burke, 2006). This device consists of four pads each containing 60 infrared diodes. Each pad can be attached to areas of the foot and leg that can be connected to a central unit that controls the production of the infrared photo energy. The concept behind this device is to encourage blood flow in the lower

extremities that can aid in repairing the peripheral nerves in diabetes. Harkless, (2006) collected the data from 2239 subjects who received treatments with the MIRE unit. These subjects were predominantly diabetics and all were confirmed to have neuropathy and peripheral sensory loss. After being treated with the MIRE unit, patients with numbness and pain improved. Yet, in a later study (Lavery, Murdoch, Williams, & Lavery, 2008; Nawfar & Yacob, 2011) of 69 subjects who were randomized to receive either the MIRE treatment versus sham did not demonstrate positive results. The sham treatment was a replica of the MIRE unit with deactivated infrared diodes. Sham treatment consisted of light and warmth (37 degrees) were emitted from the unit. At the completion of the study, the MIRE treatment was no better than the sham. The results were surprising because of the previous treatments and studies (Cliff, Kasser, Newton & Bush, 2005; Powell, Carnegie & Bush, 2006) had shown improvements in pain and function. The MIRE treatment, while it could be of benefit in pain reduction and improved sensation, is not covered by Medicare; therefore, making accessibility limited to those who can pay for the treatment. Many off-label treatments are not covered by insurers for the treatment of DPN or HIV-PN and the rationale of using these expensive and uncertain treatment outcomes make the ability to find pain relief a substantive challenge.

Risk Factors of DPN

Improving the Hemogloblin A1c level (HgA1c; a lab test that measures how much glucose binds to red blood cells over a 2-3-month period) for both individuals with Type 1 and Type 2 DM is the primary goal in preventing DPN. The process of managing homeostasis of blood sugar can be difficult for individuals where resources are limited or

culture, where rice and potatoes are dietary staples. A second risk factor for developing DPN is the length of time an individual is diagnosed with DM. Type 1 diabetics are at greater risk of developing PN, but with improved HgA1c levels, the rates of DPN are relatively lower than Type 2 diabetics (CDC, 2014). A third risk factor for developing PN is kidney disease. Toxins increase in the bloodstream and create a challenge for the kidneys to process. As a result, many people with diabetes are on dialysis and have difficulty eliminating the toxins in the blood that further damage the peripheral nerves. Other risks are smoking cigarettes and alcohol use both can contribute to damage of the vascular system that contributes to increasing damage to the peripheral nerves. People with diabetes are educated to control blood sugar and to examine their feet every day because of the risk of foot ulcer and amputation (Kasznicki, 2014). Foot care is a dominant theme in the diabetic's arsenal of care besides oral medications, diet, and weight management (Chiles et al., 2014).

Comparison of HIV-PN to DPN

In HIV-PN, the concept of foot care is not a dominant issue that is considered by clinicians. This difference may be an important contrast between these two populations that this study can potentially address. The ability to teach appropriate foot care for the prevention of amputations in the DM populations and perhaps to support function and gait in the HIV-PN population would be an interesting theme to consider within this study. When examining the literature, there are no studies or reviews in peer-reviewed journals that address comparing these two populations. Some studies discuss the many types of peripheral neuropathy and the similarities of their presentations (Moore, Wiffen,

& Kalso, 2014), but no study has compared these two populations. Other studies have looked at how each of these groups describes pain and diagnosis experience. There are many publications that discuss these two neuropathies separately, but few describe the possible similarities in pain experience, pain levels, depression, quality of life issues, or how these patients experience the challenges of living with neuropathy combined with the chronic illnesses of HIV or DM. This study examined these issues within a small group of patients who were well characterized with HIV or diabetes and extract potential themes such as foot care, prevention, PN education, stigma, and the challenges these patients face living with chronic pain.

One study examined how PN impacts the quality of life, family, and spouses of these patients (Sofaer-Bennett, Walker, Moore, Lamberty, & O'Dwyer, 2007). The authors interviewed 16 subjects with a wide variety of neuropathic pain (multiple sclerosis, stroke) to explore the consequences of living life with a chronic pain syndrome. This study found three main themes: (a) limitations due to pain, (b) uncertainties, and (c) isolation. These concepts are not new to pain investigations (Hammersla & Kapustin, 2012), but this study explored in depth the pain experiences of HIV and DM patients and provided unique information that could be incorporated into future clinical approaches, research, and educational materials.

A similar study (Henwood, Ellis, & and DuBouloz, 2012) examined the experience of patients with neuropathic pain in spinal cord injury patients. The study included seven participants who were interviewed seeking to understand pain perception and the eventual acceptance of neuropathic pain. The authors developed a step-wise

system that revealed how each participant moved towards pain acceptance. The two primary themes that were the driving forces in pain acceptance for these participants was "increasing independence" and "evolving pain view." The neuropathic pain experience of these patients could be potentially quite different from the presentation of neuropathic pain as it may relate to HIV disease or diabetes mellitus, but the issues of acceptance therapy and pain perception are not represented in the literature for these two populations. This study addresses this gap in the literature as it relates to pain perception themes of these unique patient populations that attend clinics in an urban community. An increased understanding of pain perception may assist in understanding the relationship of pain acceptance within neuropathic pain as it relates to HIV and DM. Another study investigating neuropathic pain within the context of spinal cord injury patients evaluated the prescribed pain medication regimens versus those medications patients adhered to for pain relief (Norrbrink, Lofgren, Hunter, & and Ellis, 2012). Adherence to pain treatments is another critical issue within the context of HIV-PN and DPN. Are patients taking pain medication as prescribed or are these patients using them in another manner? This is an important issue both in the HIV-PN and DPN populations to better understand whether increasing education about how to maximize pain relief by optimizing the use of pain regimens. Appropriate dosing of pain medications is important because there are limited approved pain medications for DPN and no approved treatments for HIV-PN. Clinicians need to understand how patients use these medicines to be helpful in recommendations for pain relief regimens (Robinson-Papp et al., 2015). Norrbrink et al., (2012) uncovered that educating patients to understand the limitations of pain treatment regimens, and the

context of pain experience can aid patients to manage their chronic pain experience. Understanding if this educational approach would be helpful with HIV-PN or DPN chronic pain experience.

What patients understand about their chronic pain experience, the cause of neuropathy, and how individuals experience pain within the context of HIV and DM is unknown. The complexity of the chronic pain experience and the treatments available for chronic pain are not well understood from the patient's perspective. As the world of medicine moves toward a patient-centered paradigm, understanding the perception of pain, the context of quality of life, function, and pain treatments from the viewpoint of the patient can provide invaluable information. How to best introduce the risk of neuropathy, preventative actions, treatment regimen education, and behavioral treatments all can be part of a complex educational model to help patients who develop neuropathy within the paradigm of these two diseases.

Challenges in Understanding Neuropathy

Several studies have made comparisons of various diseases that cause neuropathy to understand the chronic pain experience of these patients who suffer from this disorder. Freeman et al., (2014) reported the comparison of several clinical trials evaluating the neuropathic pain experience as measured by the Neuropathic Pain Symptom Inventory (NPSI) within the context of clinical trials studying the treatment of pregabalin. The authors selected four groups: (a) central post-stroke pain, (b) posttraumatic peripheral pain, (c) painful diabetic peripheral neuropathy, and (d) painful HIV peripheral neuropathy.

The study evaluated ten different pain adjective descriptors that are included in the NPSI when assessing pain experience from these groups. The authors concluded that there was no association between the etiology of the pain and the pain descriptors for each group. In fact, these authors suggested that the ability to use the pain descriptors as a guide for pain treatment may be a beneficial way of providing pain treatment versus etiology. Designing studies with groups of similar pain descriptors versus the source of the neuropathy might reveal a new type of primary outcome measure for clinical trials to determine pain treatments. This study supported this concept by demonstrating the similarities and differences in how patients with painful diabetic or HIV peripheral neuropathy freely described their pain or reported their pain with common pain outcome measures.

Another study of neuropathic pain evaluated sensory responses and quality of pain experience was conducted by Cepeda, Wilcox, and Levitan, (2013) as it related to pain treatment satisfaction. The authors examined a convenience sample of participants who responded to the United States National Health and Wellness Survey (NHWS). These participants consisted of two groups with post-herpetic neuralgia (shingles) and painful diabetic neuropathy. The authors correlated treatment satisfaction with symptom descriptive qualities of approximately 1500 participants who were diagnosed predominantly with painful diabetic neuropathy. Those patients with the broadest range of symptoms and symptoms related to “pins and needles sensations” and proximal pain were dissatisfied with antidepressants. Those patients who experienced throbbing or dull pain were dissatisfied with opiates. The authors discussed how the ability to understand

pain treatment satisfaction as it related to the patient's reported pain would potentially be a mode of selecting treatments. The capacity to understand what treatments are better at helping participants with neuropathic pain symptoms could be determined by the patients' perception of the pain.

This study increased the understanding of the pain experience these two groups share both those similar and dissimilar. The examined narratives of the participants who shared freely their pain history and perception combined with the pain outcome measuresaddresses the gap of knowledge of how these two groups live with pain. Helping clinicians understand of how patients describe symptoms and pain experience as it relates to either HIV or diabetes will aid in their ability to prescribe pain treatments. A study conducted by Wiklund, Holmstrom, Stoker, Wyrwich, and Devine, (2013) examined a self-assessment questionnaire of treatments for painful neuropathy. The authors studied three groups of neuropathy (HIV-PN, DPN, and postherpetic neuralgia) using both qualitative and quantitative data. The goal of this study was to determine treatment satisfaction using a scale called the Self-Assessment of Treatment (SAT). The study captured qualitative elements of pain and function in these groups, but this study did not compare the three groups, it displayed the percentages of the groups that expressed pain states or functional deficits. The examined narratives of the participants' in this study described unique areas of pain symptom experiences that were not typical. The narratives for this study were open discussions with the participant and interviewer discussing with no agenda, the pain experience, and history that these participants have experienced. This study aids in providing an increased awareness of specific pain descriptions both unique

and singular to each of the groups. This study may open other areas of unexplored pain experience because of the nature of capturing these unique narratives. Typically, most participants describe pain and pain history for the purpose of having a treatment prescribed or entry criteria into a research study and because of the nature of the study, these narratives were done purely for the purpose of understanding the participants' perception of pain. This study offered an opportunity to examine pain symptom descriptors and issues about function in these two populations and to consider how the individual narratives reflected what the participants reported on the pain outcome measures.

Chapter 2 Summary

This chapter has discussed the challenges of being diagnosed with HIV-PN and DPN, the pain treatment limitations, and the risks associated with a neuropathy diagnosis within the context of these diseases. Painful peripheral neuropathy is a disorder that is very complex, has unclear pathophysiology, and consequentially a lack of effective treatments. There are no regenerative treatments and the pain relief treatments are seldom sufficient in relieving pain. Patients with these disorders are challenged to live a quality life within the context of chronic pain. Depression, isolation, and poor quality of life are present with very little to offer these patients for successful pain management. Understanding the perspective of patients diagnosed with HIV-PN or DPN and how they manage their activities of daily living is an opportunity to develop educational tools, non-pharmacological treatments, or clinician communication strategies to serve these patients who suffer with pain. How do patients with HIV-PN compare to DPN in the management

of pain, depression, quality of life, pain treatment regimens, and the day-to-day tools of living with the presence of constant chronic pain? An opportunity to address the gap of knowledge of how patients with HIV and DM with neuropathy negotiate life can inform changes in how the clinical care of these patients need to be modified. A chance to examine pain narratives described freely within the context of the perception of HIV and DM patients diagnosed with neuropathy will help begin to aid clinicians in how to begin treatments with these patients when first diagnosed. The hopes of this study were to illuminate an understanding of the perceptions of pain by these patients, their process in coping with chronic pain, and their ability to engage in life. The knowledge gained will help in increased clinical awareness of the risk for patients with HIVand DM in developing PN, how to educate, treat, and follow up with PN assessments. As demonstrated with the spinal cord patients discussed earlier, insight of the pain experience increased pateints ability to find acceptance of the chronic pain condition; studies are moving towards examining the pain experience to understand how treatments can address the symptomology versus the pathophysiology related to the pain state.

Neuropathic pain is a complex disorder where symptoms and causes are not well understood making providing sufficient pain relief complicated. Many patients have little to no pain relief with the current treatments that are available. Studies investigating pain perception versus pain outcomes based upon the underlying disease state may potentially provide a clearer picture of how to provide sufficient pain relief. Developing an increased awareness of the perception of pain symptoms in these populations is needed to close the gap of understanding how to serve these pateints who suffer with chronic pain. The

ability to use narrative data used by this study to uncover areas of pain symptom experiences yet to be discussed in the literature.

Until better pain treatments are available or treatments that can regenerate the nerves, knowing how to provide optimal treatments for pain relief can increase the quality of life and function for those who suffer from neuropathy related to HIV of DM. Knowledge of the context of the pain experience in these patients' lives could potentially assist future patients to explore behavioral treatments when diagnosed with PN versus using pharmacological treatments alone. Decreasing the burden of chronic pain in the lives of those who are diagnosed with neuropathy due to HIV or DM is a critical need in the healthcare paradigm. Neuropathy is a challenging and complex condition with few treatments that provide sufficient pain relief. How these two patient populations experience and manage pain within the context of this study where no pain treatments were involved revealed components of pain perceptions that have not been reported. Performing this study that examined the patient pain experience using narratives and pain outcome measures yielded an increased understanding of what is important for these patients when challenged with a chronic pain condition.

Chapter 3: Research Method

Introduction

Chapters 1 and 2 introduced the current challenges of treating and understanding the complexities of painful HIV-PN and DPN: (a) there is a lack of effective treatments for pain relief; (b) no FDA-approved pain treatments are available for HIV-PN; (c) no FDA-approved treatments are available for nerve regeneration for DPN and HIV-PN; and (d) no studies have been done to examine the similarities and differences between these two disorders.

This chapter contains a discussion of the research design, theory, assessments, and statistical plan used to answer the research questions under investigation in this study. This section addresses the role of the researcher, the HIV and diabetic populations, and the setting in which the study was conducted. In this chapter, I describe the potential limitations and challenges of conducting a study in an area where no existing data have been published or previously collected. Finally, I discuss the statistical plan for the quantitative data and the plan to analyze the narratives.

HIV-PN and DPN Challenges

There is no evidence in the literature that demonstrates that previous studies have compared the pain experiences of these two groups. Previous studies have examined groups of individuals with neuropathic pain that have included these two populations, but no studies have compared these two groups based upon pain narratives and pain outcome measures. This study was the first study to examine questions about the similarities and differences between these two populations diagnosed with painful neuropathy. The

questions asked were directed toward determining whether there are intrinsic differences or similarities between HIV-PN and DPN populations. These groups have similar clinical presentations of neuropathy, yet little is understood about the differences between them, other than the physiological causes of the two different disease states. The ability to understand the relationship of pain a chronic experience in the context of HIV or DM and how it may or may not contribute to how individuals manage pain relief, quality of life, function, and depression provides insight into why pain treatments are not significantly helpful in providing pain relief in these two populations. The scientific community does not have a clear understanding of how these two groups perceive the pain experience, other than information that has been gleaned through the separate study of HIV-PN and DPN or studies that have compiled pain descriptors in conjunction with other diseases (Freeman et al., 2014; Wiklund et al., 2013).

This study examined how the context of HIV or DM changes the perception of painful neuropathy. No previous studies have examined the context of pain perception or examined similarities and differences in how these two groups report pain, functional interference, quality of life, and depression. This study compared these two populations using a group of standardized questionnaires for pain, function, and depression to examine where these two groups converged and where the results separated. This study illuminated similarities and differences between the groups, as well as statements and stories that were shared when individuals freely expressed the process of living life with chronic neuropathic pain within the context of challenging illnesses such as HIV and DM.

Theory of biopsychosocial (BPS) framework in chronic pain

This study examined the relationship of elements to a biopsychosocial framework within the context of the chronic pain condition of neuropathy. Many studies have shown the relationship of elements of this biopsychosocial theoretical framework, but no studies to date have examined in a qualitative fashion the language that demonstrates the unique biological, psychological, and social components that define this framework in these two populations. Many studies have shown the relationship of anxiety and depression in chronic pain conditions, but given the complexity of chronic pain, culture, and social dynamics could be contributing factors, including the language that is used for pain descriptors (Geisser, Roth, & Robinson, 1997; Lucey et al., 2011). As science begins to understand the neuroplasticity of the brain and the possibilities of mapping areas of the brain impacted by chronic pain, a greater understanding of how chronic pain states can have an impact on emotions and perceptions becomes possible. Craig (2002) discussed the connection of awareness of self through the neurologic pathway that gives rise to the idea of interoception. The ability to process the sense of the human body when it comes to pain, heat, cold, and hunger demonstrates an interconnectedness of the emotions and the sense of the human body. Research has demonstrated the human health condition is impacted by social and psychological conditions (Miller, Chen, & Cole, 2009). Heart disease has been shown to have a relationship with depression and aggression, demonstrating a strong psychosocial relationship linked to mortality and morbidity within this paradigm (Miller, 2009). Depression is a well-documented example of affect being

impacted by a chronic pain state in action with perceptions and thoughts due to behavior or psychological processes.

Dima, Gillanders, and Power (2013) demonstrated the chronic pain state in the context of a social paradigm incorporates both negative and positive affect as abilities to both cope and manage the chronic pain experience. The authors refer to this theory as the *dynamic model of affect* (DMA). This theory suggests that there is a relationship of emotion to pain and that it is necessary to measure the emotional context of those individuals suffering with chronic pain. A consideration for the HIV-PN group was an enmeshed experience as it related to pain and HIV stigma. The presence of resilience and stigma in the HIV population could contribute to an increased placebo response in the clinical trials conducted in this population. The idea that an individual's perceptions and body awareness change due to an HIV diagnosis within the context of chronic pain was not addressed. There are issues of recognizing stigma in the context of HIV for patients in China (Hao & Liu, 2014), Africa (Klopper, Stellenberg, & van der Merwe, 2014), and the rural South (Audet, McGowan, Wallston, & Kipp, 2013; Berg & Ross, 2014), including stigma coming from physician providers (Wagner, Hart, McShane, Margolese, & Girard, 2014).

In studies of neuropathic pain, the predominant measures of emotional perception address depression and anxiety. Understanding the emotional context of individuals who suffer with either HIV-PN or DPN could improve pain treatments, specifically those treatments that address behavioral modification or cognitive processes. This study compared standardized pain outcome measures of these two groups and then examined

narratives in relationship to the reported pain. Understanding the role of pain perceptions experienced by these participants highlights the complexities of how the construct of emotions can play a role in how pain is reported beyond depression or anxiety. Issues of stigma, resilience, and shame within the context of HIV disease constitute a known element and could be enmeshed with how individuals report pain in HIV-PN populations. In this study, I considered the element of stigma in the HIV population as it relates to chronic pain. The study discovered language in the narratives of subjects that revealed which perceptions have an impact on chronic pain. Additionally, the narratives showed how perceptions of positive or negative affect influenced how pain was perceived. The narrative component of this study contributed to the participants' perception of social and health context, as each person experienced his or her chronic pain in relationship to the management of the primary illnesses of HIV and DM.

Data gathering for this study included capturing education and socioeconomic status information to broaden the picture of emotion-pain dynamics as well as health status. The way participants managed chronic pain had a relationship to how long each participant had the primary diagnosis of his or her disease compared to when chronic pain from neuropathy became a component of the primary illness. The influence of time as a contributing factor to coping and stress management is an element that is neglected in evaluating pain perceptions by these populations. It is unknown whether the time-frame of onset of pain was considered when discussing issues of coping with a chronic pain condition. The pain history narratives of these two patient populations were reviewed to uncover coping and associated language.

Another concept for consideration is social evaluation. Understanding the driving force behind psychobiological responses as they relate to low self-evaluation is of great interest in a field where chronic pain is the result of a multifactorial condition such as HIV-PN or DPN. The perception of low self-evaluation in the context of HIV disease is one that is a predominant theme. Dickerson, Gruenewald, and Kemeny (2004) discussed the relevance of self-evaluation in the form of the emotion of shame in the context of HIV disease. Individuals report fear of being isolated socially or judged due to HIV diagnosis, which could be a driving phenomenon that plays a role in pain perception for patients with HIV-PN and could distinguish this population from those who have DPN.

Individuals diagnosed with HIV disease in the United States can be considered a highly stigmatized group, not only because of the disease, but also because many in the HIV population are members of communities which are socially seen as outsiders because of sexual orientation, drug use, poverty, education, and potentially, early life conditions that contribute to an internalized self-perception of low self-esteem, low self-worth, and self-rejection. A relationship between psychological behavior and physiological response has been studied in the HIV population (Cole, Kemeny, Fahey, Zack, & Naliboff, 2003). Lumley et al. (2011) conducted a review of the literature on pain and emotion. They showed that emotions do have a role in the perception and experience of pain that has been supported by studies that have investigated brain areas with imaging studies that show a relationship of emotions with chronic pain. Attention should be given to the emotional processes that patients with chronic pain conditions demonstrate. Catastrophizing could be the result of a combination of a patient's negative

emotional processing because of low self-efficacy, inability to disclose his or her emotions, unresolved life stressors, and anxiety. In this study, I sought to determine whether the emotion-pain dynamic was a contributing factor with HIV-PN pain perception as compared to DPN pain perception.

If treatments are not addressing these elements of pain perception as they relate to emotions, then the potential for sufficient pain relief could be elusive. Controlling for emotions as they relate to pain could be an element that needs to be addressed when performing research on pain treatments for HIV-PN. Affect could potentially be a component that differentiates the pain experience between HIV-PN and DPN. The development of chronic pain is a life-altering aspect of HIV disease and diabetes. Understanding whether emotions are a contributing risk factor may aid in finding specific psychosocial or educational tools to help patients with HIV and diabetes manage the chronic pain experience.

Research Design

This study examined differences and similarities between HIV-PN and DPN groups in the reporting of chronic neuropathic pain using standardized pain outcome measures, audio recordings, and transcripts of patient narratives. The data were originally collected during a study entitled “The Experience of Chronic Pain in Neuropathic Pain and Back Pain: A Focus Group Approach” (Appendix A). This study was conducted as part of research undertaken at the Icahn School of Medicine at Mount Sinai (ISMMS). ISMMS is a large academic center that serves a large urban population of HIV and

diabetes patients in New York City. I was a coinvestigator for the original study, which was conducted from 2010-2012.

The goal of this study was to determine whether any differences existed between the pain experiences of HIV-PN and DPN groups. A study of the data collected as part of the larger study offered an opportunity to begin to address this question because the similarities and differences in these two populations' pain experience were not addressed in the literature. The data for this study were derived from a screening visit and a baseline visit. During these two visits, participants provided consent and confirmed a primary diagnosis of either HIV-PN or DPN. The second visit consisted of a series of standardized pain outcome measures followed by recording of the participant describing in his or her own words the pain history and experience. This study used these elements collected at these two visits and compared the responses of these two groups. All of the data were deidentified, and the recordings exist as deidentified transcripts and audio files. The final element of this study consisted of 7-days' worth of pain diaries that participants completed prior to attending the focus group session. These diaries were done again to replicate the clinical trial experience where participants were asked to complete 7 consecutive days to meet a mandatory average pain score over the 7 days. The original study has not used these data in current or pending publications.

Participants and Procedures

The study enrolled a total of 44 subjects. Twelve participants enrolled into the HIV-PN group and 11 participants enrolled into the DPN group, but one individual in the DPN group withdrew from the study prior to the second visit, and 13 participants

enrolled into the chronic low back pain group. The chronic low back pain group was not included in this study. Complete data were available on 10 participants in the DPN group. One subject of the DPN group discontinued the study prior to the second visit due to amputation (Dorfmanet al., 2014), a common complication in the DPN population.

The inclusion criteria for these two groups were as follows:

1. Age 18-65 years
2. Documented diagnosis of HIV-PN, DPNP, and chronic low back pain
3. HAN and DPNP considered diagnosed by the following:
   - The presence of symptoms of pain, burning, or dysesthesia discomfort in both feet for at least 2 months prior to screening visit.
   - Absent or diminished ankle reflexes and at least one of the following: distal diminution of vibration sensation or pain or temperature sensations in the legs.
4. All patients must have been on stable pain treatment regimens during the past 30 days.

The exclusion criteria for these two groups were as follows:

1. History of schizophrenia or bipolar disorder. (Major depressive disorder allowed if patient was in remission for at least 90 days).
2. Serious illness requiring systemic treatment and/or hospitalization.
3. Treatment with any experimental agent within the past 90 days.
4. Presently seeking disability compensation related to the chronic pain condition.

5. Major symptoms related to the chronic pain condition within 12 months.
6. Any serious or unstable illnesses.

This study reports on the descriptive data collected for the HIV-PN and DPN groups concerning ethnicity, race, gender, education, and age and years of diagnosis as it relates to the primary illness and years of diagnosis with neuropathy. The study compared the pain questionnaires (VAS, NRS, SF-MPQ, BPIsc, and weekly diaries) and the Beck Depression Inventory for these two groups for the quantitative analysis. The data for the qualitative component consisted of the deidentified transcripts and audio recordings of the pain narratives of 12 HIV-PN participants and 10 DPN participants collected during Visit 2. This study included the pain diaries that were given to each of the participants to complete 1 week prior to participation in the focus group session in the quantitative analysis. Any statements that were included in these pain diaries were also extracted per participant as part of the narrative data for analysis.

Data Analysis

The primary objective of the analysis was to perform a content analysis of the narratives of the participants in the HIV-PN group versus the narratives of the DPN group using an IPS process. The initial study examined narratives that occurred during the focus group session. Four themes were uncovered concerning the narratives of the focus group sessions: (a) participants were unclear in their understanding that pain can be measured, (b) there was confusion concerning the definition of pain, (c) there was uncertainty about what pain experiences to use as referents, and (d) there was difficulty averaging pain (Robinson-Papp, George, Dorfman, & Simpson, 2015). The data reviewed for were not

included in the prior analysis because of its distinctive narrative nature. For this study, I examined the narratives of the participants and uncovered issues that contribute beyond the pain experience to share a story about issues related to the primary disease or the social dynamic of the participants' experience. The narratives of these participants revealed elements that are not considered as contributing to the pain experience.

The narrative analysis was driven by a hermeneutic perspective—story gives life meaning (Boden & Eatough, 2014). Using interpretive phenomenological analysis provided an opportunity to examine the sequence and consequences of events (Reissman & Quinney, 2005; Smith, 2004). The process of rendering a story of the pain history in the context of HIV and diabetes allowed an investigation of the how and the why of chronic pain experience as it related to managing these chronic illnesses. Each participant was asked to recall the first observation of sensations and to share the events and his or her interpretation as it related to the chronic painful neuropathy until the present time. The process of sharing these stories were perhaps the first time these participants were asked to share their story of the chronic pain experience without a clinical agenda of receiving a treatment from a clinician. The analysis of these data werr done line by line for specific content, but with the entire narrative summarized with a beginning, middle, and end to provide an opportunity for the research to reveal what was present "as if" being present in the moment of the story being shared (Charmaz, 2004). Malterud, (2001) shared three key tenements to approaching qualitative research: (a) an awareness of the context, (b) transferability, and (c) interpretation.

These analyses provided the “lived experiences” of these participants’ narratives of awareness, managing, and coping with chronic pain meaning in a greater context than prior research when participants were asked to define the pain experience by completing questionnaires where they were asked to express pain by drawing a line or making circle or selecting a number that was representative of an average pain experience. The process of examining these narratives revealed a context of life experience that is common or unique to these individuals. The lived experiences of these participants can be a source for larger investigation in the chronic pain research arena. Furthermore, the complexity of the chronic pain experience can be seen as a misunderstood paradigm that requires a different approach within research for the purpose of reporting generalizable outcomes.

Threats to External Validity

External validity for this study should not be a concern due to the comparison of two groups. Whether the results of this study are generalizable to the larger population of these two groups is unclear. The nature of HIV disease can be now be defined as a disease of individuals who are socioeconomically challenged, African American women, and Latinos (Remien et al., 2015). Likewise, diabetes affects a similar demographic (Claussen et al., 2017). Whether the narratives of this study can be generalized to other populations are living in an urban environment is possible. This study offered an opportunity to begin to illuminate themes of language in these groups that demonstrate views of pain perception attributable to these groups. The threat to external validity was that the urban populations of these two groups might not be generalizable to the greater population of these two diseases. While this may be the case, past studies contained large

numbers of participants that included Caucasians with mixed neuropathic pain (postherpetic neuralgia or shingles) diagnoses, versus the diagnoses of pain as it related to either diabetes or HIV disease neuropathy. This study provided diverse populations that included a variety of races and cultures. This study represented more of what the populations of HIV and diabetes represent socioeconomically challenged participants who are Hispanic, African-American, and multicultural. The information gained from this study offers a foundation for future studies that include these populations. This study shared a singular view of the narratives and experiences of pain that have not been represented in previous studies.

Threats to Internal Validity

This study examined archival data that was collected at two visits before a focus group session. Threats to internal validity were reduced due to the random selection of participants that occurred during the enrollment process of the original study. Some patients in both groups participated in Visit 1 and then did not take part in Visit 2, but were included in the focus group visit. There were some patients who did not complete the seven days of pain diaries, nor complete the entire packet of pain questionnaires, but the number of participants remained similar for both groups. The only patient that discontinued was in the diabetic group, a participant who experienced an amputation after Visit 1. This study participant could not continue, but the numbers of people with diabetes in the group still provided sufficient data to reduce threats to internal validity.

Trustworthiness

Qualitative data rigor relies on the design and collection of the recordings and transcripts that make up the data. The qualitative data for this study was collected with the idea of the researcher's role as purely present to obtain the participant's pain narrative as a journey from when they first experienced their pain to the engagement of medical professionals to present time. The researcher's role was not to ask questions but to provide open-ended questions to the participant to expand on his or her experience as it related to the pain, function, or the primary disease. The ability to determine if there is saturation from reviewing the narratives for this study was hard to determine but will be discussed further in Chapter 4.

Quantitative Analysis

The quantitative analysis addressed the data that consisted of the standard pain outcome measures completed at visit two. The pain outcome measures were adapted to have the same appearance concerning instructions and presentation for each of the pain groups. These packets were presented to each of the participants in the same manner as if the participants were enrolled in a research project for a pain treatment. The pain outcome measures consisted of the Visual Analog Scale (VAS), the Numeric Rating Scale (NRS), the Brief Pain Intensity sub-scale (BPIsc), the McGill Pain questionnaire short form (MS-FPQ), and the Beck Depression Inventory (BDI). To broaden the scope of these participants pain experience, each group was given a week of pain diaries to complete. These pain diaries consisted of 7 days of the NRS, an area to record the time of day, and any other statements relevant to the pain experience. The purpose of these

diaries was to mimic clinical trial design. Clinical triasl commonly use pain diaries to measure participants pain, both as a single measure prior to the study entry and as a series of diaries completed 7 days sequentially are required for a participant to be deemed eligible. Often it is required that subjects provide a minimum pain level both at the screening visit and an average pain level over a 7 to 9 day period with a minimum of 2 or 3 missing data points during the period when the pain diaries were completed. The original study captured data with an approach that mirrored these standard practices required of participants to enter a neuropathic pain clinical trial, except in the original study there was no minimum amount of pain necessary for a participant to be included on either the single study visit or the average pain reported over the 7 to 9 day period nor was there a requirement to discontinue excluded medications.

Descriptive statistics were analyzed to describe the two populations as they related to gender, race, ethnicity, education, health status, medications, length of primary diagnosis, and length of diagnosis with painful neuropathy of the two groups. Inferential statistics were done to compare the pain outcome measures and the BDI. The primary objective for the research hypothesis for the quantitative data was:

- H_1 – HIV-PN group has a different level of pain/depression than those with DPN.
- H_0 – HIV-PN and DPN have equal pain levels/depression.

Power Analysis

A two-tailed sample *t* test was used to determine whether any differences were present in the report of pain using the pain outcome questionnaires MPQSF, VASc, NRS,

BPIsc to measure function, and the BDI to measure depression. The original study was not powered for a quantitative analysis because the intent of the study was qualitative by design (Robinson-Papp et al., 2015). The efforts of this study were to examine the quantitative assessments that were collected prior to the participation in the focus group sessions. A power analysis for this proposed study of the pain outcome measures was performed to determine whether the data would provide sufficient power to address rejecting the H_0. The GPower 3.1 statistical software was used to provide an assessment of power estimation (Faul, Erdfelder, Buchner, & Lang, 2009). The comparison of painful HIV-PN and DPN was examined in the study conducted by Freeman, Baron, Bouhassira, Cabrera, and Emir, (2014). This study did not provide a mean or standard deviation for pain that could be used for this power analysis, nor did the natural history study of HIV-PN (Simpson et al., 2006). There was a mean (5.9 cm) and standard deviation (2.9) for the MPQSF that was available in the natural history study for diabetic neuropathy but the use of this mean and standard deviation for the purpose of this power provides only partial data to conduct the power analysis, therefore the power analysis relied on the effect sizes determined by Cohen's guidelines (1988), used a large effect size of .80 due to the small sample size, and the reliability of the established pain outcome measures (Sullivan & Feinn, 2012).

In preparing the power analysis using the statistical package GPower 3.1, the test family was set to a *t* test and demonstrating the statistical test of means: difference between two independent means (two groups). The type of power analysis was set at posthoc: compute achieved power - given $\alpha = 0.05$, sample size = 10 and 12, and effect

size = 0.8. Using these parameters to determine whether this study had sufficient power to reject the null hypothesis the following output was provided: noncentrality parameter = 1.92, critical $t = 2.08$, $Df = 20$ and power (1-β err probability) = 0.45.

The quantitative data for this study was underpowered because of the small numbers of the participants in each group (HIV-PN = 12 and DPN = 10), but the analysis for power using the GPower 3.1 based upon the above parameters the quantitative data showed a modest amount of power to reject the null hypothesis. These data combined with the qualitative data demonstrated the complexity of the perception of chronic neuropathic pain of these two groups. The ability to analyze and report on these two groups, provided a unique comprehensive picture of what these participants communicated about the chronic pain experience when no agenda was required.

As a coinvestigator for the original project, the idea to of capturing the pain narratives of each of the participants was my contribution to the original project. During the original protocol development, the study team included recording of the narratives of these pain histories because it was uncertain if there would be information about how pain was measured during these narratives. The study team did not know how this information would be relevant to the overall primary objective of the original study, but the opportunity to capture the pain perception of these participants prior to the focus group setting seemed important. These data were not utilized for the primary analysis of the original study. The study team agreed to the subanalysis of these two groups for the completion of this study and the Institutional Review Board at Mount Sinai extended data analysis through March 29, 2017.

Role of the Researcher

The role of the researcher in this study was to assess all of the data with the viewpoint of an outside observer. It was critical that every element of the narrative data was carefully organized and looked at from the perspective of an observer without opinion or viewpoint. The building of the cumulative story that was shared by these two groups was critical to extract common or unique themes about the neuropathic pain experience in these two groups. Using the process of analysis line by line of the narratives from a language perspective was a useful tool to uncover what stories were being shared by these two groups as it related not only to their pain experience but to other life issues that play a role in the perception of pain (i.e., HIV stigma, diabetes dietary challenges). It was necessary to divorce myself of any preconceived viewpoints or theories, look at the data collected with an impersonal, and objective view. The process of leading the focus groups for the original study and recently for several studies as part of the Neurology Department here at Icahn School of Medicine at Mount Sinai increased my experience of divorcing myself of my views and perceptions and being present to the moment. This experience allowed several discussions with patients of drug seeking on the "street" or "friend" and an open discussion of the issue of trust when seeking opiates for pain relief (Robinson-Papp & George, 2015). Further, as a researcher who has worked in the field of HIV for many more years than diabetes, I have had the opportunity to immerse myself to understand the history of diabetes and the medical consequences during the process of overseeing two large diabetic neuropathy clinical studies. I organized a support group for diabetics and worked with the study team to increase

research for pain treatments targeted for diabetics. As the researcher for this study, it was useful that the original data was collected by other individuals, even the narratives were captured by another individual from the original protocol study team. I was strategically positioned to uncover information from these data that could begin to address the gap in the field as it relates to why treating neuropathic pain in the HIV-PN group has been a scientific enigma.

Timetable

IRB approval was received from the Walden University, the narrative analysis started. The qualitative data (audio recordings and transcripts) were reviewed for each participant – a separate participant code provided. Each narrative was examined line by line for each of the participants notating initial impression. A line by line analysis was conducted to begin to shape the individual story that worked towards designing a narrative that was unique to each group. Additionally, themes were pooled as they appeared between participants. A word analysis was done using the software NVIVO notated the pain descriptors of the language that were used more frequently or used uniquely more in one group as compared to the other.

The quantitative data was placed into a separate file from the original study that is currently held on an encrypted computer that is only available to the study team. The software SPSS version 22 was used and the data were isolated so that data only to be analyzed related to the two groups and the initial visits (Visit 1 and 2). The data for the diaries were entered into the SPSS database. The timeline for completion of the analysis of this study was extended due to the findings of nonverbal and paralinguistic elements

that were notated during the initial process of listening to the audio recordings. The quantitative data was analyzed after the qualitative data was completed. The preliminary results were discussed with the dissertation Chairman, Committee, and mentor at the Icahn School of Medicine at Mount Sinai (Dr. David Dorfman). The timeframe for completion was extended so that the nonverbal and paralinguistic elements could be quantified (tone of voice, sighs, audible inhalation, pauses greater than 2 seconds, word searching, and laughter.)

Ethical Review

The study received an ethical review of the Walden University Institutional Review Board (IRB) and was approved Jan. 22, 2016. No work on the data was conducted until the approval was provided by the Walden University IRB. The original study was under ethical review by the IRB of the Icahn School of Medicine at Mount Sinai through March 29, 2017 and acknowledged the intent of this study. The data used were deidentified therefore decreasing the risk of loss of privacy. The privacy issue was addressed when discussing the narratives in the analysis no names or any recognizable information was included. Specific narratives selected to demonstrate a theme or relative components have been stripped of any possible element to maintain the privacy of the participants. This is specifically important because of the nature of working with HIV participants who are a vulnerable population. Every effort was made to work with the dissertation Chairman and committee to resolve elements of the narratives that would be sensitive in nature or risk exposing information that would place this group at risk for

loss of privacy. I structured a detailed narrative analysis plan (appendix D) and stripped the narratives of any possible identifier.

Limitations

The greatest limitation of this study was the nature of the narratives to be analyzed. The inability to probe for additional information from the narratives revealed a need for more questions and showed the challenges of communicating the pain experience and the difficulty in understanding the chronic pain experience of neuropathy in these two groups. The ability to ask questions prospectively would be a benefit when conducting qualitative studies, but the ability to do a content analysis on these data was an opportunity because patients were asked to share their pain history and pain perception without interruptions except for clarifications or probing about what the participants described. This approach, while not initially contructed for this study, showed to be meaningful for these two groups because sufficient time with a physician is not often available in many clinical settings.

The other limitation was that the data set for the quantitative analysis was small and possibly underpowered to show significance between the two groups' outcome measures. Regardless of these two specific limitations, these data were informative and provided an opportunity to examine what is communicated when patients in these two groups share their perception of pain in contrast to what was reported in the pain outcome measures. The original study was completed in 2012 and these data would languish and potentially go unreported if they were not used for this study. The academic setting this study was conducted in attributes greater emphasis to quantitative data collection and

treatment studies. This observational data set offered a rare opportunity to provide pilot data on the relationships that exist between how patients freely discussed the pain experience in a narrative as compared to how they reported the pain experience in pain questionnaires.

Chapter 3 Summary

This chapter addressed that this was a study of data collected as part of a larger study that included an additional pain group that is not included in this analysis. The larger study collected data during the second visit that included narratives of each participant's pain history and pain experience to date. These narratives were collected after the participants completed a packet of standardized pain outcome measures. This study offered a distinctive opportunity to analyze whether these two groups use similar or dissimilar language about the chronic neuropathic pain experience and whether these two groups report pain differently when completing standardized pain outcome measures. Chronic neuropathic pain has no therapies that are approved that repair the damaged peripheral nerves. DPN has few approved pain relief treatments and no approved treatments for patients with HIV-PN.

Many of these patients suffer from isolation, depression and poor quality of life coupled with the challenges of managing complicated diseases such as HIV and diabetes. This study provided the ability to evaluate narratives of well-characterized patients with these illnesses and establish pilot data that included a comprehensive story with themes that are specific to each of these conditions or similar to both. Coupled with the quantitative data of the pain measures, the relationship to pain perception between these

two groups revealed gaps in how clinicians collect pain data for clinical and research purposes. This study offered a valuable opportunity to address the gap of understanding of how patients share their chronic neuropathic pain experience, manage, and cope as they navigate their health and life.

Chapter 4: Results

Introduction

The purpose of this study was to provide a comparison of pain narratives of two groups, people living with HIV/AIDS (PLWHA) and people with diabetes, both of which had been diagnosed with painful peripheral neuropathy. Research in these two populations is rarely conducted to understand the perceptions of patients diagnosed with painful peripheral neuropathy. Often, the pain narrative experience is quantified with the use of well-established pain scales (i.e., VAS, McGill). This study offered an opportunity to examine the stories of medically well-characterized participants diagnosed with HIV and diabetes and the qualitative and quantitative pain measures captured. The primary questions to be answered by this study were the following:

1. What are the differences in the language of pain perception between HIV-PN and DPN?
2. What are the pain perception themes described as they relate both to HIV-PN and DPN?
3. How does pain perception differ when measured by standard pain questionnaires as compared to pain narratives?

This study is an examination of a single study visit from a larger study entitled "The Experience of Chronic Pain in Neuropathic Pain and Back Pain: A Focus Group Approach" conducted at the Icahn School of Medicine at Mount Sinai from 2010-2012 (see Appendix A). This chapter describes the two groups' demographics, similarities and differences in themes discovered, and elements of the narratives that were unique when

compared to the transcripts and the audio recordings. I discuss the examination of the recordings and transcripts, as well as the process of determining the themes. The process of investigation was expanded due to the nature of the audio recordings and elements unique to these audio recordings. The quantitative data offer insight into whether there were differences or similarities in how these two groups completed pain questionnaires. The quantitative data also indicate how these two groups compared concerning depression. Finally, the qualitative and quantitative data are reviewed to determine where the qualitative analysis reveals similarities or differences found in the quantitative data derived from the questionnaires.

Study

This study was an analysis of archival data collected during Visit 1 and 2 of the above-referenced research, of which I was a coinvestigator. It was my idea at the time of the study to simulate the collection of data in relation to how a patient would be asked to share his or her pain narrative when presenting to a physician for diagnosis and treatment. It is very common for patients to describe their experience and for physicians to use a standard pain scale (NRS; 0 to 10) to understand the discomfort that patients are experiencing. This information, coupled with a clinical examination, guides the physician in determining a plan of care. The primary purpose of Visit 2 for the main study was to familiarize the participants with the pain questionnaires and introduce them to discussing their pain narrative while being audio recorded. Visit 2 participants completed a packet of pain measures followed by a recording of their description of what the participants recalled about the symptoms of PN and when they began experiencing them. This study

used data that were not analyzed for the primary study to pilot information on similarities and differences between these two groups whose members suffer from neuropathic pain.

Setting

This study was the first direct comparison of HIV-PN and DPN populations comparing pain narratives and questionnaires in a mixed-method, convenience sample of well-characterized participants with HIV disease and diabetes mellitus. The original study was conducted as part of the NeuroAIDS program under the supervision of Dr. David Simpson at the Icahn School of Medicine at Mount Sinai in New York. This program is known for its work in the field of neurological complications of HIV/AIDS and has designed and conducted many studies related to peripheral neuropathy. This program's researchers are quite knowledgeable in the development, execution, and reporting of research in the field of NeuroAIDS. The population that is served by this program mirrors the populations of HIV disease and diabetes mellitus due to the location in East Harlem in New York City, a highly diverse and urban setting.

The data for this study consisted of information collected at the screening visit (Visit 1) and the baseline visit (Visit 2). The data collected during Visit 1 consisted of confirmation of eligibility, demographic information, general medical history of primary illness, pain medications, year of diagnosis of PN, and an exam by a neurologist of to confirm PN diagnosis. At Study Visit 2, the participants completed a packet of standardized pain outcome measures and the Beck Depression Inventory scale. Once this packet was completed, an audio recording was made of each subject providing a pain narrative in response to the prompt "Think back to when you first experienced symptoms

and describe what happened, who you talked to or what you did." After the recordings, participants were instructed to record their pain for 7 days in a diary provided by the study. The quantitative data collected (packet of standardized measures) from these two visits were anonymized and entered into a database for analysis. The audio recordings and transcripts were anonymized at the time of collection, as were the pain diaries. These were the elements analyzed for this study.

Participants

This study includes a convenience sample of participants who attended clinical services specifically designed to treat HIV disease or diabetes. These clinics are part of the Mount Sinai Health system (http://www.mountsinaihealth.org/locations), where the Icahn School of Medicine at Mount Sinai is situated in the heart of East Harlem in New York City. A description of the demographics of these two groups is in Table 1. The original study enrolled three groups, but only the HIV and diabetic groups had neuropathic pain and were included in this study. The two groups enrolled in sequence rather than simultaneously, with the HIV group enrolling first, followed by the diabetes group. The study enrolled a total of 12 HIV participants, all with undetectable viral loads, a range of CD4 counts of 150–1143, and stable antiviral regimens for the treatment of HIV disease. The diabetic group enrolled a total of 11 participants: two Type 1, eight Type 2, and one subject who became diabetic due to the surgical removal of a benign pancreatic tumor. A Type 2 subject was withdrawn from the study due to a complication of amputation that occurred after Visit 1 (Dorfman et al., 2012). Therefore, this participant's data are included in Table 1 but have been excluded from the data for the

remainder of the study. Ten participants in the DPN group completed both visits. The diabetic group had a mean HgA1c of 8.8, with a range of 5.5 to 15.5. The DPN participants controlled their diabetes with either insulin or oral medications, except for one participant who had non-obese bariatric surgery. All the participants knew the time frame for their primary illness, and the members of the diabetic group could recall their diagnosis of PN, but determining the specific time frame for the PN diagnosis for the HIV group was difficult. Three participants were diagnosed with PN and HIV simultaneously, while seven participants recalled having PN symptoms after taking an antiretroviral that is known for neurotoxicity and two participants couldn't recall the specific time frame for their PN diagnosis. Quantifying a mean time frame for PN diagnosis in the HIV group with accuracy was deemed difficult; therefore, a mean is not reported for either group, only a range of years for the PN diagnosis.

Table 1

Demographic Characteristics

	HIV-PN	DNP
Gender		
Male, *n*	10	5
Female, *n*	2	6
Race/Ethnicity		
African American, *n*	6	2
Other	2	2
White, *n*	4	7
Hispanic	3	2
English as a 2nd language	2	4
Age, mean (range)	52.83 (44-63)	48.90 (18-65)
Years of education	13.33 (8-24)	14.17 (13-20)
Years of primary diagnosis, mean (range)	19 (12-28)	16 (2-36)
Years with PN (range)	12-28	2-26

Pain Medications

Members of both groups needed to have been taking pain medications for a minimum of 3 months in order to meet the inclusion criteria of the study. Pain medications taken by the HIV group ranged from NSAIDS to long-acting opioids. Seven participants were taking a three- or four-medication regimen for pain control, three participants were using two pain medications, and two participants relied on over-the-counter NSAIDS. The diabetic group had two participants taking three- or four-pain-medication regimens, while five participants had only one medication for pain and three participants were taking a combination of two drugs. Table 2 describes the types of medications and the number of participants taking these for pain control.

Table 2

Pain Medications

	HIV-PN	DNP
NSAIDs	2	3
Anticonvulsant	7	6
Tricyclic antidepressant	1	2
Serotonin-and-norepinephrine reuptake-inhibitor-antidepressant	2	1
Opioids		
Short-acting (Percocet®)	1	2
Long-acting (morphine)	4	0
Opiate (narcotic)	1	1
Topical analgesic	1	1

The spectrum and combinations of medications these participants were taking demonstrated that the diabetic group was taking medications (duloxetine and pregabalin) approved for the treatment of DPN. The HIV group was prescribed a range of pain medications that were considered off-label (not FDA approved) because none of them

had been approved for the treatment of pain due to HIV-PN. The HIV-PN group was taking long-acting opiates, whereas the DPN group was taking no long-acting opioids and only a couple of participants in the DPN group included short-acting opioids as part of their pain regimen.

Data Collection

The goal was to perform a qualitative analysis of the pain narrative by examining line by line using an interpretive phenomenological analysis (IPA) to begin to understand the lived experiences of these two groups and determine their similarities and differences. A collection form was developed (Appendix D) and structured following the guidelines of Smith (2004). The structured analysis guidelines began with a macro approach of reviewing the transcripts and audio recordings, leading to a micro review of each transcript with a line-by-line analysis. A summary of each participant based upon the structured guideline form began with first impressions, followed by attention to (a) language structure; (b) pronouns, adjectives, and adverbs; (c) narrative shape—beginning, middle, and end; (d) whether the transcript correlated to the audio recording and tone of voice; (e) how the transcript revealed the story of the audio recording; (f) themes and concepts as they relate to pain; and (g) themes and concepts as they relate to life context.

The process began with stripping the narratives from the transcripts of all language that pertained to the interviewer. The audio recordings were of similar length for each group, with the HIV-PN group averaging 25 minutes and the DPN group averaging 22 minutes. Adjectives that were similar and dissimilar to both groups were

determined by an initial word analysis conducted using NVivo software version 9.0 followed by a word-by-word assessment of each narrative using the ability to search each document using the *find* feature to confirm that use of the adjective was in the context of the pain narrative. Those adjectives not used within the context of the pain narrative were eliminated from the word count. An Excel worksheet captured the adjectives and the frequency with which they occurred in each narrative.

The approach to reading and listening to these pain narratives to derive common themes, subthemes, or differences was systematically established as follows: (a) review the HIV group in its entirety, completing each of the elements in the structured guideline; (b) review the diabetes group, completing each of the elements as described in the guideline; (c) compare the elements in the groups where overlap existed; (d) begin to define themes from those areas of overlap; and (e) document elements that were unique to each group. A systematic process was used to organize and structure those statements into groups where themes of similarities and differences evolved with each line-by-line review of the transcript and audio recordings. Finally, with compilation of adjectives and the line-by-line assessment, a composition of dominant themes that described the lived experiences of these participants began to emerge. Themes defined as similar or dissimilar to each group, and the frequency of the number of participants representing these themes within the narrative were captured and summarized. Themes that were present in more than four individuals were included as dominant themes in the analysis.

The unexpected element that appeared in the qualitative analysis related to the audio recordings. When the third round of listening to the recordings occurred, vocal tone

began to present itself as different between the two groups. The HIV-PN group had a distinct lack of inflection in the voice as compared to the DPN group. A thorough examination of these audio recordings revealed that not only was there a difference in the tone of voice quality, but also nonverbal or paralinguistic phenomena became noticeable, requiring additional listening. There was enough evidence in the audio recordings of the participants to capture these audible nonverbal elements so that they could be quantified and an assessment could be made. The first listen was for tone of voice, followed by an effort to capture additional prominent elements: pauses, word searching, audible sighs or breaths, and laughter. This observation required a further series of listening to each audio recording 10 additional times, notating these elements and frequencies so that they could be summarized based on occurrences within the narrative and how many of the participants' pain narratives contained paralinguistics.

The process of documenting the quality of the tone of voice involved stating the impressions I had after multiple reviews of each of the recordings. These findings are discussed based upon the range of occurrences in each participant for each group and included in the analysis.

Data Analysis

Common Themes

The key question to be answered by these analyses was the following: What are the similar pain perception themes described in relation to both HIV-PN and DPN? Eight themes were demonstrated to be similar in both groups (see Table 3). The following discussion reviews the similar themes in both groups, followed by dissimilar themes.

Table 3

Common Themes

Themes	HIV-PN	DNP
Footwear challenges	100%	100%
Coping techniques	92%	80%
Pain and numbness coexist	75%	80%
Pain fluctuates	75%	90%
Balance disturbance	67%	70%
Delayed seeking treatment	75%	50%
Effect of medications	67%	50%
Trust	58%	50%

Footwear challenges. Each participant was asked the following question: "Think back to when you first started experiencing these sensations in your feet. Think back to what you think was happening and what did you think about those sensations? What did you do? And who did you tell?" The response to this question began with the predominant theme for all the participants in both groups: footwear. Whether the topic was socks, type of footwear, how the shoe felt on the foot, finding footwear that felt comfortable, awareness of having shoes on, or losing shoes while walking, footwear was discussed by all of the participants in both groups. Many of the participants began their pain narratives by sharing their challenges related to successes and failures with their footwear. A DPN female participant stated,

> I kept adjusting my socks. It went from itching to being sort of persistently uncomfortable ... I was continually trying to adjust my socks. I tried I don't know how many different kinds of socks—tight ones, loose ones, whatever. I changed my shoes …

A Hispanic male HIV-PN participant stated,

> Yes, I had a very hard time, (with shoes), finding the kind of shoes that would not hurt my feet. Everything hurt it … but then I was thinking maybe the shoe was wearing out. (*I*) was trying to see if I could get the medical doctors' shoes that they give you when you have diabetes … I have to get wide shoes.

Whether the subject was talking about the challenge of finding comfortable footwear or socks or keeping footwear on their feet because going without shoes or socks felt uncomfortable or noticing symptoms in the feet and attributing the discomfort in their feet to shoes, footwear was the most prominent theme in all the participant's narratives. Participants discussed the challenge of finding footwear, having to purchase multiple pairs of shoes or socks. One subject in the diabetic group did have a prescribed orthotic support from the podiatrist, and another participant in the HIV group purchased over-the-counter insole supports. The issue of finding shoes that didn't increase the discomfort or pain from the PN was a repeated theme in both groups. Another element of why shoes were an issue is that many of the participants in both groups believed the PN discomfort that they experienced originated from their footwear. A HIV-PN participant African American male stated:

> But I remember saying, wow, you know, my feet are hurting…I haven't been walking that much for my feet to be hurting… it can't be the shoes. I should change my shoes. Maybe my feet don't like these shoes anymore or something.

A DPN African American female participant stated:

> … when I got out of bed, my feet would sting. I attributed it to my shoes. I thought maybe I'm wearing my shoes too tightly. They were stinging like bees

> stinging my feet. It continued on until 1997 when I had a problem with… I was urinating quite frequently. I never put the two together. I always thought it was just my feet stinging. It was my shoes because I did wear tight shoes at the time. I assumed it was that.

Footwear, the types of shoes whether they were slip-on, sandals, or had laces, were soft, or firm, these issues made a significant difference to each participant in the two groups. Walking became more challenging if the footwear was not supportive and comfortable. Some participants purchased shoes larger than normal while other participants sought shoes that felt snug on the foot. The pain narratives shared by both groups illuminated the complex difficulty, cost, awareness, or struggle with satisfactory footwear that disrupted their activities of daily living.

Coping techniques. The theme shared by 11 participants in the HIV-PN group and eight of the DPN group described non-medical coping activities for their pain. These varied in the two groups from acupuncture, massage, essential oils, hypnotherapy, feet soaking, drinking tonics, religion, or yoga. These coping techniques were sought out by the individual, and were not recommended by their health care provider, but were sought out by the participants. Only one participant in the HIV-PN group discussed an "ultrasonic" device used during his physical therapy that was provided by his primary care doctor. A member of the DPN group mentioned the nurse educator recommending acupuncture, but when the participant stated their uncertainty of acupuncture working the educator didn't continue with any further information. Otherwise, participants

acknowledged the limitation of the pain medications providing sufficient pain relief and sought out non-medical coping strategies**.** A HIV-PN African American female stated:

> I sit down in my room. I have two lounge chairs. I put on my (hypnosis) tape. And I relax. And I say that I'm somewhere else. I'm not even here. I'm not (sic) feelin' this. And I start from the head to the toe. And it works. It smooths the pain. And it takes the pins and needles away. It works. It actually works.

A DPN female participant stated: "Some older people told me I should chop of [sic] the onion and garlic and put it on my feet; it would help. I tried everything." A HIV-PN Hispanic male participant stated: "… I know that I have a living chance if I follow my religion and follow my God in his ways." A DPN Hispanic female participant stated:

> Massage, yes, massage and I went to a class of yoga. And they helped me, so I'm going to study now more classes of yoga because that, the day I went to the class I was feeling a little more pain and after I felt less pain.

Several of the participants described alternative coping techniques to help with pain or with the course of the primary disease, such as unique physical therapy, surgery or other activities such as smoking. A HIV-PN Hispanic male participant stated: *"*When– sometimes you want to smoke a cigarette, you don't think about nothing else but smoking the cigarette… you forget about the pain." A DPN male participant stated:

> I actually went to India and had a formal bariatric surgery made for non-obese diabetics in order to cure diabetes. …my diabetes is slowly getting better. As the sugar levels are going down, so is my neuropathic pain.

A HIV-PN female participant stated:

> …to get my mind off it, I would take my shoe off. And I'm pounding my foot against the floor. Honestly, this is my way to cope. What can I say? Medication doesn't work. But it (*pounding*) kind of lessens the sting of the pain.

A HIV-PN male participant stated:

> He (physical therapist) puts me into a – like a stretching machine. …he straps my pelvis into and then straps my chest, and the table actually separates… stretches you. …immediately after there is no pain, absolutely no pain.

The coping approaches varied with hypnosis being used by the HIV-PN group because of their exposure to a previous research project, while more known approaches such as acupuncture, yoga, massage, or feet soaking were present in the DPN group. Participants did make references about the medication not working, or the participants were not certain the pain medications were working. A large percentage of the participants from both groups were seeking nonmedical approaches that would aid in coping with the pain.

Pain and numbness coexist. This dominant theme expressed by nine participants in the HIV group and eight participants in the diabetic group. The issue of pain and numbness was quite disturbing for many of the participants who found describing the coexistence of these sensations in areas of the legs or feet difficult. The concept of a numb sensation which was understood as the absence of sensation concurring with the pain sensations in the same areas was difficult to describe, understand, and to comprehend for these participants. HIV-PN participant male, Hispanic stated:

> I don't know how to really describe it. It's different because it gives me like a burning numbness. It's in between hurting, wanting to hurt and not hurting and it's troublesome because like right now my leg is numb.

A DPN male particianpt stated:

> … and it's very hard to pinpoint which area because if only one area is numb here and next to it is hurting, you know, you can't really localize it like here, and two-quarters of an inch to the left is numb; no, everything is painful. You feel pain.

A HIV-PN African American female participant stated:

> It’s the numbness. But it hurts… It’s like it’s numb. But it’s not numb… I can’t explain that. It’s numb. And it’s thick. You feel it. …But you feel pain too. I don’t understand. I can’t explain it.

A DPN female participant stated:

> I’d say pins and needles is a good description. When it’s stronger, it’s that sensation of something inside my foot moving. But the actual skin, the top layer of the skin, feels completely numb.

Numbness and how to describe the pain was quite challenging. Adjectives and descriptors will be discussed further in this analysis. Numbness is a prominent word for these two groups and finding a way to describe this sensation was puzzling, frustrating, and perplexing to find a resolution for these participants of how to share this experience of pain sensation or lack of sensation.

Pain fluctuates. This theme was shared by nine participants in both groups. The DPN participants related these fluctuations to glucose levels and the HIV-PN participants

did not state why the pain would be at different levels. The sudden presence of increased pain or an unexpected pain sensation was unpredictable and challenging for these participants to manage. These sudden pains would be unexpected and impossible to ignore. A DPN female participant stated:

> It's like getting jabbed with a fork… I was standing in the kitchen talking to my mom, and all of a sudden, I just got that stabbing. I had to just stop what I was saying and just bend over, and I had to just grab onto my foot and just sort of you know, just holding it really tight just sort of waiting for it to pass.

A HIV-PN participant female stated:

> …it's (*pain*) not in one particular spot. It feels like something shooting up my leg from the foot – ya know – maybe up to the calf... I can't say it feels as if anything is touching me. It feels like something inside shooting up my leg… it's just a sharp, intense pain. And it comes and it goes. And it hurts.

The unexpected nature of these sudden pains was not specifically associated to any rationale by the participants in the HIV-PN group. These participants never referenced why these unexpected moments of intense pain would occur. The DPN group shared their beliefs that the fluctuation of glucose caused the changes in pain. A cause was never referenced by the HIV-PN group during their narratives. The DPN participants attributed the sudden moments of pain as possibly related to glucose fluctuations, but would make statements of confusion because of the efforts of maintaining a tight control over their diets. The participants who had well-controlled HgA1c evels were unclear about the relationship between the glucose levels and sudden intense pain, but it seemed

important to many of them to mention that this fluctuation of glucose could be the cause. The HIV-PN group seemed resigned to these sudden pains, because many of the participants were long-term HIV survivors and stated that at least they were alive and knew there were other problems related to HIV disease that could make be much worse.

Balance disturbance. The two groups equally referenced some problem with standing, going up, or down stairs, and feeling unsteady when it related to fear of falling, or navigating stairs to prevent tripping or falling. The HIV-PN group had eight participants who included balance issues in their narratives and there were seven participants in the DPN group. A DPN male participant stated: "I'm at work at times where I don't have to run for a chair but I could be standing, and just it (pain) jolts you. I don't fall. I don't fall, but it's like a shock to the whole body." A HIV-PN African American male participant stated:

> My legs felt weak and like they were bending when I would walk. And I – it brought on an insurety (*sic*) that maybe I might fall… it caused me not to work anymore because it brought on, you know, I might fall."

A DPN Hispanic female participant stated:

> That sometimes I'm walking and I feel like I'm going to fall. …I walking through the stairs, downstairs, I need to stay touching the (banister) … that is going down because.. because if I don't take with my hand, I feel I'm going to fall.

A HIV-PN participant male stated: *"*Yeah, proprioception is like off. Because I – I mean I've tripped – tripped upstairs because I don't actually feel the - the edge of the stair."

Balance and falls are high risk issues as individual's age. None of the participants in either group referenced using a cane or discussing the issue of balance with their doctors.

Delayed seeking treatment. Nine of the HIV-PN group versus five of the DPN group delayed seeking treatment for the PN symptoms. Both groups delayed seeking treatment because they attributed the pain symptoms to shoes, jobs, fungus, or for the diabetic group, the issue of maintaining glucose control and ignoring symptoms of diabetes. The DPN group believed they were not providing the sufficient attention or an awareness of the diagnosis of diabetes. A DPN female participant waited six months before seeking treatment stated:

> I kept trying to make it go away. I would think when it (*pain sensations*) got a little bit worse that I was doing something wrong, and what did I need to do to fix it? I had been in great denial about whether I was a diabetic. Every person in my father's family has diabetes or had diabetes. My aunt died of gangrene infection, and my father had diabetes. I just said it wasn't me; it couldn't be me.

A HIV-PN African American male participant waited three months stated:

> Two things came to my mind was athletic feet comin' back. Yeah, start scratching and takin' my foot and rubbin' it on somethin' hard. It was more of an embarrassment. Athletic foot – your toenails – and I'm scratchin' my foot. What's goin on? I had (not) the slightest clue of what neuropathy – I never even heard the word.

While the DPN group seemed to have a context of what the sensations in their feet could possibly indicate - uncontrolled diabetes or a diagnosis of diabetes. The HIV-

PN group attributed these symptoms of pain to issues unrelated to HIV disease and believed the symptoms were caused by elements related to life (i.e. job-related, fungus), not thinking these sensations could be related to their primary illness of HIV.

Effects of medications. A larger number of the HIV-PN participants discussed side effects to the pain medication or the side effects of antiretrovirals. The DPN group had a small number of participants who expressed doubts that the pain medication was helping until they discontinued it for a brief period. Participants in both groups wanted to take over-the-counter medications because of a fear of becoming dependent on pain medications. A HIV-PN male participant stated: *"…*you kinda have to balance one (p*ain meds*) with the other. If you wanna function or if you wanna be, you know, more pain-free. …I'd rather function and have a little more pain than be zombie-like." A DPN male participant stated: "I know we tried Lyrica for a while. It made it almost impossible for me to have a good time sexually. I found it almost impossible to climax. The next doctor got me off it and started me on amitriptyline."

Pain medications were perceived by both groups as limited in an ability to relieve pain. One participant made a statement about how the pain medication made a difference in their ability to "get out of bed." The pain was always present, and no participant mentioned nonpharmacologic options from their primary care provider for pain relief. The focus for pain relief was related to medications. The participants sought out alternative solutions for themselves (research) or coping techniques to help manage pain and shared the lack of certainty whether the pain medications were working.

Trust. Participants in both groups, seven in the HIV-PN group and five in the DPN group, stated that trusting their primary care physician helped them seek out diagnosis and treatment. Trust in the physician was what helped individuals in these groups to manage their primary diagnosis of HIV or diabetes. Trust aided those who developed PN symptoms or were seeking a primary diagnosis and treatment as a result of PN symptoms. The participants expressed appreciation and gratitude for the provider who listened and developed a connection with them. A HIV-PN African American male participant stated:

> Yes because I have a good relationship with my doctor. It makes me feel good because it's like social working and doctoring and a friend all wrapped up in one… She knows some of my inner secrets. So, I could talk to her.

A DPN male participant stated: *"*He's the best (*podiatrist*). He had me get inserts. I wear the inserts. It takes a little pressure off the big toe." A HIV-PN Hispanic male participant stated:

> But luckily, I was able to go to a doctor – to a very nice doctor. She spoke to me, and in fact – She was very nice. In fact, what happened was that I went to see her, and one time I just broke down. And she said, "…go check out the mental clinic and get an HIV test.

Trust is the cornerstone to the patient provider bond. The responses shared by both groups revealed how trusting the doctor led to seeking out an HIV test, sharing inner concerns, secrets, and willingness to follow through on acting for oneself. The participants shared some issues of what they felt was crucial to build this trusting bond

and one participant shared, “that they gave me the time.” Time and attention is critical in managing challenging and complicated chronic illnesses. It is unclear that the health care climate today is measuring the value of time between patient and provider and how this can impact the actions taken by a patient on behalf of their continued health.

In summary, the number of common themes was greater between the two groups than those themes that were dissimilar. The relevance of these themes and how they related to the pain questionnaires will be discussed in Chapter 5. The goal of uncovering these themes served to reveal the lived experiences these individuals have when managing a pain disorder within the context of challenging primary diseases such as HIV and diabetes mellitus. These common themes found between these two groups have not been reported in a direct comparison of pain narratives and offer an opportunity to explore improving education and health care engagement by the primary care provider to address issues that will help those diagnosed with PN achieve goals related to activities of daily living.

Contrasting Themes

Five themes emerged that were uniquely relevant to one group of the two groups. These themes had a dominance in one group while were either not represented by any or very few of the participants in the opposite group. These themes begin a discussion about how to better serve individuals diagnosed with HIV disease or diabetes mellitus when diagnosed with the painful disorder PN. These themes provided insight into the issues as they related either to the HIV-PN group or the DPN group. Table 4 describes these themes.

Table 4

Contrasting Themes

	HIV-PN	DNP
Privacy	70%	0%
Mood	67%	20%
Sleeping difficulty	17%	80%
Exercise	17%	70%
PN interrelated to primary disease	90%	30%

These contrasing themes were determined as dominant to the group by a percentage of participants (> 40%) sharing these concepts as compared to the alternative group. Privacy was the single theme in the HIV-PN group alone while exercise was a theme that was prominent in the DPN group, but still had some relevance in a smaller percentage of the HIV-PN participants. The theme of interrelatedness to the primary disease was present in both groups, but the HIV-PN group used language referencing a relationship between the HIV diagnosis or treatments more frequently than the DPN group. The following will describe the specific theme and group and how these were or were not relevant to the group.

Privacy. The HIV-PN group spoke about pretending, and making excuses, or feigning injury when questioned by friends or family about why they demonstrated gait disturbances. An African American male participant began whispering when describing the desire to keep the PN disorder or HIV diagnosis private.

> I didn't tell a friend until I was, like, limping, and my friend said, what's wrong? I said, oh, I must have hurt my leg, my foot or something. (whispered) I was

> trying to walk in a way that no one would really notice it, that maybe they thought it was like a style walk, but it was really a pain, …but I faked it so that people wouldn't...(know)

Another HIV-PN African American male participant stated:

> …I didn't let nobody know what I was goin' through… Ya know, never act like nothin's botherin' me. I had an (pain) episode last Sunday. And I was sittin' in church. And I had to get up. So I was actin' like I was clappin' to the music.

The HIV-PN group repeatedly stated they wanted to maintain their privacy when it came to any type of symptom. While the participants did not explain the reason, they desired to keep the symptoms private there was very little discussion of sharing the challenges of coping with pain or seeking out any social support. Several of the HIV-PN group stated how they shared with their spouse or a family member, but no one spoke of openly discussing these symptoms. A HIV-PN participant tried to attend a support group and found the topics of discussion were related to housing, employment, and discontinued attending because there was no discussion directed at managing disorders related to HIV. The DPN group made no reference about hiding or pretending they were not in pain. There was openness in their discussions in the DPN group to friends, families, fellow diabetics and co-workers. There was no concern in sharing these challenges of pain symptoms with others. One participant referenced that their sharing may not result in the desired outcome. A DPN female participant stated: "…frustrating in trying to explain to other people who don't really get it, even to some diabetics who don't understand it (PN)."

Members of the DPN group knew there was a risk of a PN diagnosis because of their diabetes and the standard practice in diabetes that includes a diabetic educator. The HIV-PN group had no awareness of PN as an additional disorder in HIV and would initially think the PN symptoms were not related to HIV but to other life issues (i.e., job related, athlete's foot).

Mood. There was a greater impact on mood because of PN symptoms in the HIV-PN group versus those in the DPN group. HIV-PN group clearly described feeling pain intensify when having strong feelings (i.e., anger, fear) versus feeling no pain when they were experiencing fun or happy experiences. A HIV-PN African American male participant stated: "…it (pain) scared me because I wanted the life I had." A HIV-PN African American male participant stated: "…mean if it's (*pain*) going to come, it's going to come, but I always say, sometimes, you know, if I'm irritated, it (*pain*) seems like it'll come faster." A HIV-PN African American male participant stated: "I won't notice it (*pain*) because I'm having fun…" A HIV-PN African American male stated: "Yes, you're runnin', your dancin' and whatever (*no pain*). But when you sit and then you in that mood, somethin' like depressed, it (*pain*) bothers you. It scared me."

Moods that HIV-PN participants described were all related to a concern that the PN would progress or escalate. The HIV-PN group was composed of long-time survivors of an average of 19 years. Only one participant was infected in the year 2000 when the HIV meds were more effective. Many of the participants had experienced complications related to HIV or had witnessed friends or lovers have complications. A HIV-PN participant stated, "Because I hear some people got it in their hands… imagine numbness

in your hand where you can't lift." The idea of a condition that may just be a constant problem but doesn't really progress can be quite challenging for the HIV-PN group because of the lack of awareness of this condition existing in HIV by these participants, while in the DPN group the awareness of PN is greater due to formalized education programs.

Sleeping difficulty. The DPN group reported challenges with sleeping compared to the HIV-PN group. Awareness of the neuropathy symptoms seemed to increase during the latter part of the day or evening due to either a lack of distractions or the manner in how these participants were taking pain medications. A DPN female participant stated: I started to feel it (pain) more during the day, but especially at night. And sometime(s) difficulty sleeping…when I had a lot of trouble sleeping, I just developed this strange thing where I would have my feet outside the covers and just move my feet rapidly." A DPN participant male stated:

> …it (feet) became so sensitive that if I put a sheet at night, I couldn't sleep with a blanket. If I was covered with a sheet and the sheet touched the top of my foot, I'd be writhing in pain. It was excruciating. It (DPN) flares up occasionally at nights; mostly at nights. I still get a throbbing. Not every night. Not every night. On average, every other night just for a split second. It feels like a needle and then it goes away.

The DPN group made it clear that the PN symptoms were present but were increasingly a problem in the evening and during the night. Whether it was an overall increase in the pain symptoms would be more apparent or a sudden stabbing pain that

would happen in the night, the DPN group was quite aware of the difference in the discomfort during the day versus the challenges of the PN symptoms that would occur during the evening. A DPN Hispanic female participant stated:

> …Before I was very good sleeper, trust me, ten – between ten and eight hours of sleeping. …after that (PN diagnosis) I was a little between five hours, six sometimes. Other times that was just two hours, so one day was two hours.

Several in the HIV-PN group did mention sleep disturbance but was less frequent as compared to the DPN group where the discussion was about the awareness of the pain symptoms increasing towards the end of the day or increasing and waking the participants from sleep. There was no mention of sleep medications except by one participant in the HIV-PN group who stated they slept well due to sleep medications.

Exercise. The DPN group members stated a discontent with not being able to return to former physical activities or exercises that were part of their daily routines prior to a PN diagnosis. The issues ranged between the discomfort due to the type of shoes needed for exercise (tennis shoes) or the inability to engage in physical activities without increased pain or fatigue. A DPN female participant stated: "I ran the marathon, so I did a lot of training back in the late '90's-early 2000's. I would love to get back to it, but I did have one podiatrist warn me that I shouldn't do that anymore if I don't have feeling in my foot." A DPN male participant stated:

> I still have the strength. I determine it by the strength. My left leg is not as strong as my right leg, but I still have the strength in my right leg. I can still kick a football. The strength in the left leg has definitely diminished.

The HIV-PN group had one member who discussed how the ability to walk or ride a bike had drastically decreased, yet they still made efforts to participate in these activities. There were some members of the HIV-PN group who mentioned walking, but it was not done with an intention of returning to an active engagement in physical exercise, but due to a need to walk down the hall or walk a few blocks to run errands. The DPN group consistently shared about the inability to return to a physical pursuit of a sport or an inability to perform exercise routines due to pain, fatigue, or weakness in the physical activity that was part of their lives before being diagnosed with PN.

PN interrelatedness to primary disease. The theme of primary disease and the diagnosis of PN were extremely difficult to separate in the HIV-PN group versus the DPN group. Several participants in the HIV-PN group were diagnosed with HIV due to symptoms of PN. Antiretrovirals that are neurotoxic were used in the early years to treat HIV disease and neuropathy was a known side effect to physicians but not very well known by the patients. These occurrences established a relationship of PN within the context of the primary HIV disease that appeared to influence the perception of the pain experience for each participant in the HIV-PN group. A HIV-PN Hispanic male participant stated:

> I didn't know what neuropathy was… The whole process. The mental clinic, but also to get tested for HIV. In fact, in a way, finding out I was HIV-positive saved my life." A HIV African-American participant male stated: "...I was still getting, you know, (dealing with HIV diagnosis) I said, well, maybe this is part of the HIV stuff. You know, maybe it's affecting my feet first or something.

A HIV-PN African American male participant stated:

> I talked to my doctor. …they said it (PN) could have come from the medication – the Zerit. I was on Zerit then, or it could have just come from the HIV virus by itself. They took me off Zerit, and still hasn't gotten me any better. So it might just be from the virus, itself.

Some of the HIV group participants felt they have been coping with HIV and PN for twenty or thirty years that "it's (*PN*) like secondary to me now." Other viewpoints within the HIV group had to do with the perception of illnesses that were related to HIV disease or pain related to HIV complications that made managing or coping with PN tolerable. A HIV-PN African American female participant stated:

> To me, normal was – by me bein' HIV positive, I figure it has something to do with me bein' positive and due to the medications, that I've had or tried because some medications always interfere with your health... Because I've been sick 20 years been diagnosed 20 years.

A HIV Hispanic male participant stated:

> it's nothin' can be done for this. This is a wrap. This is part of the HIV virus this neuropathy. We gonna have this for the rest of our lives. Everybody we talk to feel the same thing.

The ability for these participants to separate their pain perception due to PN and their perceptions of being infected with HIV virus was unclear. While the DPN group appeared to understand the context of PN as it related to the disease of diabetes. Three

individuals expressed a perception of pain relative to their diabetes because of complications due to diabetes. A DPN female participant stated:

> At any rate, I didn't go on insulin until I had the diabetic amyotrophy. It took easily nine months to diagnose that, and by that time, I was crazed. I had much, much more than peripheral pain. It was sort of like this seismic shift in my health condition.

A DPN female participant shared:

> Diabetic ketoacidosis. …that was the first time I had suffered from that. I didn't really I was going into Ketoacidosis, and they didn't at the hospital either because my sugar wasn't that high. I lost a lot of weight, and it took a lot of time to recover. I'd say the rest of July and most of August, the pain was just excruciating – really, really bad.

While the concept of an interrelatedness perception of the PN disorder within the context of the primary illness was evident in the HIV-PN group at a higher level of occurrence, it is unclear whether the perception of pain was affected by these disease-related occurrences or their ability to cope with pain from PN. The DPN group while the disease-related occurrences were lower, the circumstances of an illness related to diabetes increased pain and potentially may have a greater influence on how these participants perceived pain once the complication due to diabetes resolved.

Pain Description

The largest element the participants in both groups shared were the adjectives and descriptors that each participant provided when discussing what were the sensations or

symptoms they perceived about their PN. Pain was the word frequently used by both groups and with a similar frequency (HIV-PN 200; DPN 186) during the process of discussing their narratives. Twenty-nine descriptors were similar between the two groups with varying amounts by the participants. Table 5 represents these descriptors for both groups with the number of participants and the frequency the word was used.

Table 5

Similar Pain Descriptors

Descriptor	HIV-PN # participants	Frequency	DNP # Participants	Frequency
Numbness	11	100	9	50
Hurting	6	55	3	14
Needles	6	19	3	5
Sensations	1	6	6	20
Tight	3	6	6	16
Bad	5	12	4	12
Sharp	5	5	1	3
Tingling	5	22	5	13
Burning	4	21	4	11
Cramp	4	12	3	8
Fall	4	15	3	6
Itch	4	18	3	7
Pins	4	15	3	5
Stabbing	4	6	3	15
Tired	4	4	2	9
Cold	4	21	2	8
Balance	3	4	2	3
Excruciating	1	2	3	3
Severe	2	2	3	12
Shooting	2	5	2	3
Throbbing	2	2	2	3
Hot/heat	1	1	2	3
Squeezed	1	1	2	3
Stiff	1	1	2	3
Weird	1	1	2	2
Angry	1	1	1	1
Frustrating	1	1	1	4
Intense	1	1	1	4
Weak	1	1	1	2

The interesting aspect of notating the similar descriptors between the two groups was the word *numbness* showed to be equally used by both groups. The next word that was used frequently by the DPN group was *sensations*, yet only used by one participant in the HIV-PN group. The word *sharp* was used by one participant in the DPN group while five participants in the HIV-PN group chose it for pain. The next frequent word used by the HIV-PN group was *hurting* and also used by a third of the DPN group.

The other aspect of the pain descriptors were the words that were unique to each group. (See Tables 6 and 7).

Table 6

Unique Descriptors to HIV-PN Group

Descriptor	HIV-PN	Frequency
Spasms	3	6
Afraid	3	4
Aching	2	4
Upsetting	2	4
Compressed	2	3
Distressed	1	1
Embarrassed	1	1
Freaked out	1	1
Hammering	1	1
Horrible	1	1
Irritating	1	1
Nagging	1	1
Oh my God	1	5
Scared	1	5
Sore	1	7
Thick	1	1
Tolerate	1	5
Wacky	1	1
Annoying	1	5
Bending	1	1
Buzz	1	2

Table 7

Unique Descriptors to DPN Group

Descriptor	DPN	Frequency
Swollen	4	7
Uncomfortable	4	4
Pressure	3	8
Creepy crawling	3	6
Stinging	3	7
Different	2	2
Difficult	2	2
Discomfort	2	5
Unpredictable	2	4
Heavy	2	5
Vibration	2	2
Depressing	1	5
Frequent	1	4
Hard	1	2
Jolt	1	2
Funny feeling	1	1
Prickling	1	1
Restless	1	1
Shock	1	1
Dull	1	1
Aggravate	1	1
Constant	1	1
Unpleasant	1	1
Agony	1	1
Grimace	1	1
Writhing	1	1

Twenty-one additional words were used by the HIV-PN versus 26 words used by the DPN group to describe the symptoms of PN. While many of these descriptors were used by a single person in each group, it is useful to the nature of this study to capture the distinctive nature of how each group described and experiences their PN symptoms in the effort to define their lived experiences. When participants are asked to provide descriptors within a clinical trial, it is in the process of answering a sequence outlined in

the MPQSF (See Appendix C). Table 8 is a reverse engineered table of the 15 descriptors found in the MPQSF and the percentage of participants that selected these descriptors from each group when completing the questionnaire. The descriptors used in the MPQSF shared seven words out of the 29 that were commonly used by each group (designated with an asterisk *) when freely describing their pain in this study. The HIV-PN group included the words *aching* and *fearful,* and the DPN group included the word *heavy*. The aspect of this study was to determine the similarities and differences between these two groups as it related to these descriptors of the pain experience. The number of descriptors that participants used and the challenge of describing the pain experience demonstrated that finding language for the pain experience supports the common theme *pain and numbness coexist.* Both groups demonstrated finding an accurate description of this experience problematic. The ability to describe and understand the lived experiences of these participants and how each of these participants perceive pain and the relevance of how this perception could play a role in successful pain treatment. What could be distinct to one group may not transfer to the experience of pain as perceived by another group. Perception may also be increasingly shifted when different primary illnesses are present, yet pain outcome measures are used in all types of pain syndromes.

Table 8

Descriptors in the MPQSF

Descriptor	HIV-PN *n* = 12	DPN % *n* = 9
Aching[HIV]	91.6%	77.7%
Shooting*	91.6%	66.6%
Sharp*	91.6%	77.7%
Throbbing*	83.3%	66.6%
Cramping*	83.3%	66.6%
Gnawing	83.3%	33.3%
Heavy[DM]	83.3%	44.4%
Stabbing*	75%	55.5%
Tender	75%	66.6%
Hot/Burning*	66.6%	66.6%
Splitting	66.6%	33.3%
Tiring/Exhausting*	66.6%	66.6%
Sickening	58.3%	44.4%
Punishing	58.3%	33.3%
Fearful[HIV]	41.6%	11.1%

Paralinguistics

The journey of assessing the audio transcripts began with the process of answering the questions: (a) does the transcript correlate to the audio recording and tone of voice? and (b) how does the transcript reveal the story of the audio recording? The transcripts while they contained the words used by the participant, they did not convey the story of the participant's experience. The process of extracting the words from an audio recording of a human experience leaves information that is not captured. These elements were the tone of voice, the rhythm of speech and the nonverbal expressions commonly known as paralinguistics (Trager, 1958; Trager 1961). The notable issue that was an apparent difference between the two groups was the tone of voice. This study did not establish a manner in how to measure or quantify the differences in the tone of voice

between the two groups. The study performed had not defined a method of detecting the tone of voice other than to provide a broad assessment that will be discussed further in Chapter 5. The tone of voice that the HIV-PN group demonstrated lacked in inflection as compared to the DPN group. Seven of the participants in the HIV-PN group demonstrated either flat tones or soft-spoken narratives as compared to two of the DPN group. Once tone of voice was examined, the following nonverbal and paralinguistic expressions were notated and captured in each of the narratives: laughter, breath (defined as a sigh or an audible inhale or exhale), word searching, and pauses (2 or more seconds). Table 9 provides the results of an independent sample *t* test comparing the number of incidents of each element notated in each group.

Table 9

Nonverbal and Paralinguistic Elements

	HIV-PN	DNP	*p*-value
Laughter	$M = 8.25$ $SD = 5.62$	$M = 14.60$, $SD = 14.23$	$t(20) = 1.42$, $p = 0.17$
Breath	$M = 13.66$, $SD = 11.26$	$M = 11.50$, $SD = 2.75$	$t(20) = 0.46$, $p = 0.64$
Word search	$M = 8.16$, $SD = 4.70$	$M = 15.70$, $SD = 4.11$	$t(20) = 3.95$, $p = 0.001$
Pauses (> 2 sec)	$M = 34.41$, $SD = 8.77$	$M = 38.30$, $SD = 13.63$	$t(19) = 0.80$, $p = 0.42$

A DPN participant stated: “What happened after that was, *pause* I found out in ’97 I had diabetes. *laugh* No. I had no clue. No clue that I had diabetes. *word search* When I found out, what triggered it, was urinating so frequently.” A HIV-PN Participant stated: “And a few months later is *pause* when I started really having the pains because *pause* I had time to think. I don’t think there was anything over-the-counter for neuropathy pain at all.”

Breath

The only paralinguistic that didn't occur in all the participants were the audible inhalations and sighs notated as breath in the above table. Two participants in the DPN group did not demonstrate any audible sighs or inhalations. The statistical significance of *word searching* with HIV-PN group ($M = 8.16$, $SD = 4.70$) and the DPN group ($M = 15.70$, $SD = 4.11$); $t\ (20) = 3.94$, $p = 0.001$ suggest that English as a second language coupled with the challenge of describing pain symptoms demonstrated there to be a difference in the two groups. These nonverbal and paralinguistic elements were quite noticeable in the audio recordings and changed the characterization of the narratives when incorporating these elements within the context of the shared information. Laughter, breath, and pauses were equally prominent in both groups, but what these elements represented for these two groups is unclear. The ramifications of these findings will be discussed further in Chapter 5.

Quantitative Analysis

An independent-samples *t* test was conducted comparing all of the standardized pain measurement instruments (VAS, NRS, SFMPQ, BPIsc, 7 day pain diaries, and BDI) between the HIV-PN group and the DPN group. A two-tailed independent-samples *t* test was used because of the nature of the study, and the small numbers in the group. Each questionnaire was seen as an independent inquiry (Miller, 1981). These measurements were completed by all of the participants before conducting the audio recorded interviews. The one element that is unclear is why one of the participants in the DPN group only completed the VAS and the NRS pain questionnaires. I went back to the original source, and there is no clear explanation as to why the remaining pain

questionnaires were left blank. Therefore there is a difference in the degrees of freedom in the results.

None of the primary elements of the pain intensity measures VAS, NRS MPQSF, BPIsc, or 7day pain diaries were significant between the groups ($p > 0.2$ for all). There was one-word found in the MPQSF descriptors *splitting* that showed significance with HIV-PN group ($M = 1.25$, $SD = 1.05$) and the DPN group ($M = 0.33$, $SD = 0.50$); $t(19) = 2.40$, $p = 0.02$. All the questions in the Beck Depression Inventory scale were not significant for the two groups ($p > 0.1$) except for question 5, guilty feelings. Question 5 was significant with the HIV-PN group ($M = 0.08$, $SD = 0.28$); DPN group ($M = 0.44$, $SD = 0.52$); $t(19) = 2.01$, $p = 0.05$. See Tables 9, 10, 11, and 12 for complete reporting.

Table 10

Pain Measurement Results

	HIV-PN	DNP	*p*-value
VAS	$M = 50.33$, $SD = 22.46$	$M = 41.40$, $SD = 21.43$	$t(20) = 0.82$, $p = 0.41$
NRS	$M = 5.17$, $SD = 2.03$	$M = 4.40$, $SD = 2.75$	$t(20) = 0.75$, $p = 0.46$
MPQSF Pain Intensity	$M = 2.67$, $SD = 1.23$	$M = 3.33$, $SD = 1.22$	$t(19) = 1.23$, $p = 0.23$
MPQSF VAS	$M = 57.50$, $SD = 25.56$	$M = 59.11$, $SD = 26.27$	$t(19) = 0.14$, $p = 0.88$
7-day pain diaries	$M = 4.27$, $SD = 1.73$	$M = 3.60$, $SD = 2.50$	$t(19) = 0.48$, $p = 0.72$

Table 11

Pain Measurement Results—Brief Pain Intensity Scale

	HIV-PN	DNP	*p*-value
General activity	$M = 3.92$, $SD = 2.46$	$M = 3.56$, $SD = 2.60$	$t(19) = 0.32$, $p = 0.74$
Mood	$M = 3.58$, $SD = 3.34$	$M = 4.40$, $SD = 2.75$	$t(19) = 0.51$, $p = 0.61$
Walking	$M = 4.50$, $SD = 2.93$	$M = 5.33$, $SD = 3.27$	$t(19) = 0.61$, $p = 0.54$
Normal work	$M = 4.17$, $SD = 2.94$	$M = 4.11$, $SD = 3.37$	$t(19) = 0.04$, $p = 0.96$
Relationships	$M = 3.33$, $SD = 3.36$	$M = 1.89$, $SD = 2.42$	$t(19) = 1.09$, $p = 0.28$
Sleep	$M = 4.33$, $SD = 3.52$	$M = 3.89$, $SD = 3.33$	$t(19) = 0.29$, $p = 0.77$
Enjoyment of life	$M = 4.92$, $SD = 3.52$	$M = 3.44$, $SD = 2.45$	$t(19) = 1.07$, $p = 0.29$

Table 12

Pain Measurement Results—MPQSF—Adjectives

	HIV-PN	DNP	*p*-value
1Throbbing	$M = 1.50$, $SD = 0.79$	$M = 1.33$, $SD = 1.11$	$t(19) = 0.40$, $p = 0.69$
2Shooting	$M = 1.58$, $SD = 0.90$	$M = 1.22$, $SD = 1.09$	$t(19) = 0.93$, $p = 0.41$
3Stabbing	$M = 1.50$, $SD = 1.08$	$M = 1.44$, $SD = 1.50$	$t(19) = 0.09$, $p = 0.92$
4Sharp	$M = 1.75$ $SD = 0.86$	$M = 1.53$, $SD = 1.23$	$t(19) = 0.42$, $p = 0.67$
5Cramping	$M = 1.33$, $SD = 0.88$	$M = 1.33$, $SD = 1.22$	$t(19) = 0.00$, $p = 1.00$
6Gnawing	$M = 1.42$, $SD = 0.90$	$M = 0.67$, $SD = 1.11$	$t(19) = 1.70$, $p = 0.10$
7Hot-Burning	$M = 1.17$, $SD = 1.11$	$M = 1.67$, $SD = 1.32$	$t(19) = 0.94$, $p = 0.35$
8Aching	$M = 1.83$, $SD = 0.83$	$M = 1.56$, $SD = 1.13$	$t(19) = 0.64$, $p = 0.52$
9Heavy	$M = 1.50$, $SD = 1.00$	$M = 0.78$, $SD = 1.09$	$t(19) = 1.57$, $p = 0.13$
10Tender	$M = 1.55$, $SD = 1.03$	$M = 1.33$, $SD = 1.22$	$t(19) = 0.42$, $p = 0.67$
11Splitting	$M = 1.25$, $SD = 1.05$	$M = 0.33$, $SD = 0.50$	$t(19) = 2.40$, $p = 0.02$
12Tired exhausting	$M = 1.40$, $SD = 1.16$	$M = 1.44$, $SD = 1.33$	$t(19) = 0.51$, $p = 0.96$
13Sickening	$M = 1.33$, $SD = 1.30$	$M = 0.56$, $SD = 0.72$	$t(19) = 1.06$, $p = 0.12$
14Fearful	$M = 0.75$, $SD = 0.86$	$M = 0.44$, $SD = 0.88$	$t(19) = 0.79$, $p = 0.43$
15Punishing cruel	$M = 0.92$, $SD = 0.90$	$M = 0.78$, $SD = 1.20$	$t(19) = 0.30$, $p = 0.76$

Table 13

Beck Depression Inventory Scale

	HIV-PN	DNP	*p*-value
Sadness	$M = 0.25$, $SD = 0.62$	$M = 0.56$, $SD = 1.01$	$t(19) = 0.85$, $p = 0.40$
Pessimism	$M = 0.42$, $SD = 0.90$	$M = 0.44$, $SD = 0.52$	$t(19) = 0.08$, $p = 0.93$
Past failure	$M = 0.25$, $SD = 0.62$	$M = 0.44$, $SD = 0.88$	$t(19) = 0.59$, $p = 0.53$
Loss of pleasure	$M = 0.92$, $SD = 0.79$	$M = 0.67$, $SD = 0.70$	$t(19) = 0.74$, $p = 0.46$
Guilty feelings	$M = 0.08$, $SD = 0.28$	$M = 0.44$, $SD = 0.52$	$t(19) = 2.01$, $p = 0.05$
Punishment/Feelings	$M = 0.00$, $SD = 0.00$	$M = 0.44$, $SD = 1.01$	$t(19) = 1.53$, $p = 0.14$
Self-dislike	$M = 0.33$, $SD = 0.65$	$M = 0.44$, $SD = 0.88$	$t(19) = 0.33$, $p = 0.74$
Self-criticalness	$M = 0.25$, $SD = 0.45$	$M = 0.44$, SD = 0.82	$t(19) = 0.75$, $p = 0.45$
Suicidal thoughts	$M = 0.00$, $SD = 0.00$	$M = 0.11$, $SD = 0.33$	$t(19) = 1.16$, $p = 0.25$
Crying	$M = 0.17$, $SD = 0.45$	$M = 0.56$, $SD = 0.72$	$t(19) = 1.58$, $p = 0.13$
Agitation	$M = 0.25$, $SD = 0.45$	$M = 0.67$, $SD = 0.70$	$t(19) = 1.64$, $p = 0.11$
Loss of interest	$M = 0.33$, $SD = 0.49$	$M = 0.67$, $SD = 0.70$	$t(19) = 1.27$, $p = 0.21$
Indecisiveness	$M = 0.42$, $SD = 0.51$	$M = 0.67$, $SD = 0.86$	$t(19) = 0.82$, $p = 0.41$
Worthlessness	$M = 0.17$, $SD = 0.38$	$M = 0.44$, $SD = 0.72$	$t(19) = 1.13$, $p = 0.27$
Loss of energy	$M = 0.83$, $SD = 0.38$	$M = 1.11$, $SD = 0.60$	$t(19) = 1.28$, $p = 0.21$
Changes in sleep	$M = 0.75$, $SD = 0.62$	$M = 0.78$, $SD = 0.97$	$t(19) = 0.08$, $p = 0.93$
Irritability	$M = 0.33$, $SD = 0.49$	$M = 0.44$, $SD = 0.52$	$t(19) = 0.49$, $p = 0.62$
Changes in appetite	$M = 0.25$, $SD = 0.45$	$M = 0.78$, $SD = 0.97$	$t(19) = 1.66$, $p = 0.11$
Concentration difficulty	$M = 0.58$, $SD = 0.79$	$M = 0.78$, $SD = 0.66$	$t(19) = 0.59$, $p = 0.56$
Tiredness or fatigue	$M = 0.75$, $SD = 0.62$	$M = 1.00$, $SD = 0.70$	t(19) = 0.86, $p = 0.40$
Loss of interest in sex	$M = 0.50$, $SD = 0.90$	$M = 0.56$, $SD = 0.52$	t(19) = 0.16, $p = 0.87$

While the quantitative analysis fails to reject the null hypothesis H_0 – HIV-PN and DPN have equal pain levels/depression, the qualitative data supports this analysis with the number of themes that the two groups have in common versus those themes distinct to each group. The quantitative data related to the Beck Depression Inventory demonstrated that *guilty feeling* was statistically significant and could be associated with the theme of *privacy* found in the HIV-PN group. The one element found as statistically significant in the pain descriptors of the MPQSF *splitting* could be an indicator that how these two groups describe and perceive their pain may be a challenge for both groups based on the theme found in the qualitative analysis as *pain and numbness coexist*. These issues will be discussed further in Chapter 5.

Evidence of Trustworthiness

Credibility

The researcher's role was to document systematically the process of carefully assessing the narratives with a tool that documented these procedures. The step by step assessment of the transcripts and audio recordings began with a macro review as detailed in the structured review sheet followed by an increasing assessment to the micro view of each participant. The systematic process began with the HIV-PN group followed by the DPN group for each assessment outlined in the tracking tool. Simultaneously, three volunteers (pre-medical students) reviewed the transcripts and highlighted statements as they related to pain, function or neuropathy. Each participant's audio recording and a transcript was assessed multiple times in their entirety before compiling the themes and narratives that were either similar or different in each group. The assessment of the audio

recordings review was extended to allow for the tracking of the nonverbal and paralinguistic component. As the author sought to address the question ‘does the transcript reveal that story of the audio recording?’ The transcripts did not capture elements of the tone of voice, nor the nonverbal and paralinguistic components (laughter, sighs, inhales, word searching, and pauses). The process to include these components contributed to addressing the theory of the biopsychosocial model in chronic pain. The idea of the researcher’s role was to capture the pain narrative as a journey from when the participant first experienced his/her pain to the diagnosis and treatments.

Triangulation was addressed by having supportive data through the collection of the pain diaries, the standard pain questionnaires, the Beck Depression Inventory scale (BDI), and the participant's most recent medical notes from a visit with their primary care physician. Elements of the quantitative data demonstrated a potential association between the theme of *privacy* in the HIV-PN group and the issue of *guilty feeling* (question 5 of the BDI) that was found to be significant in the quantitative data. The element of pain adjectives is discussed in Chapter Five and how these pain descriptors are relevant to current descriptions used in standard pain questionnaires.

Transferability

The study enrolled subjects randomly from the two populations, working to have a representation of the multi-cultural nature of East Harlem in New York. As with the quantitative data, the ability to have the narratives of these two populations provided an opportunity to begin to define the perceptions of the pain experience of African Americans, Latinos, and multicultural individuals. While the issue of gender and

education are possible components that demonstrate a difference between the two groups, the overall similarities of themes and data demonstrate that gender and education may not contribute a great amount of influence when describing chronic pain. The use of the narratives offered a rich description of the pain experience and showed the variation in the participant selection. This study provided a first-time comparison of these pain stories to determine the similarities and differences between these two groups. The quantitative data supports these similarities demonstrating that there were no differences in how the groups reported pain when completing pain questionnaires.

Dependability

The study team that originated the study where this data was collected was developed by a seasoned team of researchers in the field of chronic neuropathic pain. Drs. David Simpson, David Dorfman, and Jessica Robinson-Papp were all involved in the development and review of the data and the process of how the data was captured and ensured the database was confirmed by a two-step process (Two individuals separately entering and verifying all data from the source documents). The opportunity to have a mixed-methods study of well-characterized participants who were confirmed by a neurologist to have a diagnosis of PN related to the primary diagnoses of HIV or diabetes was timely for the conduct of this study. An additional level of dependability is the access to review medical records to confirm the medical history and the current status of each individuals HIV or diabetes and what pain medications were being prescribed. This critical selection process assured that the homogeneity of the two groups was without any confounding medical conditions or contributing pain syndromes from another cause. The

unique opportunity this study had was the opportunity to collect information from these participants without the agenda of a diagnosis or treatment, but purely for the ability to be heard and to share the pain narrative.

Confirmability

The process of maintaining an audit trail and an iterative approach of referring to the quantitative data, and the medical records of each of the participants assisted in bringing together a composite for each participant that was compared to the other participants in the study. This process aided me to formulate emerging themes and concepts as they related to the lived experiences of the participants in these two groups. The process of reviewing with one of the co-investigators (Dr. David Dorfman) and the committee for this dissertation process adds an additional level of confidence that should another researcher undertake a similar study in these populations the ability to find similar themes and constructs would be possible.

The use of the interpretive phenomenological analysis approach (IPS) made selecting themes a process that focused on the language that shared the story of the lives of the participants in each group. Due to the nature of the question asked of each participant to “tell their story” of what happened when they first began feeling symptoms of PN, the coding process was one that detected themes that revealed the concerns and issues that provided these participants an ability to make sense of the symptoms, seek help, and manage their lives that were changed due to the diagnosis of a pain disorder coupled with their primary illness. Selecting the codes for the themes was an iterative process. Phrases and statements within each of the narratives were grouped separately.

Once a grouping was detected, a descriptive code was selected. This process was done separately for each group. If a theme appeared in one group but was not in the other group, a process of reviewing the group without the theme to confirm no statements or language could be representative of the theme. This process was done in concert with discussions from the author's mentors at the Icahn School Medicine and a continued discussion with the Chair of the author's committee. The IPS tracking form developed for this study was used in distilling the themes frequency into an excel spreadsheet. Frequency ($\geq 40\%$) determined which themes were dominant to both groups and which themes were specific to either the HIV-PN or DPN group. The goal of this process was to add to the science and methodology for future research in these populations and in qualitative research.

Chapter 4 Summary

The process of finalizing the analyses of these data was a slow and cumulative one to determine the outcomes for the qualitative component of this study in order to define the similar and contrasting themes that provided meaning to the stories of the participants of these two groups. The eight common themes were supported by the quantitative data that failed to reject the null hypothesis. These two groups are more alike than previously considered. Yet the interesting data of the pain descriptors with such a variety and quantity plus the theme of *numbness and pain coexisting* found in both groups could be information that possibly help clinicians with better treatment scenarios and researchers with improved clinical trial design. The final element of the analysis that

demonstrated there was the theme of *privacy* found in the HIV-PN group, yet not found in the DPN group and supported by the statistically significant question relating to

Chapter 5: Discussion, Conclusions, and Recommendations

Purpose of the Study

The opportunity to compare two well-characterized patient groups whose members have confirmed diagnoses of PN and have been diagnosed with either HIV disease or diabetes mellitus is a circumstance in the pharmaceutical dynamic and occasionally is available in an academic hospital setting. This study used a convenience sample of patients who were enrolled into a larger study with a similar purpose to understand how PLWHA and diabetics perceive pain when diagnosed with PN. The goal of this study was to understand whether there were any differences or similarities between HIV-PN patients and DPN patients when discussing and measuring pain perception. Using a mixed-methods approach, the transcripts and audio recordings were reviewed to extract similar and contrasting themes. The quantitative data contained a group of the most frequently used pain questionnaires and measurement tools that are employed in the clinical trial setting. This study was designed to begin to answer the question of whether there were similarities or differences between these two groups when their members described pain or reported pain using questionnaires that measured pain or activities of daily living. The literature does not contain any studies indicating a head-to-head comparison of these two groups and how they describe and report pain. This study begins the preliminary process of building a framework to deepen the understanding of pain perception in these two populations. Although the findings are not surprising, they do offer insight into what could be done to help patients with educational tools, rehabilitation, and possible treatments.

Interpretation of the Findings

Common Themes Interpretation

The most common theme for these two groups was *footwear challenges*. PN is a disorder that occurs in the most peripheral area of the body—the feet—and infrequently also affects the hands. The ability to engage in activities of daily living (ADL) requires walking, standing, and moving, even minimally, with comfortable footwear. Time, effort, and money were discussed within these two groups in relation to the issues members had concerning finding socks and shoes that felt comfortable and helped with the process of walking and completing ADL. The peer-reviewed literature does not address assisting PLWHA who are diagnosed with PN regarding footwear. There is supportive education targeting the DPN population regarding footwear, but the goal of these studies is preventing stress fractures and foot ulcers that can lead to amputations. Robel et al. (2014) performed a study using a shear-reducing thermal insole device as compared to the usual insole to track walking stress, balance, and gait. This study showed by measuring side-to-side stresses that using these novel insoles improved gait in the participants wearing shear-reducing insoles. These types of devices need to be considered for the HIV-PN population. Although the potential for stress fractures and foot ulcers is not a concern in HIV disease, issues of balance and falls are concerns for the aging HIV population. Studies about gait, footwear, or balance need to be considered due to the symptoms of PN. Patients with HIV disease could be a targeted population to study in order to provide enhanced options for footwear. The problem with footwear was very prominent in these two groups, coupled with the theme of *balance disturbance*, which

appears to be an issue that does not go away but consistently needs to be addressed as these patients age.

The common themes of *coping* and *effects of medications* were not unexpected. Issues surrounding the benefits versus side effects of taking pain medications constitute a well-known problem in pain treatment (Margolis et al., 2017). Many patients were not sure that their pain medications were helping because they were still experiencing pain to warrant coping techniques. These coping tactics were not recommended by participants' doctor but were sought out by the participants themselves, apart from one individual in the DPN group who had a diabetic educator recommend acupuncture. *Coping* was an issue that each patient in both groups actively sought out to investigate for further pain relief. The HIV-PN group had been exposed to research in hypnotherapy and mindfulness techniques and referenced the benefit. Members of the DPN group sought out more traditional methods of coping, such as acupuncture, massage, and yoga. A recent Canadian study by Kurklinsky, Perez, Lacayo, and Sletten (2016) showed promise of a model that could be quite beneficial for chronic pain sufferers. A study of an interdisciplinary rehabilitation program focused on a 3-week outpatient program incorporating physical therapy, rehabilitation, occupational therapy, cognitive-behavioral therapy, and medication management. The study used a 6-minute walk test for participants who had failed conventional therapies and showed 39% improvement in their performance, which was 3 times what had been reported in previous studies. The common themes in this study support multidisciplinary approaches due to the complexity

of how the patients in this study reported their challenges with managing medications and discovering options for coping with pain.

The common theme of *pain and numbness coexist* was a distinct observation by these two groups. The spontaneous discussion that these participants shared about the challenges of sensing numbness and pain in the same areas have not been shared or documented before in these two groups. It is widely known that pain and numbness are symptoms that occur when members of these two groups are diagnosed, but this is the first report of participants freely stating these sensations coexist in the same areas of their body, typically the feet. This perception could be a contributing factor for poor pain relief from treatments. The current treatments provided to patients target the symptoms that are considered positive symptoms (i.e., sharp, stabbing, hot/burning; Mackey et al., 2012). Symptoms that may be related to numbness that patients felt corresponded more to theadjective *heavy* found in the DPN group, yet the descriptor that was significant between the groups was *sharpness.* Nonetheless, these subjective perceptions of pain by these participants could have clinical relevance to the type of nerve fiber damage. Several studies in these populations have examined the clinical significance of correlating symptoms, pain descriptors, pain intensity, psychological assessments, and functional testing (quantitative sensory testing and intraepidermal nerve fiber density). The process of recognizing the nature of the nerve damage and how this loss relates to pain perception (Phillips et al., 2014; Themistocleous et al., 2016) could begin to develop a deeper understanding of what patients are reporting. Why and how these nerves become damaged in these two illnesses are not clearly understood. Increasing scientific

knowledge of how this nerve loss occurs and seeking methods to repair nerve function could lead to better treatments for pain that, as participants described in this study, coexists (pain and numbness) in the same areas of the body. A first step could be to acknowledge this with the participants and confirm that what they perceive is possible when diagnosed with PN.

Treatment for both primary illnesses is still quite challenging. Individuals can have diabetes or HIV and not have awareness that anything is wrong when these PN symptoms appear. The theme *delayed seeking treatment* for both groups refers to a delay in the diagnosis of the primary illness or, for the HIV-PN group, a delay in discontinuing neurotoxic treatments. Education about signs and symptoms of PN in the HIV-group were not present at all in the discussions, while the DPN group participants were vaguely aware of the possibility of a PN diagnosis. The DPN participants ignored these signs because a PN diagnosis confirmed diabetes, therefore meaning lifestyle changes to manage diabetes. Education in high-risk groups for both would address these delays in seeking treatment. Working to provide education on the risks of developing PN, these two populations whose members suffer from symptoms in a proactive manner within the clinics where HIV or diabetes is treated could be a first step in helping individuals to speak to their clinicians about these symptoms. Delaying treatments and awareness in both groups can be detrimental in terms of engaging in activities of daily living and enjoying life. Preserving how individuals live and enjoy life within the context of these two challenging illnesses is a necessity to prevent an increase in depression, anxiety, and

social isolation, which could ultimately lead to worsening the primary diseases of HIV or diabetes in these patients.

Finally, the theme of *trust* was common to both groups. The ability to speak freely with a provider and work in partnership to manage a complex illness burdened with a secondary disorder (i.e., chronic painful PN) was comforting for the participants in these two groups. Current concerns in the health care system relate to the potential unavailability of time and attention for these challenging patients with complex medical conditions, yet this study demonstrated the value in providing patients with care and skills of listening and patient empowerment. The health care system in the United States is under scrutiny by those seeking to reduce costs. If cutting costs diminishes the ability for a clinician and a patient to develop a therapeutic bond, the ramifications for these patient populations may be quite detrimental. There needs to be a system in place that can support the clinician, build the therapeutic relationship, and manage costs. Developing a system such as this to serve these patients and develop trust with between patients and health care providers could be a real manifestation of social change for patients dealing with complex medical conditions such as HIV disease and diabetes compounded with the painful disorder of PN. The advent of technologies and wearable devices that support the patient and the provider represents a possible venue to address this need in these populations (Eckard et al., 2016).

Dissimilar Themes Interpretation

The single theme that was present in the HIV-PN group but not shared by the DPN group was *privacy.* Despite progress made in treatments for HIV and improvement

in societal views of the LGBTQ community, patients expressed quite readily an unwillingness to reveal any health issue that might result in disclosure of their HIV status. In their statements, this group of PLWHA did not share their reason for perceiving a need to be private, but it was quite apparent that they were cautious about maintaining privacy when communicating with friends or family or in social settings. A study our team conducted (George et al., 2017) found in a focus group setting unsolicited statements of a need for privacy and uncertainty regarding how to access social support when dealing with chronic pain and HIV disease. In fact, some participants remain isolated and silent, managing their illness alone. The one item that was statistically significant in this study was the question in the Beck Depression Inventory regarding guilty feelings. This finding begins to confirm the issue of privacy as having deeper psychological ramifications and perceptions about being infected with HIV. The complexity of self-perception could play a role in how patients perceive the possibility of wellness or living a healthy life when diagnosed with HIV disease, which represents an exciting area for further research to understand whether these issues contribute to the challenge of conducting research on pain medication in the HIV-PN population. Pharmaceutical companies might be willing to re-engage in seeking pain treatments for PLWHA and PN.

The themes of mood, sleeping difficulty, and exercise are not unknown topics in patients with HIV and diabetes. All of these themes are commonly queried in connection to activities of daily living when seeking to understand how much the chronic pain condition interferes with function. The theme of mood was prominent in the HIV-PN

group, whereas sleeping difficulty and exercise were more prominent in the DPN group; this may have been related to the number of participants or narratives given, which did not necessarily saturate these concepts to delineate an actual difference between the groups for these concepts. A larger percentage of the DPN group shared information about *exerci*se as compared to the HIV-PN group, but within the context of diabetes, exercise is a topic frequently discussed by educators and physicians. The themes of mood, sleeping difficulty, and exercise would need to be included in a larger study in order to understand the implications for each of these groups, especially concerning sleep. Sleep aids were not discussed and only one participant in the HIV-PN group indicating sleeping well due to medications. The question of how sleep aids are used in these two populations should be included in future research. There is evidence of a relationship between chronic pain and sleep. Lack of sufficient sleep may contribute to an increased perception of pain (Finin, Goodin, & Smith, 2013). Sleep disturbance could also be related to the theme of mood or could be more of a matter of how participants give attention to activities in their life. Participants may be more aware of PN symptoms when experiencing anger, frustration, or anxiety than when they are working or having fun, as positive distractions take attention away from PN symptoms. The ability to distract or provide deep relaxation is offered by hypnotherapy and some mindfulness practices; the HIV-PN group used this strategy readily as a coping mechanism. More research concerning activities of daily living in a qualitatively designed study could help in discovering which themes pertain specifically to one group rather than the other or are related to sleep.

Pain Descriptors Interpretation

The words chosen to describe pain by both of these groups were numerous. A list of 15 descriptors commonly used when patients discuss pain with clinicians is found in the MPQ-SF (see Appendix C). The fact that only seven of these words were freely selected by both groups is an interesting finding. Participants in both groups used 29 words in common. This is almost double the number used in the MPQ-SF or pain descriptive words used clinically or in research. The question this raises is whether the participants who were in this study completed these scales by interpreting their pain perception and mapping it into how each defined the words provided, thereby introducing a misrepresentation of their pain experience. Another possible explanation for why there are so many descriptors is the inability to describe or share the experience of these sensations that occur in the context of PN. The McGill Pain Questionnaire was designed with an array of pain conditions. During a focus group with the same population used in this study (Robinson-Papp et al., 2015) a dominant concept was uncertainty that pain could be measured. The ability to give a medical problem a name and a description helps individuals to have a context for what is happening. When a medical condition is hard to describe and a challenge to understand, this introduces uncertainty, a state that potentially contributes to the perception of pain. Helping these patient populations define this shared pain experience could provide improvement in how patients perceive pain medications. It is uncertain what would be helpful, but perhaps a narrative is developed by the patient that represents his or her pain, and it is this narrative of four or five words that anchors what is consistently referenced when determining if a pain treatment was successful.

Using descriptors that are unique to the patient and that convey the patient's pain experience could increase understanding of what the patient is experiencing and improve communication in this paradigm. Using the patient as the reference for a chronic pain condition could further empower the patient and increase the trust the patient has in the provider and medications prescribed to help with pain relief.

Nonverbal and Paralinguistic Interpretation

The presence of nonverbal elements (pauses, sighs, and deep inhalations), tone of voice, and paralinguistics (laughter and word searching) was a discovery in this data analysis that was not expected. What these elements mean is hard to know, but they may relate to the need for privacy in the HIV-PN group, the challenges of managing glucose control in the DPN group, the inability to describe pain perceptions, or perhaps a feeling of vulnerability when discussing pain and the primary illness. The one element that was statistically significant was the amount of word searching present. There were several participants who spoke English as a second language in both groups, with the DPN group having a greater number. Pain perception for these individuals could result in searching for the English word that describes the pain sensations. In a future study, it would be interesting to request the pain description in the participants' native language in order to ascertain whether word searching would still be present. It might be helpful for individuals who have chronic pain to share their pain experience in their native language. Technology could assist in relatively quick translation. More research needs to be done to investigate what these elements of communication are signaling in this very complex, multidimensional experience of chronic pain.

Limitations

In this study, I sought to compare two groups of participants: HIV-PN and DPN, both of which were well characterized medically. Participants had completed a series of patient questionnaires followed by a free discussion of the pain experience. Both groups suffered from the chronic painful disorder PN. While the findings revealed in the analysis of this retrospective data are interesting and shed light on issues such as privacy in the HIV-PN group, the challenges of describing the pain condition, and the common problems of struggling with footwear, it is unclear what is generalizable to the larger population of HIV-PN and DPN patients. The limitations concerning these data related to a single study visit contained within a larger study designed to understand what participants were considering when completing standardized pain measurements. The number of participants in both groups was small: 12 in the HIV-PN group and 10 in the DPN group. Another possible limitation was that the findings might be only relevant to patients in an urban environment and from a multicultural dynamic. An additional limitation was that the members of the HIV-PN group was familiar with the study team from previous research studies, whereas the members of the DPN group had never interacted with the study team. The two elements that were statistically significant in the quantitative data concerning Beck Depression Inventory Question 5, guilty feelings and the pain descriptor *stabbing*, were not significant because the study was not sufficiently powered. My desire for this study was to uncover in an intuitive process the "lived" experience of these individuals and to expose the challenges that are presented to these people when they are diagnosed with a pain disorder combined with a challenging illness.

Many hours of listening, relistening, and examining the transcripts could be insufficient in capturing the nonverbal or paralinguistic elements. During the entire analysis process, I sought to transcend the perspective of my life and to stand in empathy with these individuals as they shared their lived experiences openly and with frankness. Listening to the audio recordings revealed a level of emotions that was scientifically difficult to quantify. An initial step toward capturing unspoken communications was measuring the nonverbal and paralinguistic elements expressed by these participants. This study was not designed to provide a level of scientific confirmation with multiple or blinded reviewers, but to extract initial findings so that future studies could be designed to address some of the elements revealed in this study.

Recommendations

While limitations are present in this study, there were exciting areas that require further investigation. The first was the theme of *privacy* that presents itself as a long-standing issue in the HIV epidemic when the first issues of HIV surveillance and stigma were predominant themes (Sweeney et al., 2013) and continue to be a consideration now that HIV disease has become a chronic illness versus a death sentence. New educational techniques need to be introduced to help reduce the continued HIV stigma. Efforts have been made to reduce stigma, but the issue may be beyond stigma and could encompass feelings of guilt and shame (Bennett, Traub, Mace, Juarascio, & O'Hayer, 2016). A study that addresses these concepts could potentially unravel the relationship of pain perception within the context of feelings of guilt or shame. Guilt and shame are still not well defined as these states of being relate to PLWHA. The issues of stigma can be seen as a societal

view while guilt or shame can be seen as views that are internalized by an individual. Chronic pain in HIV-PN patients represents something to the individuals who participated in this study, yet is it unclear why there was a straight forward desire for the participants to maintain privacy (Bennett, Traub, Mace, Juarascio, & O'Hayer, 2015). Interrelatedness could exist between the outward sign of chronic pain and the inward feelings of shame. Non-verbal communication, paralinguistics, and tone of voice could also be signs of internalized shame or guilt. The BDI did not show that any of the participants were suffering from depression in the HIV-PN group that participated in this study. The high level of the placebo effect present in many of the clinical trials conducted for PN medications for the HIV population could be the result of inadvertently supporting individuals suffering with chronic pain that may represent feelings of unresolved shame. The efforts of treating the pain in any form could result in comforting feelings of shame or guilt. The evidence from this study demonstrated that the desire for privacy may be related to shame and/or guilt as these feelings relate to chronic pain. These feelings could be suppressed by long-term survivors of HIV-disease. This area of research would be highly beneficial for helping those long-time survivors understand more about the desire to be private as it relates to health and what deeper meanings could be associated.

The second area of research could be to address the many descriptors that participants used. When comparing to the limited number of pain descriptors selected by both groups in the SF-MPQ to describe the pain experience intrinsically raises a question about how pain is perceived when it is a chronic condition for years. The number and variety of words used by these two groups demonstrate either that the ability to describe

pain sensations is challenging or perhaps there are no words that communicate these sensations. The many pain descriptors coupled with the use of non-verbal expressions and the paralinguistics found in both group raises questions for future studies despite the size of the group. The human expression goes beyond words to give life meaning (Delafield-Butt & Trevarthen, 2015). How chronic pain may change one's meaning of life over time could be considered when measuring pain and prescribing treatments.

The third area of research would be to understand the themes uncovered in this study as related to pain would be to design a study with explicit hypotheses to examine these themes in a large series of patients and include a verbatim transcription by two transcribers so that the non-verbal and paralinguistics could be captured. The author is working with a transcription service now to develop this system for a current study with physicians in a talk aloud study. There was useful information uncovered in this study. The opportunity to carefully examine these narratives using the framework of the biopsychosocial theory demonstrates a need to extend this method to begin the development of a pain measure that captures some of the challenges uncovered by the results of this study. Further, the information here could use technology to determine how the many words that described pain could be distilled into emoji icons (Blagdon, 2013) that could be employed in a software platform as an aid to help chronic pain sufferers express the complexity of their experience.

Implications

The results of this study offer an opportunity for social change for these two populations that suffer from the challenges of managing and coping with chronic pain

while dealing with primary illnesses of HIV disease and diabetes. The concept of *trust* was present for both groups, but just a little more than a third of each group shared freely of the impact that the trust between provider and patient did when it came to taking action based on the recommendation of the physician. The continued suffering of these two populations with chronic pain to face the day-to-day struggles with footwear, balance, privacy, and medications need to have trusting physicians to support and guide with treatments and actions for the benefit of preventing further health problems. The physician-patient bond can help encourage patients diagnosed with HIV and diabetes complicated with PN to engage in activities of daily living to help their patients live full and fruitful lives. A recent qualitative study in an HIV-population in Houston, Texas Veterans Association, reported that participants sought four key elements in building the therapeutic bond: (a) reassurance, (b) it's okay to ask questions, (c) be specific, and explain lab and test results, (d) language of support and not judgment, and (e) to be included in the medical decisions (Dang, Westbrook, Njue, & Giordano, 2017).

Ultimately, when the therapeutic bond is developed between patient and physician, the issues that were shared and dissimilar between these two patient populations can be addressed because the physician is listening and including what is relevant to their patient in a manner that is supportive. The study supports that focusing on how physicians can develop and maintain the therapeutic bond would be instrumental in a great social change outcome. It is unclear that in the current healthcare climate that new and novel systems need to be developed that support the patient and the physician. Social change for these populations is of dire need and addressing elements as they

related to increased wellness activites such as a gentle yoga program for HIV-PN available where the patients receive care can help patients manage the desire for privacy and furthers the therapeutic bond. Likewise for the DPN helping with programs that address modifying exercise approaches or tactics to educate DPN patients about their sleep hygiene.

Conclusions

This study sought to understand the similarities and differences between two patient groups that suffer from chronic pain due to a disorder common neuropathy in HIV-disease and diabetes mellitus. Many topics were found to be common among the groups specifically issues that made living challenging, footwear, balance, pain fluctuations, coping with pain and the challenge of describing the pain experience. The issue of *privacy* was singular to the HIV-PN group and sleep disturbance and exercise were problems in both groups with a greater number of participants sharing this concept in the DPN group. Ultimately, what can help both these populations have improved health is to have a working, trusting relationship with a physician or care team who listens and works to provide patient-centered care. The challenge will be in how this can be adopted in a health care system that is under intense scrutiny to cut costs and to work with increased efficiency. Serving those patients with challenging illnesses such as HIV-disease and diabetes that are coupled with peripheral neuropathy that causes chronic pain may need new models that can be time efficient, yet patient effective. Technology in the healthcare arena is positioned to be the catalyst to help physicians and patients to develop and protect the patient-physician therapeutic bond and bring an impact to the social

change that is yet to be experienced and could include education, support, and improved treatment paradigms through innovation.

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Appendix A: Original Protocol

Title: The Experience of Chronic Pain in Neuropathic Pain and Back Pain: A Focus Group Approach

Brief Summary of Research:

This study uses a Focus Group approach to understand the cognitive process patients undergo when asked about painful symptoms. This study is investigating the chronic pain syndrome that arises from three conditions: HIV-associated neuropathy (HAN), Diabetic peripheral neuropathic pain (DPNP) and chronic low back pain.

Principal Investigator - David Simpson, MD

Date Revised - Protocol last revised 6/30/09

Study Number - HS#11-00570/GCO#09-1312

Objectives

This study seeks to understand the meta-cognitive processes that patients undergo when comprehending and communicating painful symptoms associated with three medical conditions: diabetic peripheral neuropathic pain, HIV-associated peripheral neuropathy, and non-neuropathic chronic low back pain.

In terms of secondary objectives, this study intends to:

- To identify the constructs patients use when responding to patient pain report outcome measures.
- To identify cognitive processes patients use in mapping their internal pain constructs into pain-rating scales and questionnaires.
- To examine the differences and/or similarities between the three groups in the patient's decision-making processes.
- To determine if there are differences between the three pain groups in terms of either the constructs or cognitive processes patients use in filling out pain rating scales and questionnaires.

Background

Since pain is not directly observable to investigators or clinicians, its measurement is by definition subjective. If the instruments used to measure pain inadequately reflect patients' experiences, the development and testing of therapeutic agents will be impeded. Many recent clinical trials of pain treatments have failed to show efficacy despite success in animal models, the expressed preferences of patients, and the experience of clinicians. It is thus unclear whether these agents truly lacked efficacy or whether the instruments used to measure pain failed to fully capture the pain experiences of the populations under study. The pain measurement instrument, such as the McGill Pain Questionnaire (MPQ), uses verbal descriptors derived from medical literature and validated in healthy subjects, rather than in chronic pain patients, thus leading to outcomes which may give rise to significant distortions of pain descriptions. For example, the SF-MPQ fails to

include terms such as “stiffness,” a common painful symptom in arthritic patients but includes infrequently used terms such as “lancinating.”

There is a need to better understand the experience and descriptive process of communicating chronic pain symptoms and how a patient translates their symptoms into responses on pain measurement instruments. Numerous authors have pointed out the challenge in translating the subjective pain experience into quantifiable data, particularly for use in clinical trials. In particular, the Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT) has drawn attention to the need for standardized instruments in measuring outcomes in clinical trials.

Setting of the Human Research - Mount Sinai Medical Center

Resources Available to Conduct the Human Research

Outreach will be done within all the practices of the study team which have many patients with neuropathic pain and chronic low back pain. The study team is using flyers previously approved by the IRB. These approved flyers are being attached for review for the next approval period. The study will use ResearchMatch.org to expand recruitment efforts to assist with enrollment of the chronic low back pain group. The information to be provided to ResearchMatch.org will be as follows:

VOLUNTEERS NEEDED WITH CHRONIC LOWER BACK PAIN
Do you suffer from pain in your back for 3 months or more?

You may be eligible for a research study at Mount Sinai School of Medicine. Dr. David Simpson is conducting a study to learn about how people who have chronic pain conditions think and make selections on pain questionnaires and how people individually and as a group think about pain.
The study will require 4 visits over approximately 90 days. Reimbursement will be provided.
For more information, please call Ms. George at xxx-xxx-xxxx.

The study team meets once per month to discuss the study and the relevant issues which have arisen.

Study Design

a. **Recruitment Methods**

Outreach will be done within all the practices of the study team which have many patients with neuropathic pain and chronic low back pain. The study team is using flyers previously approved by the IRB. These approved flyers are being attached for review for the next approval period.

b. **Inclusion and Exclusion Criteria**

Inclusion Criteria

- Age: 18 years to 65 years
- Ability and willingness of participant to provide written informed consent.

- Participants with HIV-associated neuropathy - HIV- infection, as documented by a licensed ELISA test kit and confirmed by Western blot at any time prior to study entry. HIV-1 culture, HIV-1 antigen, plasma HIV-1 RNA, or a second antibody test by a method other than ELISA is acceptable as an alternative confirmatory test. Documentation of HIV status from primary care provider will be accepted.
- Participants with diabetic peripheral neuropathic pain – documentation of diabetic mellitus, with documented history of confirmatory blood work of fasting plasma glucose levels $\geq$ 126 mg/dl or oral glucose tolerance test $\geq$ 200 mg/dl or recent abnormal hemoglobin A1C.
- HIV-associated neuropathy and diabetic peripheral neuropathic pain will be considered diagnosed by the presence of the following at the Screening Visit:
    - the presence of primary symptoms of pain, burning, or dysesthetic discomfort in both feet for at least 2 months prior to the Screening Visit,
    - AND absent or diminished, ankle reflexes,
    - OR at least one of the following: Distal diminution of vibration sensation or pain or temperature sensation in the legs.
- Documentation of a clinical diagnosis from a treating physician of chronic low back pain defined as pain restricted to the lower back (Class 1), or associated with radiation to the proximal portion of the lower limb only (Class 2, according to the Quebec Task Force on Spinal Disorders, Spitzer, Leblanc & Dupuis, 1987) and confirmed at screening by study neurologists.
- Participants in all three pain groups must be on stable pain treatment regimens during the past 30 days and are willing to continue their pain treatment regimens during the study period
- Participants are physically able to attend all study visits.
- Participants are able to read and understand English

The Mount Sinai Neurology Program will ensure that the rights and welfare of individuals are protected. We will make sure consent is given freely. If the subjects are unable to understand the consent, they will not be enrolled into study. We will not preferentially enroll vulnerable subjects, and only provide information to subjects in terms that they can fully understand. Potential subjects will be informed of alternatives to participation, including other options and other research studies that may be available to them. They will be assured that their on-going medical treatment will not be affected by their decision to enroll or not enroll in the study. We will not exert any overt or covert coercion. The study does supply travel stipend based and a stipend for the focus group for time and travel, which will be in an amount that is not coercive. The consent document will be in English. At this time all participants must be able to read and speak English because the study pain outcome measures and facilitators speak English. Subjects will be given ample time to consider participation, including being offered a copy of the consent to take home and discuss with their family members and their primary care physician before enrolling.

Exclusion Criteria

- Participants are able to read and understand English
- History of schizophrenia or bipolar disorder.
- Major depressive disorders will be allowed provided patient has been in remission for at least 90 days.
- Serious illness requiring systemic treatment and/or hospitalization within the past 90 days prior to entry, at the discretion of the principal investigator;
- Treatment with any experimental agent within the past 90 days or planning participation in an experimental treatment concurrently with this protocol.
- Presently seeking disability compensation related to their chronic pain condition.
- Major surgery related to their chronic pain condition within the past 12 months.
- Any serious or unstable illnesses including hepatic, renal, gastroenterologic, respiratory, cardiovascular, endocrinologic, neurologic (other than the conditions under study), psychiatric, immunologic, or hematologic disease or conditions that in the principal investigator's opinion would preclude successful participation in the study.
- Any other neuropathy that is not related to either HIV disease or Diabetes

c. Number of Subjects - 36 patients will be enrolled with 12 participants in each group.

d. Study Timelines - The duration of an individual subject's participation in the study (including follow-up) is expected to last 60 days

June 30, 2011 – Last patient last visit.

Dec. 31, 2011 – targeted to complete primary analysis

e. Study endpoints – not applicable

f. Procedures involved in the Human Research

All activities are done for research purposes. During the screening visit, participants from each of the pain groups will be examined by a neurologist to confirm the presence of the pain experience. Confirmation of pain must be due to either HIV- neuropathy or diabetes mellitus related neuropathy as defined by the protocol or chronic low back pain. In addition, the screening visit will include a thorough review of the participant's medical history and an interview with a psychologist to establish that the prospective participant meets neurologic and neuropsychiatric entry criteria. Each participant will be asked for a complete list of current medications and surgeries within the past five years and whether there are any planned surgeries or changes in medications for the next 90 days.

Visit 2 will occur within 3-7 days of screening. During Visit 2, the participant will complete a series of pain measurement instruments, based upon the recommendations of the Initiative on Methods, Measurement, and Pain Assessments in Clinical Trials (IMMPACT, Dworkin et al. 2008), including the 10 cm Visual Analogue Scale, Numeric Pain Rating Scale, Interference Scale of the Brief Pain Inventory, the Beck Depression Inventory, The Roland-Morris Disability Questionnaire (for chronic low back group), and the Short Form McGill Pain Questionnaire. Additionally, during Visit 2, the participants will provide a brief medical history of pain experience. This will be audio-recorded for coding. The participant will be provided a pain diary to complete that includes a Numeric Pain Scale to record the average pain each day until the focus group convenes. Visit 3 will occur within 30-45 days after Visit 2 for each of the pain conditions.

Participants will provide schedule availabilities to the study team so that the organization of the Focus Group session can be arranged for each of the pain conditions. Based upon schedules, a group of 12 participants with the same pain condition will be organized so that each participant can attend at a convenient time. The Focus Group Sessions will consist of three to four hours led by a psychologist. During the Focus Group sessions, the pain measure questionnaires and pain diary which were originally completed by each participant at Visit 2 will be projected for all of the participants to view and comment on. The Focus Group leader will ask about the participants' thinking processes to determine their responses to the pain measures that are displayed including: interpretation of the verbal descriptors, thoughts while making selections, discussion about the decision-making process, how well the questionnaires reflect the chronic pain symptoms, how well the measures reflect the impact on medical conditions and on quality of life, and what are the issues that help the patients make their selections.

The Focus Groups for this study will discuss each individual's experiences of pain, including how pain impacts feelings versus physical functioning and their decisions to seek therapy and treatment outcomes. The Focus Groups will also be asked about what quality pain care looks like to them, in order to understand the expectations patients have when seeking pain treatment and how to best address this expectation in the current patient pain outcome measures. Each Focus Group Session will be audio-recorded for coding.

During Visit 4, each participant will complete the same pain measurement instruments as completed in Visit 2, but during this session, the participants will "think-aloud" the process of completing each questionnaire using the methods developed by Ericsson and Simon (1980; 1993). The think-aloud protocols will also be audio-recorded for coding. After completing the packet of questionnaires, each participant will have a one-on-one, semi-structured interview with the Focus Group leader. The interviewer will use the pain measurement instruments as a starting point for discussion and will discuss with the participants the differences or similarities between Visit 2 and Visit 4.

g. Specimen Banking not applicable

h. Data Management and Confidentiality

The source documents will be stored as paper documents located on Annenberg 2nd Floor in a cabinet located in a locked office. Only the study team will have access. The data will be entered into the database in a timely fashion from the sources. The database will be password protected only accessible to the study team and will be stored on a departmental file server under Mount Sinai's secure data center. The server which contains the linking code files will be password- protected, encrypted, and available only to the research team. All data that is audio recorded will refer to participants by aliases. The recorded tapes will be identified by study patient identification number (MSSM 001), alias and date of recording. The tapes will be stored in a locked cabinet in a locked office with the study documents. The tapes will be destroyed using the Mount Sinai Hospital institutional process of destruction for patient identifiable information. The destruction of the tapes will occur year after the completion of the study. All tapes of the recorded sessions will be sent for transcription in a timely fashion so that coding of the data can be completed. If the information from the tapes is sent digitally to the transcription company, all information will be encrypted. The transcription company will not be provided the identification of any participant and will have only the identity of the participants by aliases. The link of the aliases to the participants will be stored in a separate sealed envelope within regulatory binder this will be stored in a locked cabinet in a locked office.

i. Provisions to Monitor the Data to Ensure the Safety of subjects

Human Research does not involve more than minimal risk to subjects.

j. Withdrawal of Subjects

Participation will be ended if the subjects do not meet the criteria after the screening visit.

Participants can quit the study at any time

All data collection stops when a participant quits the study. This study collects the data of the participant sharing a loud his or her thoughts about the pain questionnaires

Risks to Subjects There are no physical risks to the subject and minimal risks from a psychological and/or social perspective. The subject does not benefit from the study, but the contribution of the study subjects information may enable the study team to examine the nuanced thought processes individuals with chronic pain undergo and how this thinking process impacts the selection of pain outcome measures. In our opinion, the benefits greatly outweigh the risks.

Provisions for Research Related Injury - If the subject believes that they have suffered an injury related to this research as a participant in this study, they will contact Dr. David Simpson at 212-241-8748

Potential Benefits to Subjects – There is no direct benefit.

Provisions to Protect the Privacy Interests of Subjects

The study team makes every effort throughout the study to perform the following as it relates to protecting a participant's privacy and address the ease and comfort a participant experiences throughout the research process:

- Discuss the potential risk of loss of privacy during the consent form process and at each visit as it relates to the study, recordings and the focus group
- Discuss a plan of action concerning how the participant would like to be communicated with during the study e.g. Phone messages, e- mails and regular mail
- Remind the participant at each visit about the issues of privacy with special attention concerning selecting an alias for the recordings and the focus group
- Remind the participant if they do not feel comfortable answering a question or providing data that is necessary they have the ability to refrain from answering any question.
- Finally, the participant is reminded they are able to quit the study at any time without any penalty. This will not affect their ability to receive medical care at Mount Sinai or to receive any benefits to which they are otherwise entitled.
- The participant is reminded at the beginning of every visit what will happen and will be asked if there are any questions
- The participant will be asked if they still want to continue in the study at the beginning of each visit and asked if they have any concerns or questions.
- Prospective study participants are approached because of the following:

    - Study members have referred the participant to the study
    - The prospective participant has called because of seeing a flyer about the study
    - A prospective participant has called the study coordinator asking about available research related to one of the three pain conditions (HIV neuropathy, diabetic

neuropathy, chronic low back pain) because the prospective participant is knowledgeable of the research done by the study team or because of participation in a previous study

- A prospective participant has called the study coordinator because participant saw the PPHS approved flyer that provided the information about the study and where to call for more information.

Economic Impact On Subjects – There will be no costs to subjects

Payment to Subjects - Participants will be reimbursed for their time and travel $50 for Screening, Visit 2, and Visit 4. Visit 3, the Focus Group session will be reimbursed $75.00 plus food and beverages. All reimbursements are paid in cash at each visit.

Consent Process - Yes the study obtains consent. The location is an exam room on Annenberg 2nd floor behind a closed door. Interested Participants are provided a consent form either by mailing or sending through an e-mail prior to a scheduled screening appointment.
The study team is following the "SOP HRP-090 Informed Consent Process for Research"
Cognitively Impaired Adults - The study is not enrolling cognitively impaired adults.

Process to Document Consent in Writing - We will be using the standard Program for Protection of Human Subjects consent template.

Vulnerable Populations - *Indicate specifically whether you will include or exclude each of the following populations:*

Exclude: Vulnerable populations defined as

1) Adults unable to consent,

2) Individuals who are not yet adults (e.g. infants, children, teenagers)

3) Wards of the State (e.g. foster children

4) Pregnant women

5) Prisoners

Multi-Site Human Research (Coordinating Center) – exempt – this is not a multi-site human research study (coordinating center)

Community Based Participatory Research - This is not a community-based participatory research

Sharing of Results with Subjects - As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

Other collaborating research center(s) and their associated research/clinical staff who are working with the investigators on this project:

- The commercial sponsor and/or their representative: Lilly Pharmaceuticals
- The United States Food and Drug Administration

United States Department of Health and Human Services and the Office of Human Research Protection.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number or alias. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institution Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives will come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers.

IRB Review History – no external review

Control of Drugs Biologics or Devices – not applicable

Appendix B: Icahn School of Medicine Ethical Approval

APPROVAL OF RESEARCH

Date: 3/16/2016

To: **David Simpson, M.D. (David.Simpson@MSSM.edu)**

On **3/15/2016**, an Institutional Review Board of the Mount Sinai School of Medicine, in accordance with Mount Sinai's Federal Wide Assurances (FWA#00005656, FWA#00005651) to the Department of Health and Human Services approved the following human subject research from **3/30/2016** until **3/29/2017** inclusive:

Type of Review:	**Continuing Request for Approval**
Project Title:	**The Experience of Chronic Pain in Neuropathic Pain**
Investigator:	**David Simpson, M.D. (Dept: NE - Neurology)**
Project Information:	**HS#: 11-00570** **GCO#1: 09-1312(0001) Eli Lilly Pharmaceuticals**
Sites:	Mount Sinai
IND or IDE (if any):	**No INDs;No IDEs;**
Submission Details (if any):	None

Between **2/10/2017** and **2/15/2017**, or within 30 days prior to study close, whichever is earlier, you are to submit a completed FORM HRP-212: Continuing/Final Review Progress Report and required attachments, in order to request continuing IRB approval or study closure. If IRB continuing review approval is not granted before the expiration date of **3/29/2016**, IRB approval of this research expires on that date.

The IRB has determined that this research involves no greater than MINIMAL RISK. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45CFR.46.102; 21CFR50.3k).
The IRB approved this research under **expedited review procedure category(ies) 5, 6 and 7**

In conducting this research you are required to follow the requirements listed in the **Investigator Manual**. If stamped approved consent forms are attached, use copies of these forms to document consent. IRB approval does not constitute or imply institutional support for the conduct of this research.

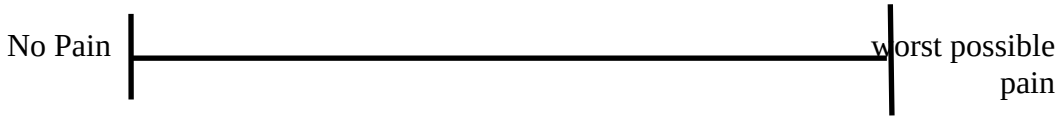
cc: Study Contact(s): Mary Catherine George (mary-catherine.george@mssm.edu)

Appendix C: Pain Scales

The following scales are shown as examples of what was provided to each subject.

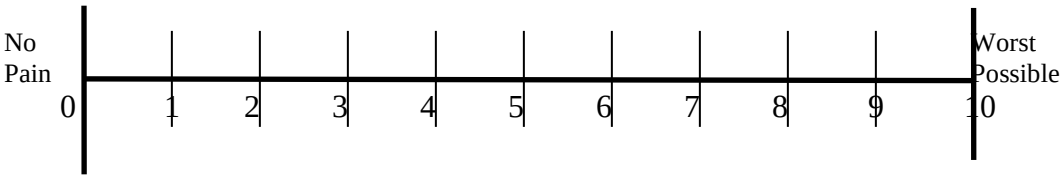
VISUAL ANALOGUE SCALE

Mark a vertical line where you feel best represents your average pain within the past 24 hours.



NUMERICAL RATING SCALE

Circle the number that you feel best represents your average pain within the past 24 hours



BRIEF PAIN INTERFERENCE SCALE

Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

1. General Activity

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

2. Mood

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

3. Walking Ability

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

4. Normal Work (includes both work outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

5. Relations with other people

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

6. Sleep

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

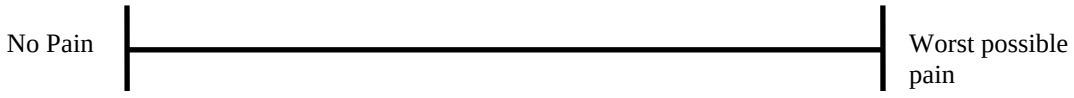
7. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

McGILL PAIN QUESTIONNAIRE

Overall severity of pain types since the last visit:	**SEVERITY**			
	None $_0$	**Mild** $_1$	**Moderate** $_2$	**Severe** $_3$
1. Throbbing	☐	☐	☐	☐
2. Shooting	☐	☐	☐	☐
3. Stabbing	☐	☐	☐	☐
4. Sharp	☐	☐	☐	☐
5. Cramping	☐	☐	☐	☐
6. Gnawing	☐	☐	☐	☐
7. Hot-burning	☐	☐	☐	☐
8. Aching	☐	☐	☐	☐
9. Heavy	☐	☐	☐	☐
10. Tender	☐	☐	☐	☐
11. Splitting	☐	☐	☐	☐
12. Tiring-exhausting	☐	☐	☐	☐
13. Sickening	☐	☐	☐	☐
14. Fearful	☐	☐	☐	☐
15. Punishing-cruel	☐	☐	☐	☐

Overall intensity of pain since the last visit analog scale (VAS)
Instructions: Place a vertical mark anywhere on the line that best describes your pain since the last visit.



Circle the word that best describes your overall pain intensity.

No pain Mild Discomforting Distressing Horrible Excruciating

Appendix D: Narrative Data Collection Form

The goal of this document is to provide a step by step manual that the author will use to guide the process of analysis of the participants "story" that captures the lived experiences of those that participated in the original study. The goal is to use the following steps to bring forth the lived experiences of these two groups who suffer with neuropathic pain (Smith, 2004):

- Initial Impressions
- Descriptive review
- Linguistic review
- Conceptual/Psychological Review
- Emergent Themes Review
- Observation of the Interview Process
- Observation of role of the Researcher
- Writing

Audio recordings:

1) Audio recordings will be reviewed to capture the following elements:

    a) Author listens and documents first impressions of the narrative focusing on specifics that relate to pain

    b) Author listens a 2nd time and documents elements relating to the following:

        1) life descriptors and pain descriptions

        2) elements of life context

3) tone of voice

c) Author listens multiple times with a focus on notating:

1) Length of pauses – introduced additional non-verbal

2) Transitions from beginning to middle to end of narrative

3) Unrelated narrative pain or life context – non-verbal and paralinguistic defined as follows – word searching, laughing and breath (sigh, audible inhalations)

2) Final review of audio recording to review and verify completeness of transcripts after a break of listening to review a final summary.

Transcript Analysis

1) Line by Line analysis of transcriptions reviewing for the following

1) Language structure

2) Pronouns, Adjectives and adverbs

3) Narrative shape – beginning, middle and end

a) Does it correlate to the audio and tone of voice?

b) How does the transcript reveal the story of the audio recording?

c) Themes and concepts as they relate to pain

d) Themes and concepts as they relate to life context

Compiling Audio and Transcripts into case descriptions

1) Compile a narrative with elements from audio and transcripts that reveals the lived experience of each participant

2) Review this with committee members discussing the process with the raw elements and compiled narrative of from HIV and diabetic population
3) Compare the narratives from each of the two groups examining the overarching themes or narratives of similarities and differences of the two groups
4) Review contents to determine if it is possible to compile representative narratives from each of the groups – will review the outcome with committee members
5) Write a summary of interview process observed
6) Write a summary of role of researcher observed

Summary

The above steps will be followed as examining the recordings and transcripts of the participants. The author will maintain the above steps unless an element in the qualitative analysis process is revealed that requires modifying the above steps. The author will discuss with committee and revise this operating guideline to incorporate this element to track the process of the analysis for reproducibility

Appendix E: Additional Narrative Samples of Themes

Common Themes

Footwear challenges

HIV-PN male participant stated: "I used to wear a size 8 ½ shoe and I can't wear that. That's what size my feet are, but I had to get to a 9 because of the pain in my feet, you know… I have more room."

DPN male participant stated: "I just bought these shoes like two weeks ago and that was after hunting and trying and not trusting a whole lot of other shoes and then ultimately paying way more than I should ever pay for a pair of shoes, but there was a difference in them the way that it felt when I put it on."

HIV-PN male participant stated: I used to walk with my slippers and half the time I'd get down the block, and my slippers, they're way back down there.
Shoes are still back there. And I don't even know it. (*Participant can't wear tight shoes too painful.)*

*DPN participant male stated "*I wear very good shoes. I wear Rockport's 99 percent of the time. Once in a while I'm going to a wedding or a bar mitzvah, I gotta put on the dress shoes just for show. Very infrequently. I have two sons the same size as me, "Dad, try my shoes." They're a little tight. I say, "Thank you. I've got my own shoes."

Coping techniques

HIV-PN male participant stated, "it's no blood circulatin'. That's what it feel like. If I get in the bath tub – hot, hot, as hot as my skin can take it. And run it on

it. It's like waking it up. Yeah, it's like wakin' it up. So I take that water as hot as I can and wiggle my toes in it and all that."

DPN female participant stated: "It (*pain*) just was unending. The only way I could get relief was to fill the bathtub absolutely as full as I could with water, and let myself float. Then I could get some relief. But if I had pressure on any part of my body, it was excruciating"

HIV-PN African American Female participant stated: So when the time I get to the train and sit down – somethin' called hypnosis yourself. I hypnosis myself without the tape. I just say hypnosis now – to myself or while I'm riding home. I calm the stiffness or the numbness down so I be all right to walk. Because I don't wanna use no canes and all that, even though I'm up in age. I'm not ready to be walkin' with canes and stuff. So I ignore it to a certain degree. I know it's there. But I'm copin' with it.

DPN female participant stated: "I tried creams, by the way, all kinds of creams. tried peppermint foot scrub, I tried – I'm very big on "there's gotta be an answer to this."

<u>Pain and Numbness Coexist</u>

HIV-PN male participant – "I noticed my feet was gettin' numb. So I panicked – ya know – what's goin' on? And when somebody tickled my foot or touched my – whoa – it was sensitive – made my foot jump. And I didn't know until I was in the hospital. The doctor took the metal thing and put it on my foot. He said, "Did your doctor tell you had neuropathy?... And I don't feel anything. But if you was

to go and just take a little knife, it'll make me jump. Sometimes it could be numb. And you could step right on my foot like this. And I won't even feel it."

HIV-PN female African American participant stated: "if I – ya know – if ya wanna massage your feet. It don't feel normal there. It feels like I'm digging inside my heel. It's like it's goin' through. It would itch or it would burn. So I don't really bother. But there's only one thing I'm afraid is, when I have the numbness to a certain degree, that I can't walk barefooted. Because if you walk barefooted, you don't know up if you're stepping on something unless it's real stingy"

Pain Fluctuates

HIV-PN male participant stated: It's (pain) always there one way or the other. It's just that some days it's lighter than the other.

DPN female participant: "I can't predict it (*pain*). I just can't. It just hits me whenever. I could be walking. I could be sitting down it starts. When I'm sitting in school, it'll start. I feel that squeezing and I start moving my feet…"

HIV-PN female African American participant stated: when I'm goin' out shopping it'll start. Or I could start out now, walking. And I'll feel good. But then after a couple a blocks, it's, like, neuropathy is comin' in. Here we go. It's always there one way or the other. It's just that some days it's lighter than the other.

DPN male participant: "Once in a while you'll get a jolt out of nowhere. Just out of nowhere. I grimace for certain, '…are you okay?' (family or friend will ask) Yeah, I'm all right. Give me a second."

Balance disturbance

*DPN female participant stated: "*I don't fall, I think, more than other people, but then I'm very careful about how I walk. Anybody who has been in as much physical therapy as I have – you sort of visualize how you need to walk, and if I think that I am in a place that's gonna be difficult, I watch myself. I fell so much when I had the onset of this disease…"

*HIV-PN male participant stated: "*It's just my feet from the knee down, if I would bend up, bend down, and try to get back up, it was like my legs would give out. They would numb out. Yeah, I tripped a couple of times. I threw out my back once at work."

Delayed seeking treatment

DPN male participant stated: You let it go for a little while and whatever. The next thing you know you go to your doctor. My doctor says, "You might have neuropathy." He said, "Let's go see a specialist." I went to see a specialist… They did a few tests where they put the needles in you, electric, I think it's called an EG or something. Whatever and a test to see the nerve damage. There was definitely nerve damage. The doctor said I had neuropathy. Peripheral neuropathy, he said that's what I believe?"

HIV-PN participant female waited three months stated: "When I come in from shoppin' or walkin' I just thought I was doin' too much work. And then I thought it was my shoes too because sometimes shoes mess up your feet. When I get

home, or if I sit on a bus, walk around stores. I feel my feet hurt. What is goin' on? What is this?"

DPN female participant waited three months stated: I switched from wearing my high heels and would go with flats or something. I couldn't really predict it, and then I started to see it seemed to be happening at the end of the day, sometime around dinner time, and then into the evening.

*HIV-PN male participant, "*Well, not immediately after I started feeling the pain because I thought it was – okay, maybe I'd been working too hard because I was doing like 12, 13 hour shifts. So I was figuring that maybe it was that. But then after a couple of years it just kept staying there, kept bothering me. I was like, "Let me go talk to the doctor."

Effect of Medications

HIV-DPN male participant shared: "I've tried like seven different kinds of medications. And nothing, none seems to work. I tried well, more now on Tramadol. And it works, but it doesn't. It just hides the pain a little bit. But when I don't take it, I can really feel the pain, you know."

DPN male participant – "I was on that (*neurontin*) for about a year and it didn't seem to be working, the Neurontin. He changed my medicine to Lyrica. I was on Lyrica for a while. …I was on Lyrica probably for another six months to another year. Two years after they started my diagnosis of neuropathy, I was in pain and then it went away. It subsided; I shouldn't say it went away completely. It subsided."

*HIV-DPN Hispanic male participant stated: "*Because thing is that Lyrica (*anticonvulsan*t) is okay, but makes me too hyper. …I'm hyper. Lyrica puts me high. I'm home… I take at 6:00. But if I'm not home, I don't take it until I go home."

DPN female participant stated: "I also tried Lidocaine patches when the pain was severe back in the summer. And they didn't work at all, …I can see how it could work. I was cutting it up into strips and putting them all over on the worst areas. It just didn't seem to help."

HIV-PN African American male particiant stated: "When they gave me the Neurontin, it was interference. It would – when they do the acupuncture, it would interfere with the Neurontin, and there was pain (from acupuncture)."

Trust

HIV-PN male participant stated: "I think it is important to have someone that you can express your feelings without being – without that person feeling sorry or, you know. You just you just need an ear. You don't really need an answer, just an ear."

DPN male participant stated: I wish I had the surgery before. I kind of feel guilty that I knew about the surgery – I was a part of their (*doctors*) study in 2008. In 2008, I did not have neuropathy; it happened only after, I would say, maybe fall of 2009, towards the end of 2009. By then, the study here was over, and I was looking for – I knew about at least one other doctor that was performing the surgery, …in Brazil. And somehow, I stumbled upon the website of the doctor in

India, who turns out to know all the doctors here that were supposed to be part of the study. And he also knows (*doctor*) in Brazil and performs exactly the same surgery for like three times less money. And I'm like, "Okay!"

Contrasting Themes

Privacy

HIV-DPN African American male participant – "Yeah, we don't even talk about it. And a friend of mine told me he had neuropathy. And the first thing I thought, do you have HIV? That's what I thought. And then he told me he was a diabetic. Good thing I didn't ask that question. Because no tellin' what conversation would've jumped from there.…you never hear anybody talk about neuropathy. They don't talk about AIDS, HIV, whatever, neuropathy."

HIV-PN male participant stated: "My sister goes, what's wrong with your feet. I smile and just, I don't know, it's something, I don't know."

Mood

*HIV-PN African American female participant stated: "*When you're hurting, you don't wanna be bothered. So when it start botherin' me, I be, like, oh, my God. Am I gonna make it to do this? – especially if I have to cook a whole meal… In my house, we have a long hallway from the bedrooms to the kitchen. And I'll be, like, oh, do I gotta walk down there again? So what I do now, I just sit and let everything cook. Stay in one spot. Because it's gonna make it worse by goin' up and down. …it's irritating."

*HIV-PN male participant stated: "*I was a little depressed because I had it (virus/PN), but I wouldn't let it stop me. I would still keep going to work; I would still take care of my kids because my kids were still No. 1 in my life. So I'm the man; I've got to stay there working, pain or no pain"

Sleeping difficulty

DPN male participant stated: "..when the sugar was really high up, it would really get painful with stabbing, and even on a few occasions woke me up at night."

HIV-PN female participant stated: "Oh yeah, it (neurontin) knocked me out. It would be the only thing that would help me go to sleep up because the feet were in so much pain down and so much irritability pause that you can't sleep. You try to take anything to go to sleep"

Exercise:

DPN female participant stated: I went to the local track and I did maybe half a mile, and then walked. It was okay during, I mean, my lungs were not good… But after, they really started to burn."

DPN Hispanic female participant stated: "…before I was more active. I want to like to walk a lot, to dance a lot, to stay moving. …sometimes I couldn't even – I try to wake up from the bed, my body was very tired. …was trying to think what was going on. I don't know I think I made a connection because I was having a lot of pain in my feet."

DPN male participant stated: I love outdoors. I love exercising. I love playing sports. I can't do it like I used to. It's that simple.

PN interrelated to primary disease

DPN female participant stated: "I was told that I needed to go on medication, so I did. I went on any number – and I can't even remember them now – Glucophage metformin, I just don't remember all of them. But I tried various assundry meds and combinations, and that didn't really do much. My blood sugar. At this point, you know, I'd sort of learned to live with - the neuropathy"

HIV-PN African American female participant stated: "But I guess now, I'm older and have other problems too. …it seems like it's getting' worse instead of better. And I don't think there's a cure for neuropathy. I think it stays with you. I'm not too sure about it. But everything I've read on neuropathy, it just says pain, feet hurt. That's it. It don't say, well, put your feet in water with the bubble bath. It don't tell you nothin'. It just says, oh, well, you got neuropathy. You gotta deal with it. That's it. It's from HIV. So I'm dealin' with it. I'm just dealin' with it. Whatever it is, I have to deal with. Just like I'm dealin' with the virus, I have to deal with this too.