

**PREVALENCE OF POSTOPERATIVE CHRONIC PAIN AFTER TOTAL HIP  
OR KNEE ARTHROPLASTY**

Masters Thesis-D. B-Susic; McMaster University- School of Rehabilitation Science.

PREVALENCE OF POSTOPERATIVE CHRONIC PAIN AFTER TOTAL HIP OR  
KNEE ARTHROPLASTY: A PILOT STUDY

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## CONTRIBUTIONS

The body of this thesis contains two separate papers, each formatted according to the requirements of the journals targeted for submission for peer review. Even though multiple authors appear on each paper, Dragana Boljanovic-Susic was responsible for all aspects of the study, including the design, analysis and writing of the manuscripts. The co-authors on the papers had varying involvement ranging from contribution to the design of the study, data collection and analysis and manuscript review.

## **ABSTRACT**

**Background:** Total joint arthroplasty (TJA) is considered the treatment of choice to alleviate pain and improve function of patients with osteoarthritis. However, recent evidence suggests that a significant proportion of patients continue to report pain, or worsening of their symptoms well after their joint replacement. We call this chronic pain “*phantom joint pain*” as it persists despite the fact that the affected joint has been replaced.

Chronic pain of neuropathic origin may be a consequence of surgery or in patients with osteoarthritis (OA); there may be a combination of nociceptive and neuropathic pain (NP) mechanisms. As there are no definitive physiological indicators for NP or gold standards for diagnosis, Guidelines on Neuropathic Pain Assessment advocate the use of screening tools to evaluate the patient’s pain experiences and potentially characterize various pain features.

Despite suggestions that phantom joint pain post TJA is a common problem there is limited information about its prevalence among Canadians. To date there are no studies that have characterized neuropathic vs. non- neuropathic chronic pain features in a TJA population.

**Purpose:** The purpose of this work was to determine the prevalence of chronic pain following total hip (THA) or knee (TKA) arthroplasty, and to identify the proportion of the cohort with chronic pain whose symptoms suggested the pain was of neuropathic origin. In addition we evaluated the ability of the NP Subscale of the McGill pain

questionnaire [NP-MPQ (SF-2)] to identify individuals with NP vs. Non NP in the TJA population.

**Methods:** A retrospective cohort study (2-4 years post joint replacement) of 148 participants with primary unilateral TJA identified from a large joint arthroplasty database (n=1143). Chronic pain was defined as post surgical pain reported 6-12 months following surgery to be 3 or higher (out of 5) on the Oxford Hip/Knee Scores, and that pain was the same or worse than reported preoperatively. A postal survey was used to administer the NP-MPQ (SF-2) and the Self-Administered Leeds Assessment of Neuropathic Signs and Symptoms (S-LANSS) (1.5-3.5 years post TJA). S-LANSS was the “non reference standard” for classification of neuropathic pain. Human research ethics approvals from Sunnybrook Health Sciences Centre and McMaster University/Hamilton Health Sciences were obtained prior to the study.

**Results:** The response rate to the postal survey to identify those with chronic pain of neuropathic origin was 53%. Thirteen percent of individuals experienced chronic pain; among individuals with chronic pain, neuropathic subtype was found in 28% (S-LANSS  $\geq 12$ ) - 43% [NP-MPQ (SF-2)  $\geq 0.91$ ]. Receiver Operating Characteristic (ROC) analysis for NP-MPQ (SF-2) yielded an area under the curve of 0.89 (95% CI: 0.82, 0.97). A cut off score of 0.91 NP-MPQ (SF-2), maximized sensitivity (89.5%) and specificity (75.0%). Our results revealed moderate correlation ( $r=0.56$ ; 95% CI: 0.40, 0.68) between the S-LANSS and NP-MPQ (SF-2) scores in patients with NP post TJA.

**Conclusion:** Based on our results, a considerable percentage of individuals (13%) experience chronic pain following TKA and THA. Moreover, among individuals with

chronic pain symptoms, a significant proportion (28-43%) of those experience pain that appears to have a neuropathic component, even 1.5 to 3.5 years following surgery. Overall prevalence of NP in TJA was 3.3 to 4.5%. The NP-MPQ (SF-2) subscale demonstrated “good” discriminatory ability, thus it might be useful in identifying patients with NP following TJA. Moderate association exists between the scales and this could affect prevalence rates in studies; or diagnosis of NP of individual patients based on the criterion used.

**DEDICATION**

**To Jana who patiently waited for mommy to be “done with school”**



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## **LIST OF ABBREVIATIONS**

AUC-area under the curve

CI-confidence interval

HHS- Harris Hip Scores

OA-osteoarthritis

OPQ- Oxford Pain Question

OPS- Oxford Pain Scores

*k*-Cohen's Kappa

KSS-Knee Society Score

MPQ (SF-2) –McGill Pain Questionnaire (Short Form-2)

NP-Neuropathic Pain

*r*-Pierson Moment Correlation

ROC –receiver operating curve

S-LANSS- self administered Leeds Assessment of Neuropathic Signs and Symptoms

SD-standard deviation

TJA –Total Joint Arthroplasty

TKA-Total Knee Arthroplasty

THA-Total Hip Arthroplasty

## **CHAPTER 1: INTRODUCTION**

### **1.1. Osteoarthritis (OA)**

Osteoarthritis (OA) is a degenerative disorder that leads to joint “wear and tear”. This slow progressive disorder of unknown cause is defined by clinical symptoms of joint pain and stiffness as well as structural cartilage destruction (Arden & Nevitt, 2006; Loeser, 2010). Epidemiological studies indicate that symptoms of OA appear in middle age and increase with age (Hunter et al., 2009; Zhang & Jordan 2010) and that 9.6% of men and 18% of women over the age of 60 worldwide, report significant clinical problems due to symptoms of OA (Woolf & Pfleger, 2003). The most commonly affected joints by OA are joints of the hand (Digital Inter-phalangeal and Carpo-Meta-Carpal), hips, knees, spine and feet (Loeser, 2010; Zhang & Jordan, 2010). In terms of affected large joints, OA of the hips and knees is one of the leading causes of reported pain, loss of function and disability, due to their significant contribution to individual’s function and mobility (McDonough & Jette, 2010). Recent reviews suggested that the pain experience in OA might be a consequence of combination of neuropathic and nociceptive pain mechanisms (Hockman et al., 2011; Lin et al., 2011).

Osteoarthritis is the most common form of joint disorder in adults worldwide (Dougados et al., 2009; Michael et al., 2010; Zhang & Jordan, 2010). Reports from the United States and Canada indicate that OA appears to be a growing epidemic with 17% of the population being affected by OA. A projected increase of over 21% by 2021 (Lawrence et al., 2008; Woolf & Pfleger, 2003) and over 53% by 2040 (AAC, 2011) is

proposed. This appears to be partly due to the aging of the “ baby boomer” population and the increase in obesity rates (Hunter & Lo, 2009). Specific to the joint affected, it appears that the incidence of hand, hip and knee OA increases with age; Women are more affected than men (Michael et al., 2010; Hunter & Lo, 2009; Quintana et al., 2008). The effect of OA on the weight bearing joints, such as hips and knees, is considered to be the main cause of an individual’s disability, particularly in females (Hunter & Lo, 2009). Consequently, OA has been considered one of the major economic burdens of health care systems on a global level (AAC, 2011; Woolf & Pfleger, 2003).

Reports of economic cost of OA in industrial countries indicate that the cost of illness has increased by 1to 2.5% in industrial countries such as: Canada, USA, UK, France and Australia (Woolf & Pfleger, 2003). According to the Public Health Agency of Canada (2011), the estimated annual costs of arthritis in Canada are around \$4.4 billion each year.

As OA is not a curable disease, current management strategies have been focused on symptomatic pain relief and improvement of mobility level while “watchfully waiting” for a joint replacement (Dougados et al., 2009; Hunter & Lo, 2009). Joint replacement surgery is considered to be an effective treatment of choice to improve an individual’s pain and function in those with end stage osteoarthritis (Bourne et al., 2010).

## **1.2 Total Joint Arthroplasty**

Hip and knee joint replacement procedures are one of the most common elective procedures performed in North America and Europe (Sharma et al., 2011; Spencer et al., 2009). According to the Canadian Institute of Health Information (CIHI) report in 2009, there has been an 87% increase in joint replacement procedures since 1995. More specifically, according to the Canadian Joint Replacement Registry the number of total knee replacements (TKA) alone has increased by more than 81%. What's more, it appears that the numbers of hip and knee replacement surgeries are rapidly rising in the 65 to 84 year age group (CIHI, 2009). According to the CIHI report (2009) from 2006-2007, 63% of Canadians that underwent a joint replacement were older than 65 years of age. Kurtz and colleagues (2007) projected that by 2030 the THA procedures would increase by 174% and TKA by 674%. As the baby boomer population approaches this age group, it is expected that the trend of upward rising cost of OA in healthcare will continue (AAC; Kurtz et al., 2007).

The reports of surgical effectiveness and patient's satisfaction with quality of life and functional improvement after hip and knee replacement have been well documented in the literature (CJRR, 2004; Gonzales STM et al., 2010, Robertsson et al., 2000). However, current reports suggest that a considerable number of patients (19%) are not satisfied with their post-surgical outcomes (Bourne et al., 2010). These reports suggest

that the surgical goal of pain relief and functional improvement are not met and that an ample proportion of patients do not experience sufficient pain relief from the TJA (Bourne et al., 2010; Nikolajsen et al; 2006). More specifically, Nikolajsen and colleagues (2006) reported that 28% of patient's experienced chronic pain after total hip replacement, and that in 12% the chronic pain was significantly affecting their function.

Post-operative chronic pain is a serious complication that is associated with decrease in physical function and quality of life as well as an increase in healthcare costs (Searle & Simpson, 2010). Chronic pain can have an unpleasant sensory, motor or sensory-motor experience; it may develop as a consequence of surgery, an injury, or disease (Bennett et al., 2007; Hochman et al., 2011). With the lack of basic definition or explicit criteria, chronic pain is often defined by it's duration or as nociceptive or neuropathic in nature (Hochman et al., 2011; Lin et al., 2011).

### **1.3 Neuropathic Pain**

**Neuropathic** and chronic pains are recognized as having different characteristics compared to other types of pains (Bouhassira & Attal, 2011; Lin et al., 2011). Besides pain as a main characteristic, chronic pain is often distinguished with additional health complaints, emotional distress and high healthcare utilizations (Searle & Simpson, 2010). Reported estimates indicate that 7% of the general population with chronic pain of any

intensity, has neuropathic pain (NP) characteristics (Bouhassira et al. 2008) and that 2 to 3% of individuals in urbanized countries develop NP (Gilron et al., 2006).

NP is been characterized as a group of specific signs and symptoms with a plethora of possible underlying causes (Crucci et al., 2010). The key characteristic features of NP include sensory changes, reports of spontaneous pain and hypersensitivity (Crucci et al., 2010; Dworkin et al., 2009). Patients with NP frequently report symptoms of “burning” or “electric shock-like pain”, dysesthesia, hyperalgesia and allodynia (stimulus evoked pain). Despite a lack of understanding of NP underlying mechanisms, there is general agreement that it has a stronger neurological component than types of pains that are more closely linked to mechanical pain and disability. (Haanpaa et al., 2011; Walsh et al., 2012). NP is associated with high physical (and social) disability (Turk et al., 2010). Recently revised guidelines from the European Federation of Neurological Societies (EFNS) define NP as “Pain arising as a direct consequence of a lesion or a disease affecting the somatosensory system” (Crucci et al., 2010; p.2). There is some indication that among patients with chronic pain, particularly post total hip and knee arthroplasties, there might be a subset of individuals with severe persistent pain that may be neuropathic in nature (Wylde et al., 2011).

In spite of the indications in the literature that the chronic post surgical pain is a common problem (Nikolajsen et al., 2006; Wylde et al., 2011), there is limited information about the prevalence of chronic pain or those with neuropathic features in the TJA population in Canada. Variability of reported prevalence of chronic pain after TJA may in part be related to differences in definition of pain and the lack of agreement on

diagnostic criteria (Bouhassira & Attal, 2011). There are some indications that the limited epidemiologic data on NP is due to the lack of explicit diagnosis (Treede et al., 2008) or valid and reliable neuropathic pain identification instruments in surveys (Torrance et al., 2006).

Thus, assessment of neuropathic pain symptoms, with specifically designed questionnaires, might help to better identify those with, or at risk of developing chronic neuropathic pain (Bouhassira & Attal, 2011; Cruccu et al., 2009). Screening tools such as the Self Administered Leeds Assessment of Neuropathic Signs and Symptoms (S-LANSS) and McGill Pain Questionnaire –short form 2 [MPQ (SF-2)] have been developed to evaluate neuropathic and non-neuropathic pain (Bennett et al., 2001; Dworkin et al., 2009; Cruccu et al., 2010). However, latest reports indicate that further validation of screening tools is required to determine which one is most appropriate for the particular task or patient population (Haanpaa et al., 2011).

#### **1.4 Thesis objectives**

Accurate and timely identification of individuals with chronic pain post hip or knee joint replacement is an essential step in alleviating unnecessary pain and suffering in order to maximize the benefits of TJA (Kumar & Indrayan, 2011). The ability to differentiate between patients post TJA who have NP vs. those who experience chronic pain that is not of neuropathic origin (Cruccu & Truini, 2009; Cruccu et al., 2010;

Haanpaa et al., 2011), could help determine the most effective intervention strategies and rehabilitation approach (Alviar et al., 2011; Brander et al., 2010). This should allow for potential pre-operative identification of individuals with NP pain in symptomatic knee OA (Hockman et al., 2011) who elect to have TJA and thus provide a better management of their care.

The overall objective of this work was to investigate the prevalence of chronic pain following TJA. A cohort of individuals with chronic pain post TJA was identified and studied to estimate the proportion of those individuals whose symptoms suggested the pain was of neuropathic origin. Diagnostic properties of a potentially useful clinical questionnaire to classify NP in patients post TJA were evaluated NP-MPQ (SF-2). This was accomplished by conducting two research studies.

The first study evaluated the ability of the NP-MPQ (SF-2) subscale to identify individuals with NP vs. Non NP in TJA population. The specific objective of this study was to: examine the discriminatory power and diagnostic accuracy of the NP-MPQ (SF-2) subscale in classification of NP.

The second study evaluated the magnitude of chronic and neuropathic pain (NP) in TJA. Specific objectives of the second study were to:

- i. identify the prevalence of chronic pain in individuals post primary, unilateral total hip or knee joint arthroplasty (TJA),
- ii. identify, the prevalence of those with potential NP features among patients with chronic pain,



- iii. explore potential predictors of NP classification in the subgroup of TJA individuals with chronic pain according to both S-LANSS and NP-MPQ (SF-2) scales,
- iv. explore the impact of chronic and NP on physical function.

To our knowledge, the S-LANSS and NP-MPQ (SF-2) measures have not been previously used to quantify the prevalence and categorize the NP characteristics in the hip and knee TJA population.

## **1.5 Organization of the Thesis**

The pertinent background information regarding osteoarthritis, TJA and chronic post surgical pain are presented in Chapter 1. Chapter 2 describes the evaluation of diagnostic properties of the NP-MPQ (SF-2) subscale and is prepared for submission to the Journal of Pain. The specific objectives of that study were to investigate the ability of NP-MPQ (SF-2) to discriminate between NP vs. Non NP in individuals with chronic pain post TJA. Chapter 3 contains the study of prevalence of chronic and neuropathic pain (NP) in TJA and is formatted for submission to the Journal of Arthroplasty. The specific aim of that study was to investigate the magnitude (prevalence) of chronic and NP in TJA population two years post surgery. Chapter 4 contains an overall summary of and

discussion of findings from these two studies as they relate to the thesis objectives and recommendations for future research directions.

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## **CHAPTER 2**

### **Does the McGill Pain Subscale Differentiate Between Neuropathic and Non-Neuropathic Chronic Pain in the Total Joint Arthroplasty Population?**

The following paper has been formatted for submission to Journal of Pain

DOES THE MCGILL PAIN SUBSCALE DIFFERENTIATE BETWEEN  
NEUROPATHIC AND NON-NEUROPATHIC CHRONIC PAIN IN THE TOTAL  
JOINTARTHROPLASTY POPULATION?

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## **Abstract**

The purpose of this study was to describe the diagnostic performance of the Neuropathic Pain Subscale of McGill' [NP-MPQ (SF-2)] and the Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire in differentiating the subgroup with neuropathic type chronic pain post Total Joint Arthroplasty (TJA). S-LANSS identified 19 subjects (28%) as having NP, while NP-MPQ (SF-2) subscale identified 29 (43%). Receiver Operating Characteristic (ROC) analysis indicated strong diagnostic power of NP-MPQ (SF-2) when the S-LANSS was used to determine the criterion diagnosis, 0.89 (95% CI: 0.82, 0.97). A cut off score of 0.91 NP-MPQ (SF-2) maximized sensitivity (89.5%) and specificity (75.0%). Correlation between the scales in the classification of NP was moderate ( $r= 0.56$ ; 95% CI: 0.40, 0.68). The NP-MPQ (SF-2) subscale demonstrated “good” discriminatory ability, thus indicating that it might be useful in identifying patients with NP following TJA. The findings of moderate association between the scales, suggest that two questionnaires have conceptual overlap but some variability in diagnosis of NP might be related to which tool is used to make the diagnosis as each scale may be tapping into different dimensions of the pain experience.

## **Perspective**

The NP-MPQ (SF-2) designed as an evaluative pain measure can be used to diagnose NP when a cut-point of 0.91 is used to differentiate NP. When used for diagnosis it provides similar conclusions to the established 12 cut-point on the S-LANNS; however, variation in diagnosis based on measure should be anticipated.

## **2.1 Introduction**

Total joint arthroplasty (TJA) procedures are considered to be a safe and cost effective treatment for those with end stage osteoarthritis (OA)<sup>25,30</sup>. Effectiveness of the procedure, combined with an aging population will result in increased utilization of joint arthroplasty. In terms of total hip and the knee replacements, reports from Canadian Institute of Health Information (2009) indicate that there has been an 87 % increase in these procedures since 1995. The projected estimates for the year 2030 indicate that THA procedures would increase by 174% and TKA by 674%<sup>23</sup>. Despite the overall effectiveness of arthroplasty procedures, current reports suggest that a considerable number of patients continue to report persistent or chronic pain, despite the fact that their damaged joint has been replaced<sup>8,34</sup>. Furthermore, latest reviews imply that among patients with severe persistent post TJA pain, there might be a subset of those who present with neuropathic pain (NP) type characteristics<sup>34</sup>.

Detection of NP is considered to be a challenging procedure, in part due to the lack of agreement on diagnostic criteria and good case identification instruments<sup>7</sup>. With no definite physiological indicators of NP, or a gold standard diagnostic test, diagnosis relies on characterization of the pain as neuropathic<sup>16</sup>. Literature indicates that the pain experience is multi-dimensional and its characterization extends beyond the pain intensity<sup>16,19</sup>. However, despite the agreement that different types of pain are associated with various pain characteristics, the research on distinctive pain qualities appears to be limited<sup>7,16</sup>. Differentiating between NP and non-NP in individuals' post TJA is crucial, as management of patients with chronic pain that manifests with neuropathic features requires different treatment strategies from chronic pain that is mechanical in nature. Consequently, there is an unmet need to provide objective evaluation tools to identify those who develop chronic neuropathic pain after TJA.

To assist with classification, screening tools, such as the Self Administered Leeds Assessment of Neuropathic Signs and Symptoms (S-LANSS) scale, have been designed to differentiate between NP and non-neuropathic pain<sup>3</sup>. The newly revised version of McGill's short form pain questionnaire has been recently modified to include a subscale for identification of NP<sup>13</sup>. The modifications were made with intent to develop a single, comprehensive pain assessment tool for characterization of various types of pain. However, the latest recommendations from Guidelines on Neuropathic Pain Assessment<sup>16</sup> (2011) suggest that diagnostic screening tools require further development and evaluation before widespread clinical use should be adopted. Currently there are no studies defining the classification of NP in the TJA population.



The purpose of this study was to evaluate the ability of the NP Subscale of McGill questionnaire to identify NP in individuals with chronic pain post TJA.

Our main objective was to evaluate the discriminatory power and diagnostic accuracy of the NP-MPQ (SF-2) subscale in classification of NP in individuals with chronic pain post TJA. In addition, the relationship between the raw scores from the two measures [S-LANSS and NP-MPQ (SF-2)] in classification of NP was explored.

## **2.2 Materials & Methods**

### *Design*

This study was a survey of a cohort of individuals who had undergone primary, unilateral total knee or hip joint arthroplasty. The project received approval from the human research ethics boards from the institution and the University.

### *Subjects and study procedure*

Subjects for the study were selected from the Total Joint Arthroplasty (TJA) registry database acquired between 2007-2009 as part of the ongoing study. This registry which includes demographics and outcome measure scores (self-reported pain and function [(Oxford Pain Scores (OPS), Harris Hip Scores (HHS) and Knee Society Score

(KSS)] was retrospectively reviewed to identify potential subjects with chronic postoperative pain. Individuals were deemed to have chronic pain if their reported overall pain score was severe at 6 month or 1 year post-surgery and that pain was the same or worse than reported preoperatively. Only individuals eligible for the postal survey completed the S-LANSS and MPQ (SF-2) questionnaires.

Individuals who met the following inclusion criteria were contacted: they had undergone primary unilateral THA or TKA at least 6 months previously, they reported their postoperative pain level to be 3 or higher (out of 5) on the Oxford Pain Questionnaire. At either 6 months or 1-year post surgery their self-reported level of pain was the same or worse than it was preoperatively. Individuals were excluded if they had undergone total joint revision surgery, bilateral or staged arthroplasties, tibial or femoral osteotomy. The time interval from operation to the completion of the postal survey varied from 1.5 to 3.5 years post surgery.

Of the 1143 total joint arthroplasty recipients, 148 individuals met all the inclusion criteria. Eligible participants received a letter in the mail from the surgeon co-investigator (JdB), who is also the Director responsible for the TJA database, inviting them to participate in this study. All potential participants were mailed information about the study and an informed consent form. Only those individuals who returned a signed written informed consent form were included in the study. Participants each received

copies of both the S-LANSS and the Short Form McGill Pain Questionnaire via mail-in survey.

In an effort to increase the mail-in survey response rate, reminder notices and replacement questionnaires were sent to the non-respondents 2-3 weeks after the initial mailing<sup>10</sup>. A total of three reminders were sent in order to improve the response rate<sup>10</sup>. All returned S-LANSS questionnaires were scored. Patients were classified as having neuropathic pain if their S-LANSS score was  $\geq 12$ , according to method proposed by Bennett and colleagues (2005). The NP-MPQ (SF-2) was scored according to method proposed by Melzack<sup>13</sup>.

### *2.2.1. Instruments (primary outcome measures)*

The S-LANSS Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs pain scale is a seven-item questionnaire: five symptom items and two examination items that are used to assess the patient's NP status<sup>2,3,4</sup>. This scale is intended as a self-administered instrument for case identification on the basis of a cutoff score. Scores range from 0-24, where a score  $\geq 12$  is indicative of neuropathic pain<sup>2, 3</sup>. Literature indicates that scores above the optimum cutoff score ( $\geq 12$ ) when S-LANSS is self-administered are considered "S-LANSS positive" and very suggestive of neuropathic pain<sup>3, 20</sup>. The sensitivity and specificity of the S-LANSS when administered (to individuals with various chronic and neuropathic pain conditions including post surgical

patients) by mail has been reported in the literature as 74% (95% CI: 65, 83) and 76% (95% CI: 68, 85) respectively, compared to the clinical exam<sup>2,3,4</sup>. Internal consistency with Cronbach's alpha of 0.76 was reported when the questionnaire was independently completed<sup>4</sup>.

The **McGill Pain Questionnaire Short Form—2** [MPQ (SF-2)] is a tool designed to provide information about the overall intensity as well as the quality of pain (sensory and affective). It consists of 22 experiences and descriptors of pain (18 sensory and 4 affective). The pain scores are derived from the sum of the intensity rating on a 10-point intensity scale (0 represents no pain, 10 represents worst possible pain). Both subscale and total scores are calculated by taking a mean of all the item ratings<sup>13</sup>. This tool is a revision of the original short form McGill Pain Questionnaire, which was modified by adding 7 questions related to neuropathic pain. In addition, the original 4-point rating scale was replaced with a 0-10 point numeric rating scale for the each question<sup>13</sup>. Good cross-sectional construct validity of MPQ (SF-2) with the Brief Pain Inventory and Multidimensional Pain Inventory scales were reported in individuals with a variety of chronic pain syndromes<sup>13</sup>. The MPQ (SF-2) has been reported as able to discriminate between those with painful diabetic peripheral neuropathy vs. those with diverse chronic pain syndromes<sup>13</sup>.

### *Secondary Outcome Measure*

**The Oxford Questionnaires** are joint specific twelve-item numeric rating scale (1-5) developed for assessment of patient's perception of pain and disability in those undergoing total hip [Oxford Hip Score (OHS)] or knee [Oxford Knee Score (OKS)] replacement<sup>9,27</sup>. Scores range from 12 to 60 with a higher score representing greater level of perceived disability. The first ten questions are the same for both scales, while the remaining two are specific to the hip or knee joint, respectively. Good internal consistency after surgery, with a range of reported Cronbach's alpha between 0.84 to 0.93 in individuals 3 to 24 months post THA has been documented for the Oxford Hip Score<sup>29</sup>. In addition, research has documented that the OHS is highly sensitive to change in patients undergoing THA<sup>28</sup> and that scores have a high correlation ( $r_s = 0.7, p < 0.001$ ) with Harris Hip Scores<sup>21</sup>. Similarly, the Oxford Knee Score has been shown to have good test-retest reliability in groups and individuals post TKA<sup>21</sup>. Good responsiveness to change in patients 6-12 months post TKR has also been documented for the OKS<sup>35</sup>.

### 2.2.2. Analysis

Collected data from the postal survey were analyzed using Statistical Package for the Social Sciences software version 19 (IBM SPSS Inc. Chicago IL). Double data entries were performed by random inspection of the paper surveys against the database entry in SPSS (version 19, IBM). To summarize the demographics of the sample population, univariate descriptive statistics were performed for all the analyzed variables.

The survey response rate was calculated as the number of questionnaires mailed out (n=148) minus the number returned with an incorrect address (4), minus the number returned with a statement that the addressee was unable to complete it because of death or incapacity (9) and minus the ineligible participants (6)<sup>17</sup>.

S-LANSS scores were used to classify participants as having positive or negative findings for the presence of predominantly neuropathic (S-LANSS scores  $\geq 12$ ) or non-neuropathic (S-LANSS scores  $< 12$ ) pain syndromes, based on recent reports that a score of 12 or greater when S-LANSS is self-administered are suggestive of neuropathic pain<sup>3</sup>.

Receiver Operating Characteristic (ROC) analysis was used to assess the overall diagnostic power and determine the optimal threshold value of the NP-MPQ (SF-2) in identification of NP in individuals with chronic pain post total hip or knee arthroplasty (by using the S-LANSS scale as a “non reference standard” for classification of NP). The optimal threshold value for NP-MPQ (SF-2) in classification of NP was established based on the visual assessment of the closest distance from the left upper corner (Area Under the Curve -AUC) and by examining the table for the curve coordinates. AUC is a method for evaluating the accuracy of a diagnostic test in differentiating between individual with and without the disease. The following guide has been suggested for categorizing the accuracy of a diagnostic test: AUC of 0.9 - 1.0 is considered to be an Excellent test, 0.8 - 0.9 Good, 0.7 - 0.8 Fair, 0.6 - 0.7 poor while the 0.5 - 0.6 is considered to be a meaningless test.

Pearson Product Moment Correlation Coefficient was used to evaluate the association between two scales [S-LANSS and NP-MPQ (SF-2)]

Differences between the groups of TJA with NP vs. Non NP were deemed to be significant at  $p < 0.05$ .

### **2.3 Results**

Seventy-five patients completed the survey (58%) (Figure 1, Flow chart summarizes the survey). Six responders were deemed ineligible (i.e. bilateral joint arthroplasty surgeries, fusions or osteotomies) and excluded from the analysis. One subject withdrew their consent after the completion of the survey. We had one individual who did not complete the S-LANSS questionnaire (missing). Thus data from 67 subjects was included in the final analysis. Participant ages ranged from 37 to 88 years with a mean age of 70 (SD= 9.3) years, Table 3.1.

Figure 2.1 Study Flow chart

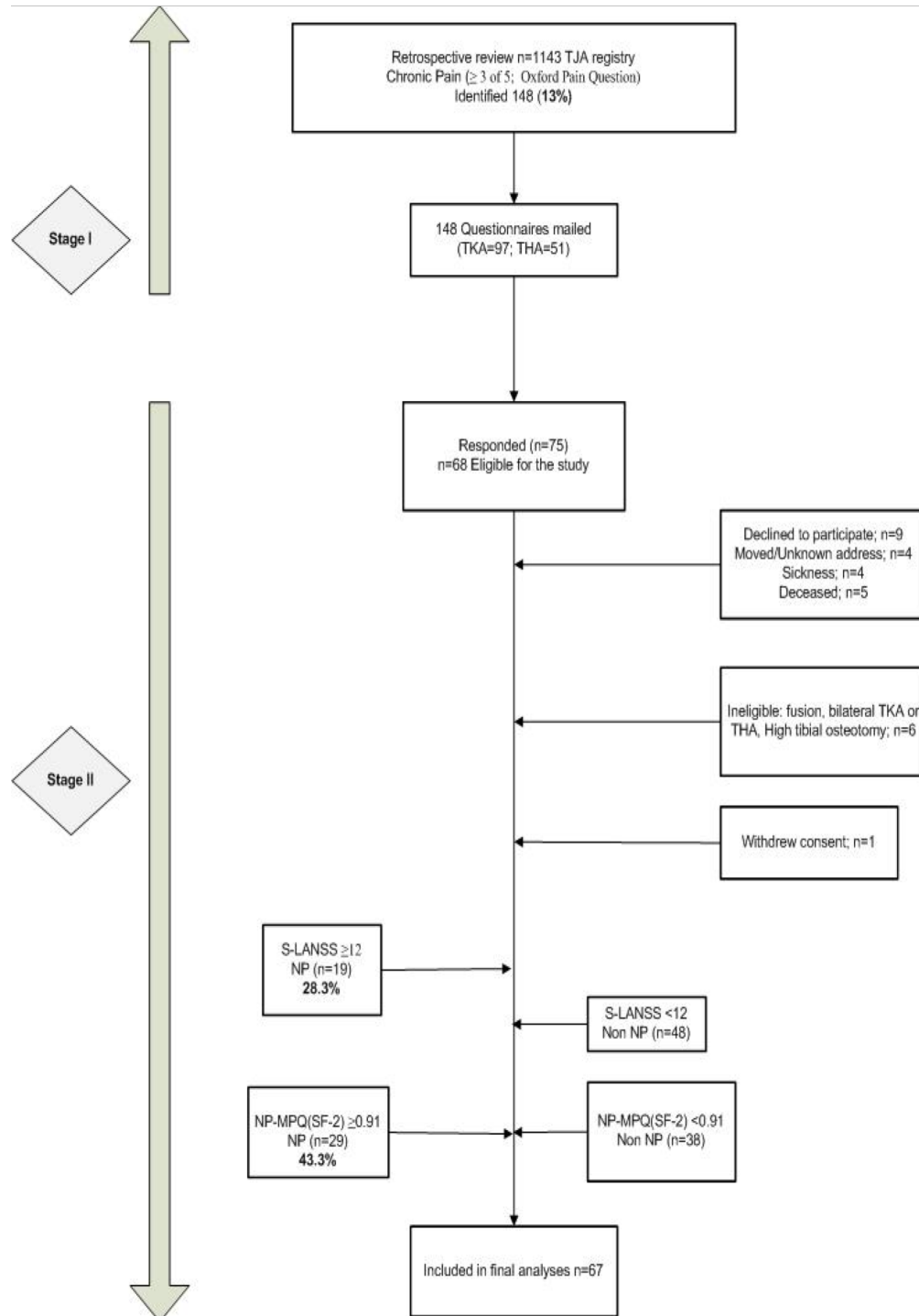




Table 2.1. Participant' Demographics

TJA Individuals (n=67)	TKA (n=42) 63%	THA (n=25) 37%
Age (years) Mean (SD)	69.67 (10.45)	70.28 (7.05)
Males (Percent)	15 (36%)	15 (60%)
Females (Percent)	27 (64%)	10 (40%)
BMI (kg/m <sup>2</sup> ) Mean (SD)	31.83 (6.38)	31.11 (5.74)
S-LANSS Mean (SD)	10.19 (7.58)	4.80 (6.75)
NP-MPQ (SF-2) Mean (SD)	1.73 (1.87)	0.81 (1.58)
Pre operative Oxford Scores Mean (SD)	37.02 (8.05)	35.92 (9.40)

Abbreviations: BMI -Body Mass Index; Oxford Scores [(12-60), higher score = greater disability]; S-LANSS=Self Assessment of Leads Neuropathic Signs & Symptoms [(0-24), scores  $\geq 12$  indicative of Neuropathic Pain (NP)]; NP Subscale of McGill's Pain Questionnaire –Shot Form 2 (NP-MPQ (SF-2) [(0-6), scores  $\geq 0.91$  indicative of NP].

Based on the S-LANSS 19 subjects (28%) scored  $\geq 12$  and were classified as having neuropathic pain. When the NP-MPQ (SF-2) questionnaire was used, 29 subjects (43%) scored  $\geq 0.91$  and were classified as having NP. Mean (SD) score on the S-LANSS was 8.18 (7.69) and 1.39 (1.81) on the NP-MPQ (SF-2) subscale.

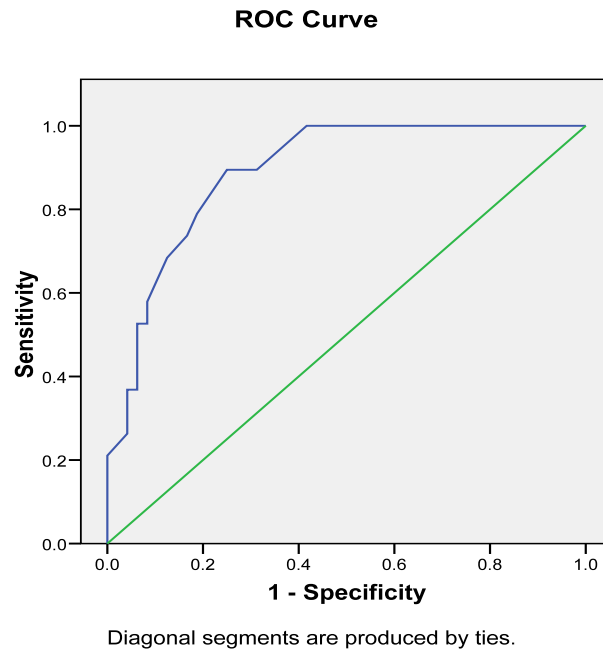
### *2.3.1 Characteristics of NP – MPQ (SF-2) subscale*

The Area under the curve (AUC) for the ROC curve comparing different cutoffs of the NP-MPQ (SF-2) yielded a good AUC=0.89 (95% CI: 0.82, 0.97). The optimal NP-MPQ (SF-2) subscale cut off score (Table 2.2) that maximized sensitivity (89.5%) and specificity (75.0%) was 0.91 points (ROC curve, Figure 2.2).

Table 2.2 Example of different cut-off scores on the prediction of NP.

Cut of Score	Sensitivity %	1-Specificity %
-1.00	100	100
.08	100	46.0
.24	100	50.0
.41	100	55.0
.58	100	59.0
.74	89.5	68.7
.91	89.5	75.0
1.08	78.9	81.2
1.24	73.7	83.3
1.41	68.4	87.5
1.58	63.2	89.6
2.66	52.6	17.0
2.99	52.6	37.0
3.49	36.8	37.0
4.83	26.3	58.0
5.88	10.5	.00

Figure 2. 2



ROC Indicating the ability of NP-MPQ (SF-2) subscale to discriminate between patients with NP and Non NP pain 2 years post TJA

*2.3.2. Association between NP-MPQ (SF-2) & S-LANSS scales*

Pearson Product Moment Correlation Coefficients was  $r = 0.56$  (95% CI: 0.40, 0.68), indicating a moderate association between two measures.

## 2.4 Discussion

This study found that the NP-MPQ (SF-2) subscale demonstrated good diagnostic accuracy (AUC=0.89) in classification of NP vs. Non NP in patients with chronic pain patients post total joint arthroplasty when the S-LANNS was regarded as the “non reference standard”. In the absence of an accurate, independent reference standard, this suggests that both scales are useful in discriminating neuropathic and non-neuropathic chronic pain. These two scales could be expected to be used for this purpose but would not necessarily agree on any individual patient since the agreement between the scales was good, but not perfect.

Based on our results, cut off score of 0.91 NP-MPQ (SF-2) displayed 89.5% sensitivity and 75.0% specificity, indicate that the NP-MPQ (SF-2) subscale may be adequate for identifying individuals in TJA population with NP features.

We chose a ROC analysis because it is considered to be a robust analysis, with ability to evaluate accuracy across a range of different scores<sup>22</sup>. This method is commonly used to identify “cut off score” or optimal threshold values for classification of those with a disease (true positives) vs. those without the disease (true negatives)<sup>22</sup>. Given a small number of perfect tests in clinical practice, the identification of optimal threshold value is often based on a balance between the sensitivity and specificity that allow optimal differentiation between those with and without the disease<sup>1, 22</sup>. The cut off scores allowed us to dichotomize the continuous data scores of the NP subscale of the NP-MPQ (SF-2) into NP and non-NP groups. With our sample we were able to determine

an optimal cut off score (0.91) for NP-MPQ (SF-2) that maximized the balance between sensitivity (89.5%) and specificity (75.0%) in classification of NP vs. Non NP in TJA population. Based on these results, NP-MPQ (SF-2) classified more individuals with NP in comparison to the S-LANSS (reported 74% sensitivity and 76% specificity in postal survey). Thus indicating that NP-MPQ (SF-2) would identify more individuals with NP in comparison to the S-LANSS scale.

With the lack of consensus on diagnosis of NP, screening tools such as S-LANSS have been recommended for identification of NP especially for clinicians<sup>16</sup>. However, literature indicates that in comparison to a clinician, NP screening tools miss detection of 20% of patients with NP features; thus they are not meant to replace a clinical examination nor should they be considered equal to a clinical diagnosis<sup>33</sup>. However, NP requires specific treatment approaches that are different from those for individuals with chronic nociceptive pain<sup>7, 11,20</sup>. Thus, in order to differentiate between specific pain qualities of different types of pains<sup>7,20</sup>, a global multidimensional outcome tool would be beneficial.

The revised version of McGill's short form pain Questionnaire [MPQ (SF-2)] was recently modified to include a subscale to identify individuals with NP<sup>13</sup>. This questionnaire is a multi-dimensional, single measure tool, intended for assessment of various types of pain<sup>13</sup>. The revisions were made with an aim to develop a comprehensive assessment tool for pain characterization of NP and Non-NP types of pains, in order to improve its clinical utility. The latest reports indicate that a considerable number of patients with chronic pain, experience a combination of nociceptive and neuropathic pain

features<sup>18, 26</sup>. Thus, clinicians require a simple and accurate screening tool in order to identify patients with potential neuropathic pain in their daily clinical practice<sup>16,20</sup>. However, since pain is a subjective experience our ability to quantify it depends on individual's perception about pain<sup>15</sup>.

Although NP-MPQ (SF-2) has not been designed for a diagnosis of NP, demonstrated diagnostic accuracy of NP-MPQ (SF-2) as a tool for classification of NP vs. Non NP potentially facilitate use of this measure for identification of individuals with NP features in clinical practice. From a clinical and epidemiological standpoint it would be advantageous, if such a comprehensive measure could be used as a potential tool for both classification and evaluation of treatment changes in TJA population. If the NP-MPQ (SF-2) could be used to identify different subtypes of pains (including NP) then it may be a useful clinical tool for classification of chronic pain of various etiologies. If this were the case it would save clinicians the burden of administering two different pain measures: one for diagnosis/classification and one for evaluation.

Even though our primary interest in this study was the extent to which the NP-MPQ (SF-2) subscale classified patients in a similar way to the S-LANSS; the association between the two scales was explored. Based on our results we found a moderate correlation between these two measures. Thus, based on this finding a positive score on one screening tool might entail a similar scoring on the other tool. However, classification of NP according to one tool did not necessarily result in the same findings for the other tool. This would suggest that although the measures both reflect some similar aspects of pain; they are also tapping into some different dimensions of the pain experience. In

addition, moderate agreement between the tools might indicate that two questionnaires are generally consistent. However, it may be possible that the difference in cut off points contributed to the moderate agreement between the scales in classification of NP in TJA population.

The findings of this study should be considered recognizing our limitations. One of our main limitations was the fact that we chose to evaluate a recently modified questionnaire by comparing it to a “non reference” standard measure. With the lack of “gold standard” or a consensus on diagnosis of NP, S-LANSS has been established as one of the tools for identification of NP in clinical setting<sup>16</sup> thus, comparison to the “non reference standard” appeared to be suitable for this study. Consequently, in the absence of consistent and testable diagnostic criterion, our study is open to the error of incorrect classification of NP due to the imperfection of the tool used for the comparison.

Limitations in our sampling size and approach should also be considered. From a large pool of data (n=1143) we focused on the smaller subset of patients who had worsening of pain following arthroplasty (n=148); and then conducted a follow-up survey that had a 53% response rate. A larger sample would have provided a more precise and stable ROC analysis. Finally, these data were acquired via mail in survey and were dependent on the accuracy of the responses provided.



## **2.5 Conclusion and future recommendations**

Despite TJA being the most common elective surgery in North America and Europe<sup>24,30</sup> relatively little attention has been paid to appropriately identifying those individuals who will benefit most from this type of surgery. Correct classification of individuals with a disease plays an important role in diagnostic accuracy, future disease management and consequently in the effectiveness of treatment outcome<sup>22</sup>. A potential application for NP-MPQ (SF-2) would be to assist clinicians such as Orthopedic Surgeons, Physiotherapists and other “non NP specialists” in screening and early identification of NP features<sup>26</sup> so that suitable and appropriate treatment could be started in a timely manner.

Our ability to detect NP would potentially lead to early identification, timely triage into appropriate treatment streams and consequently better outcomes in management of those who suffer from it<sup>31,32</sup>. A comprehensive, yet clinically practical, assessment tool is essential for further advancement of clinical detection and research in chronic and NP. Thus, comparing a newly modified measure with an existing one is necessary to evaluate the potential for being used interchangeably or to replace the existing “imperfect” tool<sup>5</sup>. It is our hope that available cut off scores predictive of identification of NP in TJA will facilitate further studies that could potentially evaluate if a single questionnaire (of NP and non NP items) is sufficient to classify those with clinical NP features<sup>7</sup> or if multiple measures are more suitable for these types of assessments.

With our study, the lack of a “gold standard” prevented us from determining whether the NP-MPQ (SF-2) pain questionnaire is superior to S-LANSS in terms of discriminatory accuracy. However, we provided sufficient evidence to suggest that studies investigating the ability of the NP-MPQ (SF-2) subscale, as a screening tool, are warranted.

Our study indicated that there are a significant number of those who experience NP post TJA [as classified by S-LANSS and NP-MPQ (SF-2) scales respectively] in the group of chronic pain sufferers. A quick and simple to use, valid questionnaire might be a first step in identification of presently under detected patients with NP symptoms<sup>7</sup>. Hence, there may be an inherent value in having a multidimensional, single tool, pain questionnaire to assist with screening and characterization of different types of pain.

Although this study focused on classification of postoperative patients, a useful extension of this work would be to test the ability of the questionnaire to classify patients as having (or not) neuropathic features prior to surgery.

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Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Activity Rating Scale (ARS), and Tegner Activity Score (TAS). *Arthritis Care Res (Hoboken)* 63 Suppl 11: S208-28, 2011

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## **CHAPTER 3**

### **Chronic Pain, Particularly of Neuropathic Subtype is Prevalent After Total Hip or Knee Arthroplasty**

The following paper has been formatted for submission to Journal of Arthroplasty



CHRONIC PAIN, PARTICULARLY OF NEUROPATHIC SUBTYPE, IS PREVALENT  
AFTER TOTAL HIP OR KNEE ARTHROPLASTY

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## **ABSTRACT**

This study aimed to identify the prevalence of chronic pain following unilateral, primary total hip (THA) and knee (TKA) arthroplasty; in particular the subgroup of those who reported neuropathic pain (NP) characteristics. A retrospective review of 1143 total joint arthroplasty (TJA) recipients identified 148 who experienced postoperative chronic pain. Chronic pain was operationally defined as pain  $\geq 3$  (out of 5) on the Oxford Pain Questionnaire, 6 months or 1-year post surgery. Participants with chronic pain completed S-LANSS and MPQ (SF-2) questionnaires. Thirteen percent experienced chronic pain following TJA; a neuropathic subtype was found in 28% (S-LANSS  $\geq 12$ ) - 43% [NP-MPQ (SF-2)  $\geq 0.91$ ], of those. Individuals with chronic pain post TJA with neuropathic subtype reported severe pain intensity and higher disability levels, even 1.5 to 3.5 years post surgery, compared to those without chronic pain.

**Key words:** chronic pain, post-operative pain, total hip arthroplasty (THA), total knee arthroplasty (TKA), prevalence

### 3.1 INTRODUCTION

Epidemiological studies suggest that osteoarthritis (OA) is a substantial and growing problem in North American with 17% of the population affected and a projected increase to over 21% by 2021 [31,32] and over 53% by 2040 [2]. As OA is not a curable disease, current management strategies focus on symptomatic relief and “watchful waiting” for a joint replacement [14].

Joint replacement surgery, particularly of the hip and knee, is one of the most common elective procedures in North America and Europe [31,32]. The benefits of the surgery and patient satisfaction have been well documented in the literature [19,24, 39,42]. However, recent reports suggest that a considerable number of patients continue to report pain, or even worsening of their symptoms, well after their joint replacement [50].

Although chronic pain is an indicator for joint replacement, the latest reviews indicate that the TJA surgical procedure itself, may contribute to the persistent chronic postoperative pain [40]. The reported estimates indicate that between 7 to 28% of individuals continue to report chronic post TJA pain [37, 50]. Canadian data indicates that the incidence of chronic pain post THA [7] may be similar (27%) to the reported estimates in other countries [37]. In addition, more recent evidence suggests that, among patients with chronic post TJA pain, there may be a subset of those with severe persistent pain that may be neuropathic in nature [50].

Chronic pain is regarded as an unpleasant sensory experience, which may develop after surgery, an injury, or disease [7,10]. It is often defined as nociceptive or neuropathic in nature [7,10,]. With the lack of a basic definition or explicit criteria, reported symptoms of chronic and NP often overlap [10, 21,33,34]. However, despite a lack of understanding of NP mechanisms, there is a general agreement that this type of pain tends to be more severe and has a more significant impact on functional impairment compared to other types of pain [2,21,34,44] and thus requires a different treatment approach than other types of pain [21,26,48]. Patients with NP frequently report symptoms of “burning” or “electric shock-like pain”, dysesthesia (abnormal sensation), and allodynia (stimulus evoked pain). With no definite physiological indicators of NP, or a gold standard diagnostic test, diagnosis relies on characterization of the pain as neuropathic [1,10,21,26,28,34]. The latest recommendations from Guidelines on Neuropathic Pain Assessment suggest that screening tools could be used to evaluate patient’s pain experiences as well as potentially identify those with NP features [4,5,8,21,34,]. Thus, pain scales such as the Self Administered Leeds Assessment of Neuropathic Signs and Symptoms (S-LANSS) [5,6,25] and the McGill Pain Questionnaire Short Form [MPQ (SF-2)] have been developed with an aim to differentiate between various types of pains [15].

Despite indications that chronic pain post TJA appears to be a significant problem [37, 50], few studies have evaluated the prevalence and characteristics of chronic pain in this population. Thus, estimating the magnitude of this problem could provide a foundation for appropriate healthcare planning and optimal treatment approaches.

The primary purpose of this study was to estimate the prevalence of chronic pain identified using the S-LANSS scale following unilateral primary total hip and knee arthroplasty, and to identify the prevalence of neuropathic pain features among those patients who have chronic pain.

Our second purpose was to examine the use of either screening tool [S-LANSS or NP-MPQ (SF-2)] to identify potential predictors of NP classification in individuals with chronic pain following TJA

Finally, the third purpose of this study was to document the characteristics of NP (intensity and duration) as defined by S-LANSS scale and explore whether physical function was worse in those individuals whose chronic pain had a neuropathic component in comparison to those with non-neuropathic features of pain.

## **3.2 MATERIALS & METHODS**

### *Design*

This study was a survey of a cohort of individuals who underwent primary unilateral total knee or hip joint arthroplasty. The project received approval from the institution and the University research ethics boards.

*Subjects and study procedure*

*Stage 1*

An existing TJA Registry database which includes standardized prospective assessment of demographics and outcome measure scores (self-reported pain and function [(Oxford Pain Scores (OPS), Harris Hip Scores (HHS) and Knee Society Score (KSS)]) was used to determine the prevalence of chronic pain post TJA. All participants whose data had been entered into the registry had consented to potential use of their data for research purposes as part of their intake questionnaires prior to their joint replacement surgery.

A retrospective review of the TJA registry records (1143) supplied by five Orthopaedic Surgeons for patients who underwent primary unilateral THA (469) or TKA (674) from 2007 to 2009 was conducted to identify participants with chronic pain. Individuals were deemed to have chronic pain if their reported overall pain score was three or higher (i.e.  $\geq 3$  out of 5) according to the Oxford Pain Question and that pain was the same or worse than reported preoperatively. Participants eligible for the postal survey completed the S-LANSS and MPQ (SF-2) questionnaires.

*Stage 2*

Individuals who met the following inclusion criteria were contacted: they had undergone primary unilateral THA or TKA at least 6 months previously, they reported their postoperative pain level to be 3 or higher (out of 5) on the pain subscale of the

Oxford Pain Questionnaire. At either 6 months or 1-year post surgery their self-reported level of pain was the same or worse than it was preoperatively. Individuals were excluded if they had undergone total joint revision surgery, bilateral or staged arthroplasties, tibial or femoral osteotomy. The time interval from operation to the completion of the postal survey varied from 1.5 to 3.5 years post surgery.

Eligible participants (n=148) identified from a retrospective review (n=1143) received a letter in the mail from the surgeon co-investigator (JdB), who is also the Director responsible for the Total Joint Arthroplasty database, inviting them to participate in this study. All potential participants were mailed information about the study and an informed consent form. Only those individuals who returned a signed written informed consent form were included in the study. Participants each received copies of both the S-LANSS and the MPQ (SF-2) questionnaire.

In order to increase response rate of postal survey, reminder notices and replacement questionnaires were sent to the non-respondents 2-3 weeks after the initial mailing [13]. A total of 3 reminders (2 weeks apart) were sent in order to improve the response rate [13]. All returned S-LANSS questionnaires were scored according to proposed method by Bennett and colleagues [6]. The NP-MPQ (SF-2) was scored according to method proposed by Dworkin and colleagues [15].

### *3.2.1 Study Measures:*



*Neuropathic Pain Instruments (primary outcome measures–postal survey)*

The **S-LANSS** is a seven-item questionnaire: five symptom items and two examination items that are used to assess the patient's NP status [6]. This scale is intended for case identification on the basis of a cutoff score. Scores range from 0-24. Total scores are calculated by adding all the items [6]. Literature indicates that scores above the optimum cutoff score ( $\geq 12$ ) when S-LANSS is self-administered are considered "S-LANSS positive" and very suggestive of neuropathic pain [6,10,21,25]. The sensitivity and specificity of the S-LANSS when administered (to individuals with various chronic and neuropathic pain conditions including post surgical patients) by mail has been reported in the literature as 74% (95% CI: 65, 83) and 76% (95% CI: 68, 85) respectively, compared to the clinical exam [5]. Internal consistency with Cronbach's alpha of 0.76 was reported when the questionnaire was independently completed [6,25].

The **McGill Pain Questionnaire-Short Form–2 [MPQ (SF-2)]** is a tool designed to provide information about the overall intensity as well as the quality of pain (sensory and affective). It consists of 22 experiences and descriptors of pain (18 sensory and 4 affective). The pain scores are derived from the sum of the intensity rating on a 10-point intensity scale (0 represents no pain, 10 represents worst possible pain). Both subscale and total scores are calculated by taking a mean of all the item ratings [15]. This tool is a revision of the original short form McGill Pain Questionnaire, which was modified by

adding 7 questions related to neuropathic pain. In addition, the original 4-point rating scale was replaced with a 0-10 point numeric rating scale for each question [15]. Good cross-sectional construct validity of MPQ (SF-2) with the Brief Pain Inventory and Multidimensional Pain Inventory scales were reported in individuals with a variety of chronic pain syndromes including neuropathic pain conditions [15]. The MPQ (SF-2) has been reported as able to discriminate between those with painful diabetic peripheral neuropathy vs. those with diverse chronic pain syndromes [15].

#### *Self Reported Functional Performance Measures*

Physical disability of individuals with chronic and NP was assessed using the existing outcome measures in the arthroplasty database: Oxford Questionnaire Scores, Harris Hip Scores and Knee Society Scores. These questionnaires are often used to evaluate long-term surgical outcomes at 6 to 12 months following TKA or THA [26,38].

**The Oxford Questionnaires** are joint specific twelve-item numeric rating scale (1-5) tools developed for assessment of patient's perception of pain and disability in those undergoing total hip [Oxford Hip Score (OHS)] or knee [Oxford Knee Score (OKS)] replacement [17,27,36,41,49]. Scores range from 12 to 60 with a higher score representing greater level of perceived disability. Research has documented that the OHS is highly sensitive to change in patients undergoing THA [38, 41] and that scores have a high correlation ( $r_s = 0.7$ ,  $p < 0.001$ ) with Harris Hip Scores [27]. Similarly, the Oxford

Knee Score has been shown to have good test-retest reliability in groups and individuals post TKA [39,49]. Good responsiveness to change in patients 6 to 12 months post TKR has also been documented for the OKS [38,49].

**The Harris Hip Score (HHS)** is a multidimensional assessment tool designed to evaluate disability related to hip symptoms (27). This scale consists of eight items that represent pain, walking, activities of daily living, and range of motion of the hip joint [27]. The total score obtained by adding the scores of all 4 domains, ranges from 0 (maximum disability) to 100 (no disability). Scores <70 are considered to be indicative of a poor outcome, while scores between 80 to 90 are considered to be a good outcome [27,39]. The HHS is frequently used in intervention trials to measure outcomes of total hip arthroplasty as it is reported to be responsive to change and have good inter-observer reliability (0.91) [27,39]. Good effect size between preoperative and 6 months post operative pain (2.80) and function (1.72) has been reported [22].

**The Knee Society Score (KSS)** is a knee rating system that evaluates a person's functional status ("functional score") and the joint itself ("knee score"). The knee score allocates points based on a patient's knee pain, stability and range of motion. The total score ranges from 0 to 100 for both functional and knee score domains. The KSS has been frequently used in studies evaluating outcomes of total knee arthroplasty due to reported responsiveness to change after surgery [29].

### *3.2.2 Statistical Analysis*

Double data entry and quality checking were performed by random inspection of the paper surveys against the database entry in SPSS. For each variable analyzed, univariate descriptive statistics were performed to summarize the demographics of both the data from the registry sample population and the data from the returned postal survey questionnaires.

Prevalence of chronic pain was calculated as the total number of individuals with chronic pain (n=148) in the TJA cohort divided by the total number of individuals in the studied cohort (n=1143)[43].

Prevalence of NP in individuals with chronic pain post TJA was calculated as the number of positive S-LANSS ( $\geq 12$ ) questionnaires returned (n=67) divided by the number mailed (n=148) corrected for those unable to participate. In other words, the denominator was (n=127) minus the number returned due to an incorrect mailing address (n=4), minus the number returned with a statement that the addressee was unable to complete it because of death or incapacity (n=9) minus the incomplete questionnaire (n=1), minus the individual that withdrew from the study (n=1) and minus the ineligible participants (n=6)

S-LANSS scores were used to classify participants into two groups, neuropathic (scores  $\geq 12$ ) or non-neuropathic (scores  $< 12$ ) pain. Bennett and colleagues [6] indicated that the optimum S-LANSS threshold value in discriminating neuropathic from

nociceptive pain was  $\geq 12$  when the scale was compared with the clinical assessment or “gold standard”.

A four-predictor logistic regression model was fitted to the data to test the influence of variables such as: preoperative pain severity (based on Oxford Pain Scores), gender, types of joint replacement (TKA vs. THA), and BMI on classification of NP by either S-LANSS or NP-MPQ (SF-2) tool in individuals with chronic pain following TJA. Backwards multiple logistic regression models were built, using NP as the dependent dichotomous (criterion) variable and the following independent variables: BMI, type of joint replacement (TKA vs. THA), pre operative pain levels (based on Oxford Pain Question Score, 1-5) and sex. Categorical dichotomous (predictor) independent variables such as type of joint replacement were coded as 1 for TKA and 0 for THA. The variable for sex was coded in a similar manner (females =1, and males = 0). BMI was used as a continuous variable.

Independent Student’ t- tests were used to determine if individuals with chronic pain (n=148) were different from those without chronic pain (n=995) in terms of pain intensity (post-pre op levels), physical function and body mass index (BMI), based on their Oxford Pain Question (OPQ), Oxford Hip/Knee Scores, Knee Society (KS) Functional Scores or Harris Hip Scores (HHS) at 6 months and 1-year post surgery. In addition, Independent Student’ t- tests comparison was performed in the subgroup with chronic pain features (n=67), between the NP vs. non-NP groups based on either the NP-MPQ (SF-2) questionnaire or S-LANSS scale classifications.

Data were analyzed using the Statistical Package for the Social Sciences software version 19 (IBM SPSS Inc. Chicago IL). Differences between the group of TJA patients with chronic pain vs. that without chronic pain and NP vs. Non NP were deemed to be significant at  $p < 0.05$ .

### **3.3 RESULTS**

The demographics of the entire (n=1143) recipient pool from the TJA registry who underwent total hip and knee arthroplasty surgery between 2007 to 2009 are presented by the type of joint replacement in Tables 1 and 2.

**Table 3.1.** Demographic of individuals with THA

	Entire Cohort	Non Chronic Pain	Chronic Pain
Individuals with Total Hip Arthroplasty (THA)	469	418	51
	Mean (SD)	Mean (SD)	Mean (SD)
Age (years)	68.20 (10.59)	68.11 (10.70)	68.73 (9.83)
Females (%)	260 (55.4%)	230 (55%)	29 (57%)
Males (%)	209 (44.6%)	188 (45%)	22 (43%)
BMI	29.61 (6.64)	29.44 (6.75)	30.42 (5.27)
OPQ (1-5) preoperatively	4.27 (0.75)	4.24 (0.77)	4.29 (0.72)
OPQ post operative 6 months	1.88 (1.02)	1.73 (0.90)	3.22 (1.22)*
OPQ post operative 1 year	1.82 (1.12)	1.50 (0.73)	4.25 (0.62)*
Oxford Score preoperative	41.26 (7.66)	41.05 (7.75)	41.65 (7.64)
Oxford Score 6 months	20.21 (7.47)	19.25 (6.56)	27.04 (9.23)*
Oxford Score 1 year	18.55 (7.48)	16.89 (5.69)	30.82 (8.56)*
HHS preoperative	45.67 (15.66)	46.39 (15.85)	43.84 (16.38)
HHS post operative 6 months	85.40 (10.06)	86.40 (9.10)	78.80 (13.92)*
HHS post operative 1 year	87.33 (8.83)	88.08 (8.42)	81.15 (10.16)

\*Differences significant at  $p < 0.05$

Abbreviations: BMI-Body Mass Index; OPQ-Oxford Pain Questionnaire (1-5); Oxford Scores (12-60), with higher score indicating more severity; HHS- Harris Hip Score (0-100), lower score indicating more disability

**Table 3.2.** Demographic of individuals with TKA

Individuals with Total Knee Arthroplasty (TKA)	Entire Cohort (n=674) Mean (SD)	Non Chronic Pain (n=577) Mean (SD)	Chronic Pain (n=97) Mean (SD)
Age (years)	68.80 (9.62)	68.68 (9.73)	70.79 (9.24)
Females (%)	428 (63.5%)	359 (62.2%)	63 (64.9 %)
Males (%)	246 (36.5%)	218 (37.8%)	34 (35.1 %)
BMI	29.61 (6.64)	31.65 (7.34)	31.86 (6.26)
OPQ (1-5) preoperatively	4.20 (0.75)	4.17 (0.76)	4.39 (0.65)
OPQ post operative 6 months	2.43 (1.07)	2.24 (0.98)	3.32 (1.05)*
OPQ post operative 1 year	2.18 (1.10)	1.80 (0.79)	3.79 (0.61)*
Oxford Score preoperative	39.07 (7.47)	38.69 (7.52)	40.91 (6.53)
Oxford Score 6 months	24.00 (7.76)	22.71 (6.77)	30.26(8.26)*
Oxford Score 1 year	22.49 (7.86)	20.16(5.87)	32.00(7.39)*
KKS Clinical Preoperative	53.96(15.25)	54.50 (15.43)	50.96 (13.82)
KKS Clinical 6 month postoperative	85.35(13.56)	87.47 (11.29)	73.79 (18.96)
KKS Clinical 1 year postoperative	87.47(12.27)	90.21 (8.86)	76.77 (17.42)
KKS Functional preoperative	42.07(13.31)	42.18 (13.39)	40.83 (12.00)
KKS Functional 6 month postoperative	61.73(22.13)	63.79 (21.89)	52.18(19.79)*
KKS Functional 1 year postoperative	63.62(23.10)	66.38 (22.53)	52.56(21.72)*

\*Differences significant at  $p < .05$

Abbreviations: BMI-Body Mass Index; OPQ-Oxford Pain Questionnaire (1-5); Oxford Scores (12-60), with higher score indicating more severity; KKS-Knee Society score; Functional (0-100) and Clinical subscales (0- 100), with lower score indicating more severity



In terms of the characteristics of non-responders (n=60) to the postal survey, their mean ( $\pm$ SD) age was  $70 \pm 8.25$  years, with a BMI of  $31.82 \pm 5.7$ ; 62% were females and the majority having undergone TKR (60%). There were no statistically significant differences in sex, age, BMI, Oxford Pain Question and Oxford Scores between the non-responders and those who completed the survey ( $p > 0.05$ ).

### *3.3.1 Prevalence of Chronic Postoperative Pain and Neuropathic Subtype in Individuals after TJA*

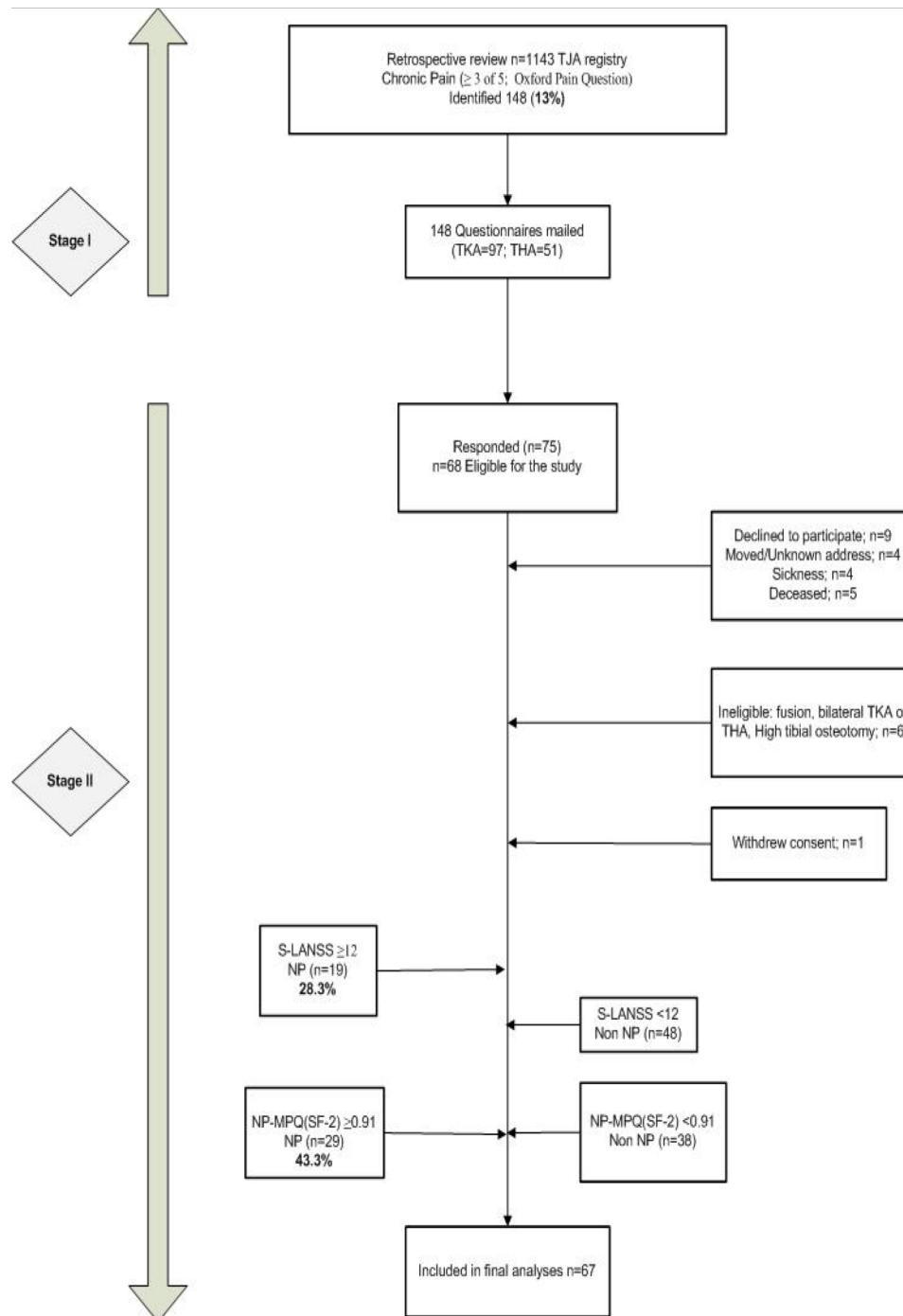
Of the entire cohort (n=1143) of total joint arthroplasty recipients, 469 individuals had total hip replacement (THA) and 674 individuals had knee replacement (TKA). Overall 13% (n=148) of individuals post TJA reported having chronic pain 6 months to 1 year after surgery, 11% after THA and 14.4% after TKA.

Seventy-five patients of the 148 eligible participants, who were deemed to have chronic pain post TJA, completed the survey (Figure 1, Flow chart summarizes the survey). Six responders were deemed ineligible (i.e. bilateral joint arthroplasty surgeries, fusions or osteotomies) and excluded from the analysis. One subject withdrew their consent after the completion of the survey and another did not complete the S-LANSS questionnaire (missing). Thus, data from 67 subjects (25 with THA and 42 with TKA) were included in the final analysis for the prospective portion of the study; evaluating the

prevalence of Neuropathic Pain characteristics among individuals with chronic pain 1.5-3.5 years post TJA.

The postal survey response rate was 53%. The subgroup of survey responders reporting chronic pain was 70 (SD±9) yrs (range: 37-88 years) with 55% of the group being females and the majority having undergone TKR (63%). The neuropathic subtype represented 28%, of the chronic pain population (13%) based on the S-LANSS classification (score  $\geq 12$ ); or 43% if the NP-MPQ-(SF-2) (score  $\geq 0.91$ ) was used. Table 3 summarizes the prevalence of NP according to S-LANSS and NP-MPQ (SF-2) classification. There were no significant differences in age or BMI between the NP vs. Non NP groups. Table 4 summarizes the characteristics of NP vs. non-NP groups according S-LANSS and NP-MPQ (SF-2) classifications. Since our prevalence of NP was specific to the subset of individuals with chronic pain post TJA, our overall prevalence of NP in this cohort of TJA individuals was 3.3-4.5%.

**Figure 3.1.** Study flow chart,



**Table 3.3.** NP-MPQ (SF-2) \* S-LANSS Cross tabulation

Count	SLANSS		Total
	NON NP (<12)	NP (≥12)	
<b>NP-MPQ (SF-2)</b>	36	2	38
Non NP (≤0.91)	(53.7%)	(3.0%)	(56.7%)
Count % of Total			
<b>NP (&gt;0.91)</b>	12	17	29
Count % of Total	(17.9%)	(25.4%)	<b>(43.3%)</b>
<b>Total</b>	48	19	67
Count % of Total	(71.6%)	<b>(28.4%)</b>	(100%)

Abbreviations: NP= Neuropathic pain=1.00; 00= Non Neuropathic Pain; S-LANSS (Self administered Leeds Assessment of Neuropathic Signs and Symptoms), NP-MPQ (SF-2) NP subscale of McGill’s Pain Questionnaire –Short Form-2

**Table 3.4.** Characteristics of NP vs. Non NP groups according to S-LANSS & NP-MPQ (SF-2) classifications

Measure	Classification using the S-LANSS Questionnaire		Classification using the NP subscale of McGill Pain Questionnaire - 2-SF	
	Non Neuropathic (n=48) Mean (SD)	Neuropathic (n=19) Mean (SD)	Non Neuropathic (n=38) Mean (SD)	Neuropathic (n=29) Mean (SD)
S-LANSS $\geq 12$ =NP < 12 Non NP	4.00 (3.79)	18.74 (3.94)*		
NP-MPQ (SF-2) $\geq 0.91$ = NP <0.91 = Non NP			0.32 (0.38)	2.90 (1.85)*
Pre op Oxford Scale Scores	35.00 (8.39)	40.68 (7.65)*	34.55 (8.21)	39.31 (8.31)*
6 mo post-op Oxford Scale Scores	26.16 (9.91)	33.47 (9.99)*	25.56 (10.21)	31.63 (9.79)*
1 y post-op Oxford Scale Scores	26.06 (9.88)	36.40 (9.20)*	25.33 (9.88)	32.89 (10.16)*
BMI	31.55 (6.19)	31.59 (6.08)	30.42 (5.43)	33.05 (6.73)
6 mo post-op Oxford Pain Question	3.24 (1.30)	3.89 (1.02)	3.28 (1.33)	3.70 (1.06)
1 year post-op Oxford Pain Question	3.16 (1.40)	4.00 (0.89)	3.14 (1.45)	3.65 (1.37)

\*Differences significant at  $p < .05$ 

Abbreviations: S-LANSS (Self administered Leeds Assessment of Neuropathic Signs and Symptoms, scores 0-24), Scores of  $12 \geq$  are indicative of NP; NP-MPQ (SF-2) (NP subscale of McGill's Pain Questionnaire –Short Form-2, Scores  $\geq 0.91$  were considered indicative of NP; Oxford Scores (12-60), with higher score indicating more disability; THA=Total Hip Arthroplasty, TKA Total Knee Arthroplasty, BMI= Body Mass Index

### 3.3.2 Characteristics of TJA samples (pain and physical function) with chronic and NP

The subgroup of individuals (n=148) deemed as having chronic post TJA pain reported significantly higher postoperative pain intensity at both 6 months ( $p < 0.001$ ) and 1-year post surgery ( $p < 0.001$ ) in comparison to the cohort of TJA (n=995) without chronic pain (Table 5). Postoperative pain severity was not different at 1-year post TJA, with a significant proportion of individuals continuing to report severe postoperative pain intensity (29%  $\geq 4$  on OPQ).

**Table 3. 5.** Comparison of TJA with chronic vs. non-chronic pain groups based on their Oxford Pain Question and their Oxford Hip/Knee Scores

Oxford Score	6 mo Post TJA Oxford Pain Question Mean (SD)	1 y Post TJA Oxford Pain Question Mean (SD)	6 mo Post TJA Oxford Hips/Knee Score Mean (SD)	1 year Post TJA Oxford Hips/Knee Score Mean (SD)
Chronic Pain (n=148)	<b>3.49*</b> (1.16)	<b>3.52*</b> (0.80)	<b>29.18*</b> (8.98)	<b>29.07*</b> (0.12)
Non Chronic Pain (n= 995)	2.05 (1.00)	1.67 (0.78)	21.36 (7.02)	18.87 (6.11)

\*Differences significant at  $p < 0.05$

Abbreviations: mo-month; y-year; Oxford Pain Question (1-5); Oxford Scores (12-60), with higher scores indicating more severity/disability

In terms of joint specific data, (n=97) individuals with chronic pain post TKA, reported significantly higher ( $p < 0.001$ ) pain intensity in comparison to the cohort of TKA without chronic pain (n=577), both at 6 months and 1 year post surgery with a significant proportion (64%) of individuals rating severe pain intensities ( $\geq 4$ ; OPQ, 1-5) both at 6 months and 1 year post surgery (39%).

The subgroup of THA individuals (n=51) with chronic pain also reported significantly higher pain intensity ( $p < 0.001$ ) in comparison to the cohort of THA without chronic pain (n=418), both at 6 months and 1-year post surgery; with 43% of individuals reporting severe pain levels ( $\geq 4$ , OPQ, 1-5) at 6 months and 35 % at 1-year post surgery (Table 6).

**Table 3.6.** Comparison of TKA & THA with chronic vs. non-chronic pain based on their Oxford Pain Question at 6 month and 1-year post surgery

Oxford Pain Question	Chronic Pain TKA (n=97) Mean (SD)	Non Chronic Pain TKA (n= 577) Mean (SD)	Chronic Pain THA (n=51 ) Mean (SD)	Non Chronic Pain THA (n=418) Mean (SD)
6 months Post TJA	<b>3.74*</b> (0.90)	2.24 (0.98)	<b>3.04*</b> (1.41)	1.73 (0.90)
1 year Post TJA	<b>3.57*</b> (0.95)	1.80 (0.80)	<b>3.44*</b> (1.51)	1.50 (0.73)

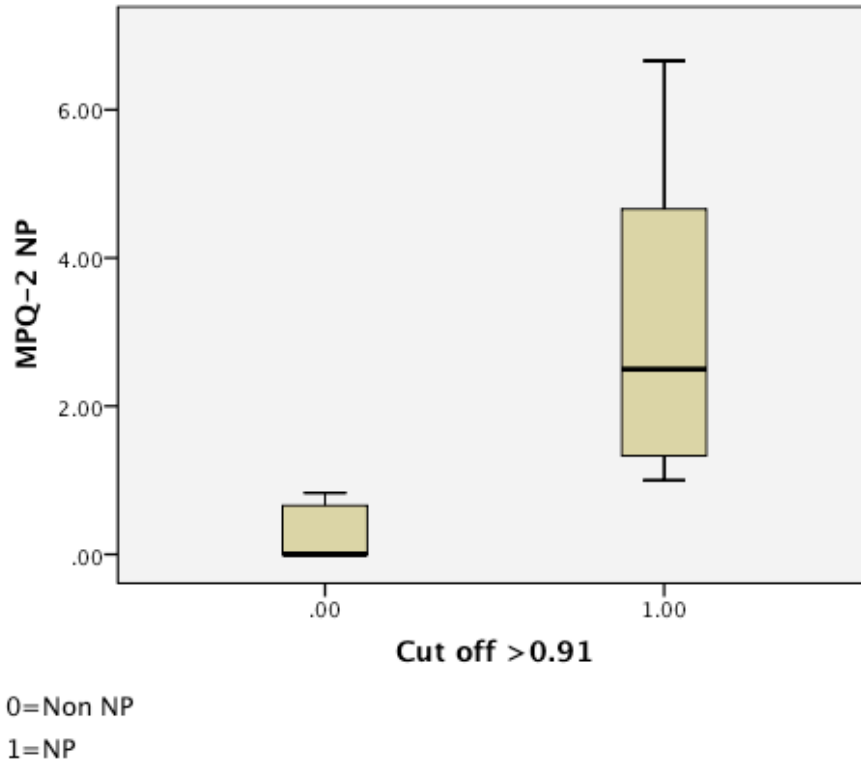
\*Differences significant at  $p < 0.05$

Abbreviations: TJA (Total Joint Arthroplasty); TKA (Total Knee Arthroplasty); THA (Total Hip Arthroplasty)

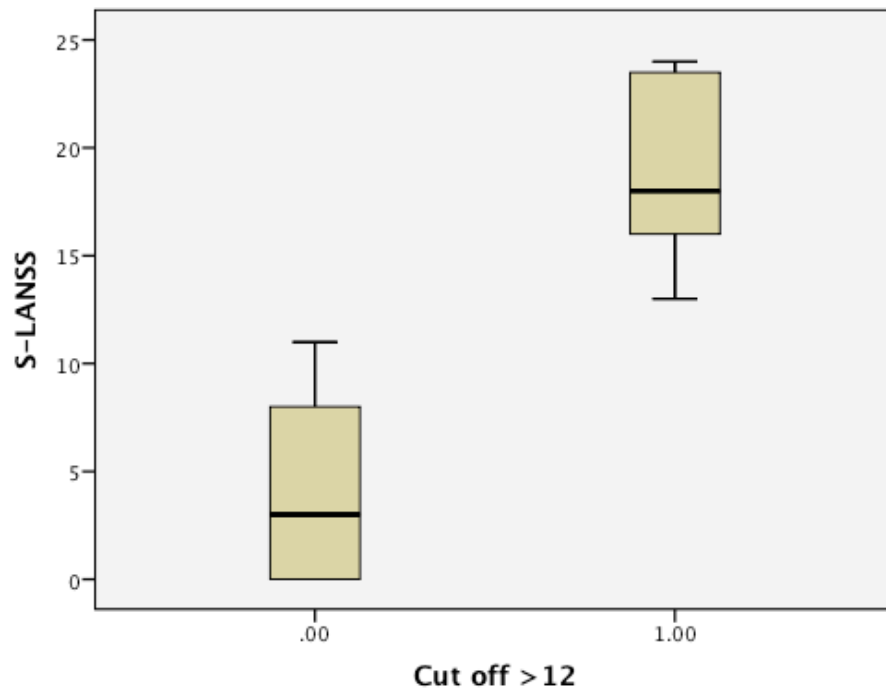
The subgroup of survey responders with chronic pain (n=67) was classified into NP vs. Non NP groups based on S-LANSS and NP-MPQ (SF-2) scores. The individuals with NP subtype had significantly higher pain scores in comparison to the Non NP group ( $p < 0.001$ ) at 1.5 -3.5 years post surgery, regardless of the tool used for classification [S-LANSS vs. NP-MPQ (SF-2)] of NP; suggesting that the chronic pain with NP characteristics was more severe (higher intensity and longer duration). Figures 2 and 3 display the comparison of NP vs. Non NP scores according to classification of both scales. Of note is that a significant percentage of individuals (37-63%) in both groups (Non NP and NP) reported high pain intensity ( $\geq 4$ , OPQ, 1-5) post TJA at 6 months and 1-year post surgery.



**Figure 3.2.** TJA Neuropathic Pain (NP) vs. Non NP scores according to NP-MPQ- (SF-2)



**Figure 3.3.** TJA Neuropathic Pain (NP) vs. Non NP scores according to S-LANSS



0-Non NP

1-NP

3.3.3. *Neuropathic Pain Predictors*

Logistic regression analyses revealed that out of all the tested variables, TKA surgery ( $p < 0.02$ ) had a significant effect on prediction of the NP classification by the NP-MPQ (SF-2) subscale (Table 9).

**Table 3.7.** Logistic regression model with variables used for predicting NP for NP-MPQ (SF-2) subscale

Covariates of model	Beta	Standard	Wald	df	p
Predicting the NP for NP-MPQ (SF-2) subscale	Error				
Joint (1)	-1.767	.721	6.012	1	.014
BMI by Oxford Pre-op Pain	.087	.071	1.518	1	.218
BMI	-.228	.269	.715	1	.398
Oxford Pain Pre-op	-2.682	2.372	1.278	1	.258
Sex (1)	-.001	.651	.000	1	.999
Age by Oxford Pain Pre-op	.008	.009	.792	1	.374
Constant	4.719	8.374	.318	1	.573

$X^2 = 16.69$

df = 6

$p = .010$

Abbreviations: TJA (Total Joint Arthroplasty);

Joint 1=TKA; 0=THA; Sex: 1=Female; 0=Male

**Table 3.8.** Logistic regression model for a best predictor of NP for NP-MPQ (SF-2) subscale

Covariates of model	Beta	Standard Error	Wald	df	p
Predicting the NP for NP-MPQ (SF-2) subscale					
Joint (1)	-1.563	.627	6.214	1	.013
Constant	-.095	.309	.095	1	.758

$X^2 = 7.30$ ;  $df = 1$ ;  $p = 0.007$       Abbreviations: Joint (1) =TKA

### 3.3.4. Impact of Pain on Functional Status in Individuals post TJA

The subgroup of TJA individuals with chronic pain appeared to be significantly more disabled at both 6 months ( $p < 0.001$ ) and 1-year post surgery ( $p < 0.001$ ) in comparison to the cohort of TJA individuals without chronic pain. The subtype of individuals with NP characteristics (mean 33.47; SD 9.92) reported a significantly higher level of disability ( $p < 0.01$ ) compared to those with Non NP (mean 26.16, SD 9.99) (according to S-LANSS classification).

The subgroup of TKA individuals (n=97) with chronic pain reported a significantly higher level of disability both at 6 months ( $p < 0.001$ ), and 1-year post surgery ( $p < 0.001$ ), in comparison to the TKA cohort (n=577) without chronic pain based

on their Oxford Knee Scores (OKS-higher score reflects greater disability) as well as their Knee Society Functional scores (KSS= lower score indicates more disability) (Table 7).

**Table 3.9.** Comparison of self reported functional status between the chronic vs. non-chronic pain TKA groups based on their Oxford Knee Scores and Knee Society Scores.

Total Knee Arthroplasty	OKS scores 6 month post TKA Mean (SD)	OKS scores 1 year post TKA Mean (SD)	KSS scores 6 months post TKA Mean (SD)	KSS scores 1 year post TKA Mean (SD)
Chronic Pain (n=97)	<b>31.15*</b> (8.34)	<b>31.40*</b> (9.05)	<b>51.88*</b> (20.58)	<b>55.96*</b> (21.86)
Non Chronic Pain (n= 577)	22.89 (6.94)	20.32 (6.01)	63.43 (22.09)	66.21 (22.55)

\*Differences significant at  $p < 0.05$

Abbreviations: TKA (Total Knee Arthroplasty); OKS-Oxford Knee Scores (higher score indicating more severity) Knee Society Scores-KSS (with lower score indicating more severity).

Similar functional comparisons of individuals post THA indicated that the subgroup of individuals with chronic pain (n=51) post arthroplasty had a significantly higher level of disability ( $p < 0.001$ ) at 6 months post surgery according to both their OHS scores (higher score indicating more disability) and their Harris Hip Scores (HHS-lower score more disability) compared to the THA cohort (n=418) without chronic pain. However, the same comparison between the THA groups at 1-year post arthroplasty

revealed that the subgroup with chronic pain continued to report a significantly higher level of disability compared to the THA cohort without chronic pain (n=418) based on their OHS ( $p < 0.001$ ), but not according to their HH scores ( $p = 0.06$ ) (Table 8).

**Table 3.10.** Comparison of self-reported functional status between the chronic vs. non-chronic pain THA groups based on their Oxford Scores and Harris Hip Scores.

Total Hip Arthroplasty	OHS score 6 mo post THA Mean (SD)	OHS score 1 y post THA Mean (SD)	HHS score 6 mo post THA Mean (SD)	HHS score 1 y post THA Mean (SD)
Chronic Pain (n=51)	<b>24.69*</b> (8.97)	<b>25.61*</b> (0.67)	<b>81.08*</b> (12.53)	84.52 (8.28)
Non-Chronic Pain (n= 418)	19.25 (6.56)	16.89 (5.69)	86.40 (9.10)	88.08 (8.42)

\*Differences significant at  $p < 0.05$

Abbreviations: mo-months; y (year); THA (Total Hip Arthroplasty); OHS-Oxford Hip Scores (higher score indicating more severity); HHS- Harris Hip Scores (lower score indicating more disability).

### **3.4 DISCUSSION**

Chronic post-operative pain is a recognized as a serious complication that is associated with a decrease in physical function and quality of life as well as an increase in healthcare costs [16,35]. Estimated incidences of chronic pain after TJA have been reported in the ranges of 10-30% [37,50]. However, in spite of indications in the literature that chronic post surgical pain is a common healthcare challenge, this topic has not been studied to any great extent [50].

The main intent of our study was to identify the prevalence of individuals with chronic pain post TJA. Moreover, among those individuals deemed to have chronic pain post TJA, the proportion of individuals with NP features as well as their overall prevalence within the TJA cohort was evaluated.

Our study sample of 1143 patients who underwent a unilateral primary hip or knee arthroplasty between 2007 and 2009 was obtained from a TJA registry. Overall, the results of our study indicated that 13% of individuals continued to report severe chronic pain ( $\geq 3/5$ ) at 6 month to 1-year post hip and knee joint arthroplasty. These results imply that a considerable proportion of individuals did not experience pain relief despite having had that joint replaced. Our findings are in keeping with the previous reviews by Wyld and colleagues [50], which indicated that the prevalence of persistent pain after TKA ranged between 7%-20% and 2%-8% for THA. Thus, our findings are consistent with Wyld and colleagues [50] who suggest that a substantial proportion of individuals post

TJA do not achieve pain relief from their arthroplasty procedure and that their treatment approach for ameliorating their chronic pain has been unsuccessful.

Based on our findings, among the subgroup of TJA with chronic pain, a significant proportion (28-43%) of individuals reported pain symptoms that have neuropathic characteristics. The subgroup with chronic pain that had NP type characteristics, reported severe pain intensity in comparison to the subgroup with Non NP even at 1.5 to 3.5 years post joint replacement. Of particular concern is that individuals with chronic pain with NP features reported higher levels of disability regardless of the type of joint replacement (TKA vs. THA). These results suggest that within the subset of TJA with chronic pain, NP characteristics might have a significant role in the intensity and duration of reported pain severity as well their perceived level of disability even 3.5 years after surgery. Our findings are in keeping with the latest reports, which indicate that NP mechanisms may contribute to the pain experience in chronic conditions such as: osteoarthritis, low back pain etc. [23,28]. A recent study by Hochman et al [23] found that 28% of older community individuals with chronic knee OA scored in NP ranges, based on modified pain DETECT questionnaire. A study by Kaki et al. [28] reported that 54.7% of individuals with chronic low back pain had symptoms suggestive of NP according to S-LANSS scale.

The current study also evaluated potential NP predictors in individuals with chronic post TJA pain. Our findings suggest that TKA surgery contributed to the prediction of reported NP characteristics in the subgroup of individuals with chronic pain



post TJA. These data support previously reported findings that individuals after TKA report poor postoperative outcome [38] and are more likely to report a higher intensity of unrelenting post-surgical pain that may have a neuropathic characteristic [50]. However, due to our small sample size, only a limited number of prognostic factors were analyzed. Establishing a true accuracy of relationship would require a larger data set and further exploration of potential explanatory variables in the model.

It is important to note that although our results signified a high prevalence of NP, our reported prevalence of NP was specific to the rates of neuropathic pain in the subgroup of patients who reported chronic pain following total joint surgery, thus bringing our overall prevalence of NP to a 3.3 to 4.5%. These findings support the previously documented reports by Wylde et al, [50] which indicated that even though a higher proportion (13% of TKA and 5% of THA) of individuals with persistent chronic pain after TJA had neuropathic pain characteristics, the overall proportion of those with NP within the entire TJA cohort was much lower (ranges of 6% for the TKA and 1% for the THA). Based on these data, the low reported prevalence of NP in TJA population could indicate that only a limited number of patients develop persistent pain with NP characteristics. However with an aging population, the increase in total joint replacement volumes [30,31] will result in an increase in individuals who might experience post-surgical chronic pain with neuropathic pain characteristics.

Recent reports suggest that epidemiologic research on neuropathic pain is hindered by lack of adequate case identification instruments [4,5,8,10]. Thus, identification and diagnosis of NP continues to be a clinical challenge [8,11,21] principally due to the lack of agreement on diagnosis of neuropathic pain [11,18]. In the absence of consensus on diagnosis of NP, screening tools such as the S-LANSS have been recommended to assist clinicians in the identification of individuals with NP [11,21,25]. The S-LANSS questionnaire was specifically designed for assessment of NP in postal research [6] it also appears to have the most empirical evidence for its ability to discriminate between NP and non-NP in diverse chronic pain populations [6,21,25,28]. Brief nature and self-examination option of this questionnaire makes it a useful tool without the need for a clinical exam by a clinician [6] especially in settings where assessment time is of essence. Thus, for this study, in the absence of a formally recognized “gold standard” for diagnosing neuropathic pain, the S-LANSS scale was regarded as the “non reference standard” against which the ability of the NP subscale of NP-MPQ (SF-2) to classify neuropathic pain was compared.

Our results should be viewed recognizing the limitation of our small sample size and our approach. Findings from our study are from one orthopaedic setting. From a large subset of individuals (n=1143) we focused on the smaller subset of patients who have worsening pain following arthroplasty; and then conducted a follow-up survey that had a 53% response rate. The composition of our sample was dependent on the accuracy of the screening for worsening pain, and the extent to which the respondents reflected the population. Despite a 6% loss to follow up at 6 months and an even larger loss of data

(28.4 %) at one year follow up; a significant percentage of individuals (13%) did not experience pain relief as a result of their hip or knee replacement surgery. Thus, it is possible that the proportion of those with potential chronic pain symptoms (with NP characteristics) might be even higher than reported.

Finally, these data were acquired via mail-in survey; and were dependent on the accuracy of the responses provided. One limitation was the lack of direct information regarding diagnosis of neuropathic pain specifically the clinical exam. In addition, we were unable to verify whether there were difficulties interpreting any of the items on the scales. Further, we are unable to determine whether the nature or location of the pain reported by patients with persistent pain has changed across the time intervals. Nevertheless, this study illustrated the need for further research in neuropathic pain domains.

### **3.5 Conclusion and Future recommendations**

In conclusion, this study has highlighted the existence of a subgroup of individuals with chronic post TJA pain, more specifically the subtype of chronic pain post TJA with NP characteristics. Despite our indications that only a small proportion of individuals experience NP features (3.3-4.5%) posts TJA, these data suggest that specific pain characteristics (NP) may have an important influence on long term prevalence of chronic pain.

Our study did not examine the extent to which a combination of pain features might contribute to the increased pain and greater disability following TJA. However, with indications that there might be a high percentage of individuals post TJA with chronic pain and that those with NP features were worse post TKA, our study illustrated that there is a need to further evaluate chronic neuropathic pain issues in post TJA population. Moreover, the latest evidence indicates that the NP questionnaire can be used as a diagnostic tool to identify individuals with NP in symptomatic knee OA [23].

Accurate classification of individuals with a disease plays an important role in diagnostic accuracy [30]. Since this study was based on a postal survey, future studies need to develop clinical tools to identify those with chronic pain following TKA or THA that have a neuropathic component and then investigate the relationship between the self-report and clinical measures in this population. Thus, a comprehensive pain measure [MPQ- (SF-2)] with ability to screen or discriminate between various types of pain or a potential combination of pain mechanisms (e.g. neuropathic +/- nociceptive pain), in individuals after TJA; might be more advantageous than a specific NP type of questionnaire (S-LANSS). Therefore, if classification and assessment of pain quality with NP-MPQ (SF-2) can assist with improved pain characterization and better screening techniques in comparison to the existing scales, then our ability to delineate characteristics of NP vs. chronic pain in patients following TJA would provide a foundation for better diagnosis and optimal treatment approaches [24].

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## **CHAPTER 4: DISCUSSION**

Despite the advancement in arthroplasty procedures, recent reports indicate that a large percentage of individuals (10-30%) continue to report chronic pain or even worsening of their symptoms after TJA surgery (Clarke et al., 2011; Whyld et al., 2011). There are some suggestions that among patients with chronic pain, post total hip and knee arthroplasties, there might be a subset of individuals with severe persistent pain that may be neuropathic in nature (Wylde et al., 2011). Despite the suggestions in the literature that chronic pain post TJA is a significant problem (Nikolajsen et al., 2006; Wylde et al., 2011) there is limited information about the prevalence and characteristics of chronic pain among the TJA population in Canada.

Quantifying a subjective entity such as pain is often challenging (Gandhi et al., 2010) especially the type of chronic pain considered to be neuropathic pain. With no standard definitions in the literature as to what constitutes NP and the lack of agreement on diagnostic criteria, NP is often under detected and poorly managed (Bouhassira & Attal, 2011). There are some indications that the limited epidemiologic data and variability of reported prevalence of chronic pain in TJA may in part be related to differences in definition of pain and the lack of agreement on diagnostic criteria and also due to lack of simple and reliable case classification tools (Bouhassira & Attal, 2011; Lin CP et al., 2011).

As total joint replacement is a common surgical procedure, there is an indisputable need to identify those who might be at “risk” of developing chronic

postoperative pain. Better identification and characterization of chronic pain as well as understanding the prevalence of it is essential, as it may lead towards better detection, adequate healthcare allocations and an overall better management of those who suffer from it (Bouhassira et al., 2008b).

This thesis intended to investigate the magnitude (prevalence) and categorize chronic pain characteristics (NP vs. Non NP) in the hip and knee TJA population. In addition, a potentially useful clinical questionnaire for classification of NP in patients post TJA was evaluated [NP-MPQ (SF-2)].

Results of this thesis pointed out that there might be a high percentage (13%) of individuals with chronic pain post TJA whose pain is not alleviated with arthroplasty procedures. Furthermore our results indicated that among the group with chronic pain post TJA, there were a high proportion of those [28% according to S-LANSS  $\geq 12$  and 43.3% according to NP-MPQ (SF-2)  $\geq 0.91$ ] who experienced NP features even 1.5-3.5 years post surgery. Our results indicated that individuals with chronic pain post TKA reported higher disability levels in comparison to THA. Although, our results signified a high prevalence of chronic pain in TJA, our reported prevalence of NP was specific to the rates of neuropathic pain in the subgroup of patients who reported chronic pain following total joint surgery, thus our overall prevalence of NP turned out to be 3.3-4.5%. These findings support the earlier reports which indicated that although a higher proportion (13% of TKA and 5% of THA) of individuals with chronic pain after TJA had NP features, the overall proportion of those with NP within the TJA cohort was much lower (ranges of 6% for the TKA and 1% for the THA)(Wylde et al, 2011).

Of great concern are our findings that chronic post TJA pain; especially the NP subtype has a significant impact on perceived level of disability. Furthermore, our results implied that TKA surgery contributed to the prediction of reported NP characteristics in the subgroup of individuals with chronic pain post TJA. These data support previously reported findings that individuals after TKA are more likely to report higher intensity of unrelenting post-surgical pain that may have neuropathic characteristics (O'Brien et al.; 2009; Wylde et al., 2011). Collectively, these results of negative influence of chronic pain highlight the fact that specific pain characteristics (NP) may have an important influence on long-term prevalence of chronic pain and disability.

Based on our data, the low reported prevalence of NP in TJA population could indicate that only a limited number of patients develop persistent pain with NP characteristics. However, as identification and diagnosis of NP continues to be a clinical challenge, a combination of an aging population and the increase in demand for joint replacement procedures (Kurtz, 2007) may result in an increase of those who might experience persistent (chronic) post-surgical pain with neuropathic characteristics.

Therefore in order to maximize the benefits of TJA surgery, differentiation between patients post TJA who have NP vs. those who experience chronic pain with non-neuropathic features is essential in order to provide more effective and appropriate treatment strategies (Bouhassira & Attal, 2011; Cruccu et al., 2010; Dworkin et al., 2007).

In the absence of agreement on diagnostic criteria, identification of individuals with NP characteristics is based on “optimal” differentiation between those with and

without the neuropathic features. Therefore, our findings of “good” diagnostic accuracy (AUC=0.89) of the NP-MPQ (SF-2), indicated that this tool might be useful in identifying patients with NP following TJA. Moderate association between the scales indicates that, although the two questionnaires are generally consistent, they also may be exploring different dimensions of pain; thus, based on the criterion used this could affect prevalence rates in studies or diagnosis of NP in individual patients.

Absence of a testable “gold standard” prevented us from establishing whether one [NP-MPQ (SF-2)] pain questionnaire is better than (S-LANSS) the other in terms of discriminatory accuracy. However, displayed (89.5%) sensitivity and (75%) specificity indicated that the NP-MPQ (SF-2) subscale might have a potential role in classification of those with NP vs. Non NP in TJA population. Although NP-MPQ (SF-2) has not been designed for a diagnosis of NP, it demonstrated good diagnostic accuracy (AUC=0.89) indicating that additional studies investigating the NP-MPQ (SF-2) subscale as a potential diagnostic tool, are warranted to further delineate the usefulness of this instrument for clinical and epidemiological use.

Our results should be viewed recognizing the limitation of our small sample size and our approach. Findings from our study are from one orthopaedic setting. From a large subset of data (n=1143) we focused on the smaller subset of patients who have worsening pain following arthroplasty; and then conducted a follow-up survey that had a 53% response rate. The data for this study were acquired via mail in survey and were dependent on the accuracy of the responses provided. It is always probable that the subset of patients who responded to our survey is in some way not typical of the



population that they are meant to represent. However, the composition of our sample was dependent on the accuracy of the screening for worsening pain and the extent to which the respondents reflected the group studied. Previous studies have reported that potential predictors of chronic postoperative pain levels are high acute post-operative pain levels (Macrae, 2008). However, since we were interested in individuals with NP characteristics as a primary issue in individuals reporting chronic pain post hip and knee arthroplasty, exclusion of individuals with “low” pain intensity might have been justified.

Further, we were unable to determine whether the nature or location of the pain reported by patients with persistent pain has changed across the time intervals. An additional limitation of this study was the lack of direct information re: diagnosis of neuropathic pain i.e.: clinical exam.

Lastly, one of our additional limitations was the fact that we chose to evaluate a recently modified questionnaire by comparing it to a “non reference” standard measure. With the lack of “ gold standard” or a consensus on diagnosis of NP, S-LANSS has been established as one of the tools for identification of NP in clinical setting (Haanpaa et al., 2011), thus comparison to the ”non reference standard” appeared to be suitable for this study. However, in the absence of consistent and testable diagnostic criterion, our study is open to the error of incorrect classification of NP (and overestimation) due to the imperfection of the tool used for the comparison. Finally, in order to establish a true accuracy of relationships and obtain more stable results a larger sample from at least two orthopaedic settings would have been more desirable.

## **CONCLUSION**

With the increases in volume of total joints in response to the Ontario Government's Wait Times Strategy, there is a potential increase in prevalence of those who might experience post-surgical chronic pain with neuropathic pain characteristics. Thus, the impacts of managing the sequelae of chronic pain post total joint arthroplasty are high – at the individual, health care system and societal levels (Smith et al., 2007; Gilron et al., 2010).

Clinical management of chronic pain continues to be a challenge, simply due to the fact that neuropathic characteristics could occur in any chronic pain condition (Bouhassira et al., 2008a). Thus, clinicians require a reliable and clinically practical assessment tool for advancement in detection, characterization and better management of individuals with NP characteristics (Mao, J. 2009).

With our study we were able to identify two different tools [S-LANSS and NP-MPQ (SF-2)] for differentiation of NP characteristics in TJA population. In addition, this study has highlighted a potential for using a simple to use [NP-MPQ (SF-2)] clinical tool for both diagnosis/classification and evaluation of treatment progress in TJA population. Consequently, if MPQ (SF-2) could be used to identify various subtypes of pains (including neuropathic pain) this could potentially limit the burden of administering two different pain measures: one for diagnosis/classification and one for evaluation.

Evidence indicates that there is a lack of a single measure for the assessment of all aspects of chronic pain characteristics and so several instruments are being required for a proper characterization of chronic pain symptoms (Grimmer–Somers et al., 2009). Thus, even administration of a few short questionnaires could be time consuming for both clinicians and patients (Grimmer–Somers et al., 2009). Furthermore, selecting the most appropriate tool for the assessment of chronic NP, between multiple instruments with similar purpose could be challenging and burdensome (Bouhassira & Attal, 2011; Grimmer-Somers et al., 2009). The MPQ (SF-2) questionnaire takes only 5-10 minutes to complete and score and requires no special training to administer or interpret it (Dworkin et al., 2009). Thus, a quick, comprehensive and a simple pain measure [MPQ (SF-2)] with ability to screen or discriminate between various types of pain or a potential combination of pain mechanisms (e.g. neuropathic +/- non-neuropathic pain) (Dworkin et al., 2009), in individuals after TJA, might be more advantageous to clinicians than a specific NP type of questionnaire (i.e. S-LANSS).

It is our hope that available cut off scores predictive of identification of NP in TJA will facilitate clinical use of this instrument and provide a foundation for better diagnosis (Toth et al., 2009) which may lead to a more individualized and appropriately tailored treatment approach. Screening tools are not meant to replace the clinical assessment, however they could assist clinicians with identification of NP (Bouhassira & Attal, 2011). Accurate and timely identification would enable clinicians to streamline

patients into the appropriate treatment streams, thus decreasing the overall cost of treatment, especially for potentially treating the “false positive ” cases (i.e. identifying individuals with NP when they do not exhibit neuropathic characteristics).

## **FUTURE RECOMMENDATIONS**

Future studies should evaluate if classification and assessment of pain quality with NP-MPQ (SF-2) can assist with improved pain characterization and better screening techniques in comparison to the existing scales.

A useful extension of our work would be an evaluation if a single questionnaire (NP-MPQ (SF-2)] is comparable to a standard criterion for diagnosis of NP (clinical assessment) and or sufficient to classify those with clinical NP features (Bouhassira & Attal, 2011), or if multiple measures are more suitable for these types of assessments.

Although TJA procedures are one of the most common elective surgeries in North America and Europe (Sharma et al., 2011; Spencer et al., 2009), relatively little attention has been paid to appropriately identifying those individuals who will benefit most from this type of surgery. A valuable extension of our study would be to test the ability of the questionnaire [(NP-MPQ (SF-2) and S-LANSS] to classify patients as having neuropathic features or not prior to surgery.

Thus, a potential clinical application of NP-MPQ (SF-2) would be to assist clinicians such as Orthopedic Surgeons, Physiotherapists and other ” non NP specialists”

in postoperative screening and early identification of NP features (May & Serpell, 2009) so that suitable treatment could be started in a timely manner. Pre operative pain assessment could potentially lead to a better understanding of whether the postoperative symptoms of NP are associated with the exacerbation of the preexisting condition or if they are potentially a result of a surgical procedure itself (Macrae, 2008).

In closing, our results indicate that there may be an opportunity to improve detection and classification of NP in the TJA population; thus it our hope that our work may facilitate future clinical use of NP-MPQ (SF-2) in this population that may lead to advancements in NP screening and potentially contribute to a more focused and adequate management of those who suffer from it. It is anticipated that these findings will contribute to the growing body of knowledge by highlighting the necessity for early identification of chronic /NP in TJA population and the need to further delineate the use of existing NP screening tools in this population.

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## APPENDIX

### **THE S-LANSS PAIN SCORE Leeds Assessment of Neuropathic Symptoms and Signs (self-complete)**

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The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale has seven items consisting of five symptom items and two examination items. Usually, the examination items are done by a doctor but the modified version (the S-LANSS or self-report LANSS) allows people to do this themselves. The purpose of these scales is to assess whether the pain that is experienced is predominantly due to nerve damage or not.

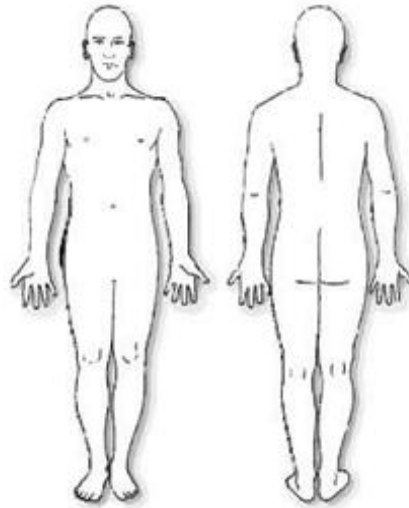
Both the LANSS and S-LANSS are scored out of 24; a score of 12 or more is strongly suggestive of neuropathic pain. Please note, however, that although the S-LANSS is a useful guide to the type of pain, it should only be viewed as an indicator, and not as a diagnosis. Always consult your doctor for a qualified opinion.

Read more ... <http://www.neurocentre.com/nep.php>

### THE S-LANSS PAIN SCORE

This questionnaire can tell us about the type of pain that you may be experiencing. This can help in deciding how best to treat it.

- Please draw on the diagram below where you feel your pain. If you have pain in more than one area, **only shade in the one main area where your worst pain is.**



On the scale below, please indicate how bad your pain (that you have shown on the above diagram) has been in the last week where '0' means no pain and '10' means pain as severe as it could be.

**NONE 0 1 2 3 4 5 6 7 8 9 10 SEVERE PAIN**

- Below are 7 questions about your pain (the one in the diagram).
- Think about how your pain that you showed in the diagram has felt **over the last week.** Put a tick against the descriptions that best match your pain. These descriptions may, or may not, match your pain no matter how severe it feels.
- Only circle responses that describe your pain.

1. In the area where you have pain, do you also have ‘pins and needles’, tingling or prickling sensations.
  - a) NO – I don’t get these sensations (0)
  - b) YES – I get these sensations often (5)
  
2. Does the painful area change colour (perhaps look mottled or more red) when the pain is particularly bad?
  - a) NO – The pain does not affect the colour of my skin (0)
  - b) YES – I have noticed that the pain does make my skin look different from normal (5)
  
3. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations or pain when lightly stroking the skin might describe this?
  - a) NO – The pain does not make my skin abnormally sensitive to touch (0)
  - b) YES – My skin in that area is particularly sensitive to touch (3)
  
4. Does your pain come on suddenly and in bursts for no apparent reason when you are completely still? Words like ‘electric shocks’, jumping and bursting might describe this.
  - a) NO – My pain doesn’t really feel like this (0)
  - b) YES – I get these sensations often (2)
  
5. In the area where you have pain, does your skin feel unusually hot like a burning pain?
  - a) NO – I don’t have burning pain (0)
  - b) YES – I get burning pain often (1)

6. Gently rub the painful area with your index finger and then rub a non-painful area (for example, an area of skin further away or on the opposite side from the painful area). How does this rubbing feel in the painful area?
- a) The painful area feels no different from the non-painful area (0)
  - b) I feel discomfort, like pins and needles, tingling or burning in the painful area that is different from the non-painful area (5)
7. Gently press on the painful area with your fingertip and then gently press in the same way onto a non-painful area (the same non-painful area that you chose in the last question). How does this feel in the painful area?
- a) The painful area does not feel different from the non-painful area (0)
  - b) I feel numbness or tenderness in the painful area that is different from the painful area. (3) non-

**Scoring: a score of 12 or more suggests pain of a predominantly neuropathic origin**

**SCORE** \_\_\_\_\_

**Short-Form McGill Pain Questionnaire-2 (SF-MPQ-2)**

This questionnaire provides you with a list of words that describe some of the different qualities of pain and related symptoms. Please put an **X** through the numbers that best describe the intensity of each of the pain and related symptoms you felt during the past week. Use 0 if the word does not describe your pain or related symptoms.

**1. Throbbing pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**2. Shooting pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**3. Stabbing pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**4. Sharp pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**5. Cramping pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**6. Gnawing pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**7. Hot-burning pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**8. Aching pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

**9. Heavy pain**

*none*

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
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*worst possible*

10. Tender

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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11. Splitting pain

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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12. Tiring-exhausting

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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13. Sickening

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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14. Fearful

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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15. Punishing-cruel

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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16. Electric-shock pain

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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17. Cold-freezing pain

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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18. Piercing

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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19. Pain caused by light touch

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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20. Itching

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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**21. Tingling or 'pins and needles'**

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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**22. Numbness**

<i>none</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<i>worst possible</i>
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