ASSESSMENT OF PRE-, POST-, AND CHANGE IN OPIOID USE: EVALUATION OF HYDROCODONE AS PART OF FUNCTIONAL RESTORATION TREATMENT IN A CHRONIC DISABLING OCCUPATIONA MUSCULOSKELETAL PAIN (CDOMP) POPULATION

by

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Abstract

ASSESSMENT OF PRE-, POST-, AND CHANGE IN OPIOID USE: EVALUATION OF HYDROCODONE AS PART OF FUNCTIONAL RESTORATION TREATMENT IN A CHRONIC DISABLING OCCUPATIONA MUSCULOSKELETAL PAIN (CDOMP) POPULATION

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The current study examines the relationship between pre-treatment, post-treatment, and change in opioid use among 1,601 chronic pain patients who participated in a functional restoration program, along with an additional investigation of pre-treatment hydrocodone use. Patients received an initial evaluation prior to treatment, including a physical examination, medical history, disability assessment, and psychological intake. In the initial phase of treatment, patients consented to be weaned from opiate medications. Assessments were repeated at program completion and structured telephone interviews were conducted at one-year post-treatment to evaluate socioeconomic outcomes. A substantial portion of patients entering the program reported opioid use upon admission (n=1054; 65.8%), and patients were divided into 5 subgroup: None (0 mg, n=547), PRN (<15mg, n=226), Low (16-30mg, n= 252), Moderate (31-60 mg, n=273) and High (>61mg) after total daily morphine equivalent (ME) doses were calculated. Pre-treatment opioid dose, post-treatment opioid dose, and change in level of opioid use all produced significant findings. Demographic differences were found related to level of opioid use and rate of program completion, area of injury, length of disability, pre-treatment surgery, and differences in racial groups. An inverse relationship was found between program completion and level of pre-treatment opioid use. One particular area of interest revealed significant findings

related to assessing Patient Reported Outcomes (PROs). Significant differences were identified in self-reported measures of psychosocial distress as they relate to opioid use at both at pre-treatment and post-treatment after controlling for demographic differences. Overall, these findings suggest that patients on PRN doses of opioids at either pre-and/or post-treatment report similar levels of pain intensity, change in pain intensity, depressive symptoms, perceived disability, and insomnia. Further studies would aid in the understanding of the connection between higher levels of self-reported distress and their association with higher levels of opioid use. Additionally, when analyzing one year socioeconomic outcomes such as work return, work retention, and healthcare utilization, opioid use at pre-treatment was found to be a predictor of work return, but perhaps a better predictor of work retention. While posts-treatments level of opioids for successful program completers did not demonstrate significant differences in work return and work retention rates, healthcare utilization at one-year was found to be significantly associated with post-treatment level of opioid use. Current health care cost require attention to these findings in that individuals who complete a functional restoration program and maintain opioid use may have similar occupational outcomes however, healthcare utilization is significantly greater for chronic pain patients who complete treatment on higher doses of opioid medications.

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Chapter 1

Introduction

The prevalence of chronic illnesses is a major concern for the healthcare system in the United States. Recent federal laws have been aimed at altering the affordability and accessibility of healthcare, however, only time will tell how these changes will affect overall costs and standards of care. Chronic pain is a health concern with vast reaching implications for Americans. With approximately 30% of the population being affected by chronic pain, the estimated cost of healthcare and loss of productivity are reported at $650 billion each year (Gaskin & Richard, 2012; Institutes of Medicine, 2011). When faced with such daunting numbers, it is essential to research and develop cost-effective treatment plans for patients with chronic pain conditions.

The most commonly available treatment for chronic pain continues to be prescription opioid medications (Garland, 2014). However, the efficacy of long-term use of opioids to treat chronic noncancerous pain remains unclear. Research indicates drugs are not ideal as a monotherapy, and up to 24% of pain patients exhibit aberrant medication use (Martell et al., 2007). Concerns about abuse and dependence, along with tolerance and hyperalgesia are just part of the problems plaguing pharmacotherapy as a primary solution to pain management. The single most prescribed medication in the United States is hydrocodone, with 129.2 million prescriptions dispensed last year (Traynor, 2014). That is actually a decrease from the peak of 136.7 million in 2011 when the Centers for Disease Control (CDC) announced that deaths from prescription medication overdoses reached epidemic proportions. They estimate that as many as 75 Americans die every day due to overdoses from prescription opiates (Traynor, 2013). For over 10 years the Drug Enforcement Agency (DEA) has made recommendations regarding concerns about the availability of opioid pain medications. The Food and Drug Administration (FDA) ultimately voted in favor of rescheduling hydrocodone-containing products as Schedule II controlled substances (Traynor, 2014). This change became effective October 6, 2014 and hydrocodone now has the same restrictions as OxyContin and other narcotics with high abuse potential.

With these current restrictions in place, it is essential to address the role of prescribing these types of medications for the treatment of chronic pain. Opioid medications have a reputation of successfully alleviating pain; however other aspects of functioning cannot be ignored. Successful treatment of chronic pain must include not just a reduction in pain, but a restoration of functional abilities such as working and maintaining activities of daily living (DeVine et al., 2011; Gagnon, Stanos, van, Rader, & Harden, 2013). Often long-term use of opioid medications can be barriers to engaging in typical daily activities such as driving. While advances in pain relieving agents have been made, the search for the "magic pill" that alleviates pain with no side effects or abuse potential has been an elusive endeavor for the pharmaceutical companies worldwide. Physicians are provided with some guidelines in an effort to optimize safety when prescribing such medications, yet no single model exists for the most effective manner to control chronic nonmalignant pain (Chou, 2009). Scientific advancements including more sophisticated technology and precision equipment that enables the examination of reward pathways of different types of opioids (Tenayuca & Nazarian, 2012) aid in understanding the mechanisms involved in pain processing (Gilron, Jensen, & Dickenson, 2013).

Combination drug regimens are commonly used when treating the complex issues of chronic pain and the possibilities for targeting specific channels and receptors in the brain adds to the utility of pharmacotherapy in the treatment of chronic pain (Gilron et al., 2013). Combination pharmacotherapy can be criticized with concerns of overmedicating or clouding single drug effects by introducing a poly pharmacy approach. Furthermore, some research indicates that over 50% of patients with chronic pain are prescribed multiple analgesic medications concurrently (Berger, Sadosky, Dukes, Edelsberg, & Oster, 2012). Treating chronic pain patients is a dynamic process and the necessary individualized adjustments for each patient is not easily simplified and studied in a typical randomized clinical trial. One often overlooked, yet extremely important, outcome measure in assessing the efficacy of chronic pain treatment is evaluating the effects of decreasing the usage of opioid medications during treatment (Grabois, 2005). Identifying factors which contribute to successfully weaning chronic pain patients from opioid use is timely and relevant in the current healthcare arena.

Using a biopsychosocial model, interdisciplinary and multidisciplinary pain management programs have become gold standard for comprehensive treatment of chronic pain conditions. Pharmacotherapy is still an integral part of the multimodal approach with one goal being to reduce dependence on opioid medications. The literature touting the benefits and long-term success rates of intensive interdisciplinary treatment, such as functional restoration, is robust (Asih, Neblett, Mayer, & Gatchel, 2014; Brede, Mayer, & Gatchel, 2012; Fore et al., 2014; Hartzell, Mayer, Asih, Neblett, & Gatchel, 2014; Mayer, McMahon, Gatchel, Sparks, Wright, & Pegues, 1998a; Mayer, Choi, Howard, & Gatchel, 2013; T. G. Mayer, Gatchel, Brede, & Theodore, 2014; Wright, Mayer, & Gatchel, 1999). These programs are tailored to the needs of individual patients and each patient agrees to participate with the knowledge that medication adjustments will be made in the direction of reducing dependence on opioids. Cognitive Behavioral Therapy (CBT) is one of the modalities used in this biopsychosocial approach. Evidence exists supporting that this component may play an important role in the opioid weaning process. A Scandinavian study reported brief CBT to be a promising treatment for successfully weaning chronic pain patients form codeine without increasing pain complaints (Nilsen et al., 2010). However, no comprehensive studies have been published looking at multiple dimensions of treatment and addressing the differences in opioid use in patients successfully completing treatment.

Completion of multidisciplinary chronic pain treatment programs is related to better long-term outcomes, including decreased health care utilization and greater rates of returning to and retaining employment (Brede et al., 2012; Mayer et al., 1985; Mayer et al., 1998a; Mayer, Anagnostis, Gatchel, & Evans, 2002; Proctor, Mayer, Theodore, & Gatchel, 2005; Wright et al., 1999). However, opioid dependence has been identified as one of the major risk factors associated with non completion of these programs (Howard, Mayer, Theodore, & Gatchel, 2009; Proctor et al., 2005). This highlights the need to focus on patients who completed a comprehensive program and evaluate the factors associated with the change in opioid use. The identification of factors related to continued use of opioids following successful completion of a functional restoration program is missing from the current literature on this topic. Additionally,

there is little known about characteristics of patients who have positive outcomes and successfully return to work while remaining on opioids long-term.

The complexity of a chronic pain population cannot be ignored in the discussion of pharmacotherapy as part of treatment. Chronic pain is highly co-morbid with psychiatric disorders including depression, anxiety, and sleep disturbance (Bair, Robinson, Katon, & Kroenke, 2003; Busch et al., 2012; Dorsten & Weisberg, 2011; Graham & Streitel, 2010; Lin, Yen, Chen, & Chen, 2014; Okifuji & Hare, 2014; Strassels, 2006). Chronic pain is a strong predictor of the onset of depression and depression can increase pain experiences for patients. Sleep disturbance co-occurs with chronic pain often causing decreases in overall function and self-reported quality of life (Okifuji & Hare, 2014). The high co-morbidity between psychiatric disorders and chronic pain requires psychotropic medication to be incorporated in chronic pain management (Turk, Wilson, & Cahana, 2011). Psychotropic medications also provide adjuvant analgesic effects, which at one time were known as off-label effects, but are being accepted as adjunctive treatment options due to independent analgesic properties. Opioid doses are often modified by concurrent use of antidepressants, which in part can assist in preventing dependency. Research in chronic pain pharmacology needs to assess all medications prescribed to the patient, including opioid analgesics, antidepressants, neuromodulators and sedatives,such as anticonvulsants and sleep-promoting medication. The literature on pharmacological interventions for chronic pain focuses on pain relief and adverse events so heavily that it often excludes or minimizes any functional outcomes (Chaparro et al., 2014; Chapman et al., 2010; Turk et al., 2011).

The aim of the present study is to examine the characteristics of patients with chronic disabling occupational musculoskeletal disorders (CDOMD) at different points in treatment to determine how demographic, occupational, psychosocial, other medications and one-year socioeconomic outcome variables vary based on opioid usage. While the success of functional restoration programs is well documented for its ability improve function and increase post-treatment work-return and work-retention (Brede et al., 2012), little is known about the relationship between tapering opioid use and the successful completion of such programs. It is known that a large majority of program completers return-to-work and sustain success based on

one-year post-treatment socioeconomic outcomes, however identifying factors that inhibit successful outcomes has not previously included opioid use or pharmacological variables.

Chapter 2

Chronic Pain

2.1 Overview of Chronic Pain and Disability

Understanding the biological mechanisms that create the experience of pain, how pharmaceutical interventions can alter the mechanisms of pain perception and the manner in which individuals cope with these bodily sensations must be addressed when exploring a comprehensive assessment of chronic pain. The transition from an acute phase to a chronic state, as well as the psychosocial and behavioral components that can complicate treatment are also an integral part to providing the context for how chronic pain is studied. The following section outlines the theories of pain, the biopsychosocial model of assessment and treatment, and the co-morbidity of psychopathology in chronic pain populations.

2.2 Theories of Pain and the Biopsychosocial Model

Understanding the mechanisms associated with pain have plagued researchers for centuries. The earliest theories of pain centered on the knowledge of pathophysiology and the biological factors relating pain to the elements of the nervous system. *Cartesian Dualism* is one of the earliest views of pain, put forth by Rene Descartes in the 17th century. This point of view separated the mind from the body, allowing for the conceptualization of pain to reflect exclusively on the sensory nervous system (Gatchel, Peng, Peters, Fuchs, & Turk, 2007). Emotional or psychosocial factors were completely removed from consideration and all illnesses and diseases were regarded purely as automatic biological processes. This theory of *Biomedical Reductionism* (Gatchel, Haggard, Thomas, & Howard, 2012) was prominent until the latter part of the 19th century. Biological understanding of pain also began to emerge by the late 1800s. At this time two prominent theories focused on the physiological mechanism of pain perception: In the S*pecificity Theory of Pain* in 1894, Maximillian von Frey suggested that there were subcutaneous nerve receptors within the nervous system that responded to specific types of sensory input, such as temperature, touch, pressure and pain (Carli, 2011). In 1896, Goldschneider proposed the *Pattern Theory of Pain,* which identified the receptors to be the same (Carli, 2011), but varied

patterns of stimulation of these receptors was said to lead to different interpretations of the sensory signals (Melzack & Wall, 1994; Theodore, Kishino, & Gatchel, 2008).

Both the *Specified Theory of Pain* and the *Pattern Theory of Pain* have led to continued research, which provided extensive knowledge about the different types of receptors and how stimulated nerve responses are relayed throughout the body. Specifically, it is now accepted that receptors that respond to touch or pressure are known as *mechanoreceptors*; *thermoreceptors* are activated by changes in temperature, and receptors responsible for the perception of pain are nociceptors. Pain perception can vary in description, and include terms such as sharp or prickly, burning, pins and needles, shooting, aching, or freezing, depending on the specific fibers stimulated, such as mechanical, thermo-mechanical, or polymodal fibers (Carli, 2011; Theodore et al., 2008). For chronic pain patients, the description can include multiple types, and it is not always simple to identify the appropriate sensation and relate it to a specific receptor. Progress in the pain theory research has also informed researchers of the greater complexities involved while assessing human subjects.

Previous theories focused on the biological mechanisms of nerve response; however, more recent findings concerning the perception of pain have focused on the integration of the mind and body. The first attempt to integrate the physiological and psychosocial components in the understanding of pain (Gatchel, Peng, Peters, Fuchs, & Turk, 2007) emerged in the 1960s when Melzack and Wall introduced *The Gate Control Theory of Pain* (Melzack & Wall, 1965). Through the dorsal horn of the spinal cord, the substantia gelatinosa is the proposed gate-control mechanism responsible for transmitting impulses from the periphery to the brain. The magnitude and severity of the signals being sent through the central nervous system is thought to be modulated by this “gating” mechanism. This theory allows for the idea that higher mental processes can contribute to inhibitory processes and can affect the transmission of signals to the brain. The *Gate Control Theory* asserts that psychosocial components can have a direct effect on pain perception (Mendell, 2014). From a clinical perspective, treating patients with chronic pain must include addressing psychosocial factors since these aspects of a patient’s life can theoretically contribute to the perception of pain. Gates can be “opened” by psychosocial distress,

helplessness, and feelings of distress over the constancy of pain, resulting in an intensification of the perception of pain. Strategies focused on lessening psychosocial distress, including utilizing coping skills and cognitive or behavioral techniques can “close” these gates resulting in a lessening of pain perception (Gatchel et al., 2007; Mendell, 2014).

In contrast to the prior theories of pain that focused solely on the biological processes, the Gate Control Theory was the first to incorporate physiological and psychosocial factors to present an integrated theory that combines cognition with the nervous system. Melzack continued to broaden this concept in 1999 when he integrated this system into the *Neuromatrix Model of Pain,* which includes stress as a major factor in understanding pain perception (Melzack, 1999). Selye provided the evidence for how stress allows the body to adapt in response to physical danger with well established foundation (Selye, 1956) and spurring on continued research into how the “fight or flight” response system is activated by the hypothalamic-pituitary-adrenocortical (HPA) axis. The HPA provides a negative feedback response to a stressful circumstance such that the body releases cortisol to inhibit the hypothalamus from releasing corticotrophin hormone (CRH) and vasopressin. The sympathetic response provided by the HPA axis also releases catecholamines (epinephrine and norepinephrine) as a positive feedback mechanism to increase the breakdown of adrenocorticotropic hormone (ACTH) by the pituitary gland. A hyperactive HPA system can actually be created by prolonged stressful situations, whether the condition is physical or psychosocial. The pain experience for chronic pain patients can be exacerbated by a hyperactive HPA response. The perception of pain can become a stressor itself, which continues to impair homeostasis and intensify pain, even if the stressor is actual pain or simply the anticipation that the pain will return once medication effects wear off. The Neuromatrix Theory acknowledges that individuals determine their own pain experience based on their own neuromatrix of genetics, cognitions, sensations and memories (Melzack, 1999; Mendell, 2014). The pattern of seeking treatment for pain relief, obtaining minimal or short-term ease from pain, followed by eventual reemerging pain, may be a cycle familiar to chronic pain patients, which can alter treatment effectiveness. Prescribing opioid medications without

integrating a holistic perspective can be problematic in seeking long-term solutions for managing chronic pain.

The *biopsychosocial model* has emerged as the ideal approach built on the gate control and neuromatrix theories, and explains how the mind and body interaction relates to the perception of pain (Gatchel et al., 2007; Theodore et al., 2008). This perspective enables physiological, psychological and social factors to interact in a way that influences the perception of pain. Individual differences in the biological, psychological and social domains vary greatly and can lead to unique experiences of pain. In 1977, Engel was the first in the medical field to propose the biopsychosocial model in the field of chronic illnesses (Engel, 1977). The continued presence of a disease state alters psychosocial dynamics and are found to complicate the assessment and treatment of an individual with a chronic disease (Freedman, 1995). The biopsychosocial perspective was later applied to the study of pain. Differentiating between the terms *nociception* and *pain* is integral to the understanding the pain process. Pain refers to the subjective individual assessment of the sensory signals, while nociception refers to the stimulation of pain receptors that are recognized by the body and sent through the nervous system. Both, however, provide valuable information about the pain experience. Suffering is related to prior experiences of pain and also to the expectation of future events. Negative emotions affiliated with nociception and pain is termed *suffering*. Embedded within the notion of suffering are elements of psychosocial distress, such as depression, panic, anxiety, moodiness, anger, and fear (Gatchel et al., 2007).

The biopsychosocial approach is not aimed at the disease, but rather is directed at the individual's illness. The distinction between the two focuses on the objectivity of the condition. A disease is a biological event that can be "cured"; however, an illness refers to the biological, psychological and social components related to the disease that can be viewed subjectively (Turk, 2001) Most view a chronic pain condition as an illness, since the treatment for this condition is usually approached through management of symptoms rather than an actual cure. Using the biopsychosocial approach is essential for understanding the individual pain experience as it holistically represents multiple theories (Gatchel et al., 2007).

The biopsychosocial model is used for both the assessment and treatment of chronic pain conditions. The assessment portion identifies co-morbid psychosocial variables that may hinder progress, including opioid dependence or sustained chronic use of opioids. Treatment of chronic pain conditions through the biopsychosocial method requires a multidisciplinary team of professionals that can work together to treat not only the injured site through medications and physical therapy, but also to provide education and psychosocial therapy to enhance social support and improve overall functioning.

2.3 Progression from Acute to Chronic Pain

Acute pain is commonly and often effectively treated with a short-term course of opioid medications, yet not all acute injuries heal in a standard time frame, resulting in chronic pain situations. Understanding the factors that contribute to the development of chronic pain conditions has been a primary goal in pain research. It is understood that individuals experience acute pain in relation to noxious stimuli often associated with physical injury (Basbaum & Jessell, 2000). In most cases, as the physical damge heals, the perception of pain fades. However, when pain lasts beyond the time frame in which typical healing processes occur, greater scrutiny is placed on the types and amounts of medications prescribed. Individuals for whom the pain state does not cease with the healing of the injury have been seen to enter an intermediate phase that can last several months following the injury. This secondary phase is marked with prolonged psychosocial distress, which can include emotions such as increased anxiety, fear or anger. During this phase, secondary symptoms not associated with the injury are often reported. The increased levels of sustained stress can be associated with other physiological disturbances, such as the respiratory and digestive systems complaints, that qualify as a somatization disorder (Gatchel, 2001).

Typically, within six months following an injury, the natural healing process restores the body back to the original condition. Although, for some, pain is experienced for a long time past the sufficient period for biological repair to have occurred (Gatchel, 2001). Long-term pain conditions are frequently found in conjunction with psychosocial issues, such as depression and sleep disturbance (Gatchel et al., 2012). Physical de-conditioning often occurs with chronic pain

conditions as well. Neglecting standard exercise routines results in the deterioration of the muscles and skeletal regions associated with the injured site (Mayer et al., 1985). Chronic pain patients often show signs of a “de-conditioned” psychosocial state as well. Personal relationships and activities once enjoyed are abandoned or neglected resulting in a weakened psychological state and waning social support system (Gatchel et al., 2012). A major factor for the chronic pain patient is often motivation. Patients lose interest in normal daily responsibilities and are distracted by the cumulative effects of constant pain, possible medication side effects, and stress which can have negative effects on their family and work performance. If medication effects or lack of motivation interfere with their ability to work, patients with chronic pain incur financial difficulties that can also contribute to their psychosocial distress. Once the individual has developed a chronic pain condition, it is essential to attend to the patient from a biopsychosocial approach, to accommodate the biological, psychological and social needs including the level of medication used to alleviate pain, while sustaining adequate functioning (AlMakadma & Simpson, 2013) . Each patient’s circumstances are unique; thus, it is vital to tailor treatment to the needs of each individual and assess which aspects of treatment can reduce dependence on opioid medications.

2.4 Psychopathology of Chronic Pain Patients

The complexity of treating chronic pain does not end with assessing and treating pain complaints. A high rate of co-morbid psychological conditions necessitates an integrative approach to pharmaceutical interventions. Pain experiences are found to intensify with the presence of psychopathology; thus, perpetuating an individual’s sense of disability. Accurate assessment of psychopathology of the patient is crucial for treating the chronic pain condition. Within chronic pain populations, three major psychiatric disorders prevail: mood disorders, anxiety disorders and substance use disorders. Additionally, increased risk for depression, suicide, and sleep disorders are all found in patients with chronic pain conditions (Bair, Wu, Damush, Sutherland, & Kroenke, 2008; Belcher et al., 2014; Dersh et al., 2007) highlighting the importance of examining the characteristics of opioid use among this vulnerable population. Pain experiences that become chronic often exacerbate emotional factors and add to patient reported

and self-perceived suffering and disability (Gatchel et al., 2012). In the general population, lifetime prevalence rates of mental disorders, as reported by the World Health Organization (Kessler et al., 2007) range from 3.3%-21.4% for Mood/Depressive Disorders and 4.8%-31.0% for Anxiety Disorders. Twelve-month, or current, prevalence rates for clinical disorders are estimated at 6.6% for Major Depressive Disorder (Kessler, Ormel, J., Demler, O., & Stang, 2003) and 18.1% for Anxiety Disorders (Kessler, Chiu, Demler, & Walters, 2005). However, within chronic pain populations, rates of psychopathology are substantially higher than in the general population. One study reported comorbid pain and depression in 20% of patients, and an additional 23% exhibited pain, depression and anxiety concurrently (Bair et al., 2008). In the general population, the 12-month prevalence rate for any substance abuse (illicit drugs or alcohol) is 8.9% and the rate for illicit drugs only is 2.8% (Substance Abuse and Mental Health Services Administration, 2009). Within chronic pain populations, the prevalence of substance abuse is much higher, estimated around 24% (Martell et al., 2007).

Research has shown that depression, anxiety and substance use disorders have a direct impact on the treatment outcomes. Depression and anxiety have been linked to poor work-return rates following treatment for musculoskeletal injuries (Bair et al., 2008; Berger et al., 2012; Gatchel, 2004; Loeser, 2006; Turk & Burwinkle, 2005). Substance abuse, in particular, is found to be a main risk factor in failure to return to work for patients with occupational musculoskeletal disorders (Gagnon et al., 2013; Garland, 2014; Kidner, Mayer, & Gatchel, 2009; Proctor et al., 2005; Provenzano & Viscusi, 2014; Vendrig, 1999; Weiss et al., 2014), highlighting the importance of further investigation of opioid use. Another common symptom among chronic pain patients is poor sleep, but is it often lumped in with depressive symptoms or medication effects. Recent studies have proposed the possibility that sleep disturbance may be a separate issue beyond depression (Asih, Neblett, Mayer, Brede, & Gatchel, 2014; Asih et al., 2014); thus, highlighting the need for further investigation into the role opioid medications have on sleep. Non-completion of multidisciplinary functional restoration has also been shown to hinder positive outcomes, such as work-return and work-retention following an occupational musculoskeletal injury (Proctor et al., 2005). Patients who prematurely dropped-out of a functional restoration

program for treatment of occupational musculoskeletal disorders present higher rates of depressive symptoms, anxiety disorders and substance use disorders (Howard et al., 2009). The role of these previously established key factors need to be examined in the context of level of opioid use prior to and upon discharge from treatment.

The biopsychosocial approach is an essential aspect of understanding a pain condition as it takes into account physiological injury, as well as various psychosocial factors that interact and can exacerbate pain perception, often altering the progress of treatment. When attempting to treat a patient rather than a disease and not simply manage medications, a comprehensive evaluation is required. Only following a full assessment, including a medical examination, current medication lists, psychological and social factors, can an appropriate treatment plan can be developed for the individual chronic pain patient. The patient's reports of current medication use is an essential component, since medications can be prescribed, but adherence to actually taking the medications can only be gained from speaking to the patient directly. While self-reported medication use may contain some variability, it typically benefits chronic pain patients in a tertiary care facility to be as accurate and honest as possible. Medication adherence is an integral aspect to the treatment of any chronic illness (Ready, Sarkis, & Turner, 1982). However, chronic pain patients often have little to gain from deceiving medical providers regarding the level of opioids they ingests. It is common practice for pain management clinics to engage in medication contracts and regular urinalysis tests to monitor and verify potential abuse issues (Passik, Narayana, & Yang, 2014). The consequences for non-adherence typically separate patients from the care they have been pursuing for long periods of time. With the advancement of technology and increased regulations, medication-seeking patients are becoming more easily identified. For example, the Veterans Administration (VA) requires urinalysis tests not just to assess higher than prescribed levels of opioids, but also to ensure that the patients who are prescribed these medications are the ones who actually ingest the drugs (Morasco & Dobscha, 2008). If a VA patient seeks a refill on a controlled substance and that substance is not found in their system, typically there will be further inquiry into the legitimacy and necessity of continuing to prescribe opioids (Morasco & Dobscha, 2008). This is thought to ensure that prescriptions are not being

shared or sold, but the actual effect might result in a patient feeling compelled to take an additional dose of PRN medication even if their pain level is not exceptionally high. Again, a comprehensive exploratory study is needed to begin the investigation into identifying characteristics of patients on varying levels of opioids.

2.5 Prevalence, Cost, and Treatment of Chronic Pain

With reported population-based estimates of chronic pain prevalence at approximately 30% of adults in the United States (Gaskin & Richard, 2012; Institutes of Medicine, 2011), and pain complaints being responsible for more than 80% of all visits to healthcare providers (Gatchel & Turk, 1996; Kerns, Otis, Rosenberg, & Reid, 2003), treatment options must be explored in depth.

Economic factors often act as an impetus and the financial impact of chronic pain promotes a sense of urgency to investigate successful cost effective treatments. Calculations for both direct and indirect costs of chronic pain in the United States are estimated around $650 billion dollars annually. Direct costs include medical care due to injury and pain (i.e. physician visits, medical devices, pharmaceuticals, hospital services, and diagnostic testing). The largest amount of money spent on direct medical costs reportedly comes from physical therapy, inpatient services, medications and physician care (Institutes of Medicine, 2011). Lost wages are an indirect cost, with estimates of costs associated with lost work days and compensation for occupational musculoskeletal disorders ranging from $13 billion to $20 billion per year (Yost, Eton, Garcia, & Cella, 2011). Additional losses occur and indirect costs increase when an individual cannot participate in typical activities they regularly accomplished prior to injury, including tasks such as childcare, food preparation, and household maintenance (Institutes of Medicine, 2011). Societal costs are incurred not only when treating chronic pain with opioids, but also when dealing with opioid abuse (Ghate, 2010). Medications tend to be less expensive and more accessible for treating patients, especially for those who do not have private health insurance. Issues with authorization and availability of appropriate treatment facilities may increase the length of time between injury and intervention. This can often extend the length of time patients remain on opioid medication without other interventions. It has been show that

increases in length of disability is correlated with higher costs and increased opioid dependence (Dersh et al., 2008; Theodore, 2009), resulting in poor long-term outcomes. One study identified co-morbid chronic pain and opioid abuse to be 10 times higher in Medicaid insured patients compared to patients with private insurance policies. However, in terms of healthcare costs, opioid abusers with private insurance incurred costs similar to Medicaid beneficiaries (i.e., $15,884 and $13,658 respectively; Ghate, 2010). These figures again illustrate the importance of characterizing factors in levels of opioid use in chronic pain patients. Not just treatment but successful and cost-effective treatment that goes beyond maintaining prescriptions for opioids must be examined in the context of this huge societal issue.

Treatment of chronic pain typically occurs in the acute injury phase, with the intent to control pain and get the body in an ideal state for proper healing to occur. Standard interventions include over-the counter (OTC) medications such as acetaminophen, or non-steroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, or a limited quantity of opioids for short term use (Verkerk et al., 2013). Other interventions include ice packs or heating pads or even electrical stimulation or ultrasound may be suggested as a short-term palliative measure until the body has had time to repair itself from the physical injury (Mayer et al., 1995). For more severe injuries or for patients whose pain persists and does not respond to the initial conventional interventions, secondary or post-acute phase of injury is addressed. At this secondary level of rehabilitation, prevention is typically the primary focus, specifically aimed at preventing physical deconditioning, medication habituation, and adverse psychological reactions. Strengthening and mobilization are key factors during this phase with the goal of restoring function to the injured area, typically through a prescribed course of physical therapy (Fore et al., 2014). Occasionally, surgical interventions occur at this level, and psychosocial interventions, or multidisciplinary care is offered to some patients (Brede et al., 2014).

Approximately 10% of patients do not respond favorably to primary or secondary rehabilitation and require tertiary care (Mayer et al., 1995). These patients typically suffer from chronic musculoskeletal conditions, and have either failed to benefit from surgical interventions or surgical interventions are not an option. Tertiary rehabilitation typically offers two options, either

palliative pain management or interdisciplinary rehabilitation. The focus of palliative pain management is explicit in the name, the goal being to ease pain, typically through opioid medications, without importance placed on restoring function. Interdisciplinary treatment however, utilizes a holistic team approach to address physical, psychological, social, and economic factors that contribute to a patient's overall health pain perception and functional abilities. The extensive costs of chronic pain, the vast number of the people it affects, and the standard levels of treatments have been discussed. Further investigation into the assessment and comprehensive quantification and analysis of all aspects in tertiary rehabilitation programs is warranted. It has been suggested that effective rehabilitation strongly relies on assessment to adequately address the needs of individual patients, including through the use of patient reported outcomes (Rose et al., 2014). Additional variables necessary for a comprehensive understanding of treatment planning include psychological factors, occupational factors, and medication use (Dworkin et al., 2005).

2.6 Functional Restoration

Utilizing the biopsychosocial approach, functional restoration is one particularly successful type of tertiary rehabilitation developed for patients with chronic pain conditions. This intensive interdisciplinary program is based on a sports medicine approach with the primary goal of restoring function and allowing individuals to avoid permanent disability. Functional restoration treatment consists of a medically-supervised, quantitatively-directed exercise progression combined with a multi-modal disability management program (MDMP). The components of MDMP include cognitive-behavioral therapy, stress management/biofeedback training, education, and vocational reintegration.

An interdisciplinary team of health care professionals assesses each patient's condition to develop a specific treatment protocol tailored to the needs of the individual. These interdisciplinary teams typically include physicians, psychologists, psychiatrists, physical therapists, occupational therapists, biofeedback specialists, and disability case managers. By incorporating interventions like education on coping strategies and stress management, the patient can continue to manage lifestyle issues or problems on the job, with the global focus of

treatment being to assist individuals in returning to their own personal level of functioning prior to their injury (Mayer et al., 1995; Moreno, Cunningham, Gatchel, & Mayer, 1991). This [unique] patient population has a higher likelihood of having developed dependency on pain medications, as most have been enduring chronic pain for many months and even years. It is no surprise that opioid dependency is a common factor in patients with chronic occupational musculoskeletal disorders (Proctor et al., 2005). One aspect of the functional restoration treatment includes assistance in detoxification from opioid dependence including modifying or rotating medications, tapering doses of or weaning off opioid use. This is a closely monitored process as the functional restoration treatment team meets regularly to discuss the progress of each patient. This enables all team members to provide recommendations for modification to the treatment regimen when sufficient progress is delayed.

Treatment outcomes for this type of interventions are consistently positive for patients with chronic pain conditions who successfully complete the functional restoration program (Brede et al., 2012; Fore et al., 2014; T. Mayer, McMahon, Gatchel, Sparks, Wright, & Pegues, 1998b; Vendrig, 1999). This tailored biopsychosocial approach, provides the opportunity to increase physical function while optimizing psychosocial responses to perceived pain, which often allows individuals to resume [certain] pre-injury lifestyle and activities. The positive treatment outcomes functional restoration provides is not limited to successful occupational outcomes. Many treatment responsiveness studies have shown tremendous success in improving patient reported outcomes of decreasing self-reported depressive symptoms, self-reported levels of disability and self-reported sleep disturbance (Hartzell et al., 2014; Kidner et al., 2009; Mayer et al., 2013; Proctor et al., 2005).

While the success of functional restoration programs is well documented for its ability to improve function and return patients to work, little is known about the relationship between tapering opioid use and the successful completion of such programs. It is known that a large majority of program completers return-to-work and sustain success in one-year socioeconomic outcomes; however, identifying factors that inhibit successful outcomes has not previously included opioid use or pharmacological variables. An important component missing from the

literature is a comprehensive characterization of opioid levels as they relate to demographic, work specific, psychosocial, medication, and one-year socioeconomic variables.

Chapter 3

Pharmacotherapy

One major component in the treatment of chronic pain is interventions involving medication. When speaking of pharmacotherapy to treat chronic pain, one automatically thinks of pain medications. The types and classes of drugs used to treat pain vary greatly. Therefore, it is essential to review some of the most common types of prescription medications utilized in the treatment of chronic pain. However, understanding the history and legalities surrounding the accessibility and availability of pain relieving medications is essential. In this context the following chapter will discuss legislation of opioid use, opioid analgesics, antidepressants, neuromodulators, and sedatives with regard to the roles each play in the treatment of chronic pain.

3.1 Legislation of Opioid Use

In the early part of the 20th Century, the United States legislators acknowledged the increasing problem of opium abuse and passed the Federal Harrison Narcotics Act of 1914. This created a tax on all opioids and mandated the monitoring of opioid trafficking through careful recording of all transfer points, including dispensing medication to patients (Savage, 1996). Court proceedings in 1919 lead to a Supreme Court rule that physicians could no longer prescribe opioids to maintain an opioid addiction. It remained legal to prescribe opioids as a part of treatment to wean addicted patients from chronic use, but many physicians feared threats to their license and the common practice of prescribing opioids was altered. However, by the 1960s federal agencies, under recommendation of the American Medical Associate, approved the study of methadone as a maintenance treatment for opioid addiction (Savage, 1996). During the Kennedy Administration, legislation permitted the opening of methadone clinics for the treatment of addiction to opioids. Advances in the availability and common practice of prescribing opioids for acute pain frequently led to chronic pain complaints, and physicians continued prescribing opioids for chronic pain, rather than to maintain addictions.

The Harrison Narcotic Act was updated in 1970, by the Comprehensive Drug Abuse Prevention and Control Act, which categorized all opioids and other drugs with abuse potential

into five schedules based on abuse potential and medical purpose (Clark & Sees, 1993). Abuse potential is based on risk for both physical and psychological dependence. Within this classification system, abuse potential decreases with each increasing schedule. Schedule I drugs have the greatest potential for abuse with no accepted medical use outside research. Heroin and cocaine are examples of Schedule I drugs. Schedules II, III, and IV include opioid medications, while Schedule V includes drugs with the lowest abuse potential. While this classification system can be helpful, Clark and Sees (1993) suggest that parameters for drug classification are not an exact science, and they fail to reflect actual prescribing practices or street demand for any given drug. Despite shortcomings of the classification system, federal regulations mandate that physicians fulfill several requirements in administering controlled substances. Critics have speculated that these laws create an environment in which physicians may become fearful of prescribing opioids and patients may be inadequately treated despite a legitimate need for pain relief (Savage, 1996). Legislation does not prohibit the use of opioids in treating known addicts for genuine medical conditions, yet the physician holds the responsibility for establishing and demonstrating the legitimacy of the medical condition and the appropriateness of the treatment plan. The subjective nature of pain can complicate this process and with unclear etiologies of some pain disorders, it can be difficult to differentiate legitimate complaints of pain from distress signals of opioid addiction (Savage, 1996).] The following section will address opioid analgesics in the treatment of chronic pain.

3.2 Opioid Analgesics

Opioids are used in treating chronic pain albeit with caution due to their tolerance and dependence issues. Opioids are used as second line treatment for moderate to severe non-cancer pain when patients do not respond to acetaminophen or NSAIDs, are experiencing pain-related functional impairment or are having diminished quality of life (Chapman et al., 2010; Chou & Huffman, 2007; Chou, 2009; Nuckols et al., 2014). A thorough assessment of potential opioid-concurrent psychiatric medication interaction risk and drug abuse history must be conducted prior to prescribing opioids to patients suffering from chronic pain co-morbid with psychiatric illness (Bair et al., 2009; Dersh et al., 2007; Nuckols et al., 2014; Rej, Dew, & Karp, 2014). A meta-

analysis of long-term opioid management for chronic non-cancer pain found that patients discontinue opioid treatment due to adverse effects (8.9-22.9%) or insufficient pain relief (5.8-10.3%) depending on mode of consumption (oral, transdermal or intrathecal) (Noble et al., 2010). Long term opioid medication, with various analgesics effects, results in pain relief. Inconclusive results were found for the effect of opioids medication on quality of life and functioning. For neuropathic pain, opioids were reported to be more effective than placebo in intermediate-term study (Eisenberg, McNicol, & Carr, 2006).

Opioids may be classified as having weak (codeine, hydrocodone and oxycodone combination medication with acetaminophen) or strong (morphine, fentanyl, oxymorphone and hydromorphone) analgesic property (Leo, 2007). Thus type of opioids prescribed depends on the patient's pain intensity. There is evidence for oxymorphone efficacy in controlling/reducing pain when compared to placebo in chronic low back pain (Hale, Dvergsten, & Gimbel, 2005). Propoxyphene (Darvon) and dextropropoxyphene are typically not recommended due to their low therapeutic/toxicity ratio (Kroenke, Krebs, & Bair, 2009). Hydrocodone-containing medications such as, Vicodin, Lortab, and Norco are currently the single most prescribed drug in the United States (Traynor, 2013). This has brought higher levels of scrutiny on the prescribing practices of care providers in this country and lead to the change in status of hydrocodone-containing medications. While hydrocodone is still considered a "weak" opioid, it currently is a schedule II controlled substance, and further investigation into this specific medication is warranted. Because of issues such as abuse potential, opioid medications are typically intended for use in the acute phase since they work well on nociceptive pain and allow patients some relief while tissues heal. In the treatment of chronic pain, opioids are not the only form of pharmacotherapy found to be beneficial. The following section will address antidepressants and their role in treating chronic pain.

3.3 Antidepressants

Antidepressants are widely used in chronic pain, as treatment for depression or as adjuvant analgesic or both. The effectiveness of antidepressants in treating neuropathic pain and non-neuropathic pain contributes to the popularity of these drugs in pain management

(Dharmshaktu, Tayal, & Kalra, 2012). Antidepressants are used due to their mood elevating effects as people suffering from chronic pain often experience depressed mood or meet criteria for a mood disorder. Antidepressants may be classified into several general classes, including tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) and monoamine oxidase inhibitors (MAOIs). MAOIs are rarely prescribed anymore due to their side effects (Leo, 2007).

Antidepressants, especially SNRIs and SSRIs are also effective in treating anxiety disorders. Over the years, more research reported the analgesic effect of antidepressants independent from mood alteration effect, thus antidepressants are also used due to the analgesics property. The popularity of antidepressants as pain relieving medication also increases because there is no dependency effect that is commonly associated with long-term use of opioid.

Antidepressants work by suppressing pain through diverse mechanisms in the central nervous system and peripheral nervous system. Antidepressants function by inhibiting serotonin, norepinephrine and dopamine reuptake, thus increasing the number of these neurotransmitters in the synaptic cleft, further inhibiting pain transmission (Leo, 2007). Serotonin and norepinephrine are specifically involved in depression; and chronic pain depletes these neurotransmitters. The analgesic property of antidepressants also works through inhibiting NMDA receptors and decreasing PGE2 production (Leo, 2007). The doses of antidepressant depend on the purpose of its prescription. Higher doses might be given to treat mood disorders comorbid with chronic pain. Lower doses are given for achieving adjuvant analgesic effects in treating chronic pain (Bair et al., 2008). Patients' age is also a factor in determining drug dose (Reid et al., 2010). Elderly patients are typically prescribed lower doses.

Tricyclics are commonly used to treat psychiatric disorders and also have the longest history of use in treatment of multiple pain conditions. Neuropathic pain responds better to TCAs than nociceptive pain; however TCAs may be effective in treating nociceptive pain comorbid with depression (Leo, 2007). Amitriptyline is widely used due to its least anticholinergic effects among TCAs and desipramine, nortriptyline and imipramine are known for their tolerance. These TCAs,

along with imipramine, inhibit norepinephrine reuptake, and are reported to be more effective than non-norepinephrine-inhibiting agents (Bair et al., 2008; Leo, 2007). TCAs have shown some efficacy in treating low back pain, but not necessarily in relieving pain in the extremities (Chou & Huffman, 2007). The daily effective dose of amitriptyline ranges from 10-30 mg in which the pain subsides at six weeks (Cascos-Romero, Vázquez-Delgado, Vázquez-Rodríguez, & Gay-Escoda, 2009). TCAs and SNRIs are typically the first line medication for neuropathic pain. Some common side effects of TCAs include sedation, dry mouth, blurred vision, urinary retention, constipation and postural hypotension, which can be reasons some patients discontinue use. SSRIs may yield effective results for patients experiencing adverse effects from TCAs even though there is limited evidence regarding SSRIs effectiveness in neuropathic pain (Leo, 2007).

Theoretically, SNRIs are thought to be more effective in treating chronic pain since it inhibits both the serotonin and norepinephrine. This assumption is validated by research findings, especially the effectiveness of SNRIs in treating neuropathic pain (Dharmshaktu et al., 2012). Duloxetine and milnacipran are SNRIs that have been shown to improve pain relief, function and quality of life in neuropathic pain patients. SSRIs such as fluoxetine and paroxetine are similarly effective for neuropathic pain, but have not shown to be effective in treating low back pain (Webster & Markman, 2014). Most common side effects of SSRIs and SNRIs included nausea, dry mouth, fatigue, diarrhea, hyperhidrosis, dizziness, and constipation (Skljarevski et al., 2010). Antidepressants are not the only alternative or adjunctive pharmacological treatment when trying to alleviate chronic pain. The next section will address neuromodulators and/or – [not all neuromodulators are anticonvulsants] anticonvulsants as they relate to the treatments of chronic pain.

3.4 Neuromodulators

Neuromodulator or anticonvulsants are also useful for treating neuropathic pain (Leo, 2007; Webster & Markman, 2014). Anticonvulsants have mood-stabilizing effects; thus, they are useful in treating pain comorbid with bipolar or schizoaffective disorders (Bair et al., 2008; Leo, 2007). The analgesic mechanism of anticonvulsant drugs works through the decrease of sodium channel activity, modulation of calcium channels, reduction of excitatory amino acids activity, and

the increase of GABA activity in the central nervous system (Ettinger & Argoff, 2007). Neuromodulators or anticonvulsants used to treat pain are: gabapentin, pregabalin, carbamazepine and topiramate, and oxcarbazepine (Chou, 2009). Gabapentin is also effective in treating/managing central pain syndrome and compression neuropathies such as carpal tunnel syndrome and radiculopathies. Gabapentin also benefits patients suffering from panic attack and social anxiety disorder, while pregabalin is effective in treating generalized anxiety disorder (Sadock & Sadock, 2007). Effective analgesia is achieved from the combination of gabapentin and morphine, each in lower dose than when prescribed as single agent (Webster & Markman, 2014). Anticonvulsants are not without side effects, and risk versus benefit is always a factor in prescribing these types of medications (Chou, 2009; Labianca et al., 2012). The next type of medication that will be addressed also requires specific attention to issues of side effects abuse or misuse. The role of sedatives including tranquilizers, anxiolytics and muscle relaxants will be briefly outlined next.

3.5 Sedatives: Tranquilizers, Anxiolytics and Muscle Relaxants

Sleep disturbance is common in chronic pain patients with or without psychiatric comorbidity; it is highly associated with depression or anxiety resulting in heightened pain intensity and decreased function (Busch et al., 2012; Graham & Streitel, 2010; O'Brien et al., 2011; Okifuji & Hare, 2014). Benzodiazepines such as diazepam, lorazepam and clonazepam can be prescribed for sleep disturbance due to the sedation and tranquilizer effects. However the use of benzodiazepine is secondary to the use of sedating antidepressants, such as amitriptyline, imipramine and trazadone (Polatin & Dersh, 2004). Sedating antidepressants such as theses have the potential to mitigate pain-associated sleep disturbance. However, the use of benzodiazepines can also result in dependence, especially when patients are also prescribed other medications including opioids (Chou, 2009; Webster & Markman, 2014). Benzodiazepine is indicated when antidepressants are not effective or result in adverse side effects. Benzodiazepines with a shorter half-life are favorable because they have less sedating effects (Sadock & Sadock, 2007). Other non-benzodiazepine sedatives used for treating sleep disturbance are Ambien (zolpidem) and Sonata (zaleplon) (Okifuji & Hare, 2014). Antidepressants

are not only beneficial in treating pain and depression, but can sometimes replace anxiolytics (anti-anxiety agents) in treating chronic pain comorbid with anxiety disorder. Antidepressants are also perceived to be more potent with fewer side effects and SNRIs and SSRIs also have less adverse withdrawal symptoms than anxiolytics, including anxiety, irritability, insomnia and muscle tension.

Muscle relaxants are antispasmodic agents used in treating acute musculoskeletal conditions. Some common antispasmodics include chlorzoxazone, cyclobenzaprine, metaxalone, baclofen, methocarbamol and orphenadrine, which are FDA approved medications for treating discomfort due to acute, painful musculoskeletal conditions (Chou, 2009). Even though muscle relaxants are approved for acute pain, they are often used in treatment of chronic pain (Webster & Markman, 2014). Cyclobenzaprine is used in treating fibromyalgia due to its tricyclic chemical structure, while baclofen might be prescribed for chronic pain arising from muscle spasticity (Leo, 2007). Side effects commonly associated with muscle relaxants are dizziness, drowsiness, dry mouth and headache. We rely on patients to report side effects and sensations which they attribute to specific medications they are taking.

Patients are increasingly playing a larger role in their own treatment. As such, the logical progression is from treatment to outcome. Evidence-based medicine no longer relies solely on objective data, but has recently put greater emphasis on a patient's self-report regarding the efficacy of treatment. This is especially true when assessing inherently subjective constructs such as chronic pain. In the following chapter, patient reported outcomes will be reviewed in the context of the role they play in the overall assessment of chronic pain treatment.

Chapter 4

Patient Reported Outcomes

Patient reported outcomes (PROs) have a long history of being utilized in chronic pain research. Due to the inherently subjective nature of pain complaints, patients are often the best, if not the only, source of information on symptoms such as pain intensity or pain interference. The accuracy of these measures are often questioned in the scientific community due to the fact that one individual's report of symptoms can vary greatly and may change over the course of a day or even an hour, making it difficult for researchers to control enough variables to feel confident about using self-reported outcomes to validate a treatment (Kirshner B, 1985). Patient-reported outcomes refers to self-reported measures of health status (Gwaltney, Shields, & Shiffman, 2008; Shields, Gwaltney, Tiplady, Paty, & Shiffman, 2006) and have important implications in clinical practice (Deutscher, Hart, Dickstein, Horn, & Gutvirtz, 2008)The FDA supports the use of PROs in clinical trials, asserting that treatment effects are often better perceived by patients, than by their treating physicians (Shields et al., 2006) Many new batteries of instruments that include PROs have been developed in recent years to quantify outcomes such as symptom relief and the ability to carry out activities of daily living. PROs can take multiple forms in a clinical practice, including symptom assessment, patient-reported function or disability, measures of health-related quality of life (HRQL), health status reports, and patient satisfaction (Rose & Bezjak, 2009). With the prolific publishing of earnest researchers trying to perfect the items that are specific and sensitive to identifying these many areas of interest, the need for brief, efficient, and reliable PROs becomes the focus of evidence-based medicine.

The National Institute of Health's (NIH) response to this need is the Patient Reported Outcome Measurement Information System (PROMIS) initiative. Originally initiated in 2004, PROMIS funding is granted by the NIH and has been publicized as an effort to make available efficient, flexible and precise item banks that provide a measurement of commonly studied PROs. The PROMIS has also developed several computerized adaptive tests (CATs) for use in clinical research and practice. It has been argued that computerized assessments have several advantages over paper-and-pencil assessments including: reduction of missing data, patient

selection of multiple answers to an item, the ability to simplify more complex skip patterns and the reduction of the burden of data-entry (Gwaltney et al., 2008). Research has been conducted to evaluate the measurement equivalence (i.e., comparability of the psychometric properties of data) between measures by administration mode (Gwaltney et al., 2008). Specifically, these studies have examined measurement equivalence for a variety of patient-reported outcome (PRO) measures and administration-mode comparisons [e.g., computer-based (via the internet at home or in the provider's office), PDA, tablet-based, telephone-based, or interactive voice response (IVR), and paper-based]. In total, the majority of studies have found measurement equivalence by administration mode (Gwaltney et al., 2008). Computerized administration carries concerns regarding proper representation and the nature of the patient population being studied; in particular, demographics, literacy, reading level, visual ability, familiarity with touch-screen computers, and manual dexterity (Rose & Bezjak, 2009). Overall, PROs are an essential aspect of measuring treatment response.

Commonly used PROs in the chronic pain population include those assessing patients' perceived level of pain intensity, typically in the form of a Visual Analog Scale (VAS). Pain disability is also of specific interest and one study examined neuromodulation in clinical practice and demonstrated patient-reported pain relief was 58.0% (±26.2%) at 3 months, 58.1% (±28.7%) at 6 months, and 57.0% (±29.4%) at 12 months. Disability scores were measured using the Pain Disability Index (PDI) and showed a reduction from 47.7 points at baseline to 33.3, 32.4, and 31.9 points, respectively ($p \leq 0.001$) (Deer et al., 2014). Pain relief was categorized by the majority of patients as 'excellent' or 'good' and who also reported their overall quality of life as 'greatly improved' or 'improved' at all time points. Additionally, over 79% of the patients were 'satisfied' or 'very satisfied' with the therapy at all time points assessed, and 47.1% of the patients 'stopped' or 'decreased' use of narcotics/opioids (Deer et al., 2014). The presence of PROs is not new to research; however, the difference now is in the recommendation for inclusion of their use in nationally funded grant projects (Deyo et al., 2014).

4.1 Scope of the Present Investigation

As previously discussed, comprehensive interdisciplinary programs that treat patients rather than illnesses have become the model and ideal standard of care for successfully treating chronic pain, yet little is known about the relationship between levels of opioid use in the context of such programs. It is known that a large majority of program completers return to work and sustain employment; however, factors that relate to successful outcomes have not previously included opioid use or other pharmacological variables. The purpose of the current study is to assess self-reported levels of opioid use upon admission to and discharge from a functional restoration program, and determine how levels of opioid use relate to demographic, occupational, patient-reported psychosocial and one-year socioeconomic variables, as well as use of other non-opioid medications. In light of the recent rescheduling of hydrocodone, it is important to analyze differences in outcomes based on the type of opioid prescribed, specifically hydrocodone alone, other opioid prescription alone, or combination of more than one opioid.

Levels of opioid use will be divided into 5 groups: 1) None; 2) PRN/Very Low: 1-15mg; 3) Low: 16-30mg; 4) Moderate: 31-60; 5) High: 61mg or greater. The specific prescriptions will be combined into groups and compared as 1) No Opioids Prescribed; 2) Single prescription for hydrocodone; 3) Single prescription for any other opioid; and 4) combination of more than one prescription opioid. It is the intent to compare each of the groups across five dimensions: 1) demographic variables, including program completion, length of disability, area of injury, race, marital status, gender, age, and pre-admission surgeries; 2) work-related variables, including job type (blue collar or white collar), net salary at time of injury, case type (workers compensation or private pay), job demand, job satisfaction, work status on admission, and SSI or SSDI disability payments upon admission; 3) patient reported psychosocial variables, Pain Intensity (PI), Beck Depression Inventory (BDI), Pain Disability Questionnaire (PDQ), Oswestry Disability Questionnaire (OSW), and Insomnia Severity Index (ISI); 4) additional medication variables will include antidepressants, neuromodulators, and/or sedatives; and 5) one-year socioeconomic outcome variables will include: work return, work retention, additional surgeries to original injury site, new injuries and visits to new healthcare providers.

The current study will be broken down into 3 separate studies: 1) Pre-admission opioid use; 2) Opioid use at discharge; and 3) Change in opioid usage from pre- to post- treatment. Furthermore, multivariate analyses will be conducted on each study to determine the key risk factors associated with each group.

4.1.1 Hypotheses

The following hypotheses were proposed for this study:

4.1.1.1. Study 1a: Self-reported level of opioid use at pre-admission.

1. Pre-treatment level of opioid use will predict differences in response to treatment, such that subjects reporting higher levels of use will have higher rates of program non-completion.
2. Pre-treatment level of opioid use will differentiate patients according to area of injury, such that subjects reporting higher levels of pre-treatment opioid use will have injuries to lumbar or cervical regions in a greater frequency than patients with injuries to extremities.
3. Pre-treatment level of opioid use will differ significantly by ethnicity in that Caucasian patients will report higher levels of pre-treatment opioid use.
4. Pre-treatment level of opioid use will differ significantly by gender in that a greater number of males will report higher levels of pre-treatment opioid use.
5. Pre-treatment level of opioid use will not differ by age, or marital status.
6. Pre-treatment level of opioid use will differ significantly in that subjects reporting higher levels of pre-treatment opioid use will exhibit higher rates of pre-admission surgery.
7. Pre-treatment level of opioid use will differ significantly in that subjects reporting higher levels of pre-treatment opioid use will exhibit longer lengths of disability.
8. Pre-treatment level of opioid use will not differentiate subjects based on most occupational variables including: job type, job demand, job satisfaction, or pre-injury wage.
9. Pre-treatment level of opioid use will vary significantly based on certain specific occupational variables such as case type, with private pay patients reporting higher levels of opioid use, work status differentiating patients reporting lower levels of opioid use with

having current employment, and patients with higher levels of opioid use being more likely to be receiving SSI or SSDI.

10. Pre-treatment level of opioid use will differentiate level of pre-treatment depressive symptoms, such that those reporting higher levels of pre-treatment opioid use will demonstrate higher pre-treatment scores on the BDI. Pre-treatment level of opioid use will differentiate level of post-treatment depressive symptoms, such that those reporting higher levels of pre-treatment opioid use will demonstrate higher post-treatment scores on the BDI. Additionally, there will be differences in change scores of self-reported depressive symptoms, with those taking lower levels of opioids at post-treatment having greater levels of change in BDI scores.
11. Pre-treatment level of opioid use will differentiate subjects according to level of pre-treatment patient reported levels of disability, such that those reporting higher levels of pre-treatment opioid use will demonstrate less desirable pre-treatment scores on the PDQ, and OSW. Pre-treatment level of opioid use will differentiate subjects according to level of post-treatment patient reported levels of disability, such that those reporting higher levels of pre-treatment opioid use will demonstrate less desirable post-treatment scores on the PDQ, and OSW. Additionally, there will be differences in change scores of self-reported disability, with those taking lower levels of opioids at pre-treatment having greater levels of change in PDQ, and OSW scores.
12. Pre-treatment level of opioid use will differentiate subjects according to level of pre-treatment patient reported levels of sleep disturbance, such that those reporting higher levels of pre-treatment opioid use will demonstrate less desirable pre-treatment scores on the ISI. Pre-treatment level of opioid use will differentiate subjects according to level of post-treatment patient reported levels of sleep disturbance, such that those reporting higher levels of pre-treatment opioid use will demonstrate less desirable post-treatment scores on the ISI. Additionally, there will be differences in change scores of self-reported insomnia, with those taking lower levels of opioids at pre-treatment having greater levels of change in ISI scores.

13. Pre-treatment level of opioid use will differentiate subjects according to level of pre-treatment additional medication use, such that those reporting higher levels of pre-treatment opioid use will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives upon admission. Pre-treatment level of opioid use will differentiate subjects according to level of post-treatment additional medication use, such that those reporting higher levels of pre-treatment opioid use will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives at discharge.
14. Pre-treatment level of opioid use will predict differences in one-year socioeconomic outcomes including healthcare utilization, such that subjects reporting higher levels of pre-treatment opioid use will demonstrate higher rates of post-treatment surgery, post-treatment injury, and higher rates of healthcare utilization at one-year follow-up.
15. Pre-treatment level of opioid use will predict differences in one-year socioeconomic outcomes including work-related outcomes, such that subjects reporting higher levels of pre-treatment opioid use will have lower rates of work-return and work-retention at one-year post-treatment.

4.1.1.2. Study 1b: Self-reported hydrocodone use at pre-admission.

1. Pre-treatment use of hydrocodone will predict differences in response to treatment, such that subjects reporting no opioid use or single opioid use of hydrocodone will have higher rates of program completion than those taking other types or a combination of opioids.
2. Pre-treatment use of hydrocodone will differentiate patients according to area of injury, such that subjects reporting a combination of multiple opioids will have injuries to lumbar or cervical regions in greater frequencies than patients with injuries to extremities.
3. Pre-treatment use of hydrocodone will differ significantly by ethnicity in that Caucasian patients will report higher levels of combination opioid use.
4. Pre-treatment level of opioid use will differ significantly by gender in that a greater number of males will by taking hydrocodone upon admission.
5. Pre-treatment use of hydrocodone will not differ by age, or marital status.

6. Pre-treatment use of hydrocodone will differ significantly in that subjects reporting higher levels of combination opioid use will exhibit higher rates of pre-admission surgery.
7. Pre-treatment use of hydrocodone will differ significantly in that subjects reporting a combination of multiple opioid medications at pre-treatment will exhibit longer lengths of disability.
8. Pre-treatment use of hydrocodone will not differentiate subjects based on most occupational variables including: job type, job demand, job satisfaction, or pre-injury wage.
9. Pre-treatment use of hydrocodone will vary significantly based on certain specific occupational variables such as case type, with private pay patients reporting higher levels of combination opioid use, work status differentiating patients reporting no opioid use or hydrocodone only will have higher rates of current/pre-admission employment, and combination opioid use will be more likely to be receiving SSI or SSDI.
10. Pre-treatment use of hydrocodone will differentiate level of pre-treatment depressive symptoms, such that those reporting a combination of prescription opioid use will demonstrate higher pre-treatment scores on the BDI. Pre-treatment use of hydrocodone will differentiate level of post-treatment depressive symptoms, such that those reporting a combination of prescription opioid use will demonstrate higher score on the BDI. Additionally, there will be differences in change scores of self-reported depressive symptoms, with those reporting a combination of prescription opioid having lower levels of change in BDI scores.
11. Pre-treatment use of hydrocodone will differentiate subjects according to level of pre-treatment patient reported levels of disability, such that those reporting a combination of opioids will demonstrate less desirable pre-treatment scores on the PDQ and OSW. Pre-treatment use of hydrocodone will differentiate subjects according to level of post-treatment patient reported levels of disability, such that those reporting higher levels of pre-treatment use of hydrocodone only will demonstrate more desirable post-treatment scores on the PDQ, and OSW than those on other opioids or combination of multiple

opioids. Additionally, there will be differences in change scores of self-reported disability, with those taking hydrocodone only or none? at pre-treatment having greater levels of change [?in what direction?] in PDQ, and OSW scores.

12. Pre-treatment use of hydrocodone will differentiate subjects according to level of pre-treatment patient reported levels of sleep disturbance, such that those reporting higher levels of combination opioid use will demonstrate less desirable pre-treatment scores on the ISI. Pre-treatment use of hydrocodone will differentiate subjects according to level of post-treatment patient reported levels of sleep disturbance, such that those reporting higher levels of combination opioid use will demonstrate less desirable post-treatment scores on the ISI. Additionally, there will be differences in change scores of self-reported insomnia, with those taking hydrocodone only at pre-treatment having greater levels of change in ISI scores.
13. Pre-treatment use of hydrocodone will differentiate subjects according to level of pre-treatment additional medication use, such that those reporting a combination of multiple opioids will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives. Pre-treatment use of hydrocodone will differentiate subjects according to level of post-treatment additional medication use, such that those reporting a combination of multiple opioids on admission will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives at discharge.
14. Pre-treatment use of hydrocodone will predict differences in one-year outcomes including healthcare utilization, such that subjects reporting a combination of multiple opioids will demonstrate higher rates of post-treatment surgery, post-treatment injury, and healthcare utilization at one-year follow-up.
15. Pre-treatment use of hydrocodone will predict differences in one-year outcomes including work-related outcomes, such that subjects reporting a combination of multiple opioids will have lower rates of work-return and work-retention at one-year post-treatment.

4.1.1.3 Study 2: Opioid use at discharge.

1. Post-treatment level of opioid use will differentiate patients according to area of injury, such that subjects reporting higher levels of post-treatment opioid use will have injuries to lumbar or cervical regions to a greater degree than patients with injuries to extremities.
2. Post-treatment level of opioid use will differ significantly by ethnicity in that Caucasian patients will report higher levels of post-treatment opioid use.
3. Post-treatment level of opioid use will differ significantly by gender in that a greater number of males will report higher levels of post-treatment opioid use.
4. Post-treatment level of opioid use will not differ by age or marital status.
5. Post-treatment level of opioid use will differ significantly in that subjects reporting higher levels of post-treatment opioid use will exhibit higher rates of pre-admission surgery.
6. Post-treatment level of opioid use will differ significantly in that subjects reporting higher levels of post-treatment opioid use will have longer lengths of disability.
7. Post-treatment level of opioid use will not differentiate subjects based on most occupational variables including: job type, job demand, job satisfaction, or pre-injury wage.
8. Post-treatment level of opioid use will vary significantly based on certain specific occupational variables such as case type, with private pay patients reporting higher levels of post-treatment opioid use. Additionally, work status will differ with patients reporting lower levels of opioid use having greater employment rates, and patients with higher levels of post-treatment opioid use will be more likely to be receiving SSI or SSDI at post-treatment.
9. Post-treatment level of opioid use will differentiate level of pre-treatment depressive symptoms, such that those reporting higher levels of post-treatment opioid use will demonstrate higher pre-treatment scores on the BDI. Post-treatment level of opioid use will differentiate level of post-treatment depressive symptoms, such that those reporting higher levels of post-treatment opioid use will demonstrate higher post-treatment scores on the BDI. Additionally, there will be differences in change scores of self-reported

depressive symptoms, with those taking lower levels of opioids at post-treatment having greater levels of change in BDI scores.

10. Post-treatment level of opioid use will differentiate subjects according to level of pre-treatment patient reported levels of disability, such that those reporting higher levels of post-treatment opioid use will demonstrate less desirable pre-treatment scores on the PDQ, and OSW. Post-treatment level of opioid use will differentiate subjects according to level of post-treatment patient reported levels of disability, such that those reporting higher levels of post-treatment opioid use will demonstrate less desirable post-treatment scores on the PDQ, and OSW. Additionally, there will be differences in change scores of self-reported disability, with those taking lower levels of opioids at post-treatment having greater levels of change in disability.
11. Post-treatment level of opioid use will differentiate subjects according to level of pre-treatment patient reported levels of sleep disturbance, such that those reporting higher levels of post-treatment opioid use will demonstrate less desirable pre-treatment scores on the ISI. Post-treatment level of opioid use will differentiate subjects according to level of post-treatment patient reported levels of sleep disturbance, such that those reporting higher levels of post-treatment opioid use will demonstrate less desirable post-treatment scores on the ISI. Additionally, there will be differences in change scores of self-reported insomnia, with those taking lower levels of opioids at post-treatment having greater levels of change in insomnia.
12. Post-treatment level of opioid use will differentiate subjects according to level of post-treatment additional medication use, such that those reporting higher levels of post-treatment opioid use will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives. Post-treatment level of opioid use will differentiate subjects according to level of pre-treatment additional medication use, such that those reporting higher levels of post-treatment opioid use will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives Better management of muscle tension, depression, and sleep may help attenuate pain and therefore, result in lower opioid use.

13. Post-treatment level of opioid use will predict differences in healthcare use, such that subjects reporting higher levels of post-treatment opioid use will demonstrate higher rates of post-treatment surgery, post-treatment injury, and higher rates of healthcare utilization at one-year follow-up.
14. Post-treatment level of opioid use will show no differences in work-related outcomes. Patients completing the program will have similar rates of work-return and work-retention at one-year post-treatment with minor differences for those completely off opioids having better work-return rates.

4.1.1.4. Study 3: Change in level of opioid use

1. Change level of opioid use will differentiate patients according to area of injury, such that subjects reporting change to no opioid use are more likely to have injuries to extremities than to cervical or lumbar regions.
2. Change in level of opioid use will differ significantly by ethnicity in that Caucasian patients will report lower rates of change to no opioid use.
3. Change in level of opioid use will not differ by age, marital status, or gender.
4. Change in level of opioid use will differ significantly in that subjects reporting change to no opioid use will exhibit lower rates of pre-admission surgery.
5. Change in level of opioid will differ significantly in that subjects reporting continuing opioid use will exhibit greater lengths of disability.
6. Change in level of opioid use will not differentiate subjects based on most occupational variables, including job type, job demand, job satisfaction, work status, or pre-injury wage.
7. Change in level of opioid use will vary significantly based on certain specific occupational variables such as case type, with worker compensation (WC) patients reporting higher rates of change to no opioid use, and patients with continued opioid use will be more likely to be receiving SSI or SSDI.
8. Change in level of opioid use will differentiate pre-treatment depressive symptoms, such that those reporting change to no opioid use will demonstrate lower pre-treatment scores

on the BDI. Change in level of opioid use will differentiate post-treatment depressive symptoms, such that those reporting change to no opioid use will demonstrate lower post-treatment scores on the BDI. Change in level of opioid use will differentiate level of change in depressive symptoms, such that those reporting change to no opioid use will demonstrate greater decrease in scores on the BDI.

9. Change in level of opioid use will differentiate subjects according to level of pre-treatment reported levels of disability, such that those reporting a change to no opioid use will demonstrate more desirable pre-treatment scores on the PDQ, and OSW. Change in level of opioid use will differentiate subjects according to level of post-treatment reported levels of disability, such that those reporting a change to no opioid use will demonstrate more desirable post-treatment scores on the PDQ, and OSW. Change in level of opioid use will differentiate subjects according to level of change in patient reported levels of disability, such that those reporting increased or continued opioid use will demonstrate less desirable change in scores on the PDQ and OSW.
10. Change in level of opioid use will differentiate subjects according to level of pre-treatment patient reported levels of sleep disturbance, such that those reporting increased or continued opioid use will demonstrate less desirable pre-treatment scores on the ISI. Change in level of opioid use will differentiate subjects according to level of post-treatment sleep disturbance, such that those reporting a change increasing or continuing opioid use will demonstrate less desirable post-treatment scores on the ISI. Change in level of opioid use will differentiate subjects according to level of change in patient reported levels of sleep disturbance, such that those increased or continued opioid use will demonstrate less desirable change in scores on the ISI.
11. Change in level of opioid use will differentiate subjects according to level of pre-treatment additional medication use, such that those reporting increased or continued opioid use will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives upon admission. Change in level of opioid use will differentiate subjects according to level of post-treatment additional medication use, such that those reporting increased or

continued opioid use will demonstrate higher rates of using antidepressants, neuromodulators, and sedatives at discharge.

12. Change in level of opioid use will predict differences in healthcare use, such that subjects reporting increased or continued opioid use will demonstrate higher rates of post-treatment surgery, post-treatment injury, and higher rates of healthcare utilization at one-year follow-up.
13. Change in level of opioid use will not predict any differences in work-related outcomes. Patients who demonstrate a change increasing opioid use may exhibit slightly lower rates of work-return and work-retention at one-year post-treatment.

Chapter 5

Methods

5.1 Participants

The study will consist of a consecutive cohort of 1601 patients presenting with chronic disabling occupational musculoskeletal disorders (CDOMD). These patients consented to and started treatment at a functional restoration treatment facility. Patients referred to a regional interdisciplinary functional restoration program (FRP) consented to the collection of information for treatment management and clinical research purposes. Information collected was part of the standard medical record, thus, the study was granted an exemption from review by the Institutional Review Board (IRB). Patients were eligible for treatment if a minimum of 4 months had passed between the date of injury and treatment; if their primary or secondary treatments were previously unsuccessful; if they were suffering from severe pain and functional limitations; and if they had the ability to communicate in either English or Spanish. Patients signed a Health Insurance Portability and Accountability Act (HIPAA) authorization before entering the program. Patients were not offered payment or reward for participation in this study, other than the benefit from various aspects of the treatment program. The participants in this study were patients who completed, or were otherwise discharged from treatment between January 2009 and September 2014 (N=1601).

5.2 Opioid Use Data

Information regarding average daily dosages of opioid mediation taken at the time of admission was gathered in several ways and from multiple locations in the patients' medical records when necessary. To standardize dosage collection and optimize accuracy, the following procedures were followed. First, information regarding opioid use was gathered from an electronic medical records program in which fields, such as medication use, were queried and downloaded into an electronic database. This information was compared to the information gathered and recorded in a medical chart by staff psychologists during the mental health evaluation (MHE) and subsequently input into a secure electronic record. All opioid medications reported by patients during the initial physician's visit and the MHE were included in the study. If

discrepancies in the dosages occurred, the paper chart was reviewed for possible data entry errors or oversight. If this did not reconcile the discrepancy, the higher reported dose noted in the chart was used for purposes of the study.

Additionally, if a medication was listed in the electronic databases without a dosage, the dosage was gathered from the initial physician's note, the MHE, or the medication record located in the medical chart. If a number of tablets were reported, but not a dose, the lowest available dose was used by default. For example, 4 hydrocodone tablets per day defaulted to four 5 mg tablets per day, which yielded an average daily dose of 20 mg per day. If a range of tablets was listed, the midpoint of this range was considered for purposes of the study. If patients reported taking an opioid medication, but gave no specific information regarding specific daily dose or number of tablets (e.g., "prn", "as needed" or "occasional" use), cases were included in the study. Medication information available from referring providers, the initial intake by the program physician, nurses' notes, and information collected by mental health professionals were reviewed approximate the overall 30 day supply of opioid medication provided. For the purposes of this study, the patients on a very low total daily dose of less than 16mg morphine equivalents were grouped with the PRN group. Again, if no information was available on the strength of the prescribed PRN medication, but number of tablets was accessible, the lowest available dose was used by default for calculation.

Information on other medications (including antidepressants, neuromodulators, and sedatives) was also gathered using the same procedures outlined for opioids. Finally, information on whether or not patients were taking opioids or other medications at the time of discharge was gathered from electronic database or from the front of the medical chart if information could not be located in the electronic medical record.

Once the average daily dose of the specific opioid medications was calculated, this information was converted into equivalent dosages of morphine and used to classify subjects into categories of pre-treatment opioid use. Multiple estimates of conversion factors for calculating morphine equivalence exist and vary slightly, many sources were considered and incorporated into the final numbers used to calculate specific values for this sample (GlobalRPh: The clinician's

ultimate reference 2015; Fisch & Cleeland, 2003; Kishner, Windle, & Schraga, 2014; Vieweg, Lipps, & Fernandez, 2005). Table 5.1 presents equianalgesic doses of various opioid analgesics used in the conversion process.

Table 5.1 Morphine Equivalents

Generic	**Brand Name Examples**	**Schedule**	**Equivalent Dose-mg**
hydrocodone	Lortab, Norco, Vicodin	II	22.5
morphine	Avinza, MS-Contin, Kadian, Oramorph	II	30
oxycodone	Oxycontin, OxyIR / Roxicodone, Percodan, Percocet	II	15
tapentadol	Nucynta	II	100
fentanyl	Duragesic Patch	II	12.5 mcg
fentanyl	Fentora	II	800 mcg
hydromorphone	Dilaudid, Pallaone, Exalgo	II	7.5
levorphanol	Levo-Dromoran	II	2
meperidine	Demerol	II	300
oxymorphone	Opana	II	10
methadone	Dolophine	II	see below*
codeine	Tylenol #3	III	200
pentazocine	Talwin	IV	100
propoxyphene	Darvocet	IV	400
ultram	Tramadol	IV	150
Agonist-Antagonists			
buprenorphine	Suboxone/Subutex	III	8
buprenorphine	Butrans Patch	III	12.5
buprenorphine	Buprenex	III	0.3

***Methadone Conversion Schedule**

Methadone Dose	**Morph:Meth**	
<30 mg	2:1	(2 mg of morphine to 1 mg methodone)
30-99 mg	4:1	
100-299 mg	8:1	
300-499 mg	12:1	
500-1000 mg	15:1	
>1000 mg	20:1	

(Fisch & Cleeland, 2003)

Study 1, examining pre- admission self-reported opioid use, will include the complete consecutive cohort of 1601 patients and will be divided into in two ways. First, levels of use opioid

use will be divided into 5 groups base on total daily milligrams of morphine and categorized as: 1) None; 2) PRN use: 1-15mg; 3) Low: 16-30mg; 4) Moderate 31-60mg; and 5) High >61mg. The second manner in which pre-treatment opioid use will be divided will put specific focus on hydrocodone. This comparison will consist of 4 groups: 1) No Opioids Prescribed; 2) Single prescription for hydrocodone; 3) Single prescription for any other opioid; and 4) Combination of more than one prescription opioid. It is the intent to compare each of the groups across five dimensions: 1) demographic variables; including: program completion, area of injury, race, marital status, gender, age, and pre-admission surgeries; 2) work-related variables including: job type (blue collar or white collar), net salary at time of injury, case type (Worker's Compensation, or other/Private pay), job demand, job satisfaction, work status on admission, SSI or SSDI disability payments upon admission, and length of disability; 3) patient reported psychosocial variables including: Pain Intensity (PI), Beck Depression Inventory (BDI), Pain Disability Questionnaire (PDQ), Oswestry Disability Questionnaire (OSW), Insomnia Severity Index (ISI); 4) additional medication variables will include: antidepressants, neuromodulators, and sedatives; and 5) one-year socioeconomic outcome variables will include: work return, work retention, additional surgeries for original injury, new injuries and healthcare utilization measured by seeking treatment from new healthcare providers.

As shown in Figure 1, Of the 1601 patients, 246 were classified as "Quality of Life" (QL) patients, who entered the functional restoration program for purposes of improving their quality of life, but did not expect nor plan to re-enter the workforce (e.g., patients who had retired). Additionally, 318 patients failed to complete the program prior to finishing the recommended course of treatment and were classified as "non-completers". Patients who failed to complete treatment regimen, "non-completers", and those who were classified as "QL" will be excluded from analyses of the discharge medication data due to incomplete, questionable, or lack of available accurate information regarding opioid use upon discharge from the program.

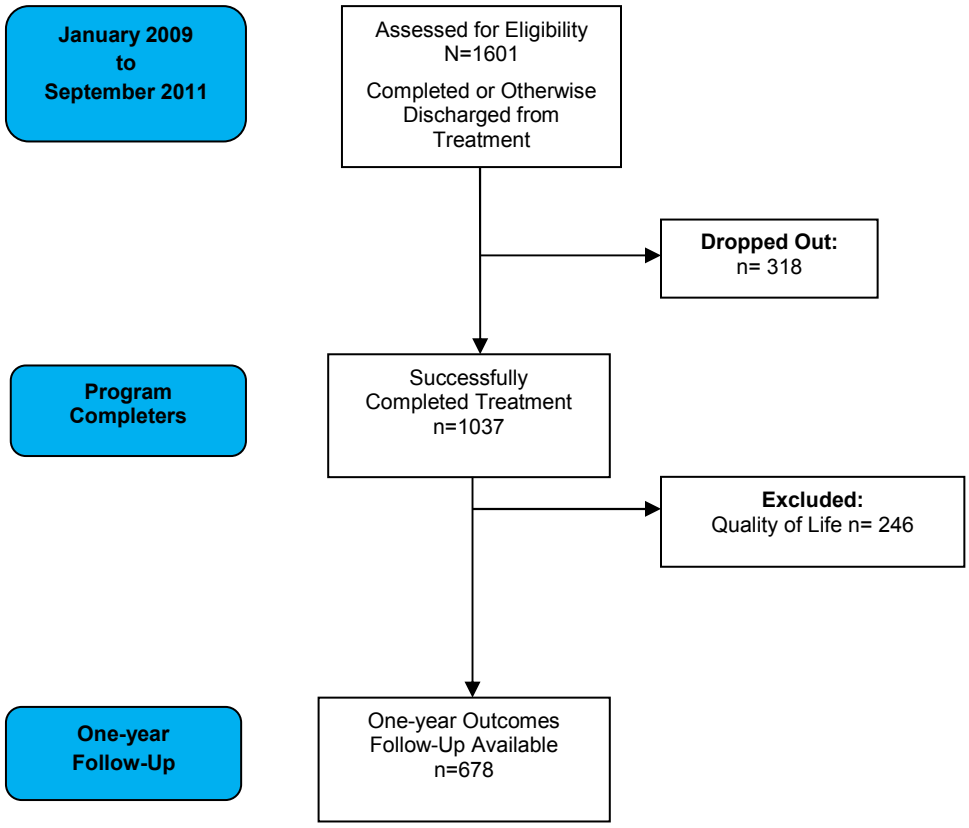

Figure 5.1 Flowchart of patients

A total number of 1037 consecutive patients who successfully completed the program during the previously stated time frame will be included in Study 2 for analyses of opioid use upon discharge. The analyses examining opioid use upon discharge will also be divided into 5 groups based on level of opioid use upon discharge from the program in the same manner as Study 1: 1) None; 2) PRN use: 1-15mg; 3) Low: 16-30mg; 4) Moderate 31-60mg; and 5) High >61mg. This study will include the same variables comparisons across the five dimensions expressed in Study 1.

Study 3 will examine the change in opioid use from pre-admission to discharge and will also exclude “QL” and “non-completers” resulting in a total number of 1037 program completers

that will be analyzed. The 491 patients who successfully completed the program, but did not enter treatment on any opioid medications will be used as a comparison group. Patients who did enter the program on opioids (n=546) will be divided into four groups based on the change in level of opioid use upon discharge: 1) Decrease to No opioids; 2) Decrease to PRN use: 1-15mg; 3) Decrease or stable use of opioids above PRN use; 4) Increase from no pre-treatment opioids to PRN use; and 5) Increase in level of opioids above PRN use. This study will also include the same variables comparisons across the five dimensions expressed in Study 1.

5.3 Procedures

All participants included in this study were chronic pain patients enrolled in a functional restoration program upon referral from a primary care physician or specialist. These participants consented to the collection of information for treatment management and research purposes at the time of admission. A functional restoration program is it an interdisciplinary rehabilitation program which follows a biopsychosocial model is medically supervised, and utilizes a sports medicine approach. Components of the program include individualized exercise programs under the supervision of physical and occupational therapists with additional participation in activities focused on managing various aspects of disability through coping skills training, educational support, counseling and biofeedback. Emphasis is placed on restoring function and reducing disabling symptoms, in addition to adequately managing pain in a manner that promotes independence. Treatment is guided by a physician, with nurses supporting medical issues and facilitating care. Physical therapy, occupational therapy, group stretching, and a multi-modal disability management program, including individual and group counseling using a CBT approach, stress management techniques, biofeedback, educational sessions, and vocational reintegration are all components of this comprehensive program and all providers interact in an interdisciplinary model since all clinicians are housed in the same building and have direct communication with each other. At the initial interview, demographic data are collected and physical and functional capacity measurements performed by appropriate staff members. The psychosocial instruments are administered upon admission to the program and again at discharge. Follow-up interviews are conducted one-year post-treatment.

5.4 Materials and Measures

5.4.1 Medical Case Management Evaluation

Demographic and occupational data were collected by the case management and nursing departments at program admission. Relevant demographic information collected included age, ethnicity, area(s) of injury, gender, education, marital status, and information about pre-admission surgeries. Occupational data included information collected about disability compensation, whether the patient was working at program admission, length of disability (the amount of time that has elapsed from the injury to rehabilitation), the patient's average weekly income, job satisfaction, and job demand, which is whether the job was classified as "blue collar" or "white collar."

5.4.2 Psychosocial Intake Evaluation

After the patient was accepted into the treatment program, he or she underwent an initial Mental Health Evaluation (MHE). Patients completed packets of patient reported outcome (PRO) questionnaires assessing psychosocial measures of pain, perceived disability, depressive symptoms, and insomnia, which were collected at admission and discharge.

5.4.3 Pain Intensity Analog

Patients marked their pain intensity on a 10mm visual analog scale (VAS) line, with the anchor points of "no pain" and "worst possible pain." Pain intensity was scored by measuring the distance from the "no pain" endpoint to the patient's marking. The VAS is usually easily understood and is useful in measuring subjective pain. Psychometric properties have been studied and accepted as a standard for assessing patient's perceived level of pain intensity (Gillian, Mian, Kendzerska, & French, 2011).

5.4.4 The Patient Disability Questionnaire (PDQ)

The PDQ is a measure of functional status and was designed for use in a CDOMD population, rather than just for low back pain populations, as the Oswestry Disability Index is (see below). In addition, the PDQ was designed to understand the biopsychosocial aspects of disability. Sample items included: "Are there emotional problems caused by your pain that interfere with your family, social, or work activities?" and "Does your pain interfere with personal

care (such as bathing, dressing, etc.)?" Responses to 15 items were scored on a 10cm VAS scale, and total scores ranged from zero, indicating optimal functioning, to 150, indicating total disability. The PDQ can be broken up categorically into 3 groupings: Mild/Moderate (0-70), Severe (71-100), and Extreme (101-150). The PDQ can also be broken down into two components: functional status and psychosocial status. The PDQ is responsive to meaningful clinical change, corresponds with psychosocial and socioeconomic outcomes, such as pain anxiety sensitivity (Cella, Bullinger, Scott, & Barofsky, 2002), coping style, insomnia somatization, psychopathology, surgery outcomes and work retention. The PDQ also demonstrates high construct-related validity and reliability.

5.4.5 The Oswestry Disability Index (ODI)

The *ODI* is a self-report scale that evaluates the degree of functional impairment in activities of daily living caused by pain (Fairbanks, Couper, Davies & O'Brien, 1980). This measure is considered to be a legacy measure and has been one of the most frequently studied disability questionnaires (Kirby, Chuang-Stein, & Morris, 2010). The ODI has demonstrated sound psychometric properties including strong validity components such as having good face validity, as well as other aspects of reliability including test-retest reliability of .99 (Kaplan, Wurtele, & Gillis, 1996; Leclaire, Blier, Fortin, & Proulx, 1997). However, it has its limitations as well, including the inability to distinguish low-scoring patients and the narrow focus on only low back pain (Kohn, Sidovar, Kaur, Zhu, & Coleman, 2014). The ODI contains ten sections asking about specific functional limitations resulting from pain. Each section has a series of six possible responses, which describe varying degrees of functional problems. Patients are instructed to mark a single box that most closely describes the patient's functional level within each section. The total maximum score (max 50) is doubled and then expressed as a percentage. Established ranges on the ODI are as follows: minimal disability (0-20%), moderate disability (20-40%), severe disability (40-60%), crippled (60-80%), and bed-bound or exaggerating (80-100%).

5.4.6 The Beck Depression Inventory (BDI)

The Beck Depression Inventory is a 21-item multiple-choice test designed to measure physical and emotional symptoms of depression, and is currently one of the most widely used

measure of depression in both medical and psychological research. It was originally developed by Beck, Ward, Mendelson, Mock and Erbaugh (1961) with the purpose of offering a reliable and valid measure of the presence and/or severity of depression. The BDI consisted of 21 items scaled on a 0-3 point scale, with zero indicating the depressive symptom is not present and three indicating that the symptom is severe. Total scores ranged from 0-63, with cutoff scores are: <10 for absence of depression; 10-18 for mild to moderate depression; 19-29 for moderate to severe depression; and >29 for severe depression (Beck, Steer, & Garbin, 1988). Reliability of the BDI is good, with internal consistency coefficients exceeding .73 in nonpsychiatric samples (Beck et al., 1988). Validity is adequate, with the BDI demonstrating a correlation of .60 with the MMPI Depression Scale in a nonpsychiatric sample, and .73 with the Hamilton Rating Scale for Depression (Beck et al., 1988). Many researchers have demonstrated the validity of the measure with chronic pain patients (Geisser, Roth, & Robinson, 1997; Novy, Nelson, Berry, & Averill, 1995; Romano & Turner, 1985; Turner & Romano, 1984), although some researchers have recommended the removal of several items (Wesley, Gatchel, Garofalo, & Polatin, 1999) and/or modification of depression cutoff scores (Geisser et al.,1997; Wesley et al., 1999) because somatic items were confounded with pain symptomatology (Wesley, Gatchel, Polatin, Kinney, & Mayer, 1991). An updated version, BDI-2, is now available, but the original was used in this study.

5.4.7 Insomnia Severity Index (ISI)

The ISI was designed to measure the severity of both nighttime and daytime insomnia components. It is measured on a 5 point Likert scale from 0 (not at all) to 4 (extremely), and generates a total score range from 0 to 28 (Bastien, VallieÁres, & Morin, 2001). Previously, a 15 point cut-off score for threshold insomnia had been used, but more recently, severity levels have been developed: No Clinically Significant Insomnia (0-7); Sub-threshold Insomnia (8-14); Moderate Clinical Insomnia (15-21); and Severe Clinical Insomnia (22-28) (Morin, Belleville, Bélanger, & Ivers, 2011). The ISI also helps determine between the 3 types of insomnia: Early (difficulty initiating sleep); Middle (difficulty staying asleep); and Late Insomnia (early morning waking). Questions about the types of insomnia are rated from 0 (none) to 4 (very severe), with a

score of 3, indicating a severe disturbance, chosen as a cut-off (Bastien et al., 2001). Patients scoring above 3 on each of the insomnia questions are likely to have that type of insomnia.

5.4.8 The Psychosocial Clinical Interview

The clinical interview, conducted by a qualified clinician, integrated the above PRO measures with a personal patient assessment. The patient was assessed for symptoms of depression, anxiety, stress, and psychiatric disorders (as diagnosed in the DSM-IV) as well as assessed on his or her home and family life and presence of social support. The psychologist also determined patient motivation for recovery, including financial disincentives for return to work, secondary gain issues, and malingering symptoms.

5.4.9 Structured One-Year Follow-Up Interview

Socioeconomically-relevant outcomes were assessed approximately one-year after discharge in a structured interview, either in person or by telephone, in order to determine the extent to which the individual had recovered from the disability phase and returned to more normal daily activities. Outcomes fell into three major domains: work status; additional healthcare utilization; and WC-related issues. Work status was determined as return-to-work (or obtaining new employment) at any time during the year following discharge from treatment; and work retention, which assessed whether the patient was still working at the time of the one-year follow-up interview. Additional healthcare utilization examined new surgery to the original site of injury, seeking healthcare from a new provider, and the associated number of visits to the new provider.

Chapter 6

Statistical Plan

All data, unless otherwise specified, will be analyzed with Statistical Package for the Social Sciences (SPSS) version 20, with the significance level set at $p = .05$.

6.1 Opioid Use and Demographic Variables

Each opioid group will be compared using analyses of variance (ANOVA) on the following: age and length of disability (months). The groups will be compared using Chi-square (χ^2) analyses on the following: program completion status, area of injury, race, marital status, gender, and pre-treatment surgery rate.

6.2 Opioid Use and Work Related Variables

Groups will be compared using analyses of variance (ANOVA) on their average income based on reported pre-injury wages. Opioid groups will be compared using Chi square (χ^2) analyses on the following: job type (blue collar or white collar), case type (Worker's Compensation or private pay/other), job demand, job satisfaction, whether or not the subject is receiving Social Security Disability Insurance (SSDI) or Supplemental Security Income (SSI) when they entered the program.

6.3 Opioid Use and PROs/ Psychosocial Variables

Univariate analyses of variance (ANOVA) will be used to identify differences between opioid use groups for the following pre-treatment variables: Pain Intensity, PDQ, BDI, OSW, and ISI. Likewise, univariate analyses of variance (ANOVA) will be used to identify differences between and among opioid use groups for the following post-treatment variables: Pain Intensity, PDQ, BDI, OSW, ISI. ANCOVAs will be used to measure how patients' opioid PROs change from admission to discharge based on opioid groups, with pre-treatment scores used as covariates.

6.4 Opioid Use and Medication Variables

Opioid use groups will be compared using Chi square (χ^2) analyses on whether or not the patients are using any antidepressant, neuromodulator and/or sedatives. Data will be analyzed for at pre-treatment and post-treatment for all three studies.

6.5 Opioid Use and One-year Socioeconomic Variables

Opioid use groups will be compared using Chi square (χ^2) analyses on the following: one-year treatment outcome variables: work return, work retention, presence of a post-treatment injury to the treated body part, post-treatment surgery to the treated body part and healthcare utilization, based on seeking treatment from new healthcare providers.

6.6 One-year Outcome Prediction

A final analysis will be to determine if discharge opioid use levels can be utilized as a predictor of one-year socioeconomic outcomes, such as return to work and work retention and health-care utilization. In order to test this, hierarchical binary logistic regression analysis will be performed. The first block in the model will contain various known predictors of work return and work retention, including length of disability, whether the patient has had surgery prior to admission, whether the patient was receiving SSi/SSDI benefits at the time of admission to the program and if the patient was working at the time of admission. The second block will contain the morphine equivalent daily dose. In order to assess the addition of each block of variables associated with the outcome variable, a Pearson Chi-Square statistic will be used, and the percentage of variance accounted for in each block will be compared using Nagelkerke's R^2. Lastly, the Wald statistic and its significance will be reported, providing information about whether the medication use remains a useful predictor after all the other variables have been added into the model. Missing data will be dealt with in a pairwise fashion, with patients not included in each analysis if they were missing data for the target variables.

Chapter 7

Results: Study 1 Pre- Admission Opioid Use

7.1. Demographic Variables

In Study 1, a total of 1601 patients were included. As previously noted, subjects in Study 1 were classified into different ways. Study 1a was based on dosage of pre-admission opioids and was divided into 5 groups: 1) None; 2) PRN/Very Low: <16mg; 3) Low: 16-30mg; 4) Moderate: 31-60; 5) High: 61mg or greater. In Study 1b the specific prescriptions were combined into groups and compared as 1) No Opioids Prescribed; 2) Single prescription for hydrocodone; 3) Single prescription for any other opioid; and 4) Combination of more than one prescription opioid. Results based on these group classifications are presented in the text and tables. A variety of demographic variables were evaluated, including: age, gender, ethnicity, marital status, area of injury, length of disability, pre-admission surgeries, program completion and total daily morphine equivalent dose. Statistical significance was set at the .05 level for all analyses performed, unless otherwise specified. Appendix A contains all of the tables describing the statistical comparisons in these studies.

7.1.1. Study 1a: Demographic Variables

Pre-admission demographic characteristics divided by level of opioid use are presented in Table A1. Analyses conducted to identify potential demographic differences between groups revealed no significant differences in age and marital status, which was predicted (hypothesis 5). Also was predicted (hypotheses 1-4), significant differences were found for gender, racial representation, rate of program completion, length of disability, pre-admission surgery, as well as area of injury. Gender differed significantly, χ^2 (4) = 11.54, p = .038, with males being overrepresented in the Moderate dose level (31-60mg). Racial representation varied significantly among the subgroups χ^2 (16) = 67.72, $p \leq .001$. Group representation of Caucasian individuals increased linearly as dosage levels increased, from 12.2% in the PRN subgroup (z=-2.3) to 26.6% in the High subgroup (z=3.7).Conversely, if opioids use was already present upon admission the proportion of Hispanic individuals decreased as dosage level increased, from 37.1% in the None subgroup (z=2.9) to 9.4% in the High subgroup (z=-4.3). Chi-square analysis

conducted for the five opioid subgroups revealed significant differences in the proportion of patients successfully completing the functional restoration program. Specifically, 70.25% of the None subgroup, 76.5% of the PRN subgroup (z=2.2), 71.4% of the Low subgroup, 58.2% of the Moderate subgroup, and 46.5% in the High subgroup (z=-3.9) completed the program. Only 13.6% of program completers were in the High does group, while 37% of patients completing the FRP represented in the No opioid use group. Pre-admission surgery rates also differed significantly between groups using chi-square analysis χ^2 (4) = 47.43, p ≤ .001. The proportion of patients who had undergone pre-treatment surgery differed significantly by subgroup with 24.6% of patients having had surgery prior to treatment in the High subgroup (z=3.9) and only 12.27% in the PRN/Very Low subgroup. Chi-square analysis of opioid subgroups revealed significant differences in the proportion of patients based on the specific area of injury χ^2 (20) = 69.52, p ≤ .001. Group representation by individuals with lumbar only injuries increased following a linear trend, with lower than expected proportions of lumbar injured patients in the None subgroup (z=-4.4), and 25.1% (z=3.0) in the High subgroup. Analysis of variance revealed significant differences in the subgroups based on length of disability, *F* (4) = 29.38, p ≤ .001. Post hoc analysis revealed that the None subgroup (M= 21.56), the PRN subgroup (M= 20.53), the Low subgroup (M= 28.35), and the Moderate subgroup (M= 30.95), all differed significantly from the High subgroup (M= 54.90).

7.1.2. Study 1b: Demographic Variables

Pre-admission demographic characteristics based on groups divided by specific use of hydrocodone are presented in Table A2. Analyses conducted to determine demographic differences between groups revealed no significant differences in age. Significant differences were found for gender, racial representation, marital status, rate of program completion, length of disability, pre-admission surgery, as well as area of injury. Gender differed significantly, χ^2 (4) = 13.91, *p* = .003, with the proportion of males being the greatest in the Hydrocodone only group, and proportionally lower then would be expected in the Combination opioid use group . Racial representation varied significantly among the subgroups χ^2 (16) = 36.95, *p* ≤ .001. Group representation of Caucasians were relatively equally distributed across groups, while proportions

of African Americans in the Other single opioid group were lower than expected (z=-2.6), and proportion of Hispanic individuals were significantly greater in the No opioid group (z=2.9). Chi-square analysis conducted for the four opioid type subgroups revealed significant differences in the proportion of patients successfully completing the functional restoration program. Specifically, differences were found between groups of program completers with a significantly lower proportion of patients completing the program if in the Combination opioid use group (z=-2.3). Pre-admission surgery rates also differed significantly between groups using chi-square analysis χ^2 (4) = 12.60, p = .006. The proportion of patients who had undergone pre-treatment surgery differed significantly by subgroup with somewhat higher proportion of patients undergoing surgery in the Other single opioid subgroup (z=1.4) and Combination opioid use subgroup (z=1.4). Additionally, Chi-square analysis of opioid subgroups revealed significant differences in the proportion of patients based on the specific area of injury χ^2 (20) = 71.85, $p \leq .001$. Group representation by individuals with lumbar only injuries was greatest in the Hydrocodone only group (z=3.7). Analysis of variance revealed significant differences in the subgroups based on length of disability, F (4) = 16.17, $p \leq .001$. Post hoc analysis revealed that the No opioid subgroup (M= 21.58), differed significantly from all other subgroups, and the Hydrocodone only subgroup (M= 29.55), differed from the Other single opioid subgroup (M= 39.54), and the Combination opioid use subgroup (M= 46.83). Marital status also revealed differences between subgroups with the greatest difference represented by a proportionally lower representation of individuals who were widowed in the No opioid subgroup (z=-2.0).

7.2. Occupational Variables

The sample was also evaluated on pre-treatment work related or occupational variables associated with pre-injury and pre-treatment. These occupational variables included: case type (workers' compensation rate); whether or not the subject is receiving Social Security Disability Insurance (SSDI) or Supplemental Security Income (SSI) at the time they entered the program; weekly net salary at time of injury; pre- injury job satisfaction, job type (i.e. white collar or blue collar); job demand; and whether or not the individual was working at the time they were admitted to the program.

7.2.1. Study 1a - Occupational Variables

Occupational variables for the five opioid subgroups are presented in table A3. As predicted in hypothesis 8, the subgroups did not show significant differences in pre-injury wage, job demand, or pre-injury job satisfaction. However, study 1a hypothesis 8 predicted that job type would not differ significantly among groups, but results revealed significant findings. Job type, characterized as blue-collar, varied significantly between subgroups χ^2 (8) = 13.37, p = .010, showing lower proportions of blue-collar workers on low levels of opioids (z=-2.6). Additionally, work status at admission, case type, and SSDI/SSI benefits on admission differed significantly among the subgroups, as predicted (hypothesis 9). Chi-square analysis revealed significant differences in the proportions of patients who were working at the time they entered the program χ^2 *(4)* = 15.67, p = .003. Revealing greater proportions of patients working at the time of admission being on a PRN dose of opioids (z=2.0), and substantially lower representation of working patients in the high subgroup. (z=-2.9). Additionally, Chi-square analysis revealed significant differences in the proportion of patients who entered the program by means other than a worker's compensation claim χ^2 (8) = 32.12, $p \leq .001$. Non-Worker's Compensation patients were proportionately higher in the None subgroup (z=3.1), and lower in both the PRN (z=-2.5) and Low subgroups (z=-3.1). Chi-square analysis also revealed significant differences between subgroups based on whether or not they were receiving SSDI/SSI benefits upon admission χ^2 (5) = 48.28, $p \leq .001$. Specifically, higher proportions of subjects receiving SSDI/SSI benefits were in the High subgroup (z=5.8) and lower proportions of patients receiving SSDI were represented in the PRN subgroup (z=-2.7).

7.2.2. Study 1b - Occupational Variables

Occupational variables for the four subgroups based on hydrocodone use are presented in table A4. The subgroups did not show significant differences in pre-injury job satisfaction, as expected (4.1.1.2 hypothesis 8) or whether or not subjects were working on admission. This finding is unlike what was hypothesized for study 1b 4.1.1.2 hypothesis 9, specifically, that pre-treatment use of hydrocodone would vary significantly based on work status on admission. However, significant differences were found between subgroups based on job type, which was

not expected in hypothesis 8. Chi-square analysis revealed significant differences in the proportions of patients who were classified as blue-collar, χ^2 (3) = 10.20, p = .017. Indicating a greater than expected proportion of white collar workers being represented in the Combination opioid use subgroup (z=1.8). Hypothesis 8 was not supported with respect to the prediction of pre-injury wage. Hypothesis 9 was confirmed in that case type, and SSDI/SSI benefits on admission varied significantly with higher proportions of patients in the combination use group reporting greater rates of SSDI benefits. Chi-square analysis revealed significant differences between Hydrocodone use subgroups in the proportion of patients who entered the program by means other than a worker's compensation claim χ^2 (3) = 38.98, $p \leq .001$. Specifically, private pay, or non-Worker's Compensation patients were proportionately lower in the Hydrocodone only subgroup (z=-3.8), and overrepresented in the No opioid subgroup (z=-3.2). Chi-square analysis also revealed significant differences between subgroups based on whether or not subjects were receiving SSDI/SSI benefits upon admission χ^2 (3) = 21.31, $p \leq .001$. A higher proportion of subjects receiving SSDI/SSI benefits were in the Combination opioid use subgroup (z=4.0).

7.3. Patient Reported Psychosocial Variables

The following section presents analysis of various pre- treatment and post-treatment patient self- reported psychosocial variables, including pain intensity, BDI, PDQ, Oswestry, and ISI. The pain intensity, depression, disability, and sleep measures were administered to all patients prior to, and upon completion of, the functional restoration program. Due to the fact that post-treatment measures were not always able to be gathered from subjects who did not complete the program, the post-treatment sample is smaller than the pre-treatment sample. Once again, comparisons among the five opioid level subgroups and comparisons between specific hydrocodone use subgroups will be presented. As expected, there were differences found with respect to the demographic variables as possible factors associated with level of opioid use. Because the differences in gender rate of completion, length of disability, pre-treatment, surgery, area of injury and ethnicity were significant, the subsequent analyses controlled for the variance attributed to those variables.

7.3.1. Study 1a - Patient reported pre-admission psychosocial variables by pre-admission opioid level

Pre-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA and ANCOVA to explore group differences based on level of opioid use. Results are displayed in table A5-A7.

The comparisons of the psychosocial variables based on level of pre-treatment opioid use revealed significant differences across all subgroups, as predicted, (4.1.1.1, hypotheses 10-12). Pre-treatment pain intensity scores differed significantly among the five opioid subgroups $F(4) = 8.86$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=6.60) and PRN subgroup (M=6.72); compared to the Low (M=7.62), Moderate (M=7.54), and High (M=7.70) subgroups. On the Beck Depression Inventory which measures depressive symptoms, as predicted by hypothesis 10, pre-treatment BDI scores differed significantly among the five opioid subgroups $F(4) = 11.32$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=16.93) compared to the Low (M=18.58), Moderate (M=19.18), and High (M=22.63) subgroups with the PRN subgroup (M=16.69) displaying similar results as the None group. As anticipated (hypothesis 11), perceived disability, as measured by the Pain Disability Questionnaire and the Oswestry disability Index were found to be significantly different between subgroups of pre-treatment opioid use. Pre-treatment PDQ scores differed significantly among the five groups $F(4) = 39.96$, $p \leq .001$. Again, Post hoc analysis showed significant differences between the None subgroup (M=89.28) compared to the Low (M=103.76), Moderate (M=105.84), and High (M=110.70) subgroups with the PRN subgroup (M=89.79), displaying similar results as the None group. Pre-treatment Oswestry scores differed significantly among the five subgroups $F(4) = 19.54$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=36.31) compared to the Low (M=43.65), Moderate (M=43.47), and High (M=50.25) subgroups with the PRN subgroup (M=37.37), displaying similar results as the None group. Additionally, as predicted (hypothesis 12), a measure of the insomnia, pre-treatment ISI scores differed significantly among all five opioid subgroups $F(4) = 6.96$, $p \leq .001$. Again, following Post hoc analysis showed significant differences

between the None subgroup (M=15.64) compared to the Low (M=18.42), Moderate (M=18.17), and High (M=19.70) subgroups with the PRN subgroup (M=16.97), displaying similar results as the None group.

7.3.2. Patient reported post-treatment psychosocial variables by pre-admission opioid level

Self-reported psychosocial factors post-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA to explore group differences based on level of opioid use. Post-treatment pain intensity scores differed significantly among the five opioid subgroups $F(4) = 6.02$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=4.72) and PRN subgroup (M=4.73); compared to the Low (M=5.31), Moderate (M=5.56), and High (M=6.05) subgroups. Results are displayed in table A6. As anticipated, (hypotheses 10), results revealed post-treatment BDI scores differed significantly among the five opioid subgroups $F(4) = 7.23$, $p \leq .001$. Post hoc analysis showed significant differences between the None (M=10.51), PRN (M=10.25), Low (M=7.62), and Moderate subgroups (M=13.18), compared to High (M=16.13) subgroup. Hypotheses 11 was confirmed by findings indicating post-treatment PDQ scores differed significantly among the five groups $F(4) = 9.47$, $p \leq .001$. Again, post hoc analysis revealed significant differences between the None (M=62.04) and PRN (M=62.47) subgroups and all other subgroups. Low (M=73.33), Moderate (M=75.65), and High (M=83.53) subgroups with PRN displaying similar results as the None group. Again, hypothesis 11 was confirmed with post-treatment Oswestry scores differing significantly among the five subgroups $F(4) = 8.49$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=23.83) and PRN subgroup (M=25.65); compared to the Low (M=29.17), Moderate (M=31.13), and High (M=36.86) subgroups, demonstrating a linear trend increasing in self-reported levels of disability as level of opioid dosage increased. Hypothesis 12 was confirmed as indicated by post-treatment ISI scores differing significantly among the five opioid subgroups $F(4) = 6.34$, $p \leq .001$. Again following Post hoc analysis showed significant differences between the None subgroup (M=10.72) and PRN subgroup (M=11.83); compared to the Low (M=12.62), Moderate (M=13.73), and High (M=15.12) subgroups.

7.3.3. Change scores in patient reported psychosocial variables by pre-admission opioid level

Change in pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANCOVA to explore group differences based on level of opioid use, with pre-treatment scores used as a covariate after pre- to post- change score was calculated, Results are displayed in table A7.

Change in pain intensity scores differed significantly among the five opioid subgroups $F(4) = 4.77$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=2.23) and PRN subgroup (M=2.27); compared to the High (M=1.48) subgroup. Contrary to hypothesis 10, change in depressive symptoms, self-reported disability, or insomnia did not differ significantly among the five opioid subgroups.

7.3.4. Patient reported pre-admission psychosocial variables by pre-admission hydrocodone use

Pre-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA to explore group differences based on level of opioid use. Results are displayed in table A8.

Pre-treatment pain intensity scores differed significantly among the four specific opioid subgroups $F(3) = 7.43$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid subgroup (M=6.61) compared to the Hydrocodone only (M=7.53); Other single opioid (M=7.21), and Combination (M=7.61) subgroups. As predicted, (4.1.1.2 hypothesis 10) Pre-treatment BDI scores differed significantly among the four opioid subgroups. $F(3) = 5.50$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid subgroup (M=16.90) and the Other single opioid (M=20.44) and Combination (M=20.62) subgroups. Pre-treatment PDQ scores differed significantly among the four groups $F(3) = 29.02$, $p \leq .001$. Again, post hoc analysis showed significant differences between the No opioid subgroup (M=89.23) and the Combination (M=110.94) subgroup. Hypothesis 11 was confirmed with findings revealing pre-treatment Oswestry scores to differ significantly among the four subgroups $F(3) = 17.51$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid subgroup (M=36.26) and the Combination (M=50.76) subgroup. As predicted (hypothesis 12), pre-treatment ISI scores differed significantly among the four opioid subgroups $F(3) = 8.10$, $p \leq .001$. Post hoc analysis

showed significant differences between the No opioid subgroup (M=15.64) and PRN subgroup (M=6.72); compared to the Combination (M=20.07) subgroup.

7.3.5. Patient reported post-treatment psychosocial variables by pre-admission hydrocodone use

Post-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA to explore group differences based on level of opioid use. Results are displayed in table A9.

Post-treatment pain intensity scores differed significantly among the five opioid subgroups $F(3) = 4.50$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid subgroup (M=4.73) compared to Combination (M=6.08) subgroup. As predicted (hypothesis 10), post-treatment BDI scores differed significantly among the four opioid subgroups. $F(3) = 3.63$, $p \leq .001$ Post hoc analysis showed significant differences between the No opioid subgroup (M=10.48) compared to the Other single opioid (M=14.11) and Combination (M=14.18) subgroups. As expected (hypothesis 11) post-treatment PDQ scores differed significantly among the four groups $F(3) = 9.33$, $p \leq .001$. Again, Post hoc analysis showed significant differences between the No opioid subgroup (M=61.97) compared to Combination (M=86.12) subgroup. As expected, (hypothesis 11), post-treatment Oswestry scores differed significantly among the four subgroups $F(3) = 11.73$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid subgroup (M=23.77) compared to the Combination (M=38.64) subgroup. AS predicited (hypothesis 12), post-treatment ISI scores differed significantly among all four opioid subgroups $F(3) = 5.08$, $p \leq .001$. Again, following post hoc analysis showed significant differences between the No opioid subgroup (M=10.77) compared to the Combination (M=15.10) subgroup.

7.3.6 Change scores of patient reported psychosocial variables by pre-admission hydrocodone use

Change in pain intensity scores differed significantly among the four opioid subgroups $F(3) = 7.43$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid subgroup (M=2.33) compared to the Combination (M=1.01) subgroup, with the patients in the Combination group showing significantly less change in pain intensity following program

completion. Contrary to what was hypothesized, change in depressive symptoms as measured by the change in BDI scores did not differ significantly among the four opioid subgroups, not did change in PDQ after bonferroni correction was applied. However, change in self-reported disability as measured Oswestry did differ significantly among the four subgroups $F(3) = 4.33$, $p \leq .001$, as expected in hypothesis 11. Post hoc analysis of the change in Oswestry scores showed significant differences between the No opioid subgroup (M=12.31) compared to the Other single opioid (M=10.27) subgroup. Change in ISI scores did not differ significantly among the four opioid subgroups.

7.4. Medication Variables

Additional medication variables were examined using a chi-square analysis to distinguish group differences in the presence of any prescription for antidepressants, neuromodulators, and/or sedatives. Data regarding the presence or absence of additional prescription for specific types of medications were gathered at both pre- and post treatment as presented in Table A11-A12.

7.4.1. Study 1a Medication variables at pre-admission

As expected, (4.1.1.1 hypothesis 13), pre-treatment use of antidepressant medications varied significantly between opioid subgroups $\chi^2(4) = 80.42$, $p \leq .001$. Significant differences between the proportion of patients taking antidepressant medications increased as the level of opioid dose increased, with the None subgroup (40.2%; z= -4.2) compared to the Moderate (62.3%; z= 2.0), and High (69.3%; z=3.8) subgroups. As anticipated, (hypothesis 13), Pre-treatment use of neuromodulators also varied significantly between opioid subgroups $\chi^2(4) = 55.49$, $p \leq .001$. Standard residuals revealed significant differences between the None subgroup (33.6%; z=-3.5); compared to the Moderate (52.0%; z=2.1), and High (57.4%; z=3.6) subgroups. Finally, as anticipated, (hypothesis 13), pre-treatment use of sedative medications varied significantly between opioid subgroups $\chi^2(4) = 152.86$ $p \leq .001$, with significant differences apparent between the None subgroup (39.9%; z=-5.9) compared to the Moderate (71.4%; z=2.7), and High (78.5%; z=4.4) subgroups.

7.4.2. Study 1a Medication Variables at post-treatment

As anticipated, (hypothesis 13), post-treatment use of antidepressant medications varied significantly between opioid subgroups χ^2 *(4)* = 39.43*,* p ≤ *.001*. Differences between the subgroups were seen with the None subgroup (44.8%; z=-3.4) compared to the Low (63.5%), Moderate (62.3%), and High (69.3%) subgroups with a linear trend as opioid doses increased. As expected, (hypothesis 13), post -treatment use of neuromodulators also varied significantly between opioid subgroups χ^2 *(4)* = 17.64*,* p ≤ *.001*. Significant differences between subgroups were found when comparing the None (33.6%; z=-2.5) and PRN subgroups (38.9%); to the Moderate (52.0%), and High (57.4%; z=2.8) subgroups. Finally, As anticipated, (hypothesis 13), post-treatment use of sedative medications varied significantly between opioid subgroups χ^2 *(4)* = 74.72 p ≤ *.001*, with significant differences between the None subgroup (39.9%; z=-4.8) compared to High (78.5%; z=2.3) subgroup.

7.4.3. Study 1b Medication Variables at pre-treatment

As anticipated, (hypothesis 13), pre-treatment use of antidepressant medications varied significantly between opioid subgroups χ^2*(3)* = 77.15*,* p ≤ *.001*. Significant differences between the proportion of patients taking antidepressant medications in the No opioid subgroup (40.1%; z= -4.2) compared to the Other single opioid subgroup (63.5%; z= 2.6), and the Combination (74.8%; z= 3.3), subgroup. As anticipated, (hypothesis 13), pre-treatment use of neuromodulators also varied significantly between opioid subgroups χ^2 *(3)* = 41.66*,* p ≤ *.001*. Standard residuals revealed significant differences between the No opioid subgroup (33.7%; z= -3.5) and the Combination (60.0%; z= 2.9), subgroup. Finally, as expected, (hypothesis 13), pre-treatment use of sedative medications varied significantly between opioid subgroups χ^2 *(3)* = 137.21 p ≤ *.001*, with significant differences apparent between the No opioid subgroup (39.7%; z= -5.9) compared to the Other single opioid subgroup (72.6%; z= 3.3), and the Combination (77.2%; z= 2.7), subgroup.

7.4.4. Study 1b Medication Variables at post-treatment

As anticipated, (hypothesis 13), post-treatment use of antidepressant medications varied significantly between opioid subgroups χ^2 *(3)* = 39.85*,* p ≤ *.001*. Differences between the

subgroups were seen with the No opioid subgroup (44.7%; z= -3.4) compared to the Other single opioid subgroup (63.0%; z= 1.9). As expected, (hypothesis 13), post -treatment use of neuromodulators also varied significantly between opioid subgroups χ^2 *(3)* = 15.47*,* p ≤ *.001*. Significant differences between subgroups were found to be driven by the No opioids subgroup (28.0%; z=-2.5. Finally, as anticipated, (hypothesis 13), post-treatment use of sedative medications varied significantly between opioid subgroups χ^2 *(3)* = 71.45 p ≤ *.001*. Standard residuals revealed significant differences in the No opioid subgroup (36.1%; z= -4.8) the Hydrocodone only subgroup (56.5%; z= 2.0), and the Other single opioid subgroup (59.3%; z= 2.3).

7.5. Socioeconomic One Year Outcome Variables

The following section presents the results of analysis of socioeconomic one year outcome data collected at one year post program. These long-term outcome data are associated with program completion, thus, group sizes are smaller than those presented in pretreatment due to missing data on some patients lost to follow-up if they were unavailable and unable to be contacted. Multiple attempts were made to contact all patients regardless of completion status and additional information such as healthcare utilization was obtained from additional sources whenever possible. Additionally, some patients in the current cohort had not yet reached the one-year date following completion, at the time the data were analyzed and therefore were excluded from analysis. Chi-square analyses were conducted to detect differences and socioeconomic outcomes as a function of pre-treatment opioid level use. Results of logistic regression analysis are presented at the end of the section.

7.5.1 Study 1a Socioeconomic One Year Outcome Variables

The one-year socioeconomic variable comparison results are depicted in Table A15. Of those patients whose outcome data were available, contrary to hypothesis 14 and 15, no significant differences were found when examining group differences in work return, work retention, new injuries or new surgeries to the original injury site. However, one aspect of hypothesis 14 was confirmed, in that there were significant differences found in the measure of healthcare utilization as whether or not a patient had sought treatment from a new provider in the

year following treatment completion χ^2 *(4)* = 36.14 *p* > *.001*, with 34.6% (z=4.6) of patients seeking treatment from a new provider at one-year in the high opioid dose subgroup, and substantially smaller proportion of patients in the None (19.2%; z=-2.3) and PRN/ Very Low (7.7%; z=-2.1) subgroups.

7.5.2 Study 1b Socioeconomic One Year Outcome Variables

The one-year socioeconomic variable comparison results are depicted in Table A16. Of those patients whose outcome data were available, overall, 87.6% of the patients who completed the program successfully returned to work by one-year following treatment. However, contrary to hypothesis 15 (4.1.1.2), no significant differences among subgroups for work return or work retention were found. No significant differences were found when examining group differences for new injuries, or new surgeries to the original injury site, which was not anticipated in hypothesis 14. However, as expected (hypothesis 14), treatment seeking from a new provider was found to vary significantly among groups with greater than expected proportions of patients seeking treatment from a new provider represented in the Combination subgroup (26.9 %; z=6.5) and fewer than expected in the No opioids subgroup (19.2%; z=-2.2) driving the statistical significance χ^2 *(3)* = 54.06 *p* > *.001.*

The binary logistic analysis for prediction of work return, work retention and healthcare utilization was undertaken, as shown in Tables A17 - A19. Binary logistic regression analyses were conducted to evaluate the prediction of one-year socioeconomic outcomes from pre-treatment level of opioid use calculated as a continuous variable of total daily morphine equivalent (ME) dose in milligrams (mg). Previously known factors influencing work return rates (length of disability, working on admission, SSDI benefits, and pre-treatment surgery) were entered into the model. Results demonstrated that pre-treatment level of opioid use is a significant factor in predicting work return and work retention in this model. Factors in this regression model, including pre-treatment opioid use, accounted and for 7.3% of the variance in work return. The overall classification rate for the binary logistic regression model was 87.1%, with 98.9% sensitivity and 6.3% specificity. (χ^2 [5] = 24.913, p < .001, R2 = .073). The same factors were entered into a model for predicting work retention. Results demonstrated that pre-

treatment level of opioid use is a significant factor in predicting work retention as well. Factors in this regression model, including pre-treatment opioid use, accounted for 5.5% of the variance in work retention. The overall classification rate for the binary logistic regression model was 77.4%, with 98.3% sensitivity and 5.1% specificity. (χ^2 [5] = 22.789, p < .001, R2 = .055). This model was slightly less predictive of work retention, possibly indicating that retaining work is less associated with higher opioid use. Finally, pre-treatment opioid level and the other factors were entered into a predictive model for treatment seeking at one year post treatment predicted whether patients had sought treatment from a new provider during the year following program completion (χ^2 (5) = 12.832, p < .001, R2 = .080. The overall classification rate for the model was not great, but the only significant predictor was pre-treatment opioid use 66.3%, with 55.7% sensitivity and 67.5%, with 8.0% of the variance being accounted for by factors in this model.

Chapter 8

Results: Study 2 – Post-Treatment Opioid Levels

In Study 2, a total of 1037 patients who completed the program were included. Study 2 was based on dosage of post-treatment opioid use and was divided into 5 groups: 1) None; 2) PRN: 1-15mg; 3) Low: 16-30mg; 4) Moderate: 31-60; 5) High: 61mg or greater. A variety of demographic variables were evaluated, including: age, gender, ethnicity, marital status, area of injury, length of disability, pre-admission surgeries. Statistical significance was set at the .05 level for all analyses performed, unless otherwise specified.

8.1 Demographic Variables

Post-treatment demographic characteristics divided by level of opioid use are presented in Table A20. As expected, (4.1.1.3, hypothesis 4) analyses conducted to determine demographic differences between groups revealed no significant differences in age; however, expected differences in gender were not found as anticipated in hypothesis 3. Significant differences were found for marital status, racial representation, length of disability, pre-admission surgery, as well as area of injury. Contrary to hypothesis 3, marital status differed significantly, χ^2 (20) = 31.79, p = .046, with the Low dose (16-30mg) group varying in lower proportions of people who are separated (z=2.0), simply because there were zero who happened to fall into that already small group. As expected, (hypothesis 2), racial representation varied significantly among the subgroups χ^2 (16) = 74.25, p ≤ .001. Group representation of Caucasian individuals increased linearly as dosage levels increased, with the exception of the High subgroup (85.7%) being slightly lower in proportion of Caucasian patients than the Moderate (91.4%). Conversely, the proportion of Hispanic individuals decreased as dosage level increased, from 28.7% in the PRN subgroup to 2.9% in the Moderate and High subgroups. As expected, (hypothesis 5), Chi-square analysis conducted for the five opioid subgroups revealed significant differences in the proportion of patients who had pre-admission surgery χ^2 (3) = 36.67, p ≤ .001. The proportion of patients who had undergone pre-treatment surgery differed significantly by subgroup with 83.3% in the High subgroup (z=2.6), 84.2% in the Moderate subgroup (z=2.8) and only 44.75% in the PRN subgroup. Chi-square analysis of post-treatment opioid subgroups revealed significant

differences in the proportion of patients based on the specific area of injury χ^2 (20) = 31.40, p ≤ .001. As expected, (hypothesis 1), group representation by individuals with lumbar only injuries varied with 22.4% in the None subgroup (z=-1.9) and 35.3% (z=3.0) in the PRN subgroup. As expected, (hypothesis 6), analysis of variance revealed significant differences in the subgroups based on length of disability, *F* (4) = 8.63, p ≤ .001. Post hoc analysis revealed that the None subgroup (M= 15.68), the PRN subgroup (M= 21.25), differed significantly from the High subgroup (M= 41.03).

8.2 Occupational Variables

Occupational variables for the five opioid subgroups are presented in Table A21. The subgroups did not show significant differences in pre-injury wage, job type, work status at admission, or pre-injury job satisfaction. Job demand, case type, and SSDI/SSI benefits on admission differed significantly among the post-treatment level of opioid subgroups. Chi-square analysis revealed significant differences in the proportion of patients who entered the program by means other than a worker's compensation claim χ^2 (8) = 38.98, $p \leq .001$, which was anticipated in hypothesis 8. Non-Worker's Compensation patients were proportionately lower in the PRN subgroup (z=-3.9), and higher in both the Moderate (z=3.2) and High subgroups (z=2.5). Unlike analyses of pre-treatment level of opioid use, post-treatment opioid use revealed differences significant differences in job demand χ^2 (20) = 42.40, $p \leq .001$, contrary to hypothesis 7. Standard residuals indicate that the significance was derived from the PRN subgroup containing proportionally lower subjects with "light" jobs (z=-2.3), subjects in the Moderate opioid level use at post-treatment with higher rates of "heavy" jobs (z=3.1), and the High subgroups containing higher rates of "sedentary" jobs (z=2.3), and lower rates of "medium" jobs (z=-2.0). As expected, (hypothesis 8), chi-square analysis also revealed significant differences between subgroups based on whether or not they were receiving SSDI/SSI benefits upon admission χ^2 (5) = 33.61, $p \leq .001$. Specifically, higher proportions of subjects receiving SSDI/SSI benefits were in the Low (z= 2.4) Moderate (z=2.1) and High subgroups (z=4.3).

8.3 Patient reported psychosocial Variables

The following section presents analysis of various pre- treatment and post-treatment patient self- reported psychosocial variables, including pain intensity, BDI, PDQ, Oswestry, and ISI. The pain intensity, depression, disability, and sleep measures were administered to all patients prior to, and upon completion of, the functional restoration program. Due to the fact that post-treatment measures were not always able to be gathered from subjects who did not complete the program, the post-treatment sample is smaller than the pre-treatment sample. Once again, comparisons among the five post-treatment opioid level subgroups are presented. The differences found with respect to the demographic variables as possible factors associated with level of opioid use. Because the differences in gender rate of completion, length of disability, pre-treatment, surgery, area of injury and ethnicity were significant, the subsequent analyses controlled for the variance attributed to those variables.

8.3.1. Patient reported pre-admission psychosocial variables at post-treatment opioid levels

Pre-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA and ANCOVA to explore group differences based on level of opioid use. Results are displayed in table A22- A24. As expected, (hypotheses 9-11), comparisons of the psychosocial variables based on level of post-treatment opioid use revealed significant differences across the subgroups. Pre-treatment pain intensity scores differed significantly among the five opioid subgroups $F(4) = 3.01$, $p = .006$. Post hoc analysis showed significant differences between the None subgroup (M=6.58) and PRN subgroup (M=7.41). As expected, (hypothesis 9), On the beck depression inventory which measures depressive symptoms, pre-treatment BDI scores differed significantly among the five opioid subgroups $F(4) = 6.19$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=16.35) compared to the High (M=23.72) subgroup. As expected, (hypothesis 10), perceived disability, as measured by the Pain Disability Questionnaire and the Oswestry disability Index were found to be significantly different between subgroups of post-treatment opioid use. Pre-treatment PDQ scores differed significantly among the five groups $F(4) = 12.42$, $p \leq .001$. Again, Post hoc analysis showed significant differences between the None subgroup (M=88.64)

compared to the PRN (M=99.38), Low (M=102.13), and High (M=103.86) subgroups. Pre-treatment Oswestry scores differed significantly among the five subgroups $F(4) = 6.92$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=36.09) compared to the PRN (M=40.92), Low (M=42.57), and High (M=45.94) subgroups. As expected, (hypothesis 11), on a measure of the insomnia, pre-treatment ISI scores differed significantly among the five post-treatment opioid subgroups $F(4) = 3.38$, $p = .010$. Again, post hoc analysis showed significant differences between the None subgroup (M=15.74) compared to the Low (M=17.24) subgroup.

8.3.2. Patient reported post-treatment psychosocial variables at post-treatment opioid levels

Self-reported psychosocial factors post-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA to explore group differences based on level of opioid use. As expected, (hypothesis 11), post-treatment pain intensity scores differed significantly among the five opioid subgroups $F(4) = 11.92$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=4.39); compared to the PRN (M=4.95), Low (M=5.38), Moderate subgroups (M=5.78), and High (M=6.60) subgroups. As expected, (hypothesis 11), post-treatment BDI scores differed significantly among the five opioid subgroups $F(4) = 9.41$, $p \leq .001$. Post hoc analysis revealed significant differences between the None (M=9.65) and PRN (M=10.87) subgroups compared to the Low (M=12.87), Moderate (M=15.50), and High (M=17.17) subgroups with PRN displaying similar results as the None group. As expected, (hypothesis 11), post-treatment PDQ scores differed significantly among the five groups $F(4) = 11.80$, $p \leq .001$. Again, post hoc analysis revealed significant differences between the None (M=58.01) subgroups and all other subgroups. PRN (M=65.42), Low (M=74.62), Moderate (M=78.62), and High (M=83.29) subgroups varied between each other. As expected, (hypothesis 11), post-treatment Oswestry scores differed significantly among the five subgroups $F(4) = 12.91$, $p \leq .001$. Post hoc analysis showed significant differences between the None subgroup (M=22.06) and PRN subgroup (M=26.70); compared to the Low (M=31.87), Moderate (M=33.97), and High (M=35.37) subgroups, demonstrating a linear trend increasing in self-reported levels of disability as post-treatment level of opioid dosage increased. As expected,

(hypothesis 11), post-treatment ISI scores differed significantly among the five opioid subgroups *F(4)* = 8.03*,* p ≤ *.001*. Again following Post hoc analysis showed significant differences between the None subgroup (M=10.57) and PRN subgroup (M=12.38); compared to the Low (M=14.29), Moderate (M=15.75), and High (M=15.33) subgroups.

8.3.3. Change scores in patient reported psychosocial variables at post-treatment opioid levels

Change in pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANCOVA to explore group differences based on level of opioid use, with pre-treatment scores used as a covariate after pre- to post- change score was calculated.

Change in pain intensity scores differed significantly among the five opioid subgroups *F(4)* = 11.07*,* p ≤ *.001*. Post hoc analysis showed significant differences between the None subgroup (M=2.26) and PRN subgroup (M=2.47); compared to the Low (M=1.68), Moderate (M=1.44), and High (M=0.88) subgroups. As expected, (hypothesis 11), change in depressive symptoms and self-reported disability as measured by the change in BDI change in showed significant differences between post-treatment opioid levels, *(4)* = 6.48*,* p ≤ *.001*. Post hoc analysis showed significant differences between the None subgroup (M=7.48) compared to the PRN (M=6.62), Low (M=5.14), Moderate (M=5.75), and High (M=6.54) subgroups. As expected, (hypothesis 11), change in self-reported disability on the PDQ showed significant differences between post-treatment opioid levels, *F(4)* = 6.13*,* p ≤ *.001*. Post hoc analysis showed significant differences between the None subgroup (M=31.53) and PRN subgroup (M=34.54); compared to the Low (M=28.56), Moderate (M=20.21), and High (M=20.23) subgroups. As expected, (hypothesis 11), change in oswestry scores as a measure of disability differed significantly among the five subgroups *F(4)* = 7.95*,* p ≤ *.001*. Post hoc analysis showed significant differences between the None (M=14.32) PRN (M=14.36), and Low subgroups (M=11.84); compared to the Moderate (M=6.61), and High (M=10.05) subgroups. As expected, (hypothesis 11), change in ISI scores differed significantly among all five opioid subgroups *F(4)* = 3.93*,* p = *.001*. Again, following post hoc analysis showed significant differences between the None (M=5.23), PRN (M=4.75), and Low (M=4.54) subgroups compared to Moderate (M=1.78) and High (M=3.93) subgroups.

8.4 Medication Variables

Additional medication variables were examined using a chi-square analysis to distinguish group differences in the presence of any prescription for antidepressants, neuromodulators, and/or sedatives. Data regarding the presence or absence of additional prescription for specific types of medications were gathered at both pre- and post- treatment as presented in Table A25-A26.

8.4.1. Medication variables at pre-admission by post-treatment opioid use

As expected, (hypothesis 12), pre-treatment use of antidepressant medications varied significantly between opioid subgroups $\chi^2(4) = 68.92$, $p \leq .001$. Significant differences between the proportion of patients taking antidepressant medications increased as the level of opioid dose increased, with the None subgroup (40.9%; z= -3.2) compared to the Low (74.6%; z= 2.9), and High (88.9%; z=3.3) subgroups. Pre-treatment use of neuromodulators also varied significantly between post-treatment opioid subgroups $\chi^2 (4) = 74.95$, $p \leq .001$. As expected, (hypothesis 12), standard residuals revealed significant differences between the None subgroup (55.6%; z=-2.4); compared to the Low (87.3%; z=2.4), and Moderate (86.8%; z=2.6) subgroups. Finally, as expected, (hypothesis 12), pre-treatment use of sedative medications varied significantly between opioid subgroups $\chi^2 (4) = 66.23$ $p \leq .001$, with significant differences apparent between the None subgroup (47.1%; z=-3.2) compared to the PRN (66.4%; z=2.1), and High (91.7%%; z=2.8) subgroups.

8.4.2. Medication variables at post-treatment by post-treatment opioid use

Post-treatment use of antidepressant medications varied significantly between opioid subgroups $\chi^2 (4) = 74.95$, $p \leq .001$. As expected, (hypothesis 12), differences between the subgroups were seen with the None subgroup (55.6%; z=-3.1) compared to the PRN (76.3.5%; z=2.2), and Low (87.3%; z=2.2), subgroups. As expected, (hypothesis 12), post -treatment use of neuromodulators also varied significantly between opioid subgroups $\chi^2 (4) = 56.50$, $p \leq .001$. Significant differences between subgroups were found when comparing the None (31.2%; z=-3.4) to the Low (63.4%; z=3.1), Moderate (60.5%; z= 2.0), and High (63.9%; z=2.3) subgroups. Finally, as expected, (hypothesis 12), post-treatment use of sedative medications varied

significantly between opioid subgroups χ^2 *(4)* = 124.30 p ≤ *.001*, with significant differences being driven by each subgroup with the None (45.4%; z=-4.5) compared to the PRN (75.6%; z=3.5), Low (84.5%; z=2.7), Moderate (86.8%; z= 2.2), and High (88.9%; z=2.3) subgroups.

8.5 Socioeconomic One Year Outcome Variables

This section presents the results of analysis of socioeconomic one year outcome data collected at one year post program. These long-term outcome data are associated with program completion, thus, group sizes are smaller than those presented in pretreatment due to missing data on some patients lost to follow-up if they were unavailable and unable to be contacted. Multiple attempts were made to contact all patients regardless of completion status and additional information such as healthcare utilization was obtained from additional sources whenever possible. Additionally, some patients in the current cohort had not yet reached the one-year date following completion, at the time the data were analyzed and therefore were excluded from analysis. Chi-square analyses were conducted to detect differences and socioeconomic outcomes as a function of pretreatment opioid level use. Results of logistic regression analysis are presented at the end of the section.

8.5.1 Socioeconomic One Year Outcome Variables by Post-Treatment Opioid Use

The one-year socioeconomic variable comparison results are depicted in Table A27. Among patients that completed the program for which outcome data were available, findings did support hypothesis 14, in that no significant differences were found when examining group differences in return to work rates, work retention at one year. However, contrary to what was anticipated (hypothesis 13), no significant differences were found for new injuries or new surgeries to the original injury site. Hypothesis 13 was supported in part with, a significant difference found in the measure of healthcare utilization as to whether or not a patient had sought treatment from a new provider in the year following treatment completion χ^2 *(4)* = 22.4 *,* p ≤ *.001.* There is an increase in treatment seeking at one year as post-treatment opioid dose levels increased. There was a substantially smaller proportion of patients on None (7.4%) or PRN (11.3%) doses compared to patients who entered the program on High (30.3%) doses of opioids.

The binary logistic analysis for prediction of work return, work retention and healthcare utilization was undertaken, as shown in Tables A28-A30. Binary logistic regression analyses were conducted to evaluate the prediction of one-year socioeconomic outcomes from post-treatment level of opioid use calculated as a continuous variable of total daily morphine equivalent (ME) dose in milligrams (mg). Previously known factors influencing work return rates were entered into the model including: length of disability, work status on admission, pre-treatment surgery, and SSDI benefits. Results demonstrated that pre-treatment level of opioid use is a significant factor in predicting work return and work retention. Factors in this regression model, including post-treatment opioid use, accounted and for 7.5% of the variance. The overall classification rate for the binary logistic regression model was 85.9%, with 11.4% sensitivity and 96.7% specificity (χ^2 [5] = 25.61, $p < .001$, R2 = .075). The same factors were entered into a model for predicting work retention. Results demonstrated that pre-treatment level of opioid use is a significant factor in predicting work retention as well. Factors in this regression model, including post-treatment opioid use, accounted and for 23.9% of the variance in work retention. The overall classification rate for the binary logistic regression model was 76.1%, with 35.9% sensitivity and 92.6% specificity. (χ^2 [5] = 25.61, $p < .001$, R2 = .075). Again the work retention model accounted for a much larger percentage of the variance indicating that of work retention is highly associated with maintaining post-treatment opioid use. Finally, post-treatment opioid level and the other factors were entered into a predictive model for treatment seeking at one year post treatment, indicating whether or not patients had sought treatment from a new provider during the year following program completion (χ^2 (5) = 19.670, $p = .001$, R2 = .059. The overall classification rate for the model was 67.2%, with 68.9% sensitivity and 52.9% with 5.9% of the variance accounted for by factors in the model.

Chapter 9

Results: Study 3 – Change

Study 3 examined the change in opioid use from pre-admission to discharge and will also exclude “QL” and “non-completers” resulting in a total number of 1037 program completers that will be analyzed. Subjects were divided into five groups based on the change in level of opioid use upon discharge: 1) No opioid use; 2) Decrease to No opioids; 3) Decrease to PRN use: 1-15mg; 4) Increase opioids to PRN use, 5) Continued stable use of opioids above PRN use. Each group was compared on demographic variables; including: program completion, length of disability, area of injury, race, marital status, gender, age, and pre-admission surgeries.

9.1 Demographic Variables

Demographic characteristics divided by change in level of opioid use are presented in Table A31. Analyses conducted to determine demographic differences between groups revealed no significant differences in age, gender, or marital status. Significant differences were found for racial representation, length of disability, pre-admission surgery, as well as area of injury. As expected, (4.1.1.4; hypothesis 2), Racial representation varied significantly among the subgroups χ^2 (16) = 72.58, p ≤ .001. Group representation of Caucasian individuals (81.5%) was the highest in the Continued use group. Conversely, the proportion of Hispanic and African American individuals decreased in the Continued use group, with only 8.1% and 10.4%, respectively. Chi-square analysis conducted for the five opioid subgroups revealed significant differences in the proportion of patients who had pre-admission surgery χ^2 (3) = 22.94, p ≤ .001. As expected, (hypothesis 4), the proportion of patients who had undergone pre-treatment surgery differed significantly by subgroup with 69.1% in the Continued use subgroup (z=2.8). Chi-square analysis of change in opioid subgroups revealed significant differences in the proportion of patients based on the specific area of injury χ^2 (20) = 49.04, p ≤ .001. As expected, (hypothesis 1), group representation by individuals with lumbar only injuries varied with 36.9% in the Decreased to PRN subgroup (z=3.2). Analysis of variance revealed significant differences in the subgroups based on length of disability, *F* (4) = 7.72, p ≤ .001. As expected, (hypothesis 5), post hoc analysis revealed that the Continued use subgroup (M= 29.70) to be significantly different from the No

opioid group (M=14.50), the Decreased to No Opioid group, the Decreased to PRN group (M=22.73), and the Increased to PRN group (M=15.9).

9.2 Occupational Variables

Occupational variables for the five opioid subgroups are presented in table A32. The subgroups did not show significant differences in job type, work status at admission, or pre-injury job satisfaction which was expected (hypothesis 6). Job demand, case type, pre-injury wage, and SSDI/SSI benefits on admission differed significantly among the change in opioid groups. Chi-square analysis revealed significant differences in the proportion of patients who entered the program by means other than a worker's compensation claim χ^2 (8) = 29.06, $p \leq .001$. As expected, (hypothesis 7), private pay patients were proportionately higher in the Decreased to PRN, Increased to PRN and Continued use subgroups. Unlike what was anticipated (hypothesis 6), change in opioid use revealed differences in job demand, with significant differences being found χ^2 (20) = 37.02, $p \leq .001$. Standard residuals indicate that the significance was derived from the sedentary subgroup containing proportionally lower subjects with Decreased to no opioids (8.5%) group and Decreased to PRN only group (7.5%). Subjects in the Continued opioid use group showed lower rates of "medium" demand jobs. Analysis of variance revealed significant differences in the groups based on pre-injury wage, F (4) = 3.17, $p \leq .001$, which was another unanticipated finding not suspected in hypothesis 6. Post hoc analysis revealed that the Continued use subgroup (M= $924.61) to be significantly different from the No opioid (M=$731.72), Decrease to none (M=$773.63), and Decrease to PRN group (M=$748.91). Chi-square analysis also revealed significant differences between subgroups based on whether or not they were receiving SSDI/SSI benefits upon admission χ^2 (4) = 32.23, $p \leq .001$, as expected (hypothesis 7). Specifically, higher proportions of subjects receiving SSDI/SSI benefits were in the Continued use group (9.4%; z= 5.1).

9.3 Patient Reported Psychosocial Variables by Change in Opioid Use

The current section presents analysis of various pre- treatment and post-treatment patient self- reported psychosocial variables, including pain intensity, BDI, PDQ, Oswestry, and ISI. The pain intensity, depression, disability, and sleep measures were administered to all patients prior

to, and upon completion of, the functional restoration program. Due to the fact that post-treatment measures were not always able to be gathered from subjects who did not complete the program, the post-treatment sample is smaller than the pre-treatment sample. Once again, comparisons among the five change in opioid use groups are presented. The differences found with respect to the demographic variables as possible factors associated with level of opioid use. Because the differences in gender rate of completion, length of disability, pre-treatment, surgery, area of injury and ethnicity were significant, the subsequent analyses controlled for the variance attributed to those variables.

9.3.1. Patient reported pre-admission psychosocial variables by change in opioid use

Pre-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA and ANCOVA to explore group differences based on change in opioid use. Results are displayed in table A33. The comparisons of the psychosocial variables based on the change in opioid use revealed significant differences across the subgroups. Pre-treatment pain intensity scores differed significantly among the five opioid subgroups $F(4) = 5.55$, $\leq .001$. Post hoc analysis showed significant differences between the Decreased to PRN group (M=7.55) and No opioid subgroup (M=6.32). On the Beck Depression Inventory which measures depressive symptoms, as expected (hypothesis 8), pre-treatment BDI scores differed significantly among the five opioid subgroups $F(4) = 6.28$, $p \leq .001$. Post hoc analysis showed significant differences between the Continued use group (M=20.27) compared to the NO opioid (M=15.39) and increase to PRN (M=15.41) groups. Perceived disability, as measured by the Pain Disability Questionnaire and the Oswestry disability Index were found to be significantly different between groups of change in opioid use. As expected (hypothesis 9), pre-treatment PDQ scores differed significantly among the five groups $F(4) = 21.20$, $p \leq .001$. Again, Post hoc analysis showed significant differences between the No opioid group (M=83.44) compared to the Decreased to PRN (M=101.14) Continued use (M=101.96) group. As expected (hypothesis 9), pre-treatment Oswestry scores differed significantly among the five subgroups $F(4) = 11.59$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid group (M=33.41) compared to the Continued use group (M=43.95) which had the highest levels of self-reported disability. On a

measure of the insomnia, as expected (hypothesis 10), pre-treatment ISI scores differed significantly among the five post-treatment opioid subgroups *F(4)* =6.13*,* p = *.000*. Again, following post hoc analysis significant differences were found between the No opioid group (M=14.46) and the Continued use group (M=18.67) group.

9.3.2. Patient reported post-treatment psychosocial variables by change in opioid use

Self-reported psychosocial factors post-treatment pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANOVA to explore group differences based on change in opioid use. Post-treatment pain intensity scores differed significantly among the change in opioid groups *F(4)* = 11.89*,* p ≤ *.001*. Post hoc analysis showed significant differences between the No opioid group (M=4.29); compared to Continued use group (M=5.87). Post-treatment BDI scores differed significantly among the change in opioid groups *F(4)* = 9.61*,* p ≤ *.001*, as expected (hypothesis 8). Post hoc analysis revealed significant differences between the No opioid (M=9.12), Decreased to no opioids (M=10.38), Decreased to PRN only (M=10.83), Increased to PRN only (M=10.54) groups compared to the Continued use (M=14.90) group. Post-treatment PDQ scores differed significantly among the change in opioid groups *F(4)* = 14.01*,* p ≤ *.001*. Again, as expected (hypothesis 9), post hoc analysis revealed significant differences between the No opioid (M=55.10) groups and the Continued opioid use group (M=79.11). As expected (hypothesis 9), post-treatment Oswestry scores differed significantly among the change in opioid groups *F(4)* = 14.97*,* p ≤ *.001*. Post hoc analysis showed significant differences between the No opioid group (M=20.45) compared to the Continued use (M=33.78). As expected (hypothesis 10), ost-treatment ISI scores differed significantly among the change in opioid groups *F(4)* = 9.61*,* p ≤ *.001*. Again, following post hoc analysis significant differences were found between the No opioid group (M=9.96) compared to the Continued use (M=15.23) group.

9.3.3. Change scores in patient reported psychosocial variables by change in opioid use

Change in pain intensity, depression, disability, and sleep variables were analyzed as continuous variables by ANCOVA to explore group differences based on level of opioid use, with pre-treatment scores used as a covariate after pre- to post- change score was calculated, Results are displayed in Table A35.

Change in pain intensity scores differed significantly among the change in opioid groups $F(4) = 10.83$, $p \leq .001$. Post hoc analysis showed significant differences between the No opioid group (M=2.13) compared to the Continued use (M=1.38) group, with significantly smaller amounts of self-reported change in pain intensity for patients who continued opioid use above a PRN level. As expected (hypothesis 8), change in depressive symptoms and self-reported disability as measured by the change in BDI change showed significant differences between change in opioid use, $F(4) = 6.32$, $p \leq .001$. Post hoc analysis showed significant differences between the group of patients who Decreased to no opioids (M=8.01) compared to the Increased to PRN (M=4.88), and Continued use (M=55.76) groups. As expected (hypothesis 9), Change in self-reported disability on the PDQ showed significant differences between change in opioid use groups, $F(4) = 6.16$, $p \leq .001$. Post hoc analysis showed significant differences between the Decreased to No Opioid group (M=34.98) and Decreased to PRN only group (M=35.82); compared substantially less change in the Continued use group (M=23.61). As expected (hypothesis 9), Oswestry scores as a measure of disability differed significantly among the change in opioid use groups $F(4) = 7.33$, $p \leq .001$. Post hoc analysis showed significant differences between Decreased to No Opioid group (M=15.85) and Decreased to PRN only group (M=14.83); compared substantially less change in the Continued use group (M=10.25). As expected (hypothesis 10), change in ISI scores differed significantly among the change in opioid groups $F(4) = 5.05$, $p = .001$. Again, following post hoc analysis significant differences were found between the Decreased to No Opioid group (M=6.32) compared to substantially less change in the Continued use group (M=3.56). .

9.4 Medication Variables

Pre-treatment use of antidepressant medications varied significantly between change in opioid groups $\chi^2(4) = 69.70$, $p \leq .001$. As expected (hypothesis 11), significant differences between the proportion of patients taking antidepressant medications were greater in the Continued use opioid group (77.7%; z=4.6) compared to the No opioid group (38.2%; z= -3.1). As expected (hypothesis 11), pre-treatment use of neuromodulators also varied significantly between change in opioid groups $\chi^2(4) = 36.97$, $p \leq .001$. Standard residuals revealed significant

differences in the No opioid group (33.4%; z=-2.2); compared to the Continued use opioid group (61.9%; z=3.8and Moderate (86.8%; z=2.6) subgroups. Finally, as expected (hypothesis 11), pre-treatment use of sedative medications varied significantly between change in opioid groups χ^2 *(4)* = 90.01 p ≤ *.001*, with significant differences apparent between the No opioid group (38.3%; z=-4.7) compared to the Decreased to PRN only (68.0%; z=2.3), and Continued use opioid group (78.4%%; z=3.3).

9.4.2. Medication variables at post-treatment by change in opioid use

Post-treatment use of antidepressant medications varied significantly between opioid change groups χ^2 *(4)* = 69.70*,* p ≤ *.001*. As expected (hypothesis 11), differences between the groups were seen with the No opioids group (53.8%; z=-2.8) compared to the Continued use opioid group (89.2%; z=3.4). Post -treatment use of neuromodulators also varied significantly between opioid change groups χ^2 *(4)* = 36.97*,* p ≤ *.001*. As expected (hypothesis 11), significant differences between subgroups were found when comparing the No opioid group (32.3%; z=-2.3), Decreased to no opioid groups (29.4%; z=-2.6), and Continued use opioid group (63.3%; z=4.3). Finally, as expected (hypothesis 11), post-treatment use of sedative medications varied significantly between opioid change groups χ^2 *(4)* = 125.94 p ≤ *.001*, with significant differences being driven by each group with the No (42.5%; z=-4.2) compared to the Decreased to no opioid (49.8%; z=-2.0), Decreased to PRN only (77.0%; z=3.5), and Continued use (85.6%; z=4.0) groups.

9.5 Socioeconomic One Year Outcome Variables

This section presents the results of analysis of socioeconomic one year outcome data collected at one year post program. These long-term outcome data are associated with program completion, thus, group sizes are smaller than those presented in pretreatment due to missing data on some patients lost to follow-up if they were unavailable and unable to be contacted. Multiple attempts were made to contact all patients regardless of completion status and additional information such as healthcare utilization was obtained from additional sources whenever possible. Additionally, some patients in the current cohort had not yet reached the one-year date following completion, at the time the data were analyzed and therefore were excluded from

analysis. Chi-square analyses were conducted to detect differences and socioeconomic outcomes as a function of pretreatment opioid level use. Results of logistic regression analysis are presented at the end of the section.

9.5.1 Socioeconomic One Year Outcome Variables by Change in Opioid Use

The one-year socioeconomic variable comparison results are depicted in Table A38. Among the patients who completed the program for which outcome data were available no significant differences were found when examining group differences in return to work rates, work retention at one year, or new injuries or new surgeries to the original injury site, which was did not support hypothesis 12 or 13. However, one aspect of hypothesis 12 was confirmed, in that, there was a significant difference found in the measure of healthcare utilization regarding whether or not a patient had sought treatment from a new provider in the year following treatment completion χ^2 *(4)* = 22.42*,* p ≤ *.001,* with significantly greater proportions of subjects in the Continued use group (28.2%; z= 3.8) and substantially smaller proportion of patients on No opioids (16.7%; z=-2.3) seeking treatment from a new provider one year following discharge from treatment.

The binary logistic analysis for prediction of work return, work retention and healthcare utilization was undertaken, as shown in Tables A39-A41. Binary logistic regression analyses were conducted to evaluate the prediction of one-year socioeconomic outcomes based on the categorical change in opioid use divided by patients ending treatment on No opioids, those ending treatment on a PRN dose and those using scheduled doses of opioid medications. The known factors influencing work return rates were entered into the model. Results demonstrated that categorical change in opioid use is a significant factor in predicting work return and work retention. Factors in this regression model, including pre-treatment opioid use, accounted and for 7.3% of the variance in work return. The overall classification rate for the binary logistic regression model was 86.6%, with 98.7% sensitivity and 3.8% specificity. (χ^2 [6] = 24.972, p < .001, R2 = .073). The same factors were entered into a model for predicting work retention. Results demonstrated that categorical change in opioid use is a significant factor in predicting work retention as well. Factors in this regression model, including categorical change in opioid use, accounted and for 5.4% of the variance. The overall classification rate for the binary logistic

regression model was 77.4%, with 98.3% sensitivity and 5.1% specificity. (χ^2 [6] = 22.143, p < .001, R2 = .054). Finally, categorical change in opioid use and the other factors were entered into a predictive model for treatment seeking at one year post treatment predicted whether patients had sought treatment from a new provider during the year following program completion (χ^2 (5) = 20.395, p = .002, R2 = .061. The overall classification rate for the model was 66.4%, with 67.6% sensitivity and 55.7% specificity.

Chapter 10

Discussion

The present study represents a comprehensive evaluation of patients with chronic pain who were admitted to a tertiary functional restoration program. The goal of this study was to identify and assess levels of opioid use upon admission to- and discharge from- treatment and determine how levels of opioid use relate to demographic, occupational, patient reported psychosocial, other medication, and one-year socioeconomic variables. The results of this study help to provide a more comprehensive understanding of chronic pain patients and the relationships between opioid doses and other previously established variables of interest. Previous researchers have identified decreasing levels of opioid use as an important outcome measure in assessing the efficacy of chronic pain treatment (Martin Grabois, 2005). By investigating patients who complete treatment and relating the various levels of change in opioid use from pre- to post-treatment, this study serves a foundation for the evaluation of opioid medication use as an important treatment outcome. A goal of this study was to aid in the understanding of factors associated with levels of opioid use and build further support for using reduction of opioid medication as an evidence-based treatment outcome. Through the use of evidence-based research, objective criteria can be identified and become benchmarks for successful outcomes. Historically, the evaluations of work return and work retention, as well as healthcare utilization in the year following treatment completion have been important objectives evidence-based research outcomes (Mayer, 2007). Thus, another aim of this study was to discover differences in one year outcomes, based on level of opioid use at various time points surrounding what is known to be a highly effective functional restoration treatment program. Subjects were classified into groups based on self-reports of pre- and post- treatment level of opioid use (PRN, Low, Moderate, and High) as well as by specific use of hydrocodone upon admission and change in level of opioid use upon discharge. This was done to determine if pre-, post- or change in level of opioid use discriminates subjects based on demographic, occupational, psychosocial, medication, and/or response to treatment. This chapter presents the findings of this examination, limitations of the study, and suggestions for future research.

10.1 Demographic Variables

As predicted in Hypothesis 1 (4.1.1.1. Study 1a), pre-treatment level of opioid use was associated with the rate of functional restoration program completion, such that patients reporting higher levels of pre-treatment opioid use were at greater risk of program non-completion. Patients enrolled in the treatment program agreed to be weaned from opioid medications at the onset of treatment. A possible interpretation of findings related to program completion rates among the opioid level is that patients taking lower doses of opioid medications are more easily weaned and thus, adhere to the guidelines of the program. Patients taking higher doses might be reluctant or have more difficulty in tapering opioid use, leading to increased program dropout. Opioid dependence has been identified as one of the major risk factors associated with non-completion of these types of programs (Howard, Mayer, Theodore, & Gatchel, 2009; Proctor et al., 2005) and findings of this study support that higher levels of opioid use are related to possible dependence which may be directly related to why completion rates were significantly different based on level of opioid use. Differences in program completion rates may be attributable to other factors as well including: varying lengths and disability, pre-treatment surgery rates, and pre-treatment pain intensity. Additionally, combination pharmacotherapy including the use of antidepressants, neuromodulators, and/or sedatives may play a role. Research into specific factors associated with completion rate have been conducted in the past (Howard, Mayer, Theodore, & Gatchel, 2009), but should be replicated with attention to level of opioid use and not limit the scope to the presence of an opioid dependence diagnosis.

Study 1b, hypothesis 1 (stated in section 4.1.1.2.), was supported, as pre-treatment use of hydrocodone did demonstrate differences in response to treatment, such that subjects reporting no opioid use or single opioid use of hydrocodone had higher rates of program completion than those taking other types or a combination of opioids. This was supported by data findings revealing 70.1% of patients who entered the program on No opioids successfully completed treatment, while patients in the Combination opioid use group only had 48.0% who completed treatment successfully. This could be due in part to the fact that when total daily

morphine equivalent (ME) dose were calculated, patients in the Combination opioid use group had significantly higher total ME doses compared to patients in the hydrocodone only group. As previously stated, opioid dependence is a known risk factor associated with failing to complete these types of programs (Howard, Mayer, Theodore, & Gatchel, 2009; Proctor et al., 2005; Kidner, Mayer, Gatchel, 2009).

Study 1a) hypothesis 2 was confirmed, evidenced by significant differences between groups based on area of injury. Patients with lumbar only injuries were underrepresented in the None subgroup, and showed a linear trend in increasing proportions as level of pre-treatment opioid use increased. Previous research has established that low back pain patients are particularly difficult population to successfully treat. One study, (Howard, Mayer, Gatchel, 2009) examined areas of injury and compared them to a lumbar only group. Results from this evaluation indicated those with chronic lumbar disorders vary in opioid use compared to other areas of injury. Study 1b) hypothesis 2 (stated in section 4.1.1.2.) was supported in that area of injury would have significant differences among hydrocodone use groups, and findings revealed there were a higher proportion of patients with a lumbar injury taking hydrocodone upon admission to the program. Again these findings are likely explained in the context of other factors associated with lumbar injuries such as length of disability and pre-treatment surgeries (Howard, et. al, 2009) resulting in greater use of hydrocodone.

Hypothesis 1 for study 2 (stated in section 4.1.1.3.) expected post-treatment level of opioid use in patients who successfully completed treatment to differentiate in demographic variables such that subjects reporting higher levels of posts treatment opioid use would have injuries to lumbar regions to a greater degree than patients with extremity injuries. Data supported this hypothesis. At post-treatment 35.3% of patients in the PRN subgroup had sustained lumbar injuries, which was significant at the $p = .05$ level. Lastly, hypothesis 1 from study 3 (stated in section 4.1.1.4.) related to area of injury for change in opioid use was supported, as findings revealed proportionally higher rates of patients with a lumbar injury in the Decreased to PRN only group, with much fewer patients in the No opioid group. These findings are congruent with respect to previous understanding of lumbar disorders accounting for a larger proportion of

patients utilizing opioid medications (Kidner, et. al, 2009; Howard, et.al., 2009). This change in opioid use as measured in program completers is a promising finding supporting positive treatment outcomes for the functional restoration program used in this study as one of the most difficult treatment groups (i.e. lumbar injured patients) were shown to be weaned down to a PRN only dose.

Study 1a) hypothesis 3 (stated in section 4.1.1.1.) addressed opioid use by ethnicity and was supported with findings that Caucasian patients reported higher levels of pre-treatment opioid use. This finding has been supported by previous research findings (Kidner, Mayer, Gatchel, 2009). This previous study exhibited lower proportions of Hispanic patients entering treatment on high levels of opioids, which were also found in the present study. Possible explanations for these findings could relate to racial and cultural differences in attitudes towards taking prescription medications, access to pharmaceutical interventions prior to entering treatment, possible biases in the prescribing practices of physicians treating chronic pain patients in specific geographical regions, complex factors of the Texas Worker's Compensation program, or other factors beyond the scope of the current study. Other investigations of cultural and racial differences in access to prescription medications have found similar disparities (Qato, D. M., Daviglus, M. L., Wilder, J., Lee, T., Qato, D., & Lambert, B., 2014). Further examination into racial differences in opioid use could be warranted in future studies. This hypothesis as related to hydrocodone use at pre-treatment (study 1b, hypothesis 3, stated in section 4.1.1.2.) was also supported in that Hispanic patients were underrepresented in the Combination opioid use group. This may be due in part to cultural differences in Latino populations and beliefs surrounding medication use. It is possible that Hispanic patients who agreed to take a prescription medication for pain relief may have been reluctant to use multiple different opioid drugs, thus showing lower proportions in the Combination group. Study 2, hypothesis 2 (stated in section 4.1.1.3.). Similar racial differences were found in both the post- level of opioid use for patients who completed treatment successfully and in the change in opioid use (Study3, stated in section 4.1.1.4.) at post-treatment. Higher proportions of Caucasians continued use of opioids above the PRN dosage

upon program completion while proportionately higher levels of Hispanic patients remained in the no opioid use group. These differences are likely due to the same previously mentioned factors.

Gender differences have been reported in previous studies, and hypothesis 4 was supported by the findings of the current study with a significantly greater proportion of males on Low or Moderate opioid doses at pre-treatment. However, the proportion of male subjects in the High dose subgroup was similar to that of the None and PRN subgroups. One possible explanation for these differences may be related to other factors including length of disability, pre-treatment surgeries or simply the fact that a greater proportion of males take opioid medications above PRN dosage. Yet at the extremes of the High subgroup or the None group, the proportions of males and females are quite similar. Gender differences related to hydrocodone only use revealed significantly higher proportions of males who were taking Hydrocodone only compared to combination opioid use. This finding could be related in part to area of injury since it is known that a greater proportion of males experience lumbar disorders (Howard, et. al, 2009). However, no significant differences in gender were found when analyzing post-treatment's opioid levels or change in opioid use upon program completion. The lack of gender differences may have been resolved at the post-treatment level due to the fact that post- treatment and change analyses were run on program completers only. This indicates that program completion rates may account for gender differences since those differences were no longer seen on post-treatment levels of opioids for completers.

Hypothesis 5 proposed that level of opioid use would not differ by age, or marital status, and was supported by pre-treatment opioid level data. Likewise, in the hydrocodone use at pre-treatment age was not a significant factor differentiating between groups. However, marital status did reveal significant differences among the hydrocodone use groups. The reason for the significance was driven primarily from the cell in the No opioids groups for patients who were widowed (z=-2.0). This can be accounted for simply due to the sample not containing equal distributions and some cells contained fewer than 5 subjects. Thus, the significance cannot be interpreted as an accurate representation of true meaningful differences. In the future, marital status might be collapsed in a more meaningful way if the intent is to assess living situations in

terms of measuring social support as a possible factor related to opioid use. Post-treatment level of opioid use and change in opioid use upon program completion both revealed no significant differences in groups based on age or marital status further confirming this hypothesis.

Hypothesis 6 regarding pre-admission surgery rates was supported by the findings. Irrespective of the proportion of patients in the None group, as the level of opioid use increased so did the proportion of patients who reported having a surgery prior to admission. This finding is not surprising given that opioids are typically prescribed initially for post-operative pain, and if a patient does not experience a positive post-surgical outcome, and continues to pursue treatments at a tertiary care level, then it makes sense that persons in the High dose subgroup would have had previous surgeries at higher proportions. Other studies also found pre-treatment surgery to be a predictor for poor one-year outcomes (Brede, E., Mayer, T. G., & Gatchel, R. J. 2012; Mayer, T. G., Gatchel, R. J., Brede, E., & Theodore, B. R., 2014). Likewise, significant differences were found in pre-treatment hydrocodone use groups with higher proportions of patients who had undergone pre-treatment surgery in the Combination opioid use group. Additionally, the other single opioid group had greater rates of pre-treatment surgery compared to those patients on hydrocodone only. Again, with length of disability as a rather important factor, it follows logical interpretation that individuals who have undergone previous surgical intervention may have initially tried hydrocodone only and then been rotated or titrated two other single opioids or perhaps combination opioid use. Similar results were found for post-treatment levels of opioid use and change in level of opioid use with pre-treatment surgery remaining significance across each time point analyzed.

Hypothesis 7 proposed that pre-treatment levels of opioid use would be associated with subjects' length of disability. It has become almost common knowledge that previously published outcomes have correlated greater length of disability with greater complexities including increased use of opioids (Theodore, 2009; Jordan, K. D., Mayer, T. G., & Gatchel, R. J., 1998; Brede, E., Mayer, T. G., & Gatchel, R. J. 2012; Mayer, T. G., Gatchel, R. J., Brede, E., & Theodore, B. R., 2014). With issues of tolerance and need for increase dosages to maintain adequate pain relief, this finding is not surprising. The greatest differences were found between

the extremes, such that individuals on No opioids or PRN only dosages had significantly shorter length of disability compared to those on High doses. An interesting finding on most of these variables was that individuals on No opioids were quite similar to those on PRN doses. This is an important finding potentially indicating that utilizing occasional opioid medications in the context of treating chronic pain can be as beneficial as remaining free from any opioid use. This hypothesis was supported in the same manner at the post-treatment opioid level analyses, as well as for change in opioid use upon completion of treatment.

10.2 Occupational Variables

Hypothesis 8 related to occupational variables was not fully supported as findings showed that greater proportions of blue-collar workers were represented in the low dose subgroup. One possible explanation for this finding could be that blue-collar workers needed to maintain adequate pain relief while doing physical jobs and were seen in this middle subgroup as a result. This hypothesis in relation to hydrocodone use at preadmission showed a significantly higher proportion of blue-collar workers taking hydrocodone only. Again this is perhaps due to the fact that hydrocodone is the most widely prescribed medication and of patients who continue to work and have physically demanding jobs hydrocodone is the most likely medication that is maintained at low level doses. However, whether or not a patient was working on admission or if they were a blue collar or white collar worker were no longer significant between levels of opioid use at post-treatment, nor were they significant for change in opioid use upon program completion. The other occupational variables addressed in this hypothesis included: job demand, job satisfaction, and pre-injury wage which did not differ significantly by subgroup. The exception was found for pre- injury wage, which did differ significantly between change in opioid use groups upon successful completion of the functional restoration program. Results found a significantly higher wage for patients who continued use above PRN dosage or for patients who increased from no opioids to a PRN dose.

Hypothesis 9 proposed that pre-treatment level of opioid use would vary significantly based on case type, with private pay patients reporting higher levels of opioid use, work status differentiating patients reporting lower levels of opioid use with having current employment, and

patients with higher levels of opioid use being more likely to be receiving SSI or SSDI. This hypothesis was supported in terms of SSDI proportions being significantly higher in those patients who entered treatments on high doses of opioids. This is understandable given the facts that if a patient is receiving disability benefits they are likely in a situation that does not require maintaining a lifestyle free of high-dose opioid use. Previous research has established that workers compensation patients have longer lengths of disability and poorer outcomes (Theodore, 2009; Carreon, Glassman, Kantamneni, Mugavin, & Djurasovic, 2010; DeBerard, Masters, Colledge, Schleusener, & Schlegel, 2001; Theodore, B. R., Kishino, N. D., & Gatchel, R. J. 2008). Work status at admission was also supported in that a proportionately lower rate of patients in the high opioid dose group actually had a job at the time of admission. Contrary to the hypothesis that private pay patients would have significantly higher opioid use, the current study found a higher percentage of private pay patients in the None group and 92.9% of patients in the PRN subgroup were workers' compensation patients. While the cells driving the significance in this chi-square analyses were from disproportionately low percentages of private pay patients in the PRN or Low dose subgroup's, the entire cohort had substantially more patients in the workers compensation group. Therefore, differences driven by lower numbers in these two cells cannot fully support or deny the hypothesis since the sample was not evenly distributed.

10.3 Patient Reported Outcomes - Psychosocial Variables

As expected, there were differences found with respect to the demographic variables under consideration as possible factors associated with level of opioid use. Because the differences in gender rate of completion, length of disability, pre-treatment, surgery, area of injury and ethnicity were significant, the subsequent analyses controlled for the variance attributed to those variables.

Hypotheses 9 through12 related to specific measures of self-reported psychosocial distress including pain intensity, depressive symptoms, perceived disability and sleep. These hypotheses proposed that higher pre- and post-treatment level of opioid use would be associated with higher levels of pre-treatment and post- treatment measures of pain intensity, depressive symptoms, perceived disability and sleep disturbance. These were all confirmed by findings

demonstrating significant differences between groups. It is interesting to note that when looking for specific differences between groups again the None and PRN groups were similar and differed significantly from the Low, Moderate or High levels of opioid use. This again may be related to patient self-reports of psychosocial distress being affected by regular doses of opioid medications which are known to have some specific side effects that could be related to such psychosocial distress. One study examined a group of patients with chronic non-cancer related pain and discovered significantly higher levels of psychosocial distress (Blake, S., Ruel, B., Seamark, C., & Seamark, D., 2007). The findings indicated that a group of patients with greater psychosocial distress were more comfortable when provided with stronger doses of pain relieving medications. Additionally, there have been studies that found an association between insomnia and opioid (Asih, Hulla, Bradford, Hartzell, & Gatchel, 2014) with high levels of self-reported insomnia being related to higher total daily morphine equivalent doses of opioid medications in chronic pain patients. Another possibility would be that these patients may reports higher levels of pain in psychosocial distress in order to justify to themselves or their treatment providers continued prescriptions for opioids above a PRN dose.

Additionally, it was hypothesized that there would be differences in change scores of self-reported pain, depression, disability, and insomnia with those taking lower levels of opioids at pre- and post-treatment having greater levels of change in these self-reported measures of distress. This was also supported by significant differences in change scores found after demographics and pre-treatment scores were used as covariates. However, only for changes in pain intensity as related to pre-treatment opioid use, showed significant change scores in pain intensity and self-reported disability (as measured by the Oswestry, but not PDQ). These findings have issues of clinical significance even though statistical significance was found between groups. Specifically, the greatest change in pain intensity was decreasing self-reported pain by an average of 2.27 points on a 10 point scale, compared to an average change of only 1.48 points for patients in the High group at pre-treatment group for pre-treatment level of opioid use. Further investigation into the true clinical meaningful difference is warranted to fully understand the importance of this particular finding. However, when assessing program completers on post-

treatment opioid levels and change in opioid levels, all measures or psychosocial distress were significant at the pre- and post-treatment and change in self-reported measures of psychosocial distress. Significant differences were expected here as this was an analysis of program completers only and their responsiveness to treatment is thought to be related in part to their level of opioid use. In levels of pre-treatment opioid use completion status is significantly related to level of opioid use, thus differences in pre-treatment's opioid use levels were controlled for demographic variables including completion status. Possible reasons for significant differences being associated with level of opioid use could include patients wanting to self-report and document higher levels of pain and distress in attempts to maintain higher levels of opioid use. For patients who entered treatments on high levels of opioids or who resists weaning entirely off of opioids is expected that their own perception of their level of disability would be related in some way to the amount of medications they use. This is further explored in the next section regarding the relationship between level of opioid use and specific additional medication usage.

10.4 Medication Variables

As communicated in hypothesis 13, it was proposed that pre-treatment level of opioid use would differentiate subjects according to level of pre-treatment additional medication use, such that those reporting higher levels of pre-treatment opioid use would demonstrate higher rates of using antidepressants, neuromodulators, and sedatives upon admission and discharge. The same thoughts were hypothesized related to post-treatment level of opioid use and change in level of opioid use. With respect to hydrocodone only use at pre-treatment it was hypothesized that the group on combination opioids would also show higher rates of additional use of antidepressants, neuromodulators, and sedatives at admission and discharge. These hypotheses were all confirmed by the current study's findings. While these findings were expected, further investigation into additional variables that might mediate or moderates the use of additional combination pharmacotherapy is warranted. It is beyond the scope of the present study to differentiate specific factors related to these particular medications of interest. However, it was interesting to find that patients on higher doses or combination medications were more likely to be on additional pharmacological interventions. This may be due in part to the fact that chronic pain

patients in this setting are typically highly motivated to avoid pain, and hence may be open to additional pharmacological interventions with the hope of these medications providing additional relief and decreasing the need for long-term opioid use. It should be noted that this is only speculation, and would require further research.

10.5 One-year Socioeconomic Outcomes

Hypothesis 14 and 15 stated that pre-treatment level of opioid use would predict differences in one-year socioeconomic outcomes including work-related outcomes, and healthcare utilization, such that subjects reporting higher levels of opioid use would demonstrate lower rates of work return and work retention and higher rates of post-treatment surgery, post-treatment injury, and higher rates of healthcare utilization at one-year follow-up. However, no differences were found in rates of work return work retention, additional surgeries or new injuries. The only part of hypothesis 14 supported was regarding, treatment seeking at one-year post program, which was higher in the High opioid group, as expected. Similar results were found based on pre-treatment hydrocodone use with healthcare utilization being the only significant variable. This further supports the fact that the specific opioid medication utilized is less important than the total daily morphine equivalent dose. There were no differences in healthcare utilization related to which opioid patients used, only on the level of morphine equivalent dose. When looking at post-treatment levels of opioid use in successful program completers, there were no differences seen in work return and work retention rates. However, healthcare utilization measured by whether or not patients sought treatment from a new provider did demonstrate significant differences between the groups based on the level of opioid dose patients were on when they completed the program. Clearly the cause of this is likely linked to the fact that maintaining prescriptions for opioid use require additional doctor visits and it could be speculated that patients on higher doses are likely to seek treatment from new providers given that one of the stated goals of program completion was to wean from opioid use. However, there may be additional factors such as comorbid conditions and unknown variables beyond the scope of the current study which might explain the significant variation between patients who completed the program on no opioids (7.4%) and those on high levels of opioids (30.3%) and their need to seek

treatment from new providers in the year following successful completion of a functional restoration program. It is possible that the comprehensive program and tailored treat the treatment were a foundation upon which patients who maintains high levels of opioid use were motivated to seek treatment from other sources.

10.5.1 Predictive Model for One Year Socioeconomic Outcomes

Binary logistic regression analyses were conducted to evaluate the prediction of one-year socioeconomic outcomes from pre-treatment level of opioid use calculated as a continuous variable of total daily morphine equivalent (ME) dose in milligrams (mg). Previously known factors influencing work return rates (length of disability, working on admission, SSDI benefits, and pre-treatment surgery) were entered into the model (Vendrig, 1999; Brede, E., Mayer, T. G., & Gatchel, R. J. 2012). Results demonstrated that pre-treatment level of opioid use is a significant factor in predicting work return and work retention in this model. Factors in this regression model, including pre-treatment opioid use, accounted and for 24.6% of the variance in work return. The overall classification rate for the binary logistic regression model was 73.1%, The same factors were entered into a model for predicting work retention. Results demonstrated that pre-treatment level of opioid use is a significant factor in predicting work retention as well. The overall classification rate for the binary logistic regression model was 76.1%. The model was slightly more predictive of work retention, possibly indicating that retaining work is more highly associated with maintain opioid use. Additional regression modeling should be explored and incorporates other significant factors identified in this study, specifically patient reported outcomes as measured by the Beck Depression Inventory, Pain Disability Questionnaire, and ISI. While work return and work retention have typically been the outcomes of interest (Vendrig, 1999; Brede, E., Mayer, T. G., & Gatchel, R. J. 2012), further predictive modeling should be done to explore the predictive factors related to opiate use. While healthcare utilization is highly associated with higher levels of continued opioid use, the possibility of using opioid medication at post-treatment and at one-year have the potential to become their own objectives outcome measures. This study is one step in laying the foundation for understanding opioid use as a standalone objective outcome.

10.6 Limitations of the Present Study

The present study represents a foundation in the exploration of the role of opioid use in chronic pain rehabilitation outcomes for patients participating in functional restoration. While this study exhibited a comprehensive analysis of an extensive number of variables among a large sample size, limitations were present. For example, the exceptionally high number of univariate comparisons, may have inflated Type I error, increasing the presence of statistical findings when truly none exist. The Holm Bonferroni procedure was utilized to adjust for multiple comparisons, however results should be interpreted in that context. Another criticism is that pre-treatment opioid use was in part based on self-report and like all patient-reported substance use, there is potential for discrepancy in accuracy. However, diligence and verification of accuracy in the data were utilized and double checked through selecting cases and comparing data with both computer records and paper medical charts. Pre-treatment level of opioid use was determined through a review of multiple sources including verifying the specific name of the medication as well as the dose, and in the process of calculating total daily morphine equivalents these data were reviewed multiple times.

Another possible limitation surrounding data accuracy could be the lack of objective confirmation of patients' pre or post-treatment opioid use. While accurate records of prescriptions were kept and verified, it is always possible that patients who had been weaned from their prescription opioid medications in the context of the program could have continued to obtain opioid medications through illicit sources or from other physicians. However, if continued opioid use was suspected by providers, concerns were discussed with the patient and when appropriate urine toxicology screening was used. If opioid use continued following these interventions, patients were offered inpatient detoxification. Patients who refused detoxification were discharged as non-completers due to non-compliance.

The ranges or cut-offs for the opioid levels utilized in the present study incorporated a PRN dose which may have varied in total daily morphine equivalents. This important subgroup was included in this investigation, even though specific total daily dose varied. It was important to capture patients who did not take a daily dose on a consistent basis. Opportunity exists for future

research designed to improve upon or further differentiate high or low levels of PRN opioid given that some patients took one pill a week, while others may have taken three or four a week.

A further limitation to this study could be found in the logistic regression model which was utilized for the dichotomous one year outcome variables. R-squared terms presented for binary logistic regression analyses in the present study are actually pseudo-R-squared statistics. Thus, interpretations of the amount of variance accounted for by opioid dose in rates of work return, work retention, and healthcare utilization must be interpreted with caution.

Additionally, the issue of findings from the present study being generalizable to larger populations needs to be considered. In the present study pre-treatment findings were based on both completers and non-completers of functional restoration, while post-treatment and one-year treatment outcomes were based on completers only. Therefore, conclusions regarding the role of pre-treatment level of opioid use may only be generalizable to patients who complete functional restoration. Additionally, there may be additional factors unique to this cohort that were not identified in the current study which further supports the need for replication via similar studies.

10.7 Future Directions

The present study raises numerous questions to be addressed by future research. Examination of the relationship between pre-treatment level of opioid use and chronic pain rehabilitation outcomes sought to identify linear relationships. However, these relationships might be better described by higher order polynomial functions. For that reason, future research might seek to identify higher-order trends that more accurately identify the associations between pre-treatment opioid use and response to functional restoration. Specifically, further investigation into additional variables that might mediate or moderate the use of additional combination pharmacotherapy including antidepressants, neuromodulators and sedatives is warranted.

Results of the present study indicate that patients who reported PRN opioid use showed similar benefits from functional restoration compared to patients who reported no opioid use, in terms of pain intensity, depressive symptoms, disability, and insomnia. Additionally, patients who reported higher levels of opioid use showed poorer socioeconomic and health outcomes at one-year follow-up, including work return, work retention, and healthcare utilization rates.

Explanations for these findings are likely multifaceted and are beyond the scope of the present study. Another avenue for exploring differences in socioeconomic and health outcomes include rates of opioid dependence. This line of research could begin by gathering information regarding opioid use, abuse, and dependence at the one year post treatment telephone screen, although, accuracy of that data would be questionable. Additional research is needed to account for differences in treatment outcomes and develop interventions that more effectively address socioeconomic and health issues among patients taking higher doses of pre-treatment opioid. As mentioned above, pre-treatment findings were based on both completers and non-completers of functional restoration, while post-treatment and one-year treatment outcomes were based on completers only. Thus, conclusions regarding the role of pre-treatment level of opioid use may not be generalizable to patients who do not complete functional restoration.

10.8 Summary and Conclusions

In summary, the present study found that pre-treatment, post-treatment and change in opioid dose were associated with similar differences in demographic variables; including length of disability, pre-admission surgery, area of injury, and ethnicity. This study differs from previous investigations in that the PRN doses were included in analysis and the higher doses were collapsed into simply a “High” dose rather than having an additional “Extremely High” group. The current study identified that patients on a PRN dose are relatively similar to those on no opioid medications. This is an important finding given that the previous research has identified differences in the extremes, while little is known about specific ranges of opioid doses that maintain beneficial outcomes. The question of how much is too much and the goal of weaning chronic pain patients completely off medications compared to allowing PRN doses to alleviate occasional severe pain that chronic pain patients may inevitably encounter following completion of a treatment program, may have future implications in setting research based goals for successful treatment.

This study further found that pre- and post-treatment, level of opioid use and change in opioid use were all associated with clinically significant differences in changes in self-reported pain. Pre-treatment and post-treatment measures of psychosocial distress (pain, depression,

disability and sleep), revealed significantly greater distress in groups taking higher doses of opioids, but the responsiveness to treatment as measured by change scores found significant differences in all measures for program completers at post-treatment levels of opioid use and change in level of opioid use. Pre-treatment level of opioid use revealed the only significant change score in psychosocial measures to be a change in pain intensity. These findings have issues of clinical significance even though statistical significance was found between groups. Specifically, the greatest change in pain intensity was decreasing self-reported pain by an average of 2.27 points on a 10 point scale, compared to an average change of only 1.48 points for patients in the High group at pre-treatment. There is a great deal of research addressing the importance of identifying Minimally Clinically Important Change (MCID) (Yost, K. J., Eton, D. T., Garcia, S. F., & Cella, D., 2011) and findings in the current study support the need for such strategies. Further investigation into the true clinical meaningful difference is warranted to fully understand the importance of this particular finding.

The present study provides continued support for the efficacy of functional restoration in the treatment of chronic pain. A substantial portion of patients entering the program reported opioid use upon admission (n=1054; 65.8%). Demographic differences were found related to level of opioid use and rate of program completion, area of injury, length of disability, pre-treatment surgery, and differences in racial groups. An inverse relationship was found between program completion and level of pre-treatment opioid use. A specific area of interest revealed significant findings related to self-reported measures of psychosocial distress as they relate to opioid use at both at pre-treatment and post-treatment after controlling for demographic differences. Overall, these findings suggest that patients on PRN doses of opioids at either pre- and/or post-treatment report similar levels of pain intensity, change in pain intensity, depressive symptoms, perceived disability, and insomnia. Further studies would aid in the understanding of the connection between higher levels of self-reported distress and their association with higher levels of opioid use. Additionally, when analyzing one year socioeconomic outcomes such as work return, work retention, and healthcare utilization, opioid use at pre-treatment was found to be a predictor of work return, but perhaps a better predictor of work retention. While post-

treatments level of opioids for successful program completers did not demonstrate significant differences in work return and work retention rates, healthcare utilization at one-year was found to be associated with post-treatment level of opioid use. Current health care costs require attention to these findings in that individuals who complete a functional restoration program and maintain opioid use may have similar occupational outcomes however, healthcare utilization is significantly greater for chronic pain patients who complete treatment on higher doses of opioid medications.

Appendix A

Tables

Table A1. Demographics by opioid use level at pre-admission - Total cohort N=1,601

Variable	None 0 mg n= 547 (34.2%)	PRN/ Very Low ≤15 mg n = 226 (14.1%)	Low 16-30 mg n = 252 (15.6%)	Moderate 31-60 mg n = 273 (16.7%)	High >61 mg n = 303 (19.5%)	F/χ^2 Value	*p* value	Effect Size
Age, mean (SD)	46.32 (10.9)	46.88 (10.8)	47.60 (10.4)	45.93 (10.2)	47.17 (10.1)	1.459	.212	
Gender, n=987/1601 **n (% male)**	325 (32.9%)	129 (13.1%)	168 (17.0%)	186 (18.8%)	179 (18.1%)	11.535	.038	.08
Completion Status						85.296	.000	.23
Completer, n=1037	384 (37.0%)	173 (16.7%) $^{+}$	180 (17.4%)	159 (15.3%)	141 (13.6%) $^{-}$			
Non-Completer, n=318	98 (30.8%)	26 (8.2%)$^{-}$	37 (11.6%)	75 (23.6%) $^{+}$	82 (25.8%) $^{+}$			
QL, n=246	65 (26.4%)$^{-}$	27 (11.0%)	35 (14.2%)	39 (15.9%)	80 (32.5%) $^{+}$			
Length of Disability, mean (SD)	21.56 (35.0)[5]	20.53 (31.4)[5]	28.35 (48.8)[5]	30.95 (49.9)[5]	54.90 (63.1)[1-4]	29.382	.000	.07
Pre- admission Surgery, n=901/1601 **n (% yes)**	299 (33.2%)	110 (12.2%)	124 (13.8%)	146 (16.2%)	222 (24.6%) $^{+}$	47.427	.000	.17
Area of Injury, n (%)						69.522	.000	.20
lumbar only, n=458	101 (22.1%) $^{-}$	67 (14.6%)	80 (17.5%)	95 (20.7%)	115 (25.1%) $^{+}$			
cervical only, n=38	11 (28.9%)	6 (15.8%)	6 (15.8%)	8 (21.1%)	7 (18.4%)			
extremity only, n=433	184 (42.5%)$^{+}$	69 (15.9%)	67 (15.5%)	57 (13.2%) $^{-}$	56 (12.9%) $^{-}$			
multiple spinal, n=161	58 (36.0%)	23 (14.3%)	27 (16.8%)	30 (18.6%)	23 (14.3%)			
multiple musculoskel., n= 447	173 (28.7%)	51 (11.4%)	66 (14.8%)	67 (15.0%)	90 (20.1%)			
other, n=64	20 (31.2%)	10 (15.6%)	6 (9.4%)	16 (25.0%)	12 (18.8%)			
Ethnicity, n (%) *valid n=1452						67.716	.000	.21
Caucasian, n=805	207 (25.7%)	98 (12.2%)$^{-}$	131 (16.3%)	155 (19.3%)	214 (26.6%) $^{+}$			
African American, n=318	84 (26.4%)	61 (19.2%)	54 (17.0%)	68 (21.4%)	51 (16.0%)			
Hispanic, n=299	111 (37.1%) $^{+}$	56 (18.7%)	60 (20.1%)	44 (14.7%)	28 (9.4%) $^{-}$			
Asian, n=16	4 (25.0%)	5 (31.2%)	1 (6.2%)	3 (18.8%)	3 (18.8%)			
Other, n=14	4 (28.6%)	3 (21.4%)	3 (21.4%)	1 (7.1%)	3 (21.4%)			
Marital Status, n (%) *valid n=1437						21.899	.330	
Single, n= 197	66 (33.5%)	29 (14.7%)	31 (15.7%)	41 (20.8%)	30 (15.2%)			
Married, n=728	200 (27.5%)	116 (15.9%)	121 (16.6%)	135 (18.5%)	156 (21.4%)			
Separated, n= 79	20 (25.3%)	15 (19.0%)	12 (15.2%)	11 (13.9%)	21 (26.6%)			
Divorced, n=332	102 (30.7%)	47 (14.2%)	59 (17.8%)	58 (17.5%)	66 (19.9%)			
Widowed, n=37	4 (10.8%)	6 (16.2%)	10 (27.0%)	9 (24.3%)	8 (21.6%)			
Cohabitating, n=64	12 (18.8%)	8 (12.5%)	13 (20.3%)	15 (23.4%)	16 (25.0%)			

$^{+/-}$ Standard residuals indicate cell driving differences *Valid n's reported in table - missing data were excluded if unavailable

Table A2. Demographics by hydrocodone use at pre- admission, Total cohort N = 1,601

Variable	No Opioids n=547 (34.2%)	Hydrocodone Only n = 577 (36.0%)	Any Other Single Opioid n = 350 (21.9%)	Combination Opioid Use n = 127 (7.9%)	F/χ^2 Value	*p* value	Effect Size
Age	46.30 (10.9)	46.42 (10.2)	47.14 (11.0)	48.41 (9.4)	1.721	.161	
Gender, 987/1601 **n (% male)**	325 (32.9%)	387 (39.2%)$^{+}$	209 (21.2%)	66 (6.7%)$^{-}$	13.909	.003	.09
Completion Status					31.599	.000	.14
Completer, n=1037	383 (36.9%)	380 (36.6%)	213 (20.5%)	61 (5.9%)			
Non-Completer, n= 318	98 (30.8%)	118 (37.1%)	70 (22.0%)	32 (10.1%)			
QL, n=246	65 (26.4%)	79 (32.1%)	68 (27.6%)	34 (13.8%)			
Length of Disability, mean (SD)	21.58 (35.0)$^{2-4}$	29.55 (48.4)^{1,3,4}	39.54 (56.8)^{1,2}	46.83 (53.6)^{1,2}	16.167	.000	.03
Pre- admission Surgery, n (% yes) 901/1601	298 (33.1%)	303 (33.6%) $^{-}$	217 (24.1%) $^{+}$	83 (9.2%) $^{+}$	12.603	.006	.09
Area of Injury, n (%)					71.845	.000	.03
lumbar only, n=458	101(22.1%)-	213 (46.5%)$^{+}$	96 (21.0%)	48 (10.5%)			
cervical only, n=38	11 (28.9%)	11 (28.9%)	12 (31.6%)	4 (10.5%)			
extremity only, n=433	183 (42.3%)$^{+}$	148 (34.2%)	83 (19.2%)	19 (4.4%)$^{-}$			
multiple spinal, n=161	58 (36.0%)	48 (29.8%)	43 (26.7%)	12 (7.5%)			
multiple musculoskel., n= 447	173 (38.7%)	130 (29.1%)$^{-}$	104 (23.3%)	40 (8.9%)			
other, n=64	20 (31.2%)	27 (42.2%)	13 (20.3%)	4 (6.2%)			
Ethnicity, n (%) *valid n=1452					36.948	.000	.16
Caucasian, n=805	207 (25.7%)	310 (38.4%)	212 (26.3%)	77 (9.6%)			
African American, n=318	84 (26.4%)	146 (45.9%)	53 (16.7%)$^{-}$	35 (11.0%)			
Hispanic, n=299	111 (37.1%) $^{+}$	105 (35.1%)	69 (23.1%)	14 (4.7%)$^{-}$			
Asian, n=16	4 (25.0%)	6 (37.5%)	6 (37.5%)	0 (0.0%)			
Other, n=14	4 (28.6%)	4 (28.6%)	5 (35.7%)	1 (7.1%)			
Marital Status, n (%) * valid n=1437					32.021	.006	.15
Single, n= 197	66 (33.5%)	73 (37.1%)	46 (23.4%)	12 (6.1%)			
Married, n=728	200 (27.5%)	272 (37.4%)	185 (25.4%)	71 (9.8%)			
Separated, n= 79	20 (25.3%)	35 (44.3%)	15 (19.0%)	9 (11.4%)			
Divorced, n=332	101 (30.4%)	130 (39.2%)	78 (23.5%)	23 (6.9%)			
Widowed, n=37	4 (10.8%)$^{-}$	18 (48.6%)	9 (24.3%)	6 (16.2%)			
Cohabitating, n=64	12 (18.8%)	40 (62.5%)$^{+}$	9 (14.1%)	3 (4.7%)			
Total Morphine daily dose in mg, mean (SD)	N/A	41.15 (31.92)	55.54 (55.34)	94.73 (46.88)	71.898	.000	.12

$^{+/-}$ Standard residuals indicate cell driving differences *Valid n's reported in table-missing data were excluded if unavailable

Table A3. Occupational variables by opioid use level at pre-admission

Variable	None 0 mg	PRN/ Very Low ≤15 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	F/χ^2 Value	*p* value	Effect Size
Case Type, n (%)						32.198	.000	.14
• **WC,** n=1392	449 (32.3%)	210 (15.1%)	237 (17.0%)	241 (17.3%)	255 (18.3%)			
• **Private Pay,** n=209	98 (17.9%) +	16 (7.7%) -	15 (7.2%) -	32 (15.3%)	48 (23.0%)			
Receiving SSI/SSDI on admission (n, % yes) n=122/1601	32 (26.2%)	6 (4.9%) -	15 (12.3%)	18 (14.8%)	51 (41.8%) +	48.277	.000	.17
Pre-injury Wage mean (SD) *valid n=1239	$754.49 (511.36)	$741.22 (513.36)	$771.06 (594.28)	$806.10 (529.39)	$792.68 (536.06)	0.572	.683	
Job Demand (n, %) *valid n=1321						23.056	.112	
• Sedentary, n=170	62 (36.5%)	32 (18.8%)	15 (8.8%)-	24 (14.1%)	37 (21.8%)			
• Light, n=236	72 (30.5%)	35 (14.8%)	39 (16.5%)	43(18.2%)	47 (19.9%)			
• Medium, n=479	154 (32.2%)	74 (15.4%)	85 (17.7%)	85 (17.7%)	81 (16.9%)			
• Heavy, n=388	112 (28.9%)	50 (12.9%)	75 (19.3%)	75 (19.3%)	76 (19.6%)			
• Very Heavy, n=48	21 (43.8%)	4 (8.3%)	4 (8.3%)	9 (18.8%)	10 (20.8%)			
Job Satisfaction Pre-Injury (n, %) *valid n=768						17.049	.382	
• Very satisfied, n=549	177 (32.2%)	88 (16.0%)	97 (17.7%)	91 (16.6%)	96 (17.5%)			
• Satisfied, n=110	26 (23.6.7%)	15 (13.6%)	18(16.4%)	27 (24.5%)	24 (21.8%)			
• Neutral, n=76	24 (31.6%)	13 (17.1%)	16 (21.1%)	12 (15.8%)	11 (14.5%)			
• Dissatisfied, n=21	10 (47.6%)	5 (23.8%)	4(19.0%)	1(4.8%)	1 (4.8%)			
• Very Dissatisfied, n=12	5 (41.7%)	3 (25.0%)	1 (8.3%)	1 (8.3%)	2 (16.7%)			
Work Status at admission *valid n=1470 **(n, % yes)** n=261	89 (34.1%)	50 (19.2%) +	44 (16.9%)	49 (18.8%)	29 (11.1%) -	15.669	.003	.10
Job Type *valid n=1486 **(n, % blue collar)**	398 (33.1%)	173 (14.4%)	213 (17.7%) +	211 (17.5%)	208 (17.3%)	13.370	.010	.09

+/- Standard residuals indicate cell driving differences *Valid n's reported in table-missing data were excluded if unavailable

Table A4. Occupational variables by pre-admission hydrocodone use

Variable	No Opioids	Hydrocodone Only	Any Other Single Opioid	Combination Opioid Use	F/χ^2 Value	*p* value	Effect Size
Case Type, n (%)					38.978	.000	.14
• **WC,** n=1392	449 (32.2%)	535 (38.4%)	296 (21.3%)	113 (8.1%)			
• **Private Pay,** n=209	98 (46.9%) [+]	42(20.1%) [-]	55 (26.3%)	14 (6.7%)			
Receiving SSI/SSDI on admission (n, % yes) n=122/1601	32 (26.2%)	37 (30.3%)	31 (25.4%)	22 (18.0%) [+]	21.312	.000	.12
Pre-injury Wage (Mean, SD) *valid n=1239	$754.49 (511.36)	$819.01 (608.93)	$739.43 (446.06)	$673.60 (379.48)	2.771 2.076*	.040 .102[#]	.01
Job Demand (n, %) *valid n=1321					42.399	.000	
• Sedentary, n=170	62 (36.5%)	41 (24.1%)	48 (28.2%)	19 (11.2%)			
• Light, n=236	72 (30.5%)	87 (36.9%)	52 (22.0%)	25 (10.6%)			
• Medium, n=479	154 (31.9%)	199 (41.5%)	96 (20.0%)	31 (6.5%)			
• Heavy, n=388	112 (28.9%)	149 (38.4%)	93 (24.0%)	34 (8.8%)			
• Very Heavy, n=48	21 (43.8%)	20 (41.7%)	4 (8.3%)	3 (6.2%)			
Job Satisfaction Pre-Injury (n, %) *valid n=768					15.855	.198	
• Very satisfied, n=549	177 (32.2%)	211 (38.4%)	129 (23.5%)	32 (5.8%)			
• Satisfied, n=110	26 (22.7%)	51 (46.4%)	25 (22.7%)	9 (8.2%)			
• Neutral, n=76	24 (31.6%)	33 (43.4%)	12 (15.8%)	7 (9.2%)			
• Dissatisfied, n=21	10 (47.6%)	10 (47.6%)	1 (4.8%)	0 (0.0%)			
• Very Dissatisfied, n=12	5 (41.7%)	5 (41.7%)	1 (8.3%)	1 (8.3%)			
Work Status at admission *valid n=1470 **(n, % yes)** n=261	89 (34.1%)	83 (31.8%)	63 (24.1%)	26 (10.0%)	5.063	.167	
Job Type *valid n=1486 **(n, % blue collar)**	398 (33.0%)	467 (38.8%)	252 (20.9%)	87 (7.2%)	10.168	.017	.08

[+/-] Standard residuals indicate cell driving differences *Valid n's reported in table-missing data were excluded if unavailable

[#] Non Significant after controlling for demographics

Table A5. Patient reported psychosocial variables pre-treatment by opioid use level at pre-admission

Variable	None[1] 0 mg	PRN[2]/ Very Low ≤15 mg	Low[3] 16-30 mg	Moderate[4] 31-60 mg	High[5] >61 mg	*F* Value	*p* value	Effect Size
Pre Pain Intensity, mean (SD) *valid n=1474	6.60 (2.06)[3-5]	6.72 (1.94)[3-5]	7.62 (5.25)[1,2]	7.54 (1.66)[1,2]	7.70 (1.52)[1,2]	8.859	.000	.02
Pre BDI, mean (SD) *valid n=1469	16.93 (10.59)[5]	16.69 (10.22)[5]	18.58 (9.90)[5]	19.18 (10.43)[5]	22.63 (10.98)[1-4]	11.325	.000	.03
Pre PDQ Total, mean (SD) *valid n=1448	89.28 (28.38)[3-5]	89.79 (26.23)[3-5]	103.76(21.98)[1,2]	105.84 (21.28)[1,2]	110.70 (19.36)[1,2]	39.959	.000	.10
Pre Oswestry, mean (SD) *valid n=1383	36.31 (18.56)[3-5]	37.37 (17.18) [3-5]	43.65 (16.29)[1,2]	43.47(16.30)[1,2,5]	50.25 (16.44)[1,2,4]	19.544	.000	.06
Pre ISI, mean (SD) *valid n=935	15.64 (7.43)[3-5]	16.97 (9.57)	18.42 (6.22)[1]	18.17 (6.36)[1]	19.70 (6.32)[1]	6.964	.000	.03

-ANCOVA utilized to control for demographic differences *Valid n's reported in table-missing data were excluded if unavailable

Table A6. Patient reported psychosocial variables post-treatment by opioid use level at pre-admission

Variable	None[1] 0 mg	PRN[2]/ Very Low ≤15 mg	Low[3] 16-30 mg	Moderate[4] 31-60 mg	High[5] >61 mg	*F* Value	*p* value	Effect Size
Post Pain Intensity, mean (SD) *valid n=1132	4.72 (2.51)[4,5]	4.73 (2.30)[4,5]	5.31 (2.34)	5.56 (2.31)[1,2]	6.05 (2.36)[1,2]	6.021	.000	.02
Post BDI, mean (SD) *valid n=1128	10.51 (9.12)[5]	10.25 (8.99)[5]	12.47 (9.62)	13.18 (10.10)	16.13 (11.22)[1,2]	7.227	.000	.03
Post PDQ, mean (SD) *valid n=1087	62.04 (33.09)[4,5]	62.47 (32.29)[4,5]	73.33 (32.91)[1,2]	75.65 (31.42)[1,2]	82.53 (32.91)[1,2]	9.466	.000	.04
Post Oswestry, mean (SD) *valid n=1071	23.83 (18.12)[3-5]	25.65 (16.64)[5]	29.17 (17.48)[1]	31.13 (17.88)[1]	36.86 (18.29)[1,2]	8.492	.000	.03
Post ISI, mean (SD) *valid n=772	10.72 (7.90)[4,5]	11.83 (7.50)[5]	12.62 (7.46)	13.73 (6.81)[1]	15.12 (7.05)[1,2]	6.343	.000	.03

-ANCOVA utilized to control for demographic differences *Valid n's reported in table-missing data were excluded if unavailable

Table A7. Change in Patient reported psychosocial variables by opioid use level at pre-admission

Variable	None[1] 0 mg	PRN[2]/ Very Low ≤15 mg	Low[3] 16-30 mg	Moderate[4] 31-60 mg	High[5] >61 mg	*F* Value	*p* value	Effect Size
Change Pain Intensity, mean (SD) *valid n=1130	2.23 (2.41)[5]	2.27 (2.62)	1.81 (6.33)	1.67 (2.18)	1.48 (2.66)[1,2]	4.768	.001	.02
Change BDI, mean (SD) *valid n=1122	7.49 (11.37)	7.24 (10.54)	7.21 (9.86)	7.55 (11.46)	8.84 (13.34)	1.698	.148	
Change PDQ Total, mean (SD) *valid n=1068	28.53 (27.47)	29.65 (31.75)	26.17 (30.88)	27.64 (29.49)	26.90 (28.62)	0.444	.777	
Change Oswestry, mean (SD) *valid n=1013	13.17 (16.45)	12.73 (16.10)	11.28 (11.95)	10.48 (15.20)	11.43 (12.42)	1.828	.121	
Change ISI, mean (SD) *valid n=667	5.56 (7.43)	5.09 (9.13)	5.02 (6.64)	4.03 (7.73)	3.06 (4.91)	2.111	.078	

-ANCOVA utilized to control for demographic differences and pre-treatment scores *Valid n's reported in table-missing data were excluded if unavailable

Table A8. Patient reported psychosocial variables pre-treatment by pre-admission hydrocodone use

Variable	No Opioids[1]	Hydrocodone Only[2]	Other Single Opioid[3]	Combination Opioid Use[4]	*F* Value	*p* value	Effect Size
Pre Pain Intensity, mean (SD) *valid n=1474	6.61 (2.07)[2,4]	7.53 (3.69)[1]	7.21 (1.81)	7.61 (1.69)[1]	7.428	.000	.04
Pre BDI, mean (SD) *valid n=1469	16.90 (10.57)[2,3]	18.69 (10.70)[1]	20.44 (10.23)[1]	20.62 (11.24)	5.504	.001	.01
Pre PDQ Total, mean (SD) *valid n=1448	89.23 (28.40)[2-4]	102.18 (23.71)[1]	102.31 (23.55)[1,3]	110.94 (19.12)[1,3]	29.016	.000	.06
Pre Oswestry, mean (SD) *valid n=1383	36.26 (18.55)[2-4]	42.56 (17.00)[1,4]	44.42 (17.63)[1,4]	50.76 (14.89)[1-3]	17.514	.000	.04
Pre ISI, mean (SD) *valid n=935	15.64 (7.45)[2-4]	18.06 (6.63)[1]	18.42 (8.41)[1]	20.07 (5.59)[1]	8.105	.000	.03

-ANCOVA utilized to control for demographic differences *Valid n's reported in table-missing data were excluded if unavailable

Table A9. Patient reported psychosocial variables post-treatment by pre-admission hydrocodone use

Variable	No Opioids[1]	Hydrocodone Only[2]	Any Other Single Opioid[3]	Combination Opioid Use[4]	*F* Value	*p* value	Effect Size
Post Pain Intensity, mean (SD) *valid n=1132	4.73 (2.51)[3,4]	5.25 (2.36)	5.54 (2.39)[1]	6.08 (2.18)[1]	4.501	.004	.01
Post BDI, mean (SD) *valid n=1128	10.48 (9.19)[3]	12.24 (10.24)	14.11 (10.23)[1]	14.18 (9.97)	3.630	.013	.01
Post PDQ Total, mean (SD) *valid n=1087	61.97 (33.11)[2-4]	69.68 (33.26)[1,4]	76.40 (33.26)[1]	86.12 (28.10)[1,2]	9.325	.000	.03
Post Oswestry, mean (SD) *valid n=1071	23.77 (18.11)[2-4]	28.23 (18.03)[1,4]	32.47 (17.48)[1]	38.64 (16.88)[1]	11.734	.000	.03
Post ISI, mean (SD) *valid n=772	10.77 (7.88)[2-4]	12.99 (7.49)[1]	13.43 (7.24)[1]	15.10 (7.55)[1]	5.083	.002	.02

-ANCOVA utilized to control for demographic differences *Valid n's reported in table-missing data were excluded if unavailable

Table A10. Change in Patient reported psychosocial variables by pre-admission hydrocodone use

Variable	No Opioids[1]	Hydrocodone Only[2]	Other Single Opioid[3]	Combination Opioid Use[4]	*F* Value	*p* value	Effect Size
Change Pain Intensity, mean (SD) *valid n=1130	2.33 (2.40)[4]	2.0 (4.71)	1.61 (2.43)[1]	1.01 (2.19)[1]	7.428	.000	.02
Change BDI, mean (SD) *valid n=1122	8.50 (11.38)	7.60 (11.45)	6.87 (10.79)	7.25 (12.89)	1.508	.211	
Change PDQ Total, mean (SD) *valid n=1068	25.87 (27.51)	31.69 (30.02)	25.03 (31.58)	22.77 (24.31)	2.761	.041†	.01
Change Oswestry, mean (SD) *valid n=1013	12.31 (16.15)[3]	13.58 (16.13)	10.27 (15.23)[1]	10.99 (13.62)	4.334	.005	.01
Change ISI, mean (SD) *valid n=667	5.23 (7.67)	4.75 (7.11)	4.54 (9.10)	1.78 (6.20)	0.988	.398	

-ANCOVA utilized to control for demographic differences and pre-treatment scores

†non-significant after Bonferroni correction

*Valid n's reported in table-missing data were excluded if unavailable

Table A11. Medication variables on admission by opioid use on admission

Variable	None 0 mg	PRN/ Very Low ≤15 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	χ^2 Value	*p* value	Effect Size
Pre-Antidepressants, n (% yes) *valid n=1601	220(40.2%)-	111(49.1%)	143(56.7%)	170(62.3%)	210(69.3%)+	80.418	.000	.22
Pre-Neuromodulators, n (% yes) *valid n=1601	184(33.6%)-	88(38.9%)	111(44.0%)	142(52.0%)	174(57.4%)+	55.488	.000	.18
Pre- Sedatives, n (% yes) *valid n=1601	218(39.9%)-	130(57.5%)	165(65.5%)	195(71.4%)	238(78.5)+	152.858	.000	.30

+/- Standard residuals indicate cell driving differences

Table A12. Medication variables upon discharge by opioid use on admission

Variable	None 0 mg	PRN/ Very Low ≤15 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	χ^2 Value	*p* value	Effect Size
Post-Antidepressants, n (% yes) *valid n=1601	245(44.8%)$^{-}$	133(58.8%)	160(63.5%)$^{+}$	165(60.4%)	185(61.1%)	39.427	.000	.16
Post-Neuromodulators, n (% yes) *valid n=1601	153(28.0%)$^{-}$	78(34.5%)	97(38.5%)	95(34.8%)	124(40.9%)$^{+}$	17.644	.001	.10
Post- Sedatives, n (% yes) *valid n=1601	197(36.0%)$^{-}$	119(52.7%)	154(61.1%)	158(57.9%)	182(60.1%)$^{+}$	74.715	.000	.21

$^{+/-}$ Standard residuals indicate cell driving differences

Table A13. Medication variables on admission by pre-admission hydrocodone use

Variable	No Opioids	Hydrocodone Only	Any Other Single Opioid	Combination Opioid Use	χ^2 Value	*p* value	Effect Size
Pre- Antidepressants, n (% yes) *valid n=1601	219(40.1%)$^{-}$	317(54.9%)	223(63.5%)	95(74.8%)$^{+}$	77.151	.000	.21
Pre- Neuromodulators, n (% yes) *valid n=1601	184(33.7%)$^{-}$	274(47.5%)	164(46.7%)	77(60.0%)$^{+}$	41.664	.000	.16
Pre- Sedatives, n (% yes) *valid n=1601	217(39.7%)$^{-}$	376(65.2%)	255(72.6%)	98(77.2%)$^{+}$	137.205	.000	.28

$^{+/-}$ Standard residuals indicate cell driving differences

Table A14. Medication variables upon discharge by pre-admission hydrocodone use

Variable	No Opioids	Hydrocodone Only	Any Other Single Opioid	Combination Opioid Use	χ^2 Value	*p* value	Effect Size
Post-Antidepressants, n (% yes) *valid n=1601	244(44.7%) -	345(59.8%)	221(63.0%) +	78(61.4%)	39.853	.000	.16
Post-Neuromodulators, n (% yes) *valid n=1601	153(28.0%)-	208(36.0%)	133(37.9%)	53(41.7%)	15.471	.001	.10
Post- Sedatives, n (% yes) *valid n=1601	197(36.1%)-	326(56.5%)	208(59.3%)	79(62.2%)+	71.452	.000	.22

+/- Standard residuals indicate cell driving differences

Table A15. Socioeconomic one-year outcome variables by pre-admission opioid use in program completers

Variable	None 0 mg	PRN/ Very Low ≤15 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	TOTAL	χ^2 Value	*p* value	Effect Size
Return-to-Work *valid n=678 **n (% yes)** $^{n=594}$	207 (34.8%)	106 (17.8%)	103 (17.3%)	96 (16.2%)	82 (13.8%)	87.6%	2.703	.609	
Work Retention *valid n=666 **n (% yes)** $^{n=516}$	178 (34.5%)	98 (19.0%)	89 (17.2%)	80 (15.5%)	71 (13.8)	77.5%	3.595	.465	
Healthcare utilization/ New provider *valid n=743 **n (% yes)**$^{n=78}$	15 (19.2%)$^{-}$	6 (7.7%)$^{-}$	19 (24.4%)	11 (14.1%)	27 (34.6%)$^{+}$	10.5%	36.143	.000	.22
New Surgery *valid n=703 **n (% yes)** $^{n=22}$	4 (18.2%)	3 (13.6%)	8 (36.4%)	3 (13.6%)	4 (18.2%)	3.0%	6.562	.161	
New Injury *valid n=696 **n (% yes)**$^{n=6}$	2 (33.3%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	2 (33.3%)	1.0%	4.621	.328	

$^{+/-}$ Standard residuals indicate cell driving differences

*Valid n's reported in table-missing data were excluded if unavailable

Table A16. Socioeconomic one-year outcome variables by pr\e-admission hydrocodone use in program completers

Variable	No Opioids	Hydrocodone Only	Other Single Opioid	Combination Opioid Use	TOTAL	χ^2 Value	*p* value	Effect Size
Return-to-Work *valid n=678 **n (% yes)** $^{n=594}$	207 (34.9%)	222 (37.4%)	122 (20.5%)	43 (7.2%)	87.6%	3.430	.330	
Work Retention *valid n=666 **n (% yes)** $^{n=516}$	178 (34.5%)	193 (37.4%)	108 (20.9%)	37 (7.2%)	77.5%	0.663	.884	
Healthcare utilization * valid n=743 **seeking treatment from new provider n (% yes)**$^{n=78}$	15 (19.2%)	28 (35.9%)	14 (17.9%)	21 (26.9%)	10.5%	54.061	.000	.26
New Surgery *valid n=703 **n (% yes)** $^{n=22}$	4 (18.2%)	6 (27.3%)	8 (36.4%)	4 (18.2%)	3.0%	6.882	.076	
New Injury *valid n=696 **n (% yes)**$^{n=6}$	2 (33.3%)	3 (50.0%)	1 (16.7%)	0 (0.0%)	1.0%	0.701	.873	

$^{+/-}$ Standard residuals indicate cell driving differences

*Valid n's reported in table-missing data were excluded if unavailable

Table A17. Binary logistic regression analysis for prediction of work return in program completers (valid n = 626) all variables at final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I.	
							Lower	Upper
Length of Disability	-.001	.005	.047	1	.828	.999	.990	1.008
Working at Admission	1.721	.477	13.002	1	.000	5.593	2.194	14.256
Pre-admission Surgery	.203	.252	.646	1	.422	1.225	.747	2.009
Receiving Social Security Income	-.957	.606	2.495	1	.114	.384	.117	1.259
Opioid use in total ME on Admission	-.003	.003	.783	1	.376	.997	.991	1.004
Constant	1.712	.194	77.760	1	.000	5.542		

Table A18. Binary logistic regression analysis for prediction of work retention in program completers (valid n = 616) all variables at final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I.	
							Lower	Upper
Length of Disability	.000	.004	.000	1	.996	1.000	.993	1.007
Working at Admission	1.105	.289	14.568	1	.000	3.018	1.712	5.322
Pre-admission Surgery	.112	.202	.309	1	.578	1.119	.753	1.663
Receiving Social Security Income	-.848	.550	2.377	1	.123	.428	.146	1.259
Opioid use in total ME on Admission	-.003	.003	1.458	1	.227	.997	.992	1.002
Constant	1.095	.160	46.698	1	.000	2.990		

Table A19. Binary logistic regression analysis for prediction of healthcare utilization in program completers (valid n = 682) all variables at final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I.	
							Lower	Upper
Length of Disability	.002	.004	.350	1	.554	1.002	.995	1.009
Working at Admission	.317	.297	1.144	1	.285	1.373	.768	2.456
Pre-admission Surgery	.456	.271	2.824	1	.093	1.578	.927	2.685
Receiving Social Security Income	.280	.694	.163	1	.686	1.323	.340	5.154
Opioid use in total ME on Admission	.011	.003	17.245	1	.000	1.011	1.006	1.016
Constant	-2.934	.238	152.202	1	.000	.053		

Table A20. Demographics by opioid use level at post-treatment, program completers n = 1,037

Variable	None[1] 0 mg n= 597 (57.6%)	PRN[2]/ Very Low ≤15 mg n = 295 (28.4%)	Low[3] 16-30 mg n =71 (6.8%)	Moderate[4] 31-60 mg n = 38 (3.7%)	High[5] >61 mg n = 36 (3.5%)	F/χ^2 Value	*p* value	Effect Size
Age, mean (SD)	45.98 (10.35)	45.77 (10.12)	45.37 (10.03)	44.58 (10.46)	43.78 (10.83)	0.546	.698	
Gender, 665/1037 **n (% male)**	370 (55.6%)	196 (29.5%)	48 (7.2%)	25 (3.8%)	26 (3.9%)	3.328	.504	
Length of Disability, mean (SD)	15.68 (19.62)[5]	21.25 (36.11)	26.42 (43.68)	24.95 (37.28)	41.03 (59.04)[1,2]	8.631	.000	.03
Pre- admission Surgery, n (% yes) n=665	304 (56.5%)	132 (24.6%)	39 (7.3%)	32 (6.0%)[+]	30 (5.6%)[+]	36.67	.000	.19
Area of Injury, n (%)						31.401	.050	.17
lumbar only, n=274	134 (48.9%)	104 (38.0%)[+]	17 (6.2%)	9 (3.3%)	10 (3.6%)			
cervical only, n=19	14 (73.7%)	2 (10.5%)	1 (5.3%)	2 (10.5%)	0 (0%)			
extremity only, n=303	188 (62.0%)	76 (25.1%)	23 (7.6%)	8 (2.6%)	8 (2.6%)			
multiple spinal, n=96	54 (56.2%)	30 (31.2%)	7 (7.3%)	2 (2.1%)	3 (3.1%)			
multiple musculoskel., n=298	177 (59.4%)	74 (24.8%)	18 (6.0%)	15 (5.0%)	14 (4.7%)			
Other, n=47	30 (63.8%)	9 (19.1%)	5 (10.6%)	2 (4.3%)	1 (2.1%)			
Ethnicity, n (%) *valid n=949						74.253	.000	.27
Caucasian, n=500	252 (50.4%)	134 (26.8%)	52 (10.4%)[+]	32 (6.4%)[+]	30 (6.0%)[+]			
African American, n=209	104 (49.8%)	91 (43.5%)	8 (3.8%)	2 (1.0%)[-]	4 (1.9%)			
Hispanic, n=223	148 (66.4%)[+]	63 (28.3%)	10 (4.5%)	1 (0.4%)[-]	1 (0.4%)[-]			
Asian, n=8	6 (75.0%)	1 (12.5%)	1 (12.5%)	0 (0%)	0 (0%)			
Other, n=9	6 (66.7%)	3 (33.3%)	0 (0%)	0 (0%)	0 (0%)			
Marital Status, n(%) *valid n=941						31.781	.046	.18
Single, n =131	63 (48.1%)	42 (32.1%)	14 (10.7%)	7 (5.3%)	5 (3.8%)			
Married, n =481	279 (58.0%)	127 (26.4%)	42 (8.7%)	18 (3.7%)	15 (3.1%)			
Separated, n=51	32 (62.7%)	13 (25.5%)	0 (0%)[-]	3 (5.9%)	3 (5.9%)			
Divorced, n=221	115 (52.0%)	82 (37.1%)	9 (4.1%)	6 (2.7%)	9 (4.1%)			
Widowed, n=16	7 (43.8%)	7 (43.8%)	2 (12.5%)	0 (0%)	0 (0%)			
Cohabitating, n=41	15 (36.6%)	16 (39.0%)	4 (9.8%)	3 (7.3%)	3 (7.3%)			

[+/-] Standard residuals indicate cell driving differences *Valid n's reported in table-missing data were excluded if unavailable

Table A21. Occupational variables by opioid use level at post-treatment, program completers

Variable	None 0 mg	PRN/ Very Low ≤15 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	F/χ^2 Value	*p* value	Effect Size
Case Type, n (%)						38.978	.000	.19
• **WC,** n=903	507 (56.1%)	256.9 (31.1%)$^{+}$	63 (7.0%)	26 (2.9%)	26 (2.9%)			
• **Private Pay,** n=134	90 (67.2%)	14 (10.4%)$^{-}$	8 (6.0%)	12 (9.0%)	10 (7.5%)			
Receiving SSI/SSDI on admission n=26/1037 **(n, % yes)**	9 (34.6%)	4 (15.4%)	5 (19.2%)$^{+}$	3 (11.5%)$^{+}$	5 (19.2%) $^{+}$	33.605	.000	.18
Pre-injury Wage (Mean, SD) *valid n=805	$750.79 (408.68)	$779.31 (686.59)	$923.56 (539.56)	$975.41 (1061.25)	$779.38 (546.06)	2.030	.088	
Job Demand(n, %) *valid n=848						42.399	.000	.22
• Sedentary, n=88	51 (58.0%)	21 (23.9%)	7 (8.0%)	2 (2.3%)	7 (8.0%)			
• Light, n=168	109 (64.9%)	34 (20.2%)	11 (6.5%)	5 (3.0%)	9 (5.4%)			
• Medium, n=308	183 (59.4%)	102 (33.1%)$^{+}$	14 (20.0%)	5 (1.6%)	4 (1.3%)			
• Heavy, n=254	128 (50.4%)	86 (33.9%)	20 (7.9%)	11 (4.3%)	9 (3.5%)			
• Very Heavy, n=30	14 (46.7%)	9 (30.0%)	3 (10.0%)	4 (13.3%)	0 (0.0%)			
Job Satisfaction Pre-Injury (n, %) *valid n=537						21.616	.156	
• Very satisfied, n=385	222 (57.7%)	111 (28.8%)	27 (7.0%)	11 (2.9%)	14 (3.6%)			
• Satisfied, n=78	35 (44.9%)	29 (37.2%)	11 (14.1%)	0 (0.0%)	3 (3.8%)			
• Neutral, n=51	28 (54.9%)	17 (33.3%)	2 (3.9%)	3 (5.9%)	1 (2.0%)			
• Dissatisfied, n=16	11 (68.8%)	4 (25.0%)	0 (0.0%)	0 (0.0%)	1 (6.2%)			
• Very Dissatisfied, n=7	2 (28.6%)	3 (42.9%)	2 (28.6%)	0 (0.0%)	0 (0.0%)			
Work Status at admission *valid n=933 **(n, % yes)**	123 (23.1%)	57 (20.9%)	13 (19.1%)	11 (40.7%)	7 (21.2%)	6.129	.190	
Job Type *valid n=963 **(n, % blue collar)**	455 (83.9%)	246 (85.1%)	56 (84.8%)	26 (78.8%)	23 (69.7%)	5.842	.211	

$^{+/-}$ Standard residuals indicate cell driving differences

*Valid n's reported in the table-missing data were excluded if unavailable

Table A22. Patient reported psychosocial variables pre-treatment by opioid use level at post-treatment, program completers

Variable	None[1] 0 mg	PRN[2]/ Very Low≤15mg	Low[3] 16-30 mg	Moderate[4] 31-60 mg	High[5] >61 mg	*F* Value	*p* value	Effect Size
Pre Pain Intensity, mean (SD) *valid n=1037	6.58 (1.97)[2]	7.41 (4.95)[1]	7.10 (1.82)	7.18 (1.81)	7.41 (1.50)[1]	3.005	.018	.01
Pre BDI, mean (SD) *valid n=963	16.35 (9.77)[4,5]	16.98 (9.74)[5]	17.67 (10.09)	20.68 (11.14)[1]	23.72 (9.12)[1,2]	6.185	.000	.03
Pre PDQ Total, mean (SD) *valid n=951	88.64 (27.99)[5,3]	99.38 (21.86)	102.13 (21.81)[1]	97.54 (21.33)	103.86 (18.59)[1]	12.416	.000	.05
Pre Oswestry, mean (SD) *valid n=911	36.09 (17.95)[5]	40.92 (15.98)	42.57 (17.17)	42.45 (13.88)	45.94 (16.09)[1]	6.922	.000	.03
Pre ISI, mean (SD) *valid n=613	15.74 (7.30)[5]	17.24 (8.57)	15.88 (7.29)[5]	17.74 (6.90)	18.86 (4.98)[1,3]	3.377	.010	.02

-ANCOVA utilized to control for demographic differences *Valid n's reported in the table-missing data were excluded if unavailable

Table A23. Patient reported psychosocial variables post-treatment by opioid use level at post-treatment, program completers

Variable	None[1] 0 mg	PRN[2]/ Very Low≤15mg	Low[3] 16-30 mg	Moderate[4] 31-60 mg	High[5] >61 mg	F Value	*p* value	Effect Size
Post Pain Intensity, mean (SD) *valid n=900	4.37 (2.36)[2-5]	4.95 (2.26)[1,5]	5.38 (2.16)[1]	5.78 (1.87)[1]	6.60 (1.40)[1,2]	11.921	.000	.05
Post BDI, mean (SD) *valid n=897	9.65 (8.35)[4,5]	10.87 (8.81)[5]	12.87 (10.22)	15.50 (11.40)[1]	17.17 (10.52)[1,2]	9.941	.000	.04
Post PDQ Total, mean (SD) *valid n=870	58.01 (31.42)[4,5]	65.42 (30.17)[5]	74.62 (30.17)	78.62 (30.38)[1]	83.29 (27.99)[1,2]	11.799	.000	.05
Post Oswestry, mean (SD) *valid n=897	22.06 (16.69)[5]	26.70 (15.99)	31.87 (17.02)	33.97 (18.57)[1]	35.37 (13.64)[1,2]	12.905	.000	.06
Post ISI, mean (SD) *valid n=623	10.57 (7.75)[4,5]	12.38 (7.03)[5]	14.29 (7.08)	15.75 (7.01)[1,2]	15.33 (6.87)[1,2]	8.027	.000	.05

-ANCOVA utilized to control for demographic differences *Valid n's reported in the table-missing data were excluded if unavailable

Table A24. Change in Patient reported psychosocial variables by opioid use level at post-treatment, program completers

Variable	None[1] 0 mg	PRN[2]/ Very Low≤15mg	Low[3] 16-30 mg	Moderate[4] 31-60 mg	High[5] >61 mg	*F* Value	*p* value	Effect Size
Change Pain Intensity, mean (SD) *valid n=900	2.26 (2.42)[4,5]	2.47 (5.59)[3-5]	1.68 (2.34)[1,2]	1.44 (2.05)[1,2]	0.800 (1.88)[1,2]	11.063	.000	.05
Change BDI, mean (SD) *valid n=928	7.48 (9.39)[5]	6.62 (10.28)[5]	5.14 (8.68)	5.75 (8.63)	6.54 (5.61)[1,2]	6.480	.000	.03
Change PDQ Total, mean (SD) *valid n=856	31.53 (29.28)[5]	34.54 (30.83)[5]	28.56 (25.69)	20.21 (28.88)	20.23 (21.97)[1,2]	6.134	.000	.03
Change Oswestry, mean (SD) *valid n=813	14.32 (16.20)[4]	14.36 (15.91)[4]	11.84 (11.85)	6.61 (16.32) [1,2]	10.05 (13.45)[4]	7.951	.000	.04
Change ISI, mean (SD) *valid n=539	5.23 (7.43)[4]	4.75 (9.13)	4.54 (6.64)	1.78 (7.73)[1,5]	3.93 (4.91) [1]	4.773	.001	.04

-ANCOVA utilized to control for demographic differences and pre-treatment scores
*Valid n's reported in the table-missing data were excluded if unavailable

Table A25. Medication variables on admission by opioid use level at post-treatment, program completers

Variable	None 0 mg	PRN/ or daily dose <16 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	χ^2 Value	*p* value	Effect Size
Pre- Antidepressants, n (% yes) *valid n=1037	244(40.9%)$^{-}$	163(55.3%)	53(74.6%)	27(71.1%)	32(88.9%)$^{+}$	68.926	.000	.25
Pre- Neuromodulators, n (% yes) *valid n=1037	332(55.6%)$^{-}$	225(76.3%)	62(87.3%)	33(86.8%)	33(91.7%)$^{+}$	74.951	.000	.19
Pre- Sedatives, n (% yes) *valid n=1037	281(47.1%)$^{-}$	196(66.4%)	51(71.8%)	30(78.9%)	33(91.7)$^{+}$	66.239	.000	.25

$^{+/-}$ Standard residuals indicate cell driving differences

Table A26. Medication variables upon discharge by opioid use level at post-treatment, program completers

Variable	None 0 mg	PRN/ Very Low ≤15 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	χ^2 Value	*p* value	Effect Size
Post- Antidepressants, n (% yes) *valid n=1037	332(55.6%)$^{-}$	225(76.3%)	62(87.3%)	33(86.8%)	33(91.7%)$^{+}$	74.951	.000	.26
Post- Neuromodulators, n (% yes) *valid n=1037	186(31.2%)$^{-}$	138(46.8%)	45(63.4%)	23(60.5%)	23(63.9%)$^{+}$	56.500	.000	.23
Post- Sedatives, n (% yes) *valid n=1037	271(45.4%)$^{-}$	223(75.6%)	60(84.5%)	33(86.8%)	32(88.9%)$^{+}$	124.295	.000	.33

$^{+/-}$ Standard residuals indicate cell driving differences

Table A27. Socioeconomic one-year outcome variables by opioid use level at post-treatment, program completers

Variable	None 0 mg	PRN/ Very Low ≤15 mg	Low 16-30 mg	Moderate 31-60 mg	High >61 mg	Total	χ^2 Value	*p* value	Effect Size
Return-to-Work *valid n=678 **n (% yes)** $^{n=594}$	352 (59.3%)	169 (28.5%)	33 (5.6%)	17 (2.9%)	23 (3.9%)	87.6%	1.401	.844	
Work Retention *valid n=666 **n (% yes)** $^{n=516}$	309 (59.9%)	145 (28.1%)	30 (5.8%)	15 (2.9%)	17 (3.3%)	77.5%	3.224	.521	
Healthcare utilization/ New provider *valid n=743 **n (% yes)**$^{n=78}$	32 (41.0%)$^{-}$	24 (30.8%)	8 (10.3%)	4 (5.1%)	10 (12.8%)$^{+}$	10.5%	22.414	.000	.17
New Surgery *valid n=743 **n (% yes)** $^{n=22}$	10 (45.5%)	8 (36.4%)	3 (13.6%)	0 (0.0%)	1(4.5%)	3.1%	4.624	.328	
New Injury *valid n=696 **n (% yes)**$^{n=6}$	3 (50.0%)	1 (16.7%)	1 (16.7%)	0 (0.0%)	1(3.7%)	1.0%	4.505	.342	

$^{+/-}$ Standard residuals indicate cell driving differences

Table A28. Binary logistic regression analysis for prediction of work return with post-treatment opioid in total ME (Morphine Equivalence) program completers (valid n=625) - all variables at the final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I.	
							Lower	Upper
Length of Disability	-.001	.005	.054	1	.815	.999	.990	1.008
Working at Admission	-1.732	.480	13.000	1	.000	.177	.069	.454
Pre-admission Surgery	-.256	.256	.998	1	.318	.774	.469	1.279
Receiving Social Security Income	.855	.620	1.904	1	.168	2.353	.698	7.929
Opioid use in total ME at discharge	-.006	.005	1.820	1	.177	.994	.984	1.003
Constant	2.812	.842	11.155	1	.001	16.636		

Table A29. Binary logistic regression analysis for prediction of work retention with post-treatment opioid in total ME (Morphine Equivalence) program completers (valid n=615) - all variables at the final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I.	
							Lower	Upper
Length of Disability	.000	.004	.000	1	.995	1.000	.993	1.007
Working at Admission	-1.109	.291	14.519	1	.000	.330	.187	.584
Pre-admission Surgery	-.144	.204	.500	1	.480	.866	.580	1.291
Receiving Social Security Income	.758	.559	1.840	1	.175	2.134	.714	6.377
Opioid use in total ME at discharge	-.006	.004	1.959	1	.162	.994	.986	1.002
Constant	1.544	.668	5.350	1	.021	4.685		

Table A30. Binary logistic regression analysis for prediction of healthcare utilization with post-treatment opioid in total ME (Morphine Equivalence) program completers (valid n=680) - all variables at the final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I. Lower	95% C.I. Upper
Length of Disability	.003	.003	.732	1	.392	1.003	.996	1.010
Working at Admission	-.313	.294	1.134	1	.287	.731	.411	1.302
Pre-admission Surgery	-.448	.271	2.731	1	.098	.639	.376	1.087
Receiving Social Security Income	.036	.723	.003	1	.960	1.037	.252	4.275
Opioid use in total ME at discharge	.013	.004	10.891	1	.001	1.013	1.005	1.021
Constant	-2.000	.814	6.039	1	.014	.135		

Table A31. Demographics by change in opioid use, program completers n = 1,037

Variable	No Opioids n= 353 (34.0%)	Increase from none to PRN dose n = 56 (5.4%)	Decreased to No Opioids n = 245 (23.6%)	Decreased to PRN only n = 244 (23.5%)	Continued use above PRN dose n = 139 (13.4%)	F/χ^2 Value	*p* value	Effect Size
Age, mean (SD)	45.88 (10.63)	44.71 (11.28)	46.11 (9.94)	46.11 (9.94)	44.55 (10.15)	0.778	.540	
Gender, n=665/1037 **n (% male)**	212 (31.9%)	38 (5.7%)	159 (23.9%)	162 (24.4%)	94 (14.1%)	4.229	.376	
Length of Disability, mean (SD)	14.50 (15.35)	15.91 (25.37)	17.33 (24.41)	22.73 (38.21)	29.70 (46.97)$^{+}$	7.719	.000	.03
Pre- admission Surgery, n (% yes) n=665	184 (34.3%)	29 (5.4%)	120 (22.3%)	108 (20.1%)	96 (17.9%)$^{+}$	22.942	.000	.15
Area of Injury, n (%)						49.044	.000	.21
lumbar only, n=274	61 (22.3%)-	15 (5.5%)	73 (26.6%)	90 (32.8%)$^{+}$	35 (12.8%)			
cervical only, n=19	6 (31.6%)	0 (0.0%)	8 (42.1%)	2 (10.5%)	3 (15.8%)			
extremity only, n=303	130 (42.9%)	20 (6.6%)	58 (19.1%)	58 (19.1%)	37 (12.2%)			
multiple spinal, n=96	34 (35.4%)	6 (6.2%)	20 (20.8%)	25 (26.0%)	11 (11.5%)			
multiple musculoskel., n=298	108 (36.2%)	14 (4.7%)	70 (23.5%)	61 (20.5%)	45 (15.1%)			
other, n=47	14 (29.8%)	1 (2.1%)	16 (34.0%)	8 (17.0%)	8 (17.0%)			
Ethnicity, n (%) *valid n=949						72.578	.000	.27
Caucasian, n=500	134 (26.8%)	26 (5.2%)	118 (23.6%)	112 (22.4%)	110 (22.0%)$^{+}$			
African American, n= 209	53 (25.4%)	18 (8.6%)	52 (53.3%)	72 (34.4%)	14 (6.7%)$^{+}$			
Hispanic, n=223	84 (37.7%)$^{+}$	8 (3.6%)	64 (28.7%)	56 (25.1%)	11 (4.9%)$^{-}$			
Asian, n=8	2 (25.0%)	0 (0.0%)	4 (50.0%)	2 (25.0%)	0 (0.0%)			
Other, n=9	2 (22.2%)	1 (11.1%)	4 (44.4%)	2 (22.2%)	0 (0.0%)			
Marital Status, n (%) *valid n=941						30.343	.064	
Single, n= 131	40 (30.5%)	12 (9.2%)	23 (17.6%)	31 (23.7%)	25 (19.1%)			
Married, n=481	146 (30.4%)	21 (4.4%)	133 (27.7%)	111 (23.1%)	70 (14.6%)			
Separated, n=51	16 (31.4%)	2 (3.9%)	16 (31.4%)	11 (21.6%)	6 (11.8%)			
Divorced, n=221	62 (28.1%)	18 (8.1%)	53 (24.0%)	64 (29.0%)	24 (10.9%)			
Widowed, n=16	2 (12.5%)	1 (6.2%)	5 (31.2%)	6 (37.5%)	2 (12.5%)			
Cohabitating, n=41	6 (14.6%)	1 (2.4%)	9 (22.0%)	15 (36.6%)	10 (24.4%)			

$^{+/-}$ Standard residuals indicate cell driving differences *Valid n's reported in table-missing data were excluded if unavailable

Table A32. Occupational variables by change in opioid use, program completers

Variable	No Opioids	Increase from none to PRN dose	Decreased to No Opioids	Decreased to PRN only	Continued use above PRN dose	F/χ^2 Value	*p* value	Effect Size
Case Type, n (%)						29.057	.000	.17
• **WC,** n=903	294 (32.6%)	53 (5.9%)	214 (23.7%)	232 (25.7%)	110 (12.2%)			
• **Private Pay,** n=134	59 (44.0%)	3 (2.2%)	31 (23.1%)	12 (9.0%)	29 (21.6%)			
Receiving SSI/SSDI on admission (n, % yes) 26/1037	5 (19.2%)	2 (7.7%)	4 (15.4%)	2 (7.7%)	13 (50%)$^{+}$	32.233	.000	.18
Pre-injury Wage (Mean, SD) *valid n=805	$731.72 (376.04)	$928.34 (1084.10)	$773.63 (450.04)	$748.91 (549.32)	$924.61 (698.02)	3.173	.013	.02
Job Demand (n, %) *valid n=848						37.021	.002	.21
• Sedentary, n=88	33 (37.5%)	5 (5.7%)	18 (20.5%)	16 (18.2%)	16 (18.2%)			
• Light, n=168	59 (35.1%)	5 (3.0%)	50 (29.8%)	30 (17.9%)	24 (14.3%)			
• Medium, n=308	98 (31.8%)	18 (5.8%)	86 (27.9%)	84 (27.3%)	22 (7.1%)$^{-}$			
• Heavy, n=254	72 (28.3%)	13 (5.1%)	56 (22.0%)	76 (29.9%)	37 (14.6%)			
• Very Heavy, n=30	13 (43.3%)	2 (6.7%)	1 (3.3%)$^{-}$	7 (23.3%)	7 (23.3%)			
Job Satisfaction Pre-Injury (n, %) *valid n=537						12.939	.677	
• Very satisfied, n=385	128 (33.2%)	18 (4.7%)	95 (24.7%)	95 (24.7%)	49 (12.7%)			
• Satisfied, n=78	16 (20.5%)	8 (10.3%)	19 (24.4%)	22 (28.2%)	13 (16.7%)			
• Neutral, n=51	16 (31.4%)	3 (5.9%)	12 (23.5%)	14 (27.5%)	6 (11.8%)			
• Dissatisfied, n=16	7 (43.8%)	1 (6.2%)	4 (25.0%)	3 (18.8%)	1 (6.2%)			
• Very Dissatisfied, n=7	1 (14.3%)	1 (14.3%)	1 (14.3%)	2 (28.6%)	2 (28.6%)			
Work Status at admission *valid n=933 **(n, % yes)**	69 (32.7%)	6 (2.8%)	54 (25.6%)	53 (25.1%)	29 (13.7%)	3.208	.524	
Job Type *valid n=963 **(n, % blue collar)**	266 (33.0%)	45 (5.6%)	190 (23.6%)	205 (25.4%)	100 (12.4%)	3.280	.512	

$^{+/-}$ Standard residuals indicate cell driving differences *Valid n's reported in table-missing data were excluded if unavailable

Table A33. Patient reported psychosocial variables pre-treatment by change in opioid use, program completers

Variable	No Opioids[1]	Increase from[2] none to PRN dose	Decreased to No[3] Opioids	Decreased to[4] PRN only	Continued use[5] above PRN dose	*F* Value	*p* value	Effect Size
Pre Pain Intensity, mean (SD) *valid n=1037	6.32 (2.01)[4,5]	6.66 (2.24)[4]	6.89 (1.88)	7.55 (5.34)[1,2]	7.26 (1.71)[1]	5.548	.000	.02
Pre BDI, mean (SD) *valid n=963	15.39 (9.74)[4,5]	15.41 (9.20)[4,5]	17.49 (9.98)	17.23 (9.86)[1]	20.27 (10.35)[1,2]	6.276	.000	.03
Pre PDQ Total, mean (SD) *valid n=951	83.44 (28.40)[4,5]	90.63 (23.10)	94.62 (26.28)	101.14 (21.50)[1]	101.96 (20.17)[1]	21.195	.000	.08
Pre Oswestry, mean (SD) *valid n=911	33.41 (17.67)[4,5]	36.81 (15.86)[5]	39.24 (17.78)	41.61 (16.03)[1]	43.95 (15.85)[1,2]	11.586	.000	.05
Pre ISI, mean (SD) *valid n=613	14.46 (7.32)[4,5]	16.62 (7.41)[5]	17.27 (6.10)	17.33 (8.82)[1,]	18.67 (6.67)[1,2]	6.132	.000	.04

-ANCOVA utilized to control for demographic differences *Valid n's reported in table-missing data were excluded if unavailable

Table A34. Patient reported psychosocial variables post-treatment by change in opioid use, program completers

Variable	No Opioids[1]	Increase from[2] none to PRN dose	Decreased to No[3] Opioids	Decreased to[4] PRN only	Continued use[5] above PRN dose	*F* Value	*p* value	Effect Size
Post Pain Intensity, mean (SD) *valid n=900	4.29 (2.35)[5]	4.68 (2.51)	4.53 (2.36)	4.98 (2.20)	5.87 (1.92)[1]	11.893	.000	.05
Post BDI , mean (SD) *valid n=897	9.12 (8.20)[5]	10.54 (10.39)	10.38 (8.54)	10.83 (8.35)	14.90 (10.76)[1]	9.607	.000	.04
Post PDQ Total, mean (SD) *valid n=870	55.10 (30.62)[5,4]	60.24 (30.425)	61.80 (32.13)	66.09 (29.95)[1]	79.11 (29.38)[1,2]	14.007	.000	.06
Post Oswestry, mean (SD) *valid n=897	20.45 (16.47)[5]	24.00 (16.54)	24.17 (16.83)	27.14 (15.74)	33.78 (16.49)[1]	14.968	.000	.07
Post ISI, mean (SD) *valid n=623	9.96 (7.94)[5,4]	10.91 (6.85)	11.46 (7.50)	12.59 (6.99)	15.23 (6.94)[1,2]	9.611	.000	.06

-ANCOVA utilized to control for demographic differences *Valid n's reported in table-missing data were excluded if unavailable

Table A35. Change in Patient reported psychosocial variables by change in opioid use, program completers

Variable	No Opioids[1]	Increase from[2] none to PRN dose	Decreased to No[3] Opioids	Decreased to[4] PRN only	Continued use[5] above PRN dose	*F* Value	*p* value	Effect Size
Change Pain Intensity, mean (SD) *valid n=900	2.13 (2.37)	1.98 (3.07)	2.41 (2.48)[5]	2.58 (5.98)[5]	1.38 (2.20)[3,4]	10.834	.000	.05
Change BDI, mean (SD) *valid n=928	6.97(9.34)	4.88 (9.45)[3]	8.01 (9.45)[2]	6.99 (10.42)	5.76 (7.96)[3]	6.319	.000	.03
Change PDQ Total, mean (SD) *valid n=856	28.57 (26.49)	30.36 (31.34)	34.98 (32.06)	35.82 (30.49)[5]	23.61 (25.73)[4]	6.157	.000	.03
Change Oswestry, mean (SD) *valid n=813	13.02 (16.05)	12.20 (17.84)	15.85 (16.27)[5]	14.83 (15.31)	10.25 (13.55)[3]	7.329	.000	.04
Change ISI, mean (SD) *valid n=539	4.34 (8.04)	5.64 (7.82)	6.32 (6.40)[5]	4.61 (9.44)	3.56 (6.57)[3]	5.046	.001	.04

-ANCOVA utilized to control for demographic differences and pre-treatment scores *Valid n's reported in table-missing data were excluded if unavailable

Table A36. Medication variables on admission by change in opioid use, program completers

Variable	No Opioids	Increase from none to PRN dose	Decreased to No Opioids	Decreased to PRN only	Continued use above PRN dose	χ^2 Value	*p* value	Effect Size
Pre-Antidepressants, n (% yes) n=1037	135 (38.2%)$^{-}$	22 (39.3%)	109 (44.5%)	133 (54.4%)	108 (77.7%)$^{+}$	69.700	.000	.25
Pre-Neuromodulators, n (% yes) n=1037	118 (33.4%)$^{-}$	25 (44.6%)	89 (36.3%)	108 (44.3%)	86 (61.9%)$^{+}$	36.965	.000	.19
Pre- Sedatives, n (% yes) n=1037	135 (38.3%)$^{-}$	34 (60.7%)	147 (60.0%)	166 (68.0%)	109 (78.4%)$^{+}$	90.009	.000	.28

$^{+/-}$ Standard residuals indicate cell driving differences

Table A37. Medication variables upon discharge by change in opioid use, program completers

Variable	No Opioids	Increase from none to PRN dose	Decreased to No Opioids	Decreased to PRN only	Continued use above PRN dose	χ^2 Value	*p* value	Effect Size
Post- Antidepressants, n (% yes) *valid n=1037	190 (53.8%)	44 (21.4%)$^{-}$	143 (58.4%)	184 (75.4%)	124 (89.2%)$^{+}$	76.678	.000	.26
Post- Neuromodulators, n (% yes) *valid n=1037	114 (32.3%)	28 (50.0%)	72 (29.4%)$^{-}$	113 (46.3%)	88 (63.3%)$^{+}$	58.071	.000	.23
Post- Sedatives, n (% yes) *valid n=1037	150 (42.5%)$^{-}$	40 (71.4%)	122 (49.8%)	188 (77.0%)	119 (85.6%)$^{+}$	125.940	.000	.31

$^{+/-}$ Standard residuals indicate cell driving differences

Table A38. Socioeconomic one-year outcome variables by by change in opioid use, program completers

Variable	No Opioids	Increase from none to PRN dose	Decreased to No Opioids	Decreased to PRN only	Continued use above PRN dose	Total	χ^2 Value	*p* value	Effect Size
Return-to-Work *valid n=678 **n (% yes)** **n=594**	194 (32.7%)	28 (4.7%)	159 (26.8%)	143 (24.1%)	70 (11.8%)	87.6%	1.781	.776	
Work Retention *valid n=666 **n (% yes)** **n=516**	168 (32.6%)	25 (4.8%)	141 (27.3%)	123 (23.8)	59 (11.4%)	77.5%	2.985	.560	
Healthcare utilization/ New Provider *valid n=743 **n (% yes)** **n=78**	13 (16.7%)$^{-}$	3 (3.8%)	19 (24.4%)	21 (26.9%)	22 (28.2%)$^{+}$	10.5%	22.415	.000	.17
New Surgery *valid n=703 **n (% yes)** **n=22**	4 (18.2%)	0 (0.0%)	6 (27.3%)	8 (36.4%)	4 (18.2%)	3.1%	4.571	.334	
New Injury *valid n=696 **n (% yes)** **n=6**	2 (33.3%)	0 (0.0%)	1 (16.7%)	1 (16.7%)	2 (33.3%)	1.0%	2.984	.561	

$^{+/-}$ Standard residuals indicate cell driving differences

*Valid n's reported in table-missing data were excluded if unavailable

Table A39. Binary logistic regression analysis for prediction of work return program completers (valid n=626) all variables at the final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I.	
							Lower	Upper
Length of Disability	-.001	.004	.054	1	.816	.999	.990	1.008
Working at Admission	-1.723	.479	12.965	1	.000	.178	.070	.456
Pre-admission Surgery	-.202	.252	.639	1	.424	.817	.498	1.340
Receiving Social Security Income	.902	.618	2.132	1	.144	2.464	.734	8.267
Change in Opioid Use : No Opioids			1.454	4	.835			
Increase from none to PRN dose	-.695	.695	1.001	1	.317	.499	.128	1.947
Decreased to No Opioids	-.358	.659	.296	1	.587	.699	.192	2.542
Decreased to PRN only	-.295	.667	.195	1	.659	.745	.201	2.754
Continued use above PRN dose	-.381	.671	.322	1	.570	.683	.184	2.544
Constant	3.028	1.004	9.096	1	.003	20.666		

Table A40. Binary logistic regression analysis for prediction of work retention in program completers (valid n=616) all variables at the final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I. Lower	95% C.I. Upper
Length of Disability	.000	.004	.003	1	.957	1.000	.993	1.007
Working at Admission	-1.095	.290	14.285	1	.000	.335	.190	.590
Pre-admission Surgery	-.102	.202	.252	1	.615	.903	.607	1.343
Receiving Social Security Income	.860	.559	2.371	1	.124	2.363	.791	7.062
Change in Opioid Use : No Opioids			1.381	4	.847			
Increase from none to PRN dose	-.225	.499	.203	1	.653	.799	.300	2.125
Decreased to No Opioids	-.063	.508	.015	1	.902	.939	.347	2.542
Decreased to PRN only	-.324	.507	.408	1	.523	.723	.267	1.955
Continued use above PRN dose	-.355	.542	.429	1	.512	.701	.242	2.029
Constant	1.566	.781	4.020	1	.045	4.787		

Table A41. Binary logical regression analysis for prediction of healthcare utilization in program completers (valid n=682) all variables at the final block

Variable	B	S.E.	Wald	df	Sig.	Odds Ratio	95% C.I. Lower	95% C.I. Upper
Length of Disability	.002	.003	.248	1	.619	1.002	.995	1.008
Working at Admission	-.349	.293	1.419	1	.234	.705	.397	1.253
Pre-admission Surgery	-.491	.270	3.311	1	.069	.612	.361	1.039
Receiving Social Security Income	-.091	.708	.016	1	.898	.913	.228	3.656
Change in Opioid Use : No Opioids			13.835	4	.008			
Increase from none to PRN dose	.922	.668	1.908	1	.167	2.515	.679	9.309
Decreased to No Opioids	-.601	.687	.766	1	.381	.548	.143	2.106
Decreased to PRN only	.014	.662	.000	1	.984	1.014	.277	3.707
Continued use above PRN dose	.219	.661	.109	1	.741	1.244	.341	4.544
Constant	-1.720	.963	3.191	1	.074	.179		

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Biographical Information

Whitney Worzer was born in Dallas, Texas and graduated from L.V. Berkner High School in Richardson, Texas. She received a Bachelor of Science degree in Rehabilitation Services from the Allied Health Sciences School at the University of Texas Southwestern Medical Center at Dallas. Whitney continued her academic pursuits and received the degree of Master of Science in Rehabilitation Counseling Psychology from the Graduate School of Biomedical Sciences at the University of Texas Southwestern Medical Center at Dallas in August 2007. Following the completion of her Master's degree she obtained credentials as a Certified Rehabilitation Counselor and Licensed Professional Counselor. Whitney obtained additional training in assessment and in 2012 began working for a small private practice where she administers neuropsychological testing. Upon completion of her PhD in 2015, Whitney will continue to work in private practice in the Dallas area and devote time to her only son, Andrew and pursue continuing education with additional training in the clinical neuroscience field.