Demography and drug prescription pattern of injured workers referred to a tertiary care chronic pain clinic by Workplace Safety and Insurance Board staff: A pilot study

By

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A thesis submitted in conformity with requirements
for the degree of Masters of Sciences
Department of Institute of Medical Sciences
University of Toronto
2012

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Abstract:

Opioid prescribing within the workers' compensation system in general has been a cause for concern. The objective of the study was to estimate the prevalence of opioid users among injured workers, referred at a Tertiary Care Pain Clinic, in 2008-2009. A cross-sectional retrospective study of 110 consecutive workers; male/female ratio was 2.3:1; mean age 45.5 years; mean pain ratings were 7.1±1.8. 21% of the workers were diagnosed with a biomedical problem (Group I), 51% with medical/psychological factors (Group II) and 25.5% had identifiable psychological factors but no physical pathology (Group III). Opioids were prescribed in 81.8%; of those 32.2% were on >200mg of daily morphine or equivalent (MED). A higher proportion of opioid users were in Group II and Group III than Group I. The vast majority of referred injured workers in this study were on opioid therapy with 1 in 3 exceeding the "watchful" dose of 200 mg MED.

Acknowledgements

"Seek knowledge from the cradle to the grave"
(Prophet Mohammed P.B.U.H)

First and foremost, my deepest gratitude goes to my supervisor Professor Dr Angela Mailis-Gagnon for giving me a wonderful opportunity to be a part of an exciting project. Without her willingness to act as my supervisor and guidance in research, this research work would not have been undertaken. Thank you- Dr. Mailis for being such a great mentor and incomparable role model.

I wish to express special thanks to my thesis committee members Prof. Dr M. Mamdani and Dr J. Hunter, whose encouragement and interest for my work have motivated me to continue my endeavor. I appreciate their edits and suggestions that helped improve this thesis.

A big thank you to my all colleague at the Comprehensive Pain Program- Toronto Western Hospital, for their constant support to achieve my goals; especially Anna Kenyon, for her invaluable assistance, and encouragement; and Drs Balaji Yegneswaran, Amol Deshpande and Keith Nicholson for contributing their expertise and time to help me with a section of my thesis.

A special thank you to my dear friends: Shahnawaz Sajid for critical mind, continuous support and friendship; Muzna Asif for listening ears; my university group and Mahjabeen Khan for uplighting prayers.

My Family!!!! How can I ever thank you all? Special tribute to my late father Haji Haroon Lakha. A very special thanks to my mother Mrs. Roshan Haroon Lakha, whose supervision assisted me in my education and her constant encouragement help build my self esteem, and my brothers Haris Haroon Lakha, Mohammed Hussain Lakha, my beloved sisters and nieces (especially Haya) for their love, encouragement and cheerfulness especially at the time of my thesis.

I would like to thank the Institute of Medical Sciences, University of Toronto for the opportunity to conduct this thesis. Particularly, I am grateful to Hazel Pollard, Dr. Mary Seeman and Dr. Howard Mount for their continuous support and words of encouragement

I am thankful to Allah who gave me the strength and courage that sent all these fabulous mentors, family, friends, coworkers and experts to help me.

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Chapter 1 – Introduction

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List of Abbreviations

ANOVA:	Analysis of variance
ASA:	Acetylsalicylic acid
CAM:	Complimentary and alternative medicine
CAT:	Computerized axial tomography
CNCP:	Chronic non cancer pain
CPP:	Comprehensive pain program
CPS:	Canadian Pain Society
CPSO:	College of Physicians and Surgeons of Ontario
CR or SR:	Controlled or sustained release
DSM-IV-TR :	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision
ED:	Emergency department
GI:	Gastrointestinal
HOU:	High opioid user
IR:	Immediate release
LBP:	Low back pain
LOU:	Low opioid users
MED:	Morphine equivalent dose
MRI:	Magnetic resonance imaging
MSK:	Musculoskeletal Pain
NCMs:	Nurse Case Managers
NOU:	Non opioid users
NP:	Neuropathic Pain
NRS:	Numerical rating scale
NSAID:	Non-steroidal anti-inflammatory drugs
PRN:	Per needed
PPI:	Present pain intensity
SAS:	Statistical analysis software
SF-MPQ:	Short form of McGill pain questionaire
SNRI:	Selective norepinephrine reuptake inhibitors
TCAs:	Tricyclic antidepressants
VAS:	Visual analogue scale

WHO: World Health Organization

WSIB: Workplace safety and insurance board

Glossary

Pain: Unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Hyperalgesia: An increased response to a stimulus which is normally painful. Increased pain from a stimulus that normally provokes pain.

Abuse: Any use of illegal drugs or the intentional self-administration of a medication for a non medical purpose.

Addiction: A primary chronic neurobiological disease with genetic, psychosocial and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving

Dependence (Physical): A state of adaptation manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing drug blood level or administration of an antagonist.

Misuse (opioid): Use of an opioid in ways other than those intended by the prescribing physicians (also called "problematic opioid use").

Source: [1]

Structure of thesis

The thesis has been structured in the following chapters

Chapter 1- Introduction and Rationale

The section provides relevant literature review on chronic pain, types of diagnoses, and drugs used for chronic pain in detail. It also provides in-depth information on opioids and their effectiveness, and rationale, objectives, the focus goal and the justification for the thesis.

Chapter 2 – Methodology

This part discusses the design and procedures of the study as well as statistical analysis.

Chapter 3 & 4 - Results

This section outlines the results of research work, and mentions exploratory results of the study.

Chapter 5- Discussions

This section of discussion summarizes outcome of the research work, mentions study limitations and finally provides recommendations for future research.

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CHAPTER 1: INTRODUCTION

Long term disability among workers with work-related injuries is the most important public health problem facing workers' compensation organizations. Usually, musculoskeletal injuries are seen as a largely self –limiting health problem, with recovery in a several weeks [2]. However, when pain does not resolve it often leads to long –term disability. As a result, constitute an immense socioeconomic burden: some 80% of health care and social costs are attributable to the 10% of cases with chronic pain and disability [3]. Risk factors associated with prolonged disability of injured workers include demographic, medical, employment and psychosocial characteristics [4-6]. In the literature this type of chronic pain has been labeled chronic non-cancer pain (CNCP) to differentiate it from cancer related pain [7].

The prevalence of CNCP in the general population varies widely in different studies (due to differences in methodology, definitions etc) and ranges from 10.1% to 55.2% [8]. In the USA more than 75 million people (25% of the entire population) have chronic and/or recurrent pain constituting an important and expanding public health issue [9]. CNCP encompasses a diverse group of diagnoses and syndromes (e.g., chronic low back pain, fibromyalgia, neuropathic pain, migraines) and there is a wide range of outcomes among workers, whose injuries initially appear similar [4]. Since CNCP may have numerous causes, treatment options vary from behavioural and rehabilitation approaches to the prescription of different medications (e.g., opioids and non opioid analgesic, antidepressants, anticonvulsants) and invasive interventions (such as nerve blocks and surgery) [10].

Opioid and non opioid drugs (i.e., NSAIDs, antidepressants, anticonvulsants) as well as non-pharmacological treatments (physiotherapy, acupuncture, cognitive behavioral therapy, chiropractic manipulation) have been found to be effective for the management of certain CNCP conditions [11]

Regarding the pharmacological management of CNCP, the World Health Organization (WHO) [12] has developed a three-step analgesic ladder as follows: For mild pain, the recommended drugs include acetaminophen, aspirin, or other non-steroidal anti-inflammatory drugs (NSAID). When pain persists or increases to moderate intensity, the prescription of weak opioids (codeine, hydrocodone or tramadol) is recommended. Because of additive analgesia, these weak opioids are often administered in fixed dosage in combination with acetaminophen or aspirin. When pain persists or increases to a severe intensity, the administration of strong opioids (morphine, hydromorphone, fentanyl etc) is recommended. This step begins by increasing the dosages of weak opioids or prescribing stronger opioids until the patient's pain is controlled. Because scheduled administration has been found to be more effective in controlling pain [13], the WHO guidelines recommend that pain medications be used on a strict schedule (e.g., every 3-6 hours), rather than "as required".

Despite the presence of several guidelines [1, 11, 14, 15] outlining the prescribing practices for opioids in CNCP, opioid prescribing remains controversial, resulting on one hand in overprescribing and, on the other hand, in underprescribing of opioids . Recent data from Ontario report an increase in prescription-opioid-related deaths by two-fold in 10 years in the province, from 13.7 per million in 1991 to 27.2 per million in 2004. Prescription of Oxycodone rose by

850% between 1991 and 2007 [16]. Also, prescription-opioid-related admissions to substance-use treatment programs doubled between 2004 and 2009 [17]. On the other hand, The National Institute on Drug Abuse (NIDA) has noticed that health care providers under-prescribe painkillers as they frequently overrate the potential for patients to become addicted to medications, for instance morphine and codeine [18].

Opioids are only effective for certain patients and certain chronic neuropathic and musculoskeletal non-malignant conditions (e.g. low back pain, rheumatoid arthritis and connective tissue disorders, post herpetic neuralgia and painful peripheral neuropathy). They are not considered the solution for all chronic pain conditions [19].

Physicians and policy maker must know the indications, utility and efficacy of opioids, in order to decide decide how much risk is acceptable before it offsets the benefits of using opioids [20]. However, opioid prescribing patterns vary widely. A survey of CNCP patients documented a 10 fold variation in opioid use that ranges from only 3.4% in patients with spinal pain [21] to 33% in a sample of veterans with pain condition [22]. Canada is one of the world's leading consumers (per capita) of several opioids (e.g., hydromorphone, oxycontin, fentanyl patch, morphine), which creates for an ''opioid-rich'' environment [23, 24]. There is evidence that long term opioid use may be associated with lack of functional improvement, adverse effects on the immune system and sexual function, opioid-induced hyperalgesia, impaired cognition, possible addiction and increase in non-medical use of opioids [25-30]

Even though the goals of long term opioid therapy are reduction in disability and increase in activity, a recent epidemiological study in Denmark, which suggested that these goals are not

being met . CNCP chronic opioid users faced poorly when compared to non-opioid users [26]. These authors reported that opioid use was significantly associated with reported moderate/severe or very severe pain, poor self-rated health, higher unemployment, greater use of health care and worse quality of life. The study demonstrated the significant association betweeen opioid use and several negative health-related factors. However there is a possibility that the study had some inherent selection bias. It can be argued that those prescribed opioids have greater biomedical pathology, weighing down on the outcomes. In other studies, opioid administration emerged as an important factor associated with poor prognosis for return of injured workers to employment [27, 31, 32].

In CNCP, existing guidelines [1, 11, 15] recommend that opioids should not be a "stand alone" primary treatment of CNCP, but part of a comprehensive treatment program that combines physical rehabilitation and psychosocial/ behavioral approaches.

Drug prescription databases and pharmaco-epidemiological data in general may provide insights into aspects of drug utilization, such as aggregation of drug use at various levels and information on indications, doses and dosage regimens. Without information on how drugs are being prescribed and used, it is difficult to initiate a debate on rational drug use and to suggest measures to change prescribing habits for the better. It is in this context, that I sought to collect detailed information on a subset of injured workers in regards to their characteristics and opioid/other drug use.

Contextual Background

In 2000, the Workplace Safety and Insurance Board (WSIB) of Ontario published a report produced by an expert advisory panel which reviewed the chronic pain literature [33]. The panel outlined specific suggestions for the identification and management of injured workers with chronic pain. In 2001, given the complexity of managing CNCP, the WSIB formed a unique relationship with the Comprehensive Pain Program (CPP) a tertiary care Pain Clinic in Toronto Western Hospital, University Health Network, affiliated with the University of Toronto. This relationship allows WSIB Nurse Case Managers (NCMs) and WSIB physicians to directly refer complex cases of injured workers with chronic pain to the CPP. An earlier pilot study at the CPP suggested that many injured workers with CNCP referred directly to the program by WSIB staff, use high doses of opioids which do not always correlate with the severity of their medical condition [34, 35]. These findings were in accordance with a study conducted at a VA hospital [36] that showed that emotional distress (but not the degree of biomedical pathology) was one of the determining factors which differentiated veterans who were on opioids for low back pain as compared to those on no opioids. Therefore, knowledge concerning detailed characteristics and prescription drug patterns in injured workers is useful in adding to our understanding of factors associated with CNCP and its treatment in work related injuries.

Literature Review

1-1-1 Chronic Non-Cancer Pain

Chronic pain is usually defined as pain persisting over 3 - 6 months, and constitutes a prominent societal and economical burden. Since chronic pain arises primarily from non cancer causes, in this thesis the terms chronic pain and chronic non cancer pain (CNCP) are used interchangeably. According to Statistics Canada about 1.5 million Canadians aged 12 to 44 reported experiencing chronic pains [37]. In that age group back pain, migraines and other chronic pains affect about 1 in 10 Canadians [38]. Pain is more common in elderly population than younger age group [39]. Given the aging of the Canadian population, the problem of CNCP is expected to grow substantially over time.

It has been suggested indeed that there is an "epidemic" of chronic pain [40] and that the cost of current treatment and compensation are “threatening national economies” [41]. Chronic pain costs more than cancer, heart disease and HIV combined [42]. Estimates place direct health care costs for pain in Canada to be more than $6 billion per year and productivity costs related to job loss and sick days at $37 billion per year [42, 43]. Remarkably, less than 10% of the chronic pain population consumes as much as 70-80% of the resources including sick leave benefits and health care visits [31]. Conversely, a large number of people with chronic or recurrent pain do not pursue medical attention and take little, if any, time off work [44, 45].

1-1-2 Pain Mechanisms/ causes

CNCP encompasses a diverse group of diagnoses and syndromes. Physiologically, pain originates from nociceptive, neuropathic, or mixed mechanisms.

Neuropathic pain results from pain initiated or caused by a primary lesion or dysfunction of the nervous system (IASP 1994)[7]. Examples include post stroke pain syndrome, spinal cord injury pain, multiple sclerosis, post amputation pain, peripheral nerve damage due to injury, disease or surgery, diabetic neuropathy, post herpetic neuralgia. The Canadian Pain Society (CPS) reported that about 1 million Canadians have neuropathic pain based on literature interpretation [46]. However, a general population study in the UK estimated that neuropathic pain has a much higher prevalence [47], which raises the domestic figure to 2.5-3 million Canadians possibly suffering from painful neuropathic conditions.

Nociceptive pain is the result of tissue injury and arises primarily from disorders of musculoskeletal tissues and less so visceral tissues, such as the stomach, bowels, heart, kidney etc. In the United States, headache, back pain, arthritis, and other musculoskeletal pains are the most common conditions of CNCP that result in lost work time [48]. The United Nations noted the burden to society of musculoskeletal disorders and declared 2000 to 2010 as The Bone and Joint Decade [49]. The total direct and indirect costs of musculoskeletal disorders in Canada, surpass those reported for cardiovascular diseases, with the highest expenditure reported for back and spine disorders, arthritis and rheumatism [50]. Specifically, in Canada, musculoskeletal pains are the major single reason of work disability [51] and account for 10% of the short-term disability costs and 39% of the approximate long-term disability costs [52]. Additional serious

costs are associated with lost productivity, income replacement, or disability payments.

In many cases of chronic pain, there is no apparent peripheral biomedical pathology; the type and degree of organic pathology does not distinguish between those who develop chronic disabling pain from those who do not; often the severity of pain and related disability appears grossly disproportionate to the degree of peripheral injury [53]. These and other considerations have given rise to psychosocial concepts in an effort to understand CNCP, such as the development of the biopsychosocial movement [54], the distinction between the subjective experience of pain versus pain behavior [55], response bias in the reporting of pain [56, 57], impairment versus disability [58], and concepts of abnormal illness behavior [59]).

One conclusion drawn from the literature is that psychological or psychosocial variables seem to be more important than biomedical factors underlying chronic pain in predicting outcomes, as several studies have shown [60, 61]. To cite a few, in a study of 33 low back pain patients, Vlaeyen et al [62] found that physical pathology was not predictive of disability, whereas pain-related fear was. Severeijns et al [63] studied a group of 211 patients with heterogeneous pain complaints. Catastrophizing proved to be the most potent predictor of each of the outcome variables while physical pathology made a modest contribution to the variance in pain intensity and pain interference.

1-1-3 Painful work-related injuries

Workers' Compensation programs protect employees from the monetary hardships associated with work-related injuries and occupational illnesses [64]. It is a form of insurance in which workers' give up their right to sue in exchange for compensation benefits. In Canada, each

province and territory has its own exclusive Workers' Compensation Board/Commission (WCB) [65].

Chronic pain and its management constitute a substantial problem in the work place, as 10 % of the American population suffers from work disability at any one time [66]. In 1992, there were 2.7 million disabling work injuries in the USA which were eligible for workers compensation insurance benefits and were calculated to cost US$129 billion (this figure translates to US$180 billion in 2005 dollars) [67]. In addition, Ontario's Workplace Safety and Insurance Board (WSIB) reports usual lost time injury costs more than $106,500/ injury (2007 data) [68]. This number contains direct expenses to the WSIB of nearly $21,300. Indirect costs to the corporation, including lost productivity and human resource expense, constitute the bulk of the total financial burden. Using these approximation and the fact the WSIB reported more than 80,000 accepted lost time injuries, the WSIB financial burden in Ontario for 2008 was CDN $8.5 billion [68].

The types of workers and job duties have changed over time, leading to differences in the occurrence and kinds of workplace injuries and predictors of disabilities. For instance, new machinery has increased time spent keyboarding but has reduced the duration of several procedures in industries. Additionally, the workers are getting older and the proportion of females and minorities is mounting [69].

Painful musculoskeletal conditions are frequent causes for work loss and reduced efficiency while at employment [48]. It is estimated that about 70% of the compensable workplace injuries have a musculoskeletal basis arising both from acute traumas and from

persistent cumulative biomechanical challenges [70]. The cost of painful musculoskeletal disorders in the workplace is significant but estimates vary. Webster and Snook [71] reported an average direct cost of US$ 8,070 per case for "upper extremity cumulative trauma disorder" claims in 1989 from a large national worker compensation insurance carrier. In another report on "cumulative injury" (which, however, included mental stress and back claims), the average cost per claim was US$24 in 1992 ($158 in 1989 dollars) based on a random sample of lost time from participating insurers [72].

Back pain is extremely common, with up to 50 percent of workers suffering an episode each year. Back pain is a major cause of absence from work and of correspondingly high economic losses [73]. In another study, a multi-employer database that links medical, prescription drug, absence, and short term disability data at the patient level, was analyzed to uncover the 10 most costly physical disorders affecting American businesses. The top-10 were: angina pectoris; essential hypertension; diabetes mellitus; mechanical low back pain; acute myocardial infarction; chronic obstructive pulmonary disease; back disorders not specified as low back; trauma to spine and spinal cord; sinusitis; and diseases of the ear, nose and throat or mastoid process [74].

Since the release of the College of Physicians and Surgeons Evidence Based Guidelines for the management of CNCP in 2000, the CPP as well as other pain clinics have seen a rapidly increasing number of general patient referrals from the medical community with ineffective or problematic management, many of whom are on opioids [75]. On the other hand, in an attempt to evade multiple issues associated with opioid analgesia, these medications are avoided altogether

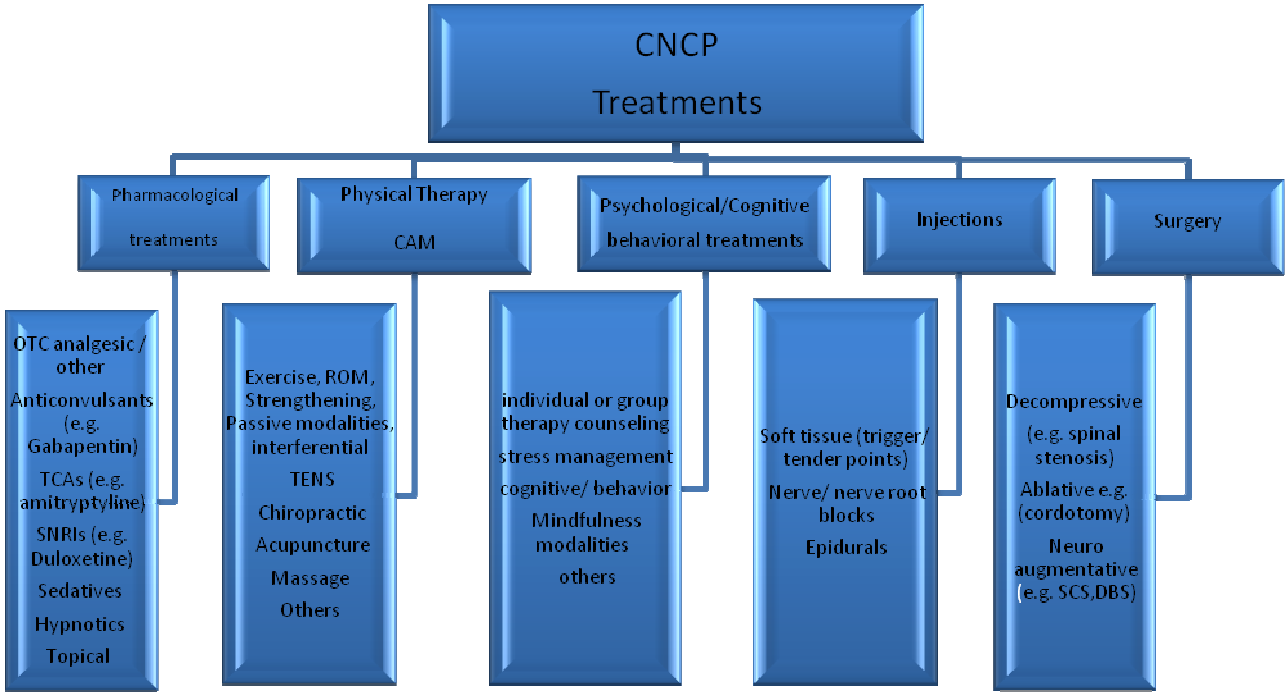
by many physicians [76]. However, opioids in small to moderate doses may be required to control certain types of pain [19] and may make the difference between a successful return to work or increased quality of life and permanent unemployment and disability.

1-1-4 Management of CNCP

Understanding the challenges in the management of CNCP, in 2000, a task force appointed by the College of Physicians and Surgeons of Ontario (CPSO) provided a systematic review of randomized trials and other clinical studies on the effectiveness of various treatment modalities [11]. CNCP can be treated with a multiplicity of modalities such as pharmacotherapy; physical treatments including exercise, local ice and heat, joint/ tissue mobilization etc; psychological/ behavioral treatments; injections to soft tissues and nerves or nerve roots, and more invasive (surgical) treatments [10, 77].

1-1-5 Pharmacological and Non-pharmacological Treatment options:

The range of options available for chronic pain management was summarized as follows [1]. While CNCP patients are very often prescribed sedatives and hypnotics for concomitant sleep disorders, the present study limited to review of medication given specifically for pain.



1-1-6 Simple analgesics and Non Steroidal Anti-inflammatory Drugs (NSAIDS)

Acetaminophen is a commonly used oral analgesic and antipyretic for treatment of pain. It works in most kinds of pain excluding inflammatory arthritic pain [78] and most preparations containing acetaminophen are available over the counter (OTC) without the need for a doctor's prescription. Similarly, Acetylsalicylic acid (ASA) is one of the oldest non-opioid analgesics, also available without prescription. Gastric problems and bleeding are general side-effects of therapeutic doses of ASA [79].

Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, and naproxen can provide relief in pain [78]. Many of these drugs can also be obtained OTC. NSAIDs are most beneficial in cases of acute pain, or flare-ups in patients with chronic nociceptive pain [80]. Originally, it was thought that pain relief was due to their action on curtailing inflammation. However, research [81] has shown that there is poor correlation between anti-inflammatory activity and analgesic effectiveness. NSAID analgesic action occurs not only through peripheral inhibition of prostaglandin synthesis, but also through a variety of other peripheral and central mechanisms [82, 83]. In general, NSAID use is often limited for patients with chronic nociceptive pain because of gastrointestinal (GI) side effects [84]. The newer, so-called COX-2 selective inhibitors (also called COXIBs), such as Celebrex, were designed to avoid this complication and indeed, large, randomized, controlled trials demonstrated improved GI safety for rofecoxib and other similar drugs [85]. Caution should still be exerted when using these medications for long periods of time [78].

Topical NSAID preparations are also effective in relieving pain in certain acute and

chronic nociceptive conditions [86].

1-1-7 Antidepressants and anticonvulsants

Several reviews of randomized controlled trials have concluded that a class of older antidepressants, the tricyclic antidepressants (TCAs) have analgesic effectiveness in several chronic pain conditions [86-89]. Specifically, TCAs have demonstrated analgesia in pain due to diabetic neuropathy, postherpetic neuralgia, tension headache, migraine, atypical facial pain, fibromyalgia and low back pain.

Other classes of antidepressants include Selective Norepinephrine Reuptake Inhibitors (SNRIs) and Selective Serotonin Reuptake Inhibitors (SSRIs). While Venlafaxine (SNRI) is an effective antidepressant, uncontrolled reports indicate that it is effective in pain conditions such as postherpetic neuralgia, painful polyneuropathy, headache, neuropathic pain, atypical facial pain and radicular back pain [90, 91]. Duloxetine (SNRI) has been shown in randomized controlled trials to be effective in the treatment of several CNCP conditions [92] and has been approved by Health Canada for the treatment of anxiety, depression, certain neuropathic pains, fibromyalgia and more recently chronic low back pain.

Anti-convulsant medications are used to relieve neuropathic pain, based on their ability to decrease neuronal excitability [93]. There are variations among agents which relate to particular mechanisms of action. The most well studied agents are gabapentin, pregabalin and carbamazepine [78]; though, there is increasing evidence for lamotrigine, topiramate and oxcarbazepine [78]. Several large randomized, controlled trials have provided evidence that

gabapentin provides significantly more pain relief than placebo in postherpetic neuralgia [94, 95], diabetic neuropathy [96, 97] and mixed diagnoses of neuropathic pain [98]. A newer "gabapentinoid" is pregabalin. Large, randomized, controlled trials have shown that pregabalin has significant analgesic effectiveness in postherpetic neuralgia [87, 99] and painful diabetic peripheral neuropathy [100, 101]. The drug is approved by Health Canada for the treatment of diabetic neuropathy pain, post-hepretic neuralgia, spinal cord injury pain and fibromyalgia.

The early anticonvulsants phenytoin, valproate and carbamazepine and the newer anticonvulsants lamotrigine, pregabalin, gabapentin, lacosamide, topiramate and levetiracetam, act through a multiplicity of mechanisms which may interfere with different pathways and neurotransmitters involved in chronic pain [77].

1-1-8 Opioids

Opioids are a class of medications that act on delta, kappa, and mu receptors found in brain, spinal cord, peripheral sensory neurons and intestinal tract. They are natural, synthetic or semi–synthetic derivatives of morphine. Opioids are available in both short and long acting preparations. They have been shown to be effective for both pain and function in patients with certain nociceptive and neuropathic pain syndromes when compared to placebo [19]. Furlan et al [102] have recently conducted a systematic review of opioids for CNCP. This systematic review of sixty-two randomized trials confirmed the previous findings, namely: Opioids were more effective than placebo in patients with nociceptive pain and neuropathic pain, and that there was no difference in efficacy between weak and strong opioids.

Opioids may be given parentally (SC/IV/IM), orally or topically. They are effective for severe pain; however there is a risk of dependence and side effects. There are different types of opioids, classified as either weak or strong. Weak opioids include codeine and tramadol where strong opioids include oxycodone, fentanyl, hydrocodone, hydromorphone, morphine, oxymorphone and pentazocine.

The studies cited below paint the picture of the opioid "dilemma" in North America and demonstrate the need to strike the balance between the benefits and hazards of opioid use.

Opioid effectiveness versus adverse effects

The best available evidence indicates that long-term use of opioids provides 30% pain relief based on pain scores and often does not improve function [29]. Unfortunately, the effort to improve CNCP management has focused on increasing access to opioids [103], which has not been matched by increasing access to other treatments also proven effective for CNCP such as cognitive-behavioral and multidisciplinary treatments [104].

Opioid related side effects are very well documented. Noble et al [105] who conducted meta-analysis of 3079 patients treated with opioids for CNCP for at least 6 months, found a 32.5% dropout rate in consumers of intrathecal, oral, and transdermal opioids, with the maximum dropout rates being in oral usage. In a meta-analysis of 6019 patients [19] dropout rate was 33% from opiate therapy. Side effects like nausea and constipation were the most challenging compared to those found with other non-opioid pain medications. Compared with other drugs, statistically significant risk differences were found (defined as risk in one group divided by the risk in the other) for nausea (14%, 95% CI 4%–25%) and for constipation (9%,

1%–17%) [19]. Many side effects, such as somnolence, nausea, and pruritis, occur during the initial titration of opioids which can be difficult to manage and prevent many patients from continuing with their therapy. As medications that influence the central nervous system, opioids may affect cognition and psychomotor performance [106]. Additionally, long term adverse effects include misuse and addiction, disturbance of immune regulation, sexual dysfunction and opioid induced-hyperalgesia with associated need for escalating doses to provide desired pain relief and stabilization of mood [28, 30].

Opioid prescribing guidelines

The increased use of opioids has compelled the authors of several recent studies [16, 107, 108] to caution regarding the risks of treating CNCP with opioids. It has also led to several organizations producing guidelines to assist physicians with opioid prescribing [1, 14, 15].

These guidelines state that opioids are for certain nociceptive and neuropathic conditions, although higher doses may be required for neuropathic pain [109]. Stable and moderate opioid doses have the fewer cognitive effects or long-term side effects than non-stable doses. The guidelines stress vigilance during initial titration particularly in the elderly and those on sedating drugs. In addition, considerable caution should be exercised if the patient is to drive, depending on the dose/type of opioids (short versus long acting), the concomitant prescription of other psychotropic drugs, the presence of mood/anxiety disorders and suboptimal management of pain [1]. Both the American and the Canadian guideline stress that at baseline, the patient should be assessed for the risk of substance abuse and for possible mood and anxiety disorder, a treatment agreement should be considered (verbal or written) and informed consent should be obtained.

Opioid management should be pooled with other medical treatments and counseling and these drugs should be used with caution as a stand alone treatment. The Canadian Guideline suggests that the patient should experience a graded analgesic response with each dose increase and should be switched to controlled release opioids once the optimal dose is established with immediate-release opioids, to help prevent the "off and on" switch of fluctuating opioid blood levels that lead to euphoria alternating with cravings. Additionally, the Canadian Guideline suggests that no more than one-third of the total daily opioid should be used for breakthrough pain and cautioned that most patients with chronic pain should be managed on less than 200 mg morphine or equivalent dose (opioids doses are converted to daily morphine dose equivalents, (MED) per day). In particular, the 200 mg MED has been considered the "watchful dose", though it does not constitute the "optimal" or "maximal" dose. The physicians are advised that if the patients are in need of higher doses, the prescribers should take a fresh look at indications and effectiveness and proceed very carefully.

Evidence of increased opioid prescribing

The use of opioids in pain management for both palliative care and CNCP has been escalating in recent years. Market data indicate that since 2000, long acting and short acting opioids have experienced a 26.5% and 39% compound annual growth rate, respectively [110]. On per capita basis, Canada has become the world's third largest consumer of prescription opioids, behind the United States and Belgium [111]. Canada's recorded prescriptions for opioids increased by about 50% between 2000 and 2004 [23]. There has also been a consistent increase in the use of narcotic analgesic-related US emergency department (ED) visits from 41,687 cases in 1994 to 90,232 cases in 2001 [112]. Dependence was the most frequently

reported motive underlying narcotic analgesic visits (38,941 visits), followed by suicide (24,576), and psychiatric effects (13,949). In Canada, prescriptions for oxycodone rose by 850% during a period of 1991 to 2007 [16]. Studies have acknowledged a striking increase in opioid-related problems, including rising rates of opioid addiction, overdose, emergency department visits and hospitalizations. These problems closely parallel the exceptional increase in prescribing of controlled release opioids and they seem to be dose-related [113, 114]. .

Opioid abuse and addiction

In recent years, the number of CNCP patients addicted to opioids who seek treatment in mental health facilities has increased considerably [115]. Savage [116] reported that based on review of the literature, addictive disorders of any sort occur in approximately 3-26% of the general population, in 19-25% of hospitalized patients, and in 40-60% of patients who sustain major trauma. In regards to chronic pain, it is estimated that 3% [117] to 19% of CNCP patients [118] may be abusing or be addicted to opioids. The large variations in reported prevalences in the above cited studies relate to methodological issues including definitions and inclusion of low versus high risk populations. In the United States there has been an increase in the reported cases of non-medicinal use of OxyContin® from 221,000 cases in 1999 to 1,900,000 in 2002 [119]. Additionally, prescription opioids have replaced heroin as the substance of choice for addicts in many Canadian cities [16, 120].

Increased opioid prescribing in patients with psychological/ psychiatric co-morbidity

Breckenridge et al [36] showed that, rather than underlying biomedical pathology, characteristics such as age, depression, personality disorder, and substance abuse, distinguished

veterans with chronic low back pain who were on opioids from those who were receiving non-opioid treatments. Gartner and Schiltenwolf [121] studied patients with unremitting strong pain arising from the musculoskeletal system despite long-term opioid medication and recommended that in such patients, psychiatric comorbidities should be considered as basis for the unremitting pain. Chelminski et al [25] found that 32% of a sample of CNCP patients had problems with substance misuse associated with high psychiatric comorbidity. A very recent study from the CPP showed that community physicians prescribe high doses of opioids for patients in distress with significant psychosocial factors contributing to their disability, despite the presence of little or no biomedical pathology [75].

Opioid related mortality

Recent studies have shown that patients who are at higher doses of opioids (>100 mg of morphine equivalent) are at increased risk of opioid related death compared to patients who are at lower dose of opioids (<20 mg) [107, 108]. In addition, a recent Canadian study [122] reviewed sequential trends in opioid prescribing among Ontario Drug Benefit recipients. This study showed 2 year opioid related mortality rates of 1.6 per 1000 people among individuals prescribed MED of less than 200 mg/day; 7.9 per 1000 among those prescribed an MED of 200 to 400 mg/day; and 9.9 per 1000 for those prescribed an MED of more than 400 mg/day. Dhalla et al in another recent Canadian study [123] provided insight into factors associated with the increase in opioid-related mortality. They concluded that the problem is partially related to the large variance between family physicians who prescribe opioids, with a certain subgroup been responsible for high opioid prescribing.

The other side of the problem: Opioid under-prescribing

On the other hand, opioids are under-prescribed even for patients with serious biomedical conditions for fear that they may lead to problems of addiction or abuse, or because of possible regulatory consequences [124]. A survey probing 100 Canadian physicians about their attitudes towards opioid use for chronic pain, confirmed that 35% of general practitioners and 23% of palliative care physicians would "never" use opioids even for the management of severe CNCP [125]. This Canadian study is in accordance with the findings of other surveys and focus groups in the United States, as physicians are concerned about the risk of dependence and uncertain about the indications for opioids [126, 127]. Clinicians reluctant to use opioids in CNCP perceive that the risk of addiction, somnolence with resulting impairment of function, and general ineffectiveness of opioids plus fear of regulatory interference, far outweigh any benefit that may exist [103].

Opioids in the workplace

Opioid therapy is one of the available forms of therapy for chronic pain conditions, with the aim of reducing pain and increasing function [128, 129] .

In Washington state workers' compensation system, prescriptions for narcotics in general were shown to have increased moderately from 1996 to 2002 [130]. However, specifically prescriptions for strong opioids increased from 19.3 % to 37.3%. The study presented evidence of increasing doses of long-acting opioids and opioid-related deaths, primarily involving men (84%) and smokers (69%) [130].

Opioid prescribing within the workers' compensation system in general has been a cause for concern as long term opioids are reportedly related to poorer outcomes. Webster et al [32] examined the association between early opioid use and subsequent outcomes of claimants with acute disabling low back pain during the period 2002-2003. Claimants receiving opioids within 15 days after filing a workers' compensation claim, were more likely to experience increased disability duration, increased medical costs, and subsequent surgery. Workers who received more than 450 mg morphine equivalent dose in total were disabled 69 days longer than those who received no early opioids.

A recent study in USA, examined whether prescription of opioids within 6 weeks of low back injury is associated with work disability at 1 year [31]. The authors analyzed detailed data on paid bills for opioids prescribed within 6 weeks of the first medical visit for a back injury among 1843 workers with lost work-time claims in the Washington State Workers' Compensation Program from July 2002 to April 2004. This study found that nearly 14% of the workers (254/1843) were receiving work disability compensation at 1 year. About one-third of the entire workers cohort (34.1%) received an opioid prescription within 6 weeks, and 50.7% of those on opioids, received them at the first medical visit. Franklin et al concluded that prescription of opioids for more than 7 days and receipt of more than 1 opioid prescription in workers with acute low back injuries was a risk factor for work disability at 1 year [31].

Another prospective study [131] involved patients with chronic disabling occupational spinal disorders (CDOSD) diagnosed with or without post-injury opioid-dependence disorder (ODD). This study showed that opioid-dependent patients were 1.7 times less likely to return to

work, 2 times less likely to retain work at the 1-year, and 1.7 times more likely to engage in healthcare utilization as compared with non opioid-dependent patients.

In contrast, a recent Canadian study examined the association between early opioid prescription and future recovery in injured workers and found contradictory results to the previously cited studies [31, 32, 131] regarding early opioid prescriptions and disability [132]. This study showed that in Alberta prescriptions for opioid analgesia appear to be decreasing over time within worker compensation claimants. Claimants with more severe injuries were more likely to receive opioids, if the opioid prescription was given in the early period.

To address the issue of opioid prescriptions in the workplace, different workers compensation systems in Canadian jurisdictions have attempted to establish policies. In 2004, The Workplace Health, Safety & Compensation Commission of Newfoundland and Labrador implemented the Policy HC-14 titled *The Use of Opioid Medication for Compensable Injuries*. The purpose of this policy was to establish the parameters for appropriate coverage of opioids (narcotic pain medication) in the treatment of compensable injuries. It clarifies the responsibilities of the injured worker and those of the prescribing and dispensing health care provider(s) and the Commission and defines an appropriate effective monitoring and reporting process for opioids covered by the Commission. The Commission's opioid policy had an influence, as new claims in 2005 and 2006 of injured workers receiving opioids, were less than one third of those of the previous years [133].

The Workmen's Compensation Board in Ontario was formed in 1915, through an Act of the Ontario government, and is accountable for supervising the Workplace Safety and Insurance

Act (WSIA). It was renamed later as Workplace Safety and Insurance Board (WSIB). WSIB is fully subsidized by the employers of Ontario and obtains no government financial support. Its primary objectives are to supply income assistance and subsidize medical treatment to workers injured at the workplace. Each year, an average of 300,000 new claims are registered with the WSIB [134].WSIB accepts claims for chronic pain disability (CPD) when it results from a work-related injury and there are adequate reliable subjective and objective facts confirming the disability. The eligibility criteria to qualify for compensation for CPD were developed by a panel of experts.

WSIB introduced on February 2010 a new policy on opioid administration for acute pain. After a new injury or recurrence, the WSIB initially only allows prescriptions for short-acting narcotics for a maximum of 12 weeks. Long-acting drugs will not be allowed during this period. After 12 weeks of continued narcotic use, WSIB clinical staff will review the worker's case regarding the ongoing use of opioids and commencement of a long-acting opioid. Workers already on opioids for severe injuries or those with chronic work- related diseases, do not fall under this policy. Indeed, there is no WSIB policy in existence for CNCP to address the large numbers of workers receiving opioids, though currently WSIB is working on establishing an opioid policy for chronic users. Of note, 40% more claimants are prescribed opioids currently, than 10 years ago [134].

1-2 Research Questions:

The **research questions** of the study are:

a) What is the prevalence of a) opioid users in general and b) high dose opioid users in particular among injured workers referred to the Toronto Western Hospital Comprehensive Pain Program directly by WSIB staff from 2008-2009?

b) What are the demographics and pain characteristics of injured workers who are opioid users and have been referred to the Toronto Western Hospital, Comprehensive Pain Program directly by WSIB staff?

c) What doses of opioids are prescribed to injured workers with different types of underlying pathology associated with their pain?

d) What is the prevalence of co-prescriptions of psychoactive medications prescribed to injured workers who are opioid users and are referred to the Toronto Western Hospital, Comprehensive Pain Program directly by WSIB staff?

1-3 Rationale: Innovation, statement of importance and major contribution

Recent studies have shown an increase in expenditures for opioids used for back pain of 423% between 1997 and 2004, without demonstrable progress in patient outcomes or reduction in disability rates. During the same time, the number of opioid prescriptions rose 108% [135]. A 2008 study of the California Worker's Compensation Institute involved 166,366 injured workers with medical back conditions without spinal cord involvement. For this group, 854,244 opioid prescriptions were dispensed, with an average of 5.2 prescriptions per injured worker [136].

Given the current debate on the use of opioids in CNCP, the increase in problematic opioid use in patients referred to pain clinics, the recent data regarding opioid related mortality, and the lack of evidence of long term effectiveness in this patient population, the current study aimed to determine the prevalence of opioid prescribing in WSIB patients attending a tertiary pain clinic with emphasis on the common factors that are significantly associated with high levels of opioid use. Without information on how drugs are being prescribed and used, it is difficult to initiate a debate on rational drug use and to suggest measures to change prescribing habits for the better.

The study's innovation is the attempt to provide prevalence and utilization estimates among a very poorly studied population. In addition, the study used the Canadian guideline's watchful dose of 200 mg MED as the benchmark dose that separates high from low opioid users, a benchmark already used in several studies [16, 108].

The treatment of CNCP with opioids in Canada seem to be polarized in two extremes, under and over prescribing [137]. When it comes to opioid "recipients" in the work place, an understanding of the actual prescribing of opioids, indications and dosing, particularly in injured workers seen in a tertiary pain clinic setting, is of paramount importance. These workers are referred because they have failed current management and continue to be highly disabled. Understanding of the factors associated with administration of opioids in conjunction with poor outcomes may detect a subset of variables contributing to these poor outcomes and guide further research into potentially modifiable factors.

The study also generates valuable information for the WSIB by identifying several factors that may be useful for resource allocation and to guide policy, as well as by highlighting key areas for future research on community-based opioid prescribing. This study is the first in Ontario to delineate the factors associated with opioid prescribing in a subset of injured workers.

1-3-1 Area of interest

Opioids in the management of CNCP continue to remain a challenging issue. The literature to date provides conflicting evidence on the benefits, risks and potential complications of opioid use. An understanding of the actual prevalence and prescribing of opioids particularly in injured workers referred to a tertiary pain clinic setting, is an important topic with social consequences and an excellent area to develop this thesis.

1-3-2 Objectives of present investigation

The primary objective of the present pilot study was to estimate the prevalence of opioid users among injured workers who were referred at a Tertiary Care Pain Clinic of Toronto Western Hospital, by WSIB staff in 2008-2009.

The secondary objectives were:

1) To assess the prevalence of low dose opioid users (less than 200 mg of morphine or morphine equivalent does –MED -) and high dose opioid users (more than 200 mg MED) among these injured workers.
2) To describe the demographic and pain characteristics of non opioid users and low and high dose opioid users among these injured workers.
3) To assess the gender distribution between non opioid users and low and high dose opioid users among these injured workers.
4) To assess the country of origin distribution between non opioid users and low and high dose opioid users among these injured workers.
5) To assess the prevalence of diagnostic groups (with a) medical only, b) medical and psychological factors, and c) psychological factors only underlying their disability) among non opioid users and low and high dose opioid users.
6) To describe the combination of different types of pain medications and other psychoactive drugs prescribed among non opioid users and low and high dose opioid users.

CHAPTER 2- METHODOLOGY

2-1 Study Design:

This was a cross-sectional pilot study of injured workers with chronic pain who were referred to the Toronto Western Hospital by WSIB staff in one year period.

2-2 Sample:

All patients referred to the CPP of the Toronto Western Hospital by WSIB physicians or NCMs as difficult management problems (see definition below) during a period of one year (August 2008 to July, 2009) (n=110).

2-3 Source population:

The study population included consecutive series of injured workers referred to the CPP by WSIB physicians or NCMs because of difficulties in management, such as: unclear or poorly investigated diagnosis; failure to respond to all available treatments; questions regarding worker's eligibility to re-enter labour market; appropriateness of repeat trigger point blocks or "nerve blocks", and concerns regarding administration of analgesics (especially opioids and other drugs). Of note, most workers had more than one management issue as defined above.

2-4 WSIB Database Privacy Protection:

Standard privacy protection principles were observed during the assembly of the CPP data for this project. The CPP data remained on the program's main computer and claim numbers were used as the index in data assembly. Only the principal investigator had access to the data at this stage and conducted all data assembly. CPP files were archived and no data were removed from the hospital's premises.

Once the records for this study were assembled, the claim number was removed and replaced by a study number developed for the purposes of the research project. The mapping between the unique identifier (WSIB claim number) and the study number was kept in a separate file on the computer. The structure of the database is outlined in extraction form with some basic descriptive information provided below.

2-5 Procedure and Data Collection

2-5-1 Data from the Comprehensive Pain Program:

Data are collected routinely at the time of original consultation for all subjects with the CPP as follows: Upon arriving at the clinic for their initial visit, patients are asked to complete a standardized intake form (Appendix 1) that includes the following information: age, gender, marital status, country of origin, education, employement status, sleep problems, pain information retrieved from the short form of McGill pain questionaire (SF-MPQ), and a body map where the patients mark their pain areas.

All patients are then interviewed and examined by a pain clinic physician and additional

data are collected through the clinical interview and retrieved from the .clinical charts as follows: a) type/mechanism of work related injury; b) duration of pain condition in months (from onset of symptoms to time of consultation); c) numbers/types of pain conditions if more than one; d) current pharmacological treatments with emphasis of opioids (all opioids are recorded and doses are converted to daily morphine dose equivalents –MED); f) tricyclic antidepressants, other antidepressants, anticonvulsants, sedatives and hypnotics (without details of dose); g) current pain ratings utilizing a Numerical Rating Scale (NRS 0 to 10); h) diagnosis as furnished by the pain clinic physician etc.

Equianalgesic dose information for each opioid type is adapted from the Canadian Guideline group for safe and effective use of Opioids for CNCP [1] (Appendix 2). All drugs (opioids or other) are reported with their generic names in this study, though in the consultation notes drugs are reported with either the brand or generic name. The data were collected directly from the consultation notes for all the medications prescribed to the patients and were later classified into therapeutic categories.

The countries of origin were classified as per the 2005 World Population Data Sheet [138].

2-5-2 Morphine Equivalent Dose

The equation to determine morphine equivalent dose (MED) is as follows: Strength (mg) × equianalgesic dose. For example, the conversion to MED of a common opioid like codeine 30 mg is as follows: 30 (mg) × 0.15 = 4.5 mg MED. Appendix 1 charts the equianalgesic doses for

conversion to MED for common opioids.

Below is an excerpt from the data extraction form for opioid prescriptions, as well as other drugs.

Table 1 : Opioid Prescription Example: Patient A

Drug class	Drug Name	Dosing Schedule	Total daily dose	Morphine Equivalent
Strong Opioid	Oxycodone immediate release	5 mg X 5 tabs/day	25 mg	37.50 mg

Table 2: Other medications

Antiepileptics	TCAs/	Other antidepressants	Sedatives/ hypnotics	NSAIDS	Others	Smoked marijuana
For the above current medications (other than opioids), the generic name of the drug (but not the does) is recorded.						a/ Yes b/ No

In regards to opioid consumption, patients were classified as Non Opioid Users (NOU), Low Opioid users (LOU), or High Opioid User (HOU), with 200 mg MED daily as the cut-off point between the two opioid groups. MED was calculated whether the opioid was weak or strong. The 200 mg level was based on the "watchful dose" recommended by the 2010 Canadian Guideline that treats effectively the vast majority of CNCP patients [1] . Tramadol users were placed in the LOU group, but were excluded from morphine calculation as equivalency has not been established between morphine and tramadol. Opioids were classified as weak (propoxyphene, meperidine, codeine, tramadol) and strong (morphine, fentanyl, hydromorphone

and oxycodone preparations alone or in combination with acetaminophen, ASA etc). Action of medication at onset such as controlled or sustained use (CR or SR) versus immediate release (IR) was also noted.

2-6 Instruments and classification system to be used in the study

2-6-1 Short form Of McGill pain Questionnaire (SF-MPQ):

The McGill Pain Questionnaire (MPQ) [139] is one of the most widely used tests for the measurement of pain. It provides valuable information on the pain experience and is capable of discriminating among different pain problems. The MPQ has three components: a descriptive component (asking the patient to mark words from a specific group list which characterize the patient's pain and also assign a category of pain intensity: none, mild, moderate and severe), the Present Pain Intensity (PPI), for which the patients are asked to use one word to overall describe their pain severity, and a Visual Analogue Scale (VAS) to provide a numerical value to the patient's perceived pain. A short and more versatile form of the MPQ was used in the current study (SF-MPQ). The difference with the original MPQ is the number of words available to characterize the pain, making it in this aspect, much shorter and easier to administer. The SF-MPQ contains eleven words referring to the sensory dimension of the pain experience and four related to the affective dimension (total of 15). Each descriptor is ranked on a four point intensity scale as stated for the long form of the questionnaire (0=none, 1=mild, 2=moderate, 3=severe). The SF- MPQ can be interviewer-administered or self administered. The PPI and VAS are included to provide indices of overall pain intensity, though in the current study NRS scores were used. The reason for this is that most subjects present with more than one pain. The VAS captures "all pain collectively" at the time the patient fills the form, while the NRS ratings were

obtained separately for the different pains. The highest NRS pain score from the primary region of pain was used in the current study, though most subjects had more than one pain area and more than one NRS scores.

Although there has been no evaluation of the reliability of the SF- MPQ [140], it has been shown to be correlated highly with the sensory, affective and total Pain Rating intensity scores of the original MPQ [139] and is highly sensitive to clinical changes brought about by various therapies [141]. The SF- MPQ also has been shown to have high content validity [142] (Appendix 3).

In this study data were collected for the total number of words used by the subjects in the moderate and severe pain intensity category (maximum number of words possible 15) and the total score was calculated from the SF-MPQ (score range 0-45).

2-6-2 Comprehensive Pain Program classification system:

The classification system of the American Psychiatric Association (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision DSM-IV-TR)[143] has been adapted with modifications by the CPP physicians since 1994 for all patients attending this program in both inpatient and outpatient facilities. It should be stressed that there are very few diagnostic classification systems for which there are meaningful gold standards of validity. The DSM-IV-TR criteria and categories specifically have problems and lack reliability and validity [144], though the diagnostic classification is used widely around North America and particularly in medicolegal context in personal injuries. One of the weak points of the DSM IV TR

classification system is the lack of specific descriptors for the psychological factors that contribute to the maintenance, aggravation and perpetuation of pain, as such factors are considered tantamount in the DSM IV classification of two somatoform Chronic Pain Disorders, namely a) Chronic Pain Disorder associated with a general medical condition and psychological factors, and b) Chronic Pain Disorder associated primarily with psychological factors. Both these disorders are defined as psychiatric disorders, in contrast to Chronic Pain Disorder associated (only) with a general (bio) medical condition, which is NOT a psychiatric diagnosis.

To bypass these problems, the CPP has applied an empirically derived system adapted from DSM IV TR in an effort to define non biomedical factors that contribute to pain disability, which has resulted in several recent publications [75, 145, 146]. The CPP system uses three diagnostic groups based on a standardized approach to the diagnosis applied by all pain clinicians at the program. Patients classified as belonging to Group I have a significant biomedical condition responsible for their pain with lack of undue psychological influences (this is similar to DSM IV TR Chronic Pain Disorder associated (only) with a general medical condition). Group II patients have underlying biomedical pathology but additional non physical factors are deemed to play a significant role in their disability (similar to DSM IV TR Chronic Pain Disorder associated with a general medical condition and psychological factors). Group III patients display very high levels of disability, but lack detectable biomedical pathology (with the currently available diagnostic means available to clinicians such as x-rays, electromyographic and nerve conduction studies, MRI and CAT scans, bone scans, findings during surgical interventions etc). This last group is similar to DSM IV TR Chronic Pain Disorder associated primarily with psychological factors. The CPP system used in several studies published and currently in progress, is an experience-based system which tries to address the most contentious

and criticized part of the DSM IV classification, i.e., the lack of definition of what psychological factors exist that contributes to disability. The CPP system records in detail a) underlying biomedical pathology based on results of investigations, operative findings and pertinent clinical examination findings, and b) observational and historical information which allows the physicians to record non-biomedical factors that enhance disability [75, 145, 146]. It is this empirical system that has allowed the CPP clinicians to institute appropriate management by employing medical, psychological treatment or both when needed, depending exactly on the presence or absence of biomedical and/or psychological contributors to disability. Despite the lack of validation (studies are currently in progress for this), the system has allowed the CPP physicians to detect consistently substantial differences in regards to type of complaints, consumption and effectiveness of medications and response to treatments in both inpatient and outpatient populations. The CPP diagnostic classification form is attached in the Appendix 4.

2-6-3 Numerical Rating Scale

The Numeric Rating Scale (NRS) is a helpful tool that assists patients to describe how much pain they are feeling and measures how well treatments are relieving the patient's pain. It is based on a scale from zero to 10; this scale assigns a measurable number to the patient's pain level. Zero represents no pain at all while 10 represent the worst imaginable pain. The NRS is considered to be a valid measure [147] and has good feasibility, reliability (internal consistency) and convergent validity [148]. Pain ratings 1-3 are considered to represent mild pain, 4-6 moderate pain and >7 severe pain [149].

2-6-4 Body map

Patients mark the pain areas on a body-map diagram. Patients are asked to rank their pain areas in order of severity and intrusiveness (Appendix 5), so that the number of painful areas and the order of importance can be documented in each patient.

2-7 Validity of Comprehensive Pain Program Data:

CPP maintains all data related to demographics, diagnosis, types of injury, duration of pain and drug prescription at the time of consultation, linked with the patients' referral reports. In order to standardize the collection of drug prescription information and to control for the accuracy of provided pharmacological data, a specific procedure was followed. First, information regarding opioid use was gathered from the initial referral notes. This information was compared with the data gathered by the consultant during the patient's evaluation. Additionally, in order to determine the reliability and validity of drug information data, consultants examined actual pharmacy prescription records when available, and medical records documenting prescriptions and/or labeled prescription containers. All medications reported by patients during the assessment and from the referral reports, were included in the study. There were no discrepancies were found in the quantity of medication noted, during assessment and from the referral notes.

2-8 Statistical Analysis:

The data were analyzed using the SAS program version 9.2 (SAS Institute Inc., Cary, NC). The descriptive analysis composed of means and proportions according to the nature of the variables. As a dispersion measurement the standard deviations were calculated. Standard descriptive statistics (frequencies, percentage, mean) were used to describe the general characteristics of the WSIB population.

Prevalence estimates of opioid users in injured workers were calculated using the data of opioid use at the point of entry to the CPP over a period of one year (2008-2009) and the total population of injured workers seen in the clinic during the study period was the denominator. Similarly, the prevalence rate of low dose opioid users and high dose opioid users among these injured workers was calculated by using the opioid users's population as the denominator.

For categorical data, proportion and size of each category for all demographic characteristics (such as sex, marital status, education, employment status, and language spoken at home), were calculated. Comparisons of proportions were made using Pearson's Chi-square test or the Fisher's exact test (in cases where cell counts were less than or equal to 5) among NOUs, LOUs and HOUs. For continuous variables, differences between groups were evaluated using two-sample t-tests or ANOVA for more than two groups. When ANOVA test showed significant differences among groups, Bonferroni tests were further conducted to observe which group was actually significantly different from another between NOUs, LOUs, HOUs. For nonparametric

data, differences between groups were assessed with the appropriate corresponding tests – the Mann-Whitney U test for two samples and Kruskal-Wallis test for more than two groups. The Shapiro-Wilk normality test was used to assess normality.

Prevalence of diagnostic groups in NOUs, LOUs and HOUs were calculated using the data of injured workers in each opioid group as the denominator. Also, descriptive statistical analyses were conducted for the total number of drugs prescribed in each class (opioids, antiepileptic, TCA's, Other Antidepressants, Sedatives and Hypnotics, NSAIDs, Acetaminophen) and for the frequency of the most commonly prescribed drugs within each category.

2-9 Ethics Approval

Permission to conduct this study was obtained from the investigator's thesis committee, and the ethical review committee of the hospital. The study has been approved by the University Health Network, Institution's Research Ethics Board on December, 2009 (Appendix 6).

CHAPTER 3- RESULTS

3-1 General Characteristics

A total of 110 injured workers directly referred by WSIB were seen over the one year period. Demographic characteristics are summarized in table 1.

Men in general outnumbered women in the study with the male/female ratio 2.3:1. The mean (± SD) age at presentation for all injured workers was 45.5 years ±8.85 (range 22-68years). Based on country of birth, 69.0% (76/110) of the injured workers were born in Canada and identified as the "Canadian" group. The rest of the injured workers were born outside of Canada and are labeled as "foreign born" in the study. Of the foreign born, 65% (22/34) spoke the language of their native country at home. In regards to employment, the majority of injured workers (80% or 88/110) were unemployed. Half of the unemployed (51% or 45/88) reported skilled labor as their last occupation (Table 1).

Based on the CPP diagnostic classification system, 20.9% (N=23) of injured workers were classified as Group I, 50.9% (N=56) as Group II, and 25.5 % (N=28) were considered to meet the criteria for Group III. A very small number of injured workers (2.7% or N=3) had not been diagnosed yet as while further investigations were pending the workers were lost to follow up.

Based on pain drawings, low back pain (LBP) was indeed the commonest pain complaint

(61.0%), though it was not necessarily the primary or sole complaint. Isolated LBP (as the sole site of pain) occurred only in 4.5% of all cases with low back pain. Other pain areas in the total population (N=110) are listed in Table 5, in order of occurrence (Fig 1).

The mean duration of pain was 6 years (median 51 months, range 8-420), with half of the injured workers having over 4 years history of pain. In regards to NRS pain ratings, more than half of the injured workers (72%, N=79) were in severe pain (NRS scores >7) and the primary pain area at the time of the original interview/examination was rated as 7.2 ± 1.84 (range 1.5-10) (Table 1).

In addition 84.5 % (93/110) injured workers reported fragmented sleep.

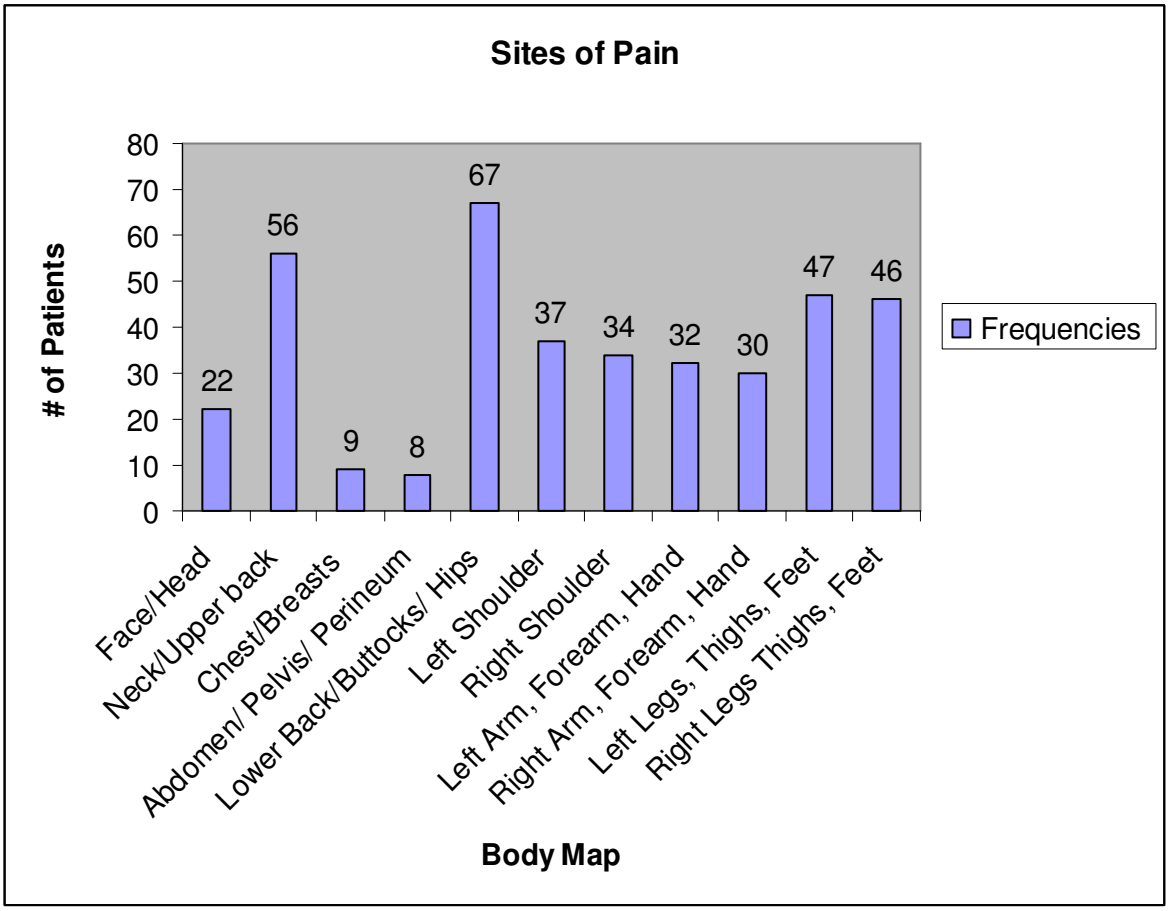
Table 1. General Characteristics

VARIABLES	RESPONSE	OVERALL (N=110)	%
Gender	Male	77	70.0
	Female	33	30.0
Age	mean +/- stdv	45.45±8.85	
	Range	22-68	
Marital status	Single	25	22.7
	Married/ common law	69	62.7
	Divorced and/Separated	13	11.8
	Widow	3	2.7
Country of birth	Canadian born	76	69.1
	Foreign born	34	30.9
Language spoken at home	English	88	80.0
	Other	22	20.0
Highest education	Elementary or less	18	16.4
	High School	54	49.0
	College	32	29.0
	University	4	3.6
	Not specified	2	1.8
Country of Education	Canada	82	74.5
	Other	26	23.6
	Not specified	2	1.8
Employment status	Employed	18	16.3
	Unemployed	88	80.0
	Other (housewife, student)	4	3.6
Last Occupation prior to pain onset (n=94)	Professional	11	11.7
	White collar	9	9.5
	Skilled manual labor	45	47.8
	Unskilled manual	25	26.6
	Other	4	4.2
Fragmented sleep	Yes	93	84.5
	No	17	15.5

OTHER VARIABLES	RESPONSE	OVERALL (N=110)	%
Pain duration (months)	mean +/- stdv Median, range	71.92 ±66.6 51, 8-420	
NRS pain ratings (0-10)	mean +/- stdv (range)	7.2 ± 1.8 (1.5-10)	
McGill Total pain Score (0-45)	mean +/- stdv (range)	26.29±9.8 (9-45)	
McGill questionnaire: combined number of moderate and severe pain intensity words chosen	mean +/- stdv (range)	9.4±3.7 (0-15)	
Pain Diagnosis	Group I	23	20.9
	Group II	56	50.9
	Group III	28	25.5
	Group IV	3	2.7
Classification of Opioid use	NOU	20	18.2
	LOU	61	55.4
	HOU	29	26.3
Total Morphine dosage (N=90) in mg of morphine or equivalent (mean equivalent dose –MED-)	mean +/- stdv Range	225.78±367.0 4.5-1702.5	

NRS: Numerical rating score; Group I: Biomedical diagnosis; Group II: Biomedical diagnosis and Psychological factors; Group III: Psychological factors; Group IV: Not yet diagnosed (NYD); HOU: High opioid user; LOU: Low opioid user; NOU: Non opioid user

Fig 1. Sites of pain



Group I (Biomedical diagnosis) and II (Biomedical diagnosis and Psychological factors) ; N =72,
* Many workers had many more than one site of pain

3-2 Prevalence of Opioid Users in injured workers

In regards to the **primary objective** of the present pilot study (prevalence of opioid users among injured workers at the point of entry to the CPP), 81.8% of the injured workers (90/110) were on opioids. The mean dosage for all opioid users expressed in mg MED was 225.78± 367.06 (range 4.5-1702 mg) (Table 1). The most frequently (55.5%, 50/90) prescribed opioid was an oxycodone preparation in both short and long acting forms.

3-3 Prevalence of LOUs and HOUs

In regards to the injured workers (N=110) in this study, 55.4% (n=61) were prescribed <200mg of daily MED (Low Opioid Users/LOUs); 26.3% (n=29) were prescribed >200mg MED (High Opioid Users/ HOUs), and the remaining patients (18.1%, n=20) were considered Non Opioid Users/ NOUs.

Of those prescribed opioids (N=90), 32.2% (n=29) of opioid users exceeded 200 mg MED (HOUs) and the remaining 67.7% (n=61) were LOUs (Table1). The mean daily MED consumption in HOUs and LOUs was 589±469 and 53±53 mg, respectively.

3-4 Demographics and Pain characteristics of NOUs, LOUs and HOUs

When NOUs, LOUs and HOUs were compared in regards to their demographics, no statistically significant differences were found in age (p= 0.98), marital status (p=0.17), first language spoken at home (p=0.58), and highest education (Fisher p= 0.19). More patients were employed in the NOU group (35.0%) as compared to LOU (16.4%) and HOU (3.0%) groups;

these differences were statistically significant ($p<0.01$) (Table 3).

There was no statistically significant differences between NOU, LOU and HOU groups with respect to NRS scores ($p=0.38$), SF-MPQ total pain score ($p=0.33$) and SF-MPQ combined moderate and severe words ($p=0.17$), although HOUs had significantly longer pain duration in months (104 ± 87) than NOUs (50±67) and LOUs (64±49), ($p=0.006$) (Table 3).

3-5 Gender Distribution between NOUs, LOUs and HOUs

In regards to gender differences, males were twice as likely to be LOU and 4 times as likely to be HOU when compared to females (M/F ratio1:1 NOU; 2:1 LOU; and 3.8:1 in HOU) ($p=0.0072$) (Table 3).

3-6 Country of Origin of NOUs, LOUs and HOUs

When the data were analyzed of NOUs, LOUs and HOUs related to country of birth, the proportion of Canadian Born increased substantially in parallel with the use of opioids. Specifically, among NOUs 55.0% were Canadian born (11/20) and 45.0% were foreign born (9/20). Among LOUs, 65.6% were Canadian born (40/61) and) 34.4% were foreign born (21/61. Among HOUs, 86.2% were Canadian born (25/29), while only 13.7% were foreign born (4/29). There was a statistically significant difference between the proportion of Canadian and foreign born among NOUs, LOUs and HOUs ($p=0.03$) (Table 3).

3-7 Prevalence of Diagnostic Groups among NOUs, LOUs and HOUs

When NOUs, LOUs and HOUs data were analyzed based on the diagnostic groups, among NOUs, 45.0% (9/20) and 15.0% (3/20) of injured workers were classified as Group II and

III, respectively, relative to 35.0% (7/20) of the workers classified as Group I. Among HOUs and LOUs (collectively analyzed) 52.2% (47/90) and 27.7% (25/90) of injured workers were classified as Group II and Group III respectively, relative to 17.7% (16/90) of Group I. This was considered a trend as no statistical significant difference between the proportions of NOUs, LOUs, and HOUs and diagnostic groups was found (p=0.15) (table 3)

Table 2. Analysis per opioid use group

VARIABLES	p value	RESPONSE	NOU (n=20)	%	LOU (n=61)	%	HOU (n=29)	%
Gender	P=0.0072	Male*	10	50.0	*41	67.2	*26	89.7
		Female	10	50.0	20	32.7	3	10.3
Age	P=0.977	mean +/- stdv	45.8±10.11		45.4±8.3		45.2±9.2	
		Range	25-65		22-68		29-61	
Marital status	P=0.168	Single	4	20.0	11	18.0	10	34.4
		Married/ common law	13	65.0	41	67.2	15	51.7
		Divorced and/Separated	1	5.0	8	13.1	4	13.7
		Widow	2	10.0	1	1.6	0	0
Country if Birth	P= 0.039	Canadian*	11	55.0	40*	65.6	25*	86.2
		Foreign	9	45.0	21	34.4	4	13.8
Language spoken at home	P=0.538	English	15	75.0	48	79.0	25	86.2
		Others	5	25.0	13	21.0	4	13.8
Highest education	P=0.1869	Elementary or less	2	10.0	14	23.0	2	7.0
		High School	10	50.0	24	39.0	20	69.0
		College	6	30.0	19	31.0	7	24.0
		University	1	5.0	3	5.0	0	0
		Not specified	1	5.0	1	2.0	0	0
Employment status	P=0.0066	Employed*	7*	35.0	10	16.4	1	3.4
		Unemployed/ retiree	11	55.0	49	80.3	28	96.6
		Others (housewife, student)	2	10.0	2	3.3	0	0
Pain Diagnosis	P=0.15	Group I	7	35.0	13	21.3	3	10.3
		Group II	9	45.0	27	44.3	20	69.0
		Group III	3	15.0	19	31.1	6	20.7
		Group IV	1	5.0	2	3.3	0	0

OTHER VARIABLES	p value	RESPONSE	NOU (n=20)	LOU (n=61)	HOU (n=29)
McGill Total pain Score (0-45)	P=0.33	mean +/- stdv range	29±9.5 (12-45)	26±10.1 (9-45)	25±9.4 (9-45)
McGill questionnaire: combined number of moderate and severe intensity words chosen words chosen	P=0.17	mean +/- stdv range	10.6±3.2 (0-15)	9.4±3.7 (4-15)	8.6±3.6 (5-15)
Pain duration (months)	P=0.006	mean +/- stdv range	50±67 (8-303)	64±49 (10-216)	104±87* (14-420)
NRS pain ratings (0-10) (range)	P=0.38	mean +/- std range	6.75±2.1 (2-10)	7.1±1.68 (1.5-10)	7.5±1.83 (2-10)

Statistical significance is marked by *. There were statically significance differences between NOUs, LOUs and HOUs with respect to gender, place of birth, and employment status.

HOU: High opioid user; LOU: Low opioid user; NOU: Non opioid user; NRS: Numerical rating score; Group I: Biomedical diagnosis; Group II: Biomedical diagnosis and Psychological factors; Group III: Psychological factors; Group IV: Not yet diagnosed

3-8 Types of Pain Medications and Psychoactive Drugs Prescribed Among NOUs, LOUs and HOUs

Opioids

The most frequently prescribed opioids were calculated separately for the HOU and LOU groups. The top three opioids prescribed to HOUs included: oxycodone CR (long acting) (55.1%); fentanyl patch (long acting), (24.1%); and oxycodone (short acting) in combination with acetaminophen (13.7%). The top three opioids for the LOU group included: oxycodone CR (49.1%), codeine alone (short acting) or in combination with acetaminophen (26.2%) and fentanyl patch, tramadol and hydromorphone hydrochloride (3.3% each) (the later two in both long or short acting forms).

Psychoactive co-prescriptions

When psychoactive co-prescriptions (tricyclic antidepressants, other antidepressants, anticonvulsants and sedatives or hypnotics) drugs were examined among NOUs, more than half (55%) received no psychoactive drugs, while 25% received one and 20% received two such drugs. Psychoactive co-prescriptions were also often reported in conjunction with opioids. In the LOU subgroup, 41.0% of injured workers received an opioid alone, while 31.1%, 23.0% and 5% received one, two, and three or more additional psychoactive drugs, respectively. In the HOU subgroup, 51.7% of injured workers received opioids alone, while 17.2%, 27.6% and 3.4% received one, two and three or more additional psychotropic drugs, respectively (Table 4). In summary, half or more of the opioid users (58.1% of the LOUs and 48.2% of the HOUs) received opioids combined with at least one other psychotropic drugs.

Table 3. Prescription of psychotropic drugs (other than opioids)

# of psychotropic drugs*	NOU (n=20)	%	HOU (n=29)	%	LOU (n=61)	%	Total (n=90)	%
0	11	55.0	15	51.7	25	41	40	44.4
1	5	25.0	5	17.2	19	31.1	24	27.0
2	4	20.0	8	27.6	14	23	22	24.4
3	0	0	1	3.4	3	5	4	4.4

HOU: High opioid user; LOU: Low opioid user; NOU: Non opioid user.
*HOU and LOU received opioids as well.

CHAPTER 4- RESULTS OF EXPLORATORY ANALYSIS

Given the fact the population of injured workers in this research is poorly studied, I conducted an exploratory analysis of variables not included in my objectives, in an effort to detect further information that defines my study group better and will also direct future research.

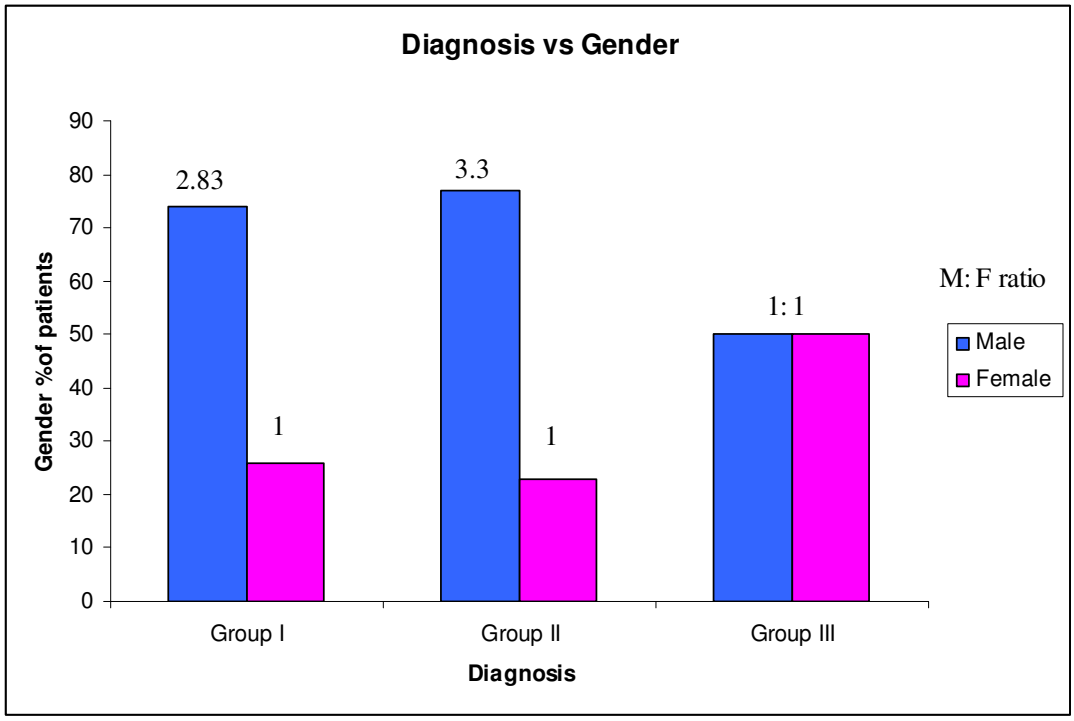
4-1 Pain Characteristics

Females had higher NRS pain ratings than males and the difference was statistically significant (mean 7.6 ± 1.4vs. 6.9 ±1.9 p=0.002). Additionally, females obtained significantly higher scores than the males in the SF-MPQ total scores (mean 30.0±9.6 vs 24.8±9.5 respectively, p=0.01) and selected more words than males (mean 11.1±3.5 vs 8.7±3.8, p=0.002) in the moderate and severe pain intensity categories of the SF-MPQ. Foreign born scored significantly higher in the SF-MPQ as compared to Canadian born (mean 29.2±9.9 vs. 25.0±9.5, p=0.04), but this was not reflected in their NRS scores (mean 7.5± 1.5 vs 7.0±1.9, p=0.36, respectively).

4-2Group Diagnostic and Demographics

In terms of gender and country of birth, there were more males (p= 0.04) and Canadian born (p=0.04) in Groups I (patients with pure biomedical problem) and Group II (patients with mixed medical/ psychological factors) as compared to Group III (patients with psychological factors but no physical pathology) (see Fig 2 and Fig 3).

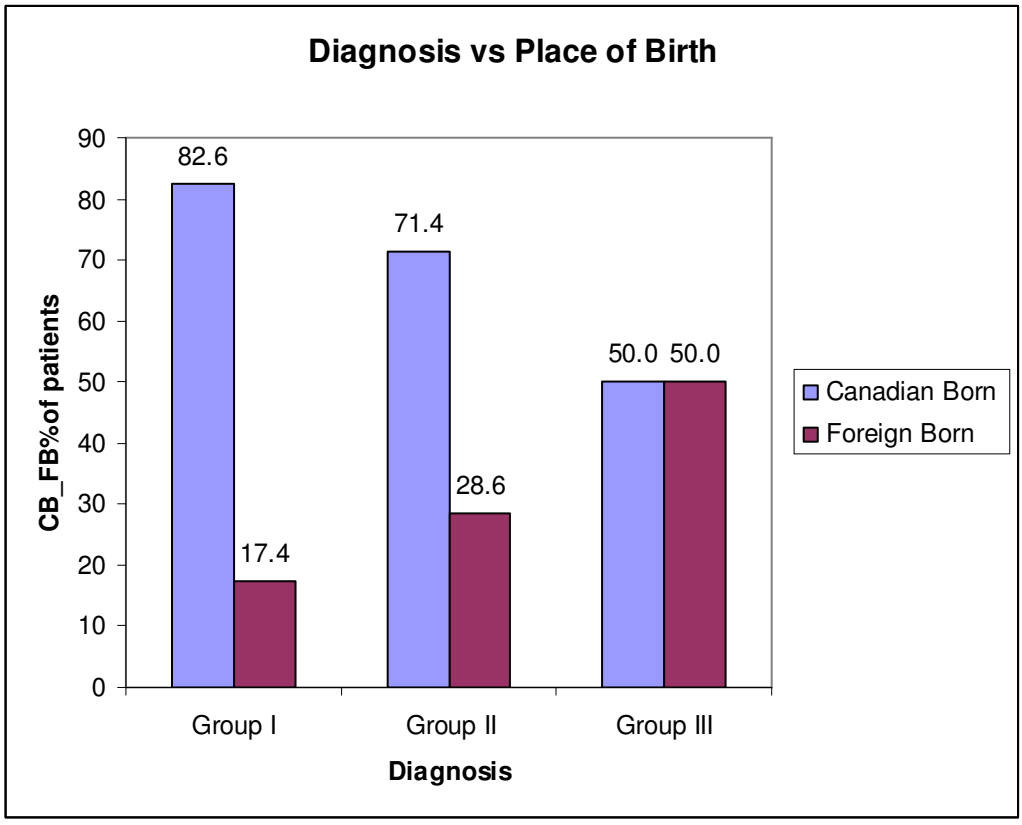
Fig 2



There were statically significant differences between males and females ratio in diagnostic groups (Group I, and II and III) (p=0.04)

(M: male; F: female; I: Group I Biomedical diagnosis; II: Group II Biomedical diagnosis and Psychological factors; III: Group III Psychological factors.)

Fig 3



There were statistically significant difference between the proportions of Canadian Born and Foreign born in Group I, Group II and Group III (p=0.04)

(CB: Canadian Born; FB: Foreign born Group; I: Biomedical diagnosis; Group II: Biomedical diagnosis and Psychological factors; Group III: Psychological factors.)

4-3 Disease appropriate drugs for Neuropathic and Musculoskeletal conditions

Specific attention was paid to prescription of disease-appropriate drugs for neuropathic (NP) or musculoskeletal (MSK) conditions (TCAs or anticonvulsants for NP and NSAIDS for MSK conditions). The results show that only a minority of all subjects were receiving such drugs (1/3 to 1/2), while opioids were the most frequently prescribed class of drugs irrespective of the underlying condition (Table 5). Some of these injured workers might have been treated with disease appropriate drugs prior to referral and experienced either lack of efficacy or side effects that led to the discontinuation of these drugs.

Table 4. Drugs prescribed in types of biomedical conditions

Drugs	NP frequency(n=24)	MSK frequency (n=33)	NP+MSK frequency (n=6)	Mixed mechanism Pain Syndrome (n=15)	Total
Opioids (n=90)	19 (79.1%)	23(69.6%)	5(83.3%)	15(100%)	62
AEs (n=33)	8 (33.3%)	8 (24.2%)	3(50.0%)	3 (20.0%)	22
TCAs (n=20)	3 (12.5%)	4(12.1%)	2 (33.3%)	3 (20.0%)	12
SNRI's (n=7)	1(4.1%)	0 (0 %)	1(16.6%)	2 (13.3%)	4
Other Antidepressants (n=26)	2(8.3%)	7 (21.2%)	2(33.3%)	3 (20.0%)	14
Sedatives and Hypnotics(n=35)	8 (33.3%)	7 (21.2%)	2(33.3%)	6 (40.0%)	23
NSAIDs (n=31)	5(20.8%)	11(33.3%)	2(33.3%)	1(6.6%)	19
Acetaminophen(n=9)	2(8.3%)	3(9.09%)	1(16.6%)	0 (0%)	6

NP: Neuropathic pain; MSK: Musculoskeletal pain; AE: antiepileptic; TCA: tricyclic antidepressant; SNRI's: Selective norepinephrine reuptake inhibitors; NSAIDs Non-steroidal anti-inflammatory drugs.

CHAPTER 5- DISCUSSION AND CONCLUSION

5-1 Discussion

The current study on 110 consecutive injured workers who were referred to the CPP provides the first detailed information about the prevalence of opioid use and its association with underlying biomedical and/or psychological factors contributing to pain disability in a subset of injured workers in Ontario. The vast majority of these injured workers were on opioid therapy with 1/3 of them exceeding by far the "watchful" dose of 200 mg MED suggested by the 2010 Canadian Guideline. In particular, opioid administration varied with the underlying diagnosis. However, the "watchful" dose of 200 mg morphine was not publicized until 2010, before the study sampling time, and that there will likely be a delay before this information is disseminated to primary care providers. The data showed that the more distress and psychological factors are involved in the injured worker's presentation, the greater the likelihood of receiving opioids and at higher doses. Additional novel findings in this study relate to the associations of high opioid use with male gender and Canadian born origin The study is the first in Canada (to the best of our knowledge) to correlate underlying biomedical pathology (or lack thereof) and opioid prescribing habits in a subset of injured workers. In the study sample, psychological factors accounted partially or totally for displayed disability in three quarters of the study patients (Group II and III).

The most important assumption opioid proponents use in justifying high opioid doses in CNCP [150] is that "patients taking higher doses of opioids may be suffering from more severe

injuries that are less amenable to conventional treatment". This did not prove to be true in my study and the recent CPP study [146]. A telling example is Group III injured workers, where psychological factors were considered the primary contributors to their disability in the absence of detectable physical pathology, who consistently received high doses of opioids. The results of the present study confirm the findings of other recent publications [75, 151], which concluded that physicians prescribe high doses of opioids to patients who present with significant psychoemotional issues.

Further important findings from the current study are as follows: While women outnumber men in pain clinics [146], males predominated in this WSIB sample. This may reflect the complexity of recalcitrant chronic pain cases in injured workers. Interestingly, while LBP is the predominant cause of chronic pain and disability in the work force, the study injured workers proved to have more than one pain complaint as LBP was the only pain complaint in a minority of subjects.

High opioid users are predominantly Canadian born and males, a finding similar to the demography seen in a large sample of CNCP patients referred to the CPP by community physicians [75]. Specifically, the gender difference in consumption of opioids in general and high doses of opioids in particular cannot be explained on biological differences as there is no literature supporting such differences. In general, substantial differences in many perception and other pain related differences are summarized in a large study in our pain program [152].

In regards to the observation that high opioid use is associated with Canadian born origin,

one may argue that foreign born individuals are not offered opioids. The latter does not seem a valid reason for the observed differences as 34.4% of LOU workers were foreign born, therefore, it is obvious that foreign born have no difficulty been offered or accepting opioids in low doses. An alternative and most plausible explanation is that foreign born injured workers are hesitant to accept these drugs in "high doses" for fear of addiction or other side effects of drugs, or because of culturally based aversion to "many pills".

The fact that females had higher NRS scores and greater numbers of SFMPQ words in the moderate and severe pain intensity category is not surprising, as women in general seem to demonstrate lower pain thresholds, reduced capability to distinguish painful sensations, higher pain ratings, and a lower acceptance for pain [153].

Co-prescriptions of drugs that can affect the sensorium (TCAs, anticonvulsants etc) are important considerations for possible cumulative cognitive impairment in individuals with chronic pain on opioids. In the current study, more than a third of injured workers consuming high doses of opioids, received at least two other psychoactive medications. Additionally, the vast majority of injured workers reported sleep disturbance known to affect cognition [154] and high pain scores (even in the presence of high doses of opioids). Poorly treated pain of severe intensity (>7/10 on a NRS scale) is shown by itself to consume attentional resources [155]. The combination of opioids, psychoactive co-prescriptions, sleep difficulties and high levels of pain, is quite concerning as it impacts the ability of injured workers to attend school, be retrained, drive cars or use machinery.

The fact that less than 1/3 of opioid users received adjuvant neuropathic medications or

NSAIDs, respectively for their NP or MSK condition respectively, raises some important concerns. Some of these injured workers might have been treated with NP or MSK types of medication prior to or at the point of referral and experienced either lack of efficacy or adverse effects that led to the discontinuation of these drugs. However, opioids continued to be prescribed in high or very high doses despite significant levels of pain. Alternatively, these injured workers may have been offered opioids just after the injury instead of drugs appropriate for the underlying pain condition, making opioids "the first drugs of choice".

The results of my study are very much in accordance with recently published CPP data on CNCP patients referred by community physicians to the CPP [75]. This study analyzed a cohort of 455 patients referred by general physicians to the CPP, by using similar methodology and data collection procedure like my own pre-selected sample of injured workers.

Both studies confirmed the following:

- The mean age of CNCP patients referred to a tertiary care pain clinic is in the mid-40s and associated with high level of unemployment.
- Isolated LBP occurred only in a minority of subjects with low back pain complaints (namely, 8% of CPP community subjects and 4.5% of injured workers), as the majority had more than one pain complaint.
- Male gender and Canadian born origin were associated with higher rates of opioid prescribing and higher doses of opioids.
- Approximately less than 1/3 of opioid users with NP or MSK pathology, were receiving appropriate disease-related medications for their biomedical condition, while opioids were

the predominant prescribed class of drugs.

- Community physicians (both primary care practitioners and specialists) may administer opioids liberally primarily in patients with psychological distress.
- . Physicians may be unaware that they are treating emotional distress instead of physical origin of pain using high doses of opioids. In particular, Canadian born males with chronic pain associated with psychological factors seem to be the "population at risk" for administration of opioids and high doses of opioids identified by both studies.

Noteworthy differences between injured workers and community referred CNCP patients to CPP, were:

- A much higher proportion of injured workers were on opioids as well as high doses of opioids as compared to the community referred sample. Specifically, at the point of entry to the CPP, 81.8% of the injured workers were on opioids as compared to 63% of the CPP patients, while 19% of CPP opioid users exceeded 200 mg MED (HOUs) as compared to 32% of WSIB population. These results are to be expected, however, as opioid use and high opioid use was one of the primary reasons for referral of these workers to CPP for assessment.
- The two samples differed in their NRS scores for Group I patients with biomedical conditions underlying their disability. Group I referred by community physicians to the CPP [19] had much lower pain scores as compared to Groups II and III , while this difference was not observed in the study sample of injured workers who maintained very high pain ratings irrespective of the underlying condition across all 3 groups. This may be attributed to factors relating to the compensable nature of their claim as follows: a) as a "cry to be heard and

believed", b) enhanced pain perception due to the stress generated by encounters with WSIB or c) conscious exaggeration of pain ratings for secondary gains of compensation.

5-2 Limitations

The present study has several limitations.

This is a pilot study which is intended to provide preliminary information on this poorly studied patient population. Such preliminary investigations typically lack the sample size that is needed to determine statistical significance to validate a hypothesis [156, 157].

Additionally the results can not be generalized to other populations of injured workers or CNCP patients in the general population as the study subjects were pre-selected (selection bias) and represent a specific subset of injured workers with treatment resistant problems, including opioid insensitive pain. However, the data are likely to indeed represent at least a subgroup of injured workers within the community.

Another limitation of this study is its retrospective design and its inherently small and diverse clinical population where data have been collected in a clinical context. However, the patient group in this study was quite homogenous.

Error in recall of information is another potential limitation of a retrospective study. However, the use of detailed pharmacy or medical records at entry stage minimizes the recall bias. The current study relied on pharmacological data gathered through injured workers' statements, chart review and prescription reviews when available, which does not necessarily confirm that opioids prescribed were accurately recorded in the study for all subjects. Previous publications, though, report that in general the concordance between patient report and medical

records for current medication intake is generally accurate [158, 159].

The use of the CPP diagnostic classification system is unique to the CPP where the present study was conducted, and the system has not been validated. To its defense, however, the CPP classification system is much more detailed, several publications have demonstrated remarkable similarity of meaningful findings in different cohorts and it is easy to apply [75, 145, 160]. Furthermore, it is much more specific than the widely used DSM IV TR Pain Disorder Classification across North America (after which the CPP system is adapted), which lacks validation or detailed information regarding psychological factors affecting pain related disability.

5-3 Conclusions

Despite these limitations, the study has notable strengths. First, this is the first cross-sectional Canadian study of recalcitrant to treatment injured workers with chronic pain that detailed workers' characteristics and prescription patterns. Second, opioid prescription data were linked to workers' diagnosis.

The fact that opioids were prescribed at high doses in this sample of injured workers by their physicians in the face of significant psychological factors contributing to the workers' disability and in the absence of substantial (or any) biomedical pathology, leads inevitably to the conclusion that *physicians may treat emotional distress rather than the physical origin of pain with high dose opioids*. This further questions the need for high dose opioids in particular in CNCP. Studies like the present one in conjunction with published guidelines are important in guiding both physicians and workers compensation policy makers to establish criteria for appropriate opioid administration.

5-4 Recommendations for future research

There is a need to evaluate not only the recipients of high doses of opioids in CNCP populations but also those physicians who tend to be high opioid prescribers. It is unknown who comprise of the high opioid prescriber group, their level of CNCP treatment education, their familiarity with opioid guidelines, and the treatments that had been used and failed.

Future research should also address gender and cultural differences as they seem to be significantly associated with the level of opioid administration.

Similar studies should be carried out in other pain clinics (in academic hospitals or community set ups, and in specialized populations) as well as primary care practices, in order to establish opioid prescription patterns in different clinical settings for management of CNCP. While the study data profile a certain type of very high opioid users, it would be important in future studies to collect data on the prescribers as well in an effort to understand the characteristics of physicians who tend to prescribe high doses of opioids (gender, education, country of birth, years of practice, type of practice and specialization if any).

In addition, a comparative study of no-opioid, low-opioid, and high opioid prescriber's regarding their competency, training, and attitudes to opioid use in CNCP is urgently needed so that policymaker and providers can best assists all Canadians to receive better and safe chronic pain care.

Comprehensive Pain Program Standard intake form (Appendix 1)

Date:_____ Referral Date :_____

MRN #:_____

Health card number: _____ Version code: _____

WSIB Claim number: _____

Date of Accident:_____

Name: _____

Surname: _____

Date of Birth:_____

Home Address: _____Apt:_____

City:_____ Province :_____

Postal Code:_____

Mailing Address:_____

_____

Referring Doctor:_____

Address:_____

_____

_____

Family Doctor: _____Billing #: _____

Address: _____

_____

_____

Home Ph: _____Work Ph_____

Name of next of Kin: _____

Relationship to Patient:_____

1. Type of clinic visit ☐ New visit ☐ Follow up visit

2. Sex ☐ Female ☐ Male

3. Age ___ yrs

4. Marital Status ☐ Married
    a. Single
    b. Divorced
    c. Widow/ widower

5. What is your country of birth?
    _____

6. Date immigrated to Canada: _____

7. Language spoken at home:
    First: _____ Second: _____

8. Education (highest level of formal schooling **completed/graduated**)
    a. No formal schooling
    b. Grade school
    c. High school
    d. College
    e. University (post secondary education that leads to a degree)

9. Employment status ☐ Full –Time Employed
    a. Part-Time/Casual Employed
    b. On medical leave from work
    c. Unemployed
    d. Student
    e. Housewife
    f. Retiree
    g. Other (specify) _____

10. If not working now because of pain, how long have you been out of work (**specify number of years or months**)**?** _____

11. Do you receive any payments while you are off work?

☐ Yes ☐ No

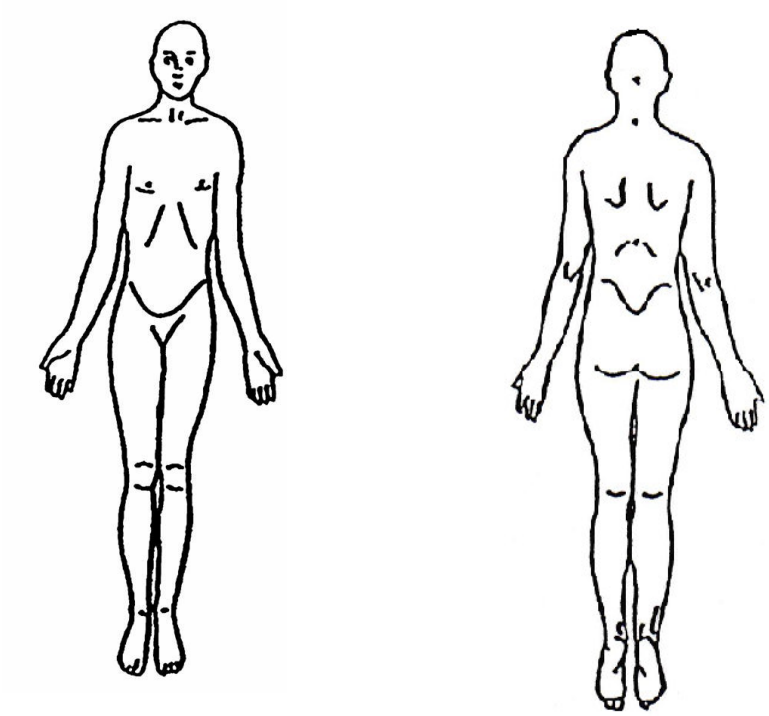
12. If Yes, what kind of payment?
    a. CPP
    b. Workers' compensation
    c. Long term disability
    d. ODSP
    e. Other (specify) _____

DEPENDING ON YOUR WORK STATUS PLEASE ANSWER THE APPROPRIATE QUESTION

13. If you are working currently Full Time or Part time/ Casual, what type of work are you doing?
    a. Professional (i.e, accountant, doctor, lawyer, nurse, teacher, psychologist, engineer, architect, computer/ information consultant etc)
    b. White collar (i.e. office worker, lab technician)
    c. Skilled manual labour (includes trades i.e. electrician, plumber, carpenter, mechanic, pilot, interior designer etc)
    d. Unskilled labour (i.e nanny, domestics, etc)
    e. Other (specify:_____)

14. If you are NOT working currently Full Time or Part time/ Casual, what was your last occupation (**see definitions at 10a**)?
    a. Professional
    b. White collar
    c. Skilled manual labour
    d. Unskilled labour
    e. Other (specify:_____

16. Mark the areas of **ALL pains** that bother you currently in the following body map (*The interviewer should be instructed to tell the patient that bothersome pains can be constant, intermittent or recurrent over the past 6 months at least*)



17. Over the **<u>past week</u>** rate the intensity of your **OVERALL** pain (**if patients ask which pain, advise them to rate the worst**) (Interviewer enter a check mark in appropriate box)

No pain	Mild	Discomforting	Distressing	Horrible	Excruciating

18. In regards to the 3 MOST IMPORTANT pain areas, answer the following

PAIN RATINGS In a scale 0= no pain to 10= worse imaginable pain	Primary pain site (state what the area is)	Secondary pain site (state what the area is)	Tertiary pain site (state what the area is)
Now			
Highest it can go			
Lowest it can be			
Average			
PAIN DURATION Specify how many months or years			

NOUGG OPIOID EQUIVALENCE TABLE (Appendix 2)

	Equivalence to oral morphine 30 mg:	**To convert to oral morphine equivalent multiply by:**	**To convert from oral morphine multiply by:**
Morphine	30 mg	1	1
Codeine	200 mg	0.15	6.67
Oxycodone	20 mg	1.5	0.667
Hydromorphone	6 mg	5	0.2
Meperidine	300 mg	0.1	10
Methadone and tramadol	Morphine dose equivalence not reliably established.		

Equivalence between oral morphine and transdermal fentanyl:

Transdermal fentany[1]	60-134 mg morphine = 25mcg/h 135-179 mg = 37 mcg/h 180-224 mg = 50 mcg/h 225-269 mg = 62 mcg/h 270-314 mg = 75 mcg/h 315-359 mg = 87 mcg/h 360-404 mg = 100 mcg/h

SHORT-FORM McGILL PAIN QUESTIONNAIRE

RONALD MELZACK

PATIENT'S NAME: _____ DATE: _____

	NONE	MILD	MODERATE	SEVERE
THROBBING	0) _____	1) _____	2) _____	3) _____
SHOOTING	0) _____	1) _____	2) _____	3) _____
STABBING	0) _____	1) _____	2) _____	3) _____
SHARP	0) _____	1) _____	2) _____	3) _____
CRAMPING	0) _____	1) _____	2) _____	3) _____
GNAWING	0) _____	1) _____	2) _____	3) _____
HOT-BURNING	0) _____	1) _____	2) _____	3) _____
ACHING	0) _____	1) _____	2) _____	3) _____
HEAVY	0) _____	1) _____	2) _____	3) _____
TENDER	0) _____	1) _____	2) _____	3) _____
SPLITTING	0) _____	1) _____	2) _____	3) _____
TIRING-EXHAUSTING	0) _____	1) _____	2) _____	3) _____
SICKENING	0) _____	1) _____	2) _____	3) _____
FEARFUL	0) _____	1) _____	2) _____	3) _____
PUNISHING-CRUEL	0) _____	1) _____	2) _____	3) _____

NO PAIN ——— WORST POSSIBLE PAIN

P P I

0 NO PAIN _____
1 MILD _____
2 DISCOMFORTING _____
3 DISTRESSING _____
4 HORRIBLE _____
5 EXCRUCIATING _____

Appendix3

Appendix 4

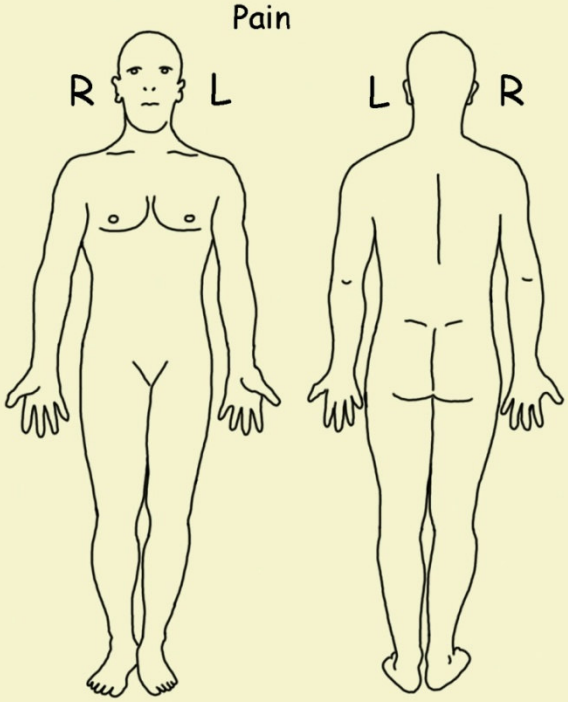
Comprehensive Pain Program Group diagnostic classification system

Category A Factors consistent with biomedical pathology	Category B Factors consistent with non-biomedical pathology
1. Symptoms congruent with medical condition and/or anatomy, including pain severity and level of disability 2. Supporting investigations for relevant pathology 3. Findings on physical examination supporting relevant condition	**OBSERVATIONS BY PAIN CLINICIAN** 1. Multiple verbal and non verbal pain behaviours in excess of underlying pathology 2. Significant fear of pain or movement resulting in guarding or immobility 3. Incongruent affect and pain ratings, e.g., happy demeanor despite very high pain ratings 4. Consistently high pain ratings with little fluctuation 5. Disability in excess of underlying pathology 6. Bizarre or non physiological signs incongruent with a known pathology or disease 7. Discrepancy in performance between formal and informal examination (manifested by substantial differences in SLR, range of movement, reaction to palpation etc) 8. Behaviours and pain ratings altered significantly in the presence of a solicitous caregiver **HISTORICAL INFORMATION** 1. Patient reports that pain increases with psychosocial stressors or subsides when relaxed 2. Unusual and inexplicable patterns of pain (rhythmical, cyclical etc) 3. Recurrent short term benefits or exacerbations with unrelated interventions (medications, injection, therapy etc, representing a reproducible nocebo or placebo effect) 4. Known history of multiple pre-exisiting pain issues suggestive of psychological factors contributing to presentation (eg. pseudoseizures, somatisation disorder etc) 5. Onset of pain in the context of emotionally stressful situations followed by persistent manifestations of emotional distress (e.g. PTSD etc) 6. Presence of a mood or anxiety disorder (other than PTSD) during the interview or documented by a treating psychiatrist or psychologist 7. History of psychiatric disorder other than mood or anxiety 8. History of physical, emotional or sexual abuse or significant psychological trauma 9. Presence of significant other with chronic pain related disability within the family of origin 10. OTHER _____
Presence of one or more Category A factors only qualifies the patient for Group I diagnosis (biomedical pathology only) Presence of Category A and at least two Category B factors renders the diagnosis of Group II (biomedical and psychological factors together) Presence of two or more Category B factors only renders the diagnosis of Group III (psychologically based pain disorder in the absence of biomedical pathology detected with currently available means)	

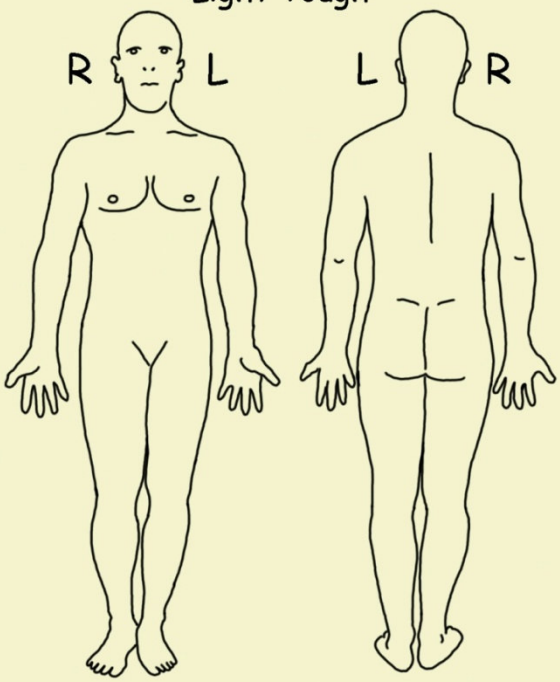
Appendix 5

Name:_____ Date:_____

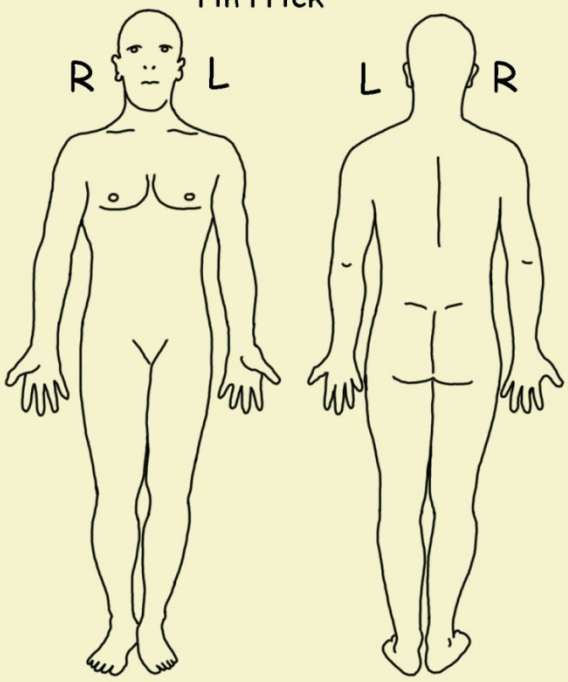
Pain



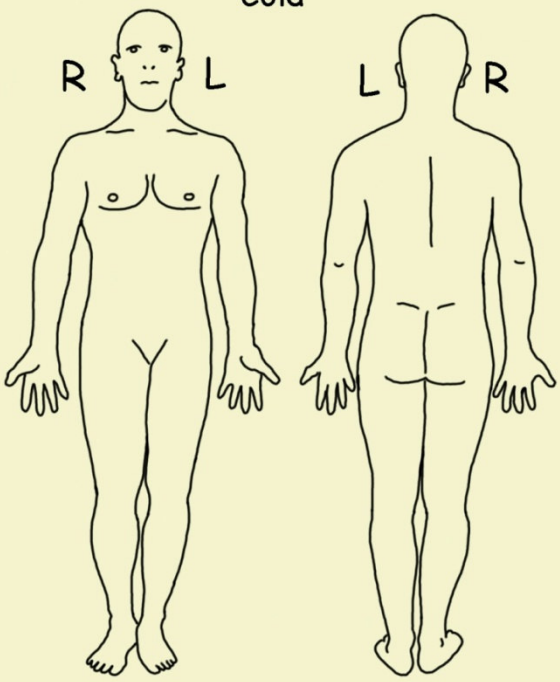
Light Tough



Pin Prick



Cold



Vibration Sense:_____

Deep Pain Sensitivity:_____

Comprehensive Pain Program, Toronto Western Hospital

Appendix 6

University Health Network
Toronto General Toronto Western Princess Margaret

University Health Network
Research Ethics Board
8th Floor South, Room 8-23
700 University Ave
Toronto, Ontario, M5G 1Z5
Phone: (416)946-4438

Notification of REB Approval for Access to Retrospective Data for Research Purposes

Date: December 10th, 2009
To: Dr. Angela Mailis
Rm 4F811, FP, TWH

Re: 09-0805-AE
WSIB Claimants Referred to the Toronto Western Hospital Tertiary Pain Clinic: Who Are They? What Medication are they Prescribed?

REB Review Type:	Expedited
REB Initial Approval Date:	December 10th, 2009
REB Expiry Date:	December 10th, 2010
Documents Approved:	
Data Collection Form	Received on: December 1st, 2009

We wish to remind you that access to personal health records for research purposes without patient consent is a privilege granted by the REB. Please be sure to adhere at all times to the UHN Policy on Information and Data Security as noted in the Confidentiality Agreement signed as part of this submission.
If, during the course of the research, there are any confidentiality concerns, changes in the approved project, or any new information that must be considered with respect to the project, these should be brought to the immediate attention of the REB. In the event of a privacy breach, you are responsible for reporting the breach to the UHN REB and the UHN Corporate Privacy Office (in accordance with Ontario health privacy legislation - Personal Health Information Protection Act, 2004). Additionally, the UHN REB requires reports of inappropriate/unauthorized use of the information.

Please be aware that it is UHN policy that research-related activities involving an external party require a research agreement. An 'external party' refers to a corporation other than UHN or an individual who is not UHN personnel. Should a research agreement be required in this case, the study may not begin at UHN until the agreement has been signed by all parties. Should the negotiation process raise concerns, the REB reserves the right to reconsider its approval.
Please note that approval for this study will expire on this date unless the UHN REB is otherwise notified.
The UHN Research Ethics Board operates in compliance with the Tri-Council Policy Statement, ICH/GCP Guidelines, the Ontario Personal Health Information Protection Act (2004), and Part C, Division 5 of the Food and Drug Regulations of Health Canada.

Sincerely,
Ronald Hesslegrave, Ph.D.
Chair, University Health Network Research Ethics Board

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