AN EXAMINATION OF THE VALIDITY OF THE CENTRAL SENSITIZATION INVENTORY WITH CHRONIC DISABLING OCCUPATIONAL MUSCULOSKELETAL DISORDERS

by

YUNHEE CHOI

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Abstract

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YunHee Choi, PhD

The University of Texas at Arlington, 2013

Supervising Professor: Robert J. Gatchel

Central Sensitivity Syndrome (CSS) includes a group of related conditions that share a common pathophysiological mechanism called central sensitization (e.g., fibromyalgia, irritable bowel syndrome, tension headache/migraine, etc.). Individuals with these conditions display increased pain sensitivity in response to painful stimuli, pain in response to normally non-painful stimuli, and expansion of the receptive field. Depression and anxiety frequently occur among individuals with CSS, as well as disturbed sleep, somatic symptoms and emotional distress. The Central Sensitization Inventory (CSI) is a newly developed self-report measure to assess the full array of 25 somatic and emotional symptoms associated with CSS. The present study sought to examine the concurrent validity of the CSI, and the predictive ability of the pre-determined cut-off point of 40, and the proposed severity cutoffs of 30, 40, 50, and 60 on the CSI associated with program completion and/or one-year socioeconomic outcomes. A total of 681 patients with a Chronic Disabling Occupational Musculoskeletal Disorder (CDOMD) were collected from a regional functional restoration program (FRP). A series of univariate and multivariate regression analyses were utilized to identify key factors contributing to the total CSI scores at FRP admission. Results revealed that CDOMD patients with high CSI scores

were likely; to be diagnosed with post-injury Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD); to have spinal disorders (opposed to extremity disorders); to report previous history of CSS; and to have an abuse experience history. The CSI was moderately associated with other psychosocial instruments measuring components involving CSS, such as somatization-related symptoms, depression, and sleep disturbance. For FRP completion rate, the high CSI score predicted a lower rate of program completion. After completing the FRP, the average CSI scores were significantly reduced. The CSI score at FRP discharge was a significant independent predictor of work retention one-year post FRP. The five CSI ordinal severity categories, rather than a single CSI cutoff, were successfully associated with substantially lower rate of work retention one-year post FRP and high frequency of the treatment seeking behaviors. The results support that the CSI is a clinically valid and useful instrument, which can be used to assess CSS-relevant multiple symptoms, and to monitor treatment outcomes. The established five CSI severity levels provide a guideline for clinicians in interpreting and using CSI scores in clinical trials.

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Chapter 1

Introduction

Musculoskeletal disorders describe a wide range of inflammatory and degenerative conditions affecting the muscles, tendons, ligaments, joints, peripheral nerves, and supporting blood vessels. The most prevalent musculoskeletal pains are low back pain, neck pain, shoulder pain, arm/wrist/hand conditions and widespread pain (Punnett & Wegman, 2004). With our growing knowledge of pain mechanisms, musculoskeletal pain is often classified as nociceptive pain, peripheral neuropathic pain, and central sensitization pain on the basis of its underlying mechanisms that contribute to generation and maintenance of pain (Smart, Blake, Staines, & Doody, 2010; Woolf et al., 1998). Nociceptive pain refers to pain originating from somatic tissues in response to noxious stimuli, as might occur in response to traumatic, degenerative, or inflammatory conditions. Peripheral neuropathic pain refers to pain arising from a primary injury or dysfunction in the peripheral nervous system. Finally, central sensitization pain refers to pain that arises or persists as a result of altered pain processing (i.e., hyperexcitability) within the central nervous system (CNS). The mechanism of central sensitization provides an explanation of variations in the nature and severity of clinical presentations of musculoskeletal pain, in particular, such as widespread pain in the absence of identifiable pathology and persisting pain after the resolution of injury or pathology (Smart, Blake, Staines, & Doody, 2011).

A recent empirical finding indicates that 34% and 23% of chronic musculoskeletal pain have components of central sensitization pain, such as chronic widespread pain and fibromyalgia, respectively (Howard et al., 2010). In the study, patients with fibromyalgia were found to experience higher levels of perceived disability and depression, compared to those without chronic widespread pain. Additional research also has suggested that

individuals classified with a dominance of central sensitization pain were associated with more severe pain, and greater level of pain-related disability, depression, and anxiety, compared to those classified as nociceptive pain or peripheral neuropathic pain (Smart, Blake, Staines, & Doody, 2012). Since chronic patients tend to experience increased and prolonged pain, many individuals with chronic musculoskeletal disorders may have prominent central nervous system contributions to their pain, as well as peripheral nerve injuries. One of the major features related to central sensitization includes multifocal pain with a high current and lifetime history of pain in various regions of the body (Goldenberg, Clauw, & Fitzcharles, 2011). Therefore, the presence of central sensitization in patients with chronic musculoskeletal pain can make clinical trials more challenging due to an increase in multiple symptoms (Nijs, Van Houdenhove, & Oostendorp, 2010).

Given the increasing evidence supporting the clinical significance of central sensitization in patients with chronic musculoskeletal disorders, a new self-report measure of central sensitization was developed to alert clinicians and physicians to a patient's multiple somatic and emotional symptoms related to central sensitization (Mayer et al. 2012). This new instrument (the Central Sensitization Inventory: CSI) is the first tool to assess the full array of key comorbid symptoms associated with central sensitization, and quantify the degree of these symptoms. The items of the CSI were derived from the theoretical and clinical research literature of comorbid symptoms associated with central sensitization, and were reviewed for face validity by an interdisciplinary team (psychiatrists, orthopedic surgeons, rehabilitation specialists, clinical psychologists, health psychologists, and psychophysiological specialists) who work closely with chronic pain patients (Mayer et al., 2012).

The major aim of this study was to examine the concurrent validity of the CSI, while also establishing its utility in chronic musculoskeletal pain patients. Several

baseline risk factors for multi-symptom conditions in chronic musculoskeletal pain patients were identified and controlled, in order to ensure the validity of the CSI. Furthermore, the predictive ability of the CSI for rehabilitation outcomes at different time points (admission, discharge, one year) was examined.

Chapter 2

Work-Related Musculoskeletal Pain

Overview of Occupational Musculoskeletal Pain

Musculoskeletal pain disorders frequently result from workplace injuries including accidents or cumulative and repetitive motion. According to the United States Department of Labor, Bureau of Labor Statistics, musculoskeletal injuries accounted for 33% of all workplace injuries and illnesses that required days away from work in 2011 (Bureau of Labor Statistics, 2012). Back injuries accounted for 42% of musculoskeletal injuries and required a median of 7 days away from work. The next common injury was shoulder (13%), followed by leg (11%), wrist (6%), and arm (5%). Data for musculoskeletal injury conditions analyzed in 2004 showed that the estimated cost of treating all musculoskeletal injuries was $ 127.4 billion (Bone and Joint Decade, 2008). Musculoskeletal injuries often produce significant indirect costs related to days spent in bed or lost work days, thus further escalating costs (Bone and Joint Decade, 2008). It is well documented that some patients experience persistent pain after resolution of injury, resulting in limited activity and long-term disability (Turk & Gatchel, 2002). In a 2000 disability report based on data from the Centers for Disease Control & Prevention, direct and indirect disability lost-time costs were $ 458,150 per 100 workers, and medical costs were $ 268, 539 per 100 workers (Denniston, 2003). Several risk factors, both occupational and non-occupational, have been associated with the development and exacerbation of work-related musculoskeletal injuries, including physical, individual predisposition, and psychological conditions (Barbe & Barr, 2006; Punnett & Wegman, 2004; Schultz & Gatchel, 2005). For example, advanced age, female sex, certain past or current medical condition, work capacity, and physical and psychological factors were found to increase the severity and duration of work-related musculoskeletal disorders.

A more comprehensive biopsychosocial model of pain was proposed to emphasize the complex interactions of biological, psychological, and social factors that need to be taken into account for better understanding of chronic musculoskeletal conditions (Engel, 1977; Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Turk & Gatchel, 2002). This model highlights the potentially significant role of psychosocial factors in the development and maintenance of pain behaviors. Subsequently, a number of multidisciplinary/interdisciplinary approaches were developed to deal with a various range of physiological, psychological, and social problems that are associated with the high levels of pain-related disability for each individual with chronic pain (Turk & Gatchel, 2002). Complex chronic pain conditions were considered to be best managed by a team of specialists, including a medical director, nurse, physical therapist, occupational therapist, and psychologist. The body of scientific literature has provided evidence that such multidisciplinary pain treatment have been effective in improving the overall function of chronic pain patients (Flor, Fydrich, & Turk, 1992; Gatchel & Okifuji, 2006; Schatman & Campbell, 2007).

Functional Restoration Program

During the last decade, a more comprehensive and effective interdisciplinary program for chronic musculoskeletal pain, functional restoration program (FRP), has been developed based upon the biopsychosocial model of pain (Hazard et al., 1989; Mayer et al., 1987; Mayer et al., 1985). The FRP is a medically-directed, interdisciplinary pain and disability management approach, designed for patients who have developed chronic spinal disorders (Mayer & Gatchel, 1988), as well as those with other chronic musculoskeletal disorders (Howard, Mayer, & Gatchel, 2012; Mayer, Cohen, & Mayer, 2011). The major treatment components of the FRP consists of a comprehensive evaluation, a structured exercise program, a disability management program (e.g.,

cognitive-behavioral therapy, vocational reintegration, biofeedback, stress management, and education), and medication management (e.g., opioid tapering and psychotropic medications) The reduction of pain, disability, and an improvement in the quality of life, as well as return to work rate, work retention, and health-care utilization have widely been used as outcomes or treatment goals (Gatchel & Mayer, 2011; Mayer et al., 1985; Mayer et al.,1987; Mayer, Prescott, & Gatchel, 2000).

In the evaluation phase of the FRP, there have been many clinical research efforts to identify risk factors and barriers for patients who many need more focused care to complete the program, as well as those who are less likely to return to work and retain work at one-year post-treatment. Many risk factors have been related to unsuccessful treatment completion, including: a longer duration of disability between injury and admission to the program; a higher post-injury opioid dose; a high level of pain intensity; a socially problematic Cluster B personality disorder; panic disorder; and dysfunctional coping profile (Choi, Mayer, Williams, & Gatchel, 2012; Howard, Mayer, Theodore, & Gatchel, 2009; Kidner, Mayer, & Gatchel, 2009; McGeary, Mayer, & Gatchel, 2006). A multivariate logistic regression analysis also revealed significant demographic, psychological, and occupational predictors of failure to retain work for chronic musculoskeletal pain patients: older age, female sex, extreme disability at admission, antisocial personality disorder, nonworking status at discharge, receipt of government disability benefits at admission, and dependence on opioid pain medications (Brede, Mayer, & Gatchel, 2012). A subset of chronic musculoskeletal pain patients with fibromyalgia was associated with many of these same risk factors (e.g., female sex, disability at admission, greater length of time the patient was not working any capacity before admission to treatment), and also found to be related to poorer rates of work return and work retention one-year post FRP (Howard et al., 2010). Furthermore, chronic

musculoskeletal disorder patients with fibromyalgia were more likely to report multiple injuries that may be contributing to a wide range of widespread pain and multiple symptoms (Howard et al., 2010).

From Acute Localized Pain to Chronic Pain

In some cases, individuals with acute localized musculoskeletal disorders develop chronic widespread pain and fibromyalgia from persisting local pain (Nijs & Van Houdenhove, 2009; Sarzi-Puttini, Atzeni, & Mease, 2011). Several studies have shown that physical trauma (e.g., motor vehicle collision, work injury, surgery) often triggers or worsens chronic widespread pain. It was found that 61% of patients noted the onset of fibromyalgia symptoms after a motor vehicle accident, 13% after a work injury, 7% after surgery (Waylonis & Perkins, 1994). Another study reported that 22% of patients with neck injury developed fibromyalgia 1 year after a motor vehicle collision (Buskila & Mader, 2011). Finally, a long-term study revealed that workplace low-level mechanical trauma, such as pushing/pulling heavy weights, repetitive wrist movements, and kneeling, was predictive of the later development of chronic widespread pain (McBeth, Harkness, Silman, & Macfarlane, 2003). The advancement of scientific knowledge related to these associations indicated that initial injury may lead to chronic pain via the development of peripheral, spinal or supraspinal sensitization within the central nervous system. Although fibromyalgia is the prototypical central nervous system sensitization syndrome, it is well known that it has overlapping characteristics with other central sensitization-related syndromes, such as chronic fatigue syndromes, irritable bowel syndrome (IBS), temporomandibular (joint) disorder (TMD/TMJ), and multiple chemical sensitivity.

Chapter 3

Central Sensitivity Syndrome (CSS)

The Concept of CSS

Central sensitization syndrome (CSS) is a term first used by Yunus in 2000 to describe a group of overlapping conditions of fibromyalgia that share a common pathophysiological mechanism of central sensitization (Yunus, 2000, 2007a). Groups of individuals with these conditions display the increased pain in response to normally painful stimuli (i.e., hyperalgesia), pain in response to normally non-painful stimuli (i.e., allodynia), and/or expansion of the receptive field (Yunus, 2007a). A modified list of CSSs proposed by Neblett and colleagues (Neblett, Cohen, Choi, Hartzell, William, Mayer et al., 2013) includes CSSs such as fibromyalgia, IBS, TMD/TMJ, chronic fatigue syndrome, tension headache/ migraines, restless leg syndrome, multiple chemical sensitivities, interstital cystitis, myofascial pain syndrome, post-traumatic stress disorder (PTSD), and CSS-related conditions such as neck injury (including whiplash), anxiety/panic attack, depression, and an abuse history. The term of CSS is advantageous over other previously defined names for this condition, such as somatization disorder, functional somatic syndromes, and medically unexplained symptoms, because it incorporates both biological and psychosocial components with the demonstrable pathophysiology (Yunus, 2008).

The Mutual Association among CSS

Increased understanding of shared pathophysiological mechanism among CSSs found that several CSS diagnoses are often commonly overlapping to a significant degree. A mutual association between CSS members was reviewed by Aaron and Buchwald in 2001 (Aaron & Buchwald, 2001), and more recently by Yunus in 2005 (Yunus, 2005). Overlapping syndromes have been primarily focused fibromyalgia with

other core CSSs, such as IBS, tension headache/migraine, chronic fatigue syndrome, and temporormandibular disorder. For example, among patients with FM, 32% - 70% have comorbid IBS (Campbell, Clark, Tindall, Forehand, & Bennett, 1983; Hudson, Goldenberg, Pope, Keck, & Schlesinger, 1992; Romano, 1988; Sivri, Cindas, Dincer, & Sivri, 1996; Sperber et al., 1999; Triadafilopoulos, Simms, & Goldenberg, 1991; Veale, Kavanagh, Fielding, & Fitzgerald, 1991; Wolfe, Ross, Anderson, Russell, & Hebert, 1995; Wolfe et al., 1990; Yunus, Inanici, Aldag, & Mangold, 2000; Yunus, Masi, Calabro, Miller, & Feigenbaum, 1981), 44% – 90% have tension headache and migraine, (Campbell et al., 1983; Hudson et al., 1992; Marcus, Bernstein, & Rudy, 2005; Nicolodi, Volpe, & Sicuteri, 1998; Yunus, 2000; Yunus, Masi, & Aldag, 1989; Yunus et al., 1981), 21% - 70% have CFS, (Aaron, Burke, & Buchwald, 2000; Buchwald & Garrity, 1994; Hudson, et al., 1992; White, Speechley, Harth, & Ostbye, 2000; Wysenbeek, Shapira, & Leibovici, 1991), and 69%- 75% have TMD, (Dao, Reynolds, & Tenenbaum, 1997; Eriksson, Lindman, Stål, & Bengtsson, 1988; Plesh, Wolfe, & Lane, 1996). The wide-ranging prevalence estimates partly from different methodology and criteria, but these comorbid rates are much higher than those found in control groups (Yunus, 2007b). Less overlap, but still high number of patients with restless leg syndrome (31%) (Yunus & Aldag, 1996) and multiple chemical sensitivity (33-55%) (Slotkoff, Radulovic, & Clauw, 1997) has been observed in fibromyalgia patients. When patients with interstitial cystitis were evaluated for fibromyalgia, 12% to 25 % patients met criteria for fibromyalgia (Alagiri, Chottiner, Ratner, Slade, & Hanno, 1997; Clauw et al., 1997).

Psychiatric Disorders and CSS

Similar to studies on overlaps in CSSs, depression and anxiety frequently occurred among individuals with fibromyalgia and other pain conditions (Arnold et al., 2004; Arnold et al., 2006; Fischer, Gaab, Ehlert, & Nater, 2013; Henningsen,

Zimmermann, & Sattel, 2003). Like other chronic conditions, a meta-analytic review of CSSs (described as medically unexplained physical symptoms), anxiety, and depression revealed that fibromyalgia, IBS, chronic fatigue syndrome, and non-ulcer dyspepsia were moderately related to depression and anxiety (Henningsen et al., 2003). The degrees of association were highly significant, when compared with healthy individuals and controls with medical disorder of known organic pathology (Henningsen et al., 2003). A recent Web survey of 3,054 nonclinical respondents also supported a high comorbidity of depressive and anxiety disorders among persons with CSS (described as functional somatic syndromes). The results of two family studies of fibromyalgia found a substantial lifetime psychiatric cormobidity in fibromyalgia pro-bands and their relatives (Arnold et al., 2004; Arnold et al., 2006). The lifetime prevalence of major mood disorder (including major depressive disorder and bipolar disorders) probands was 74.4% (Arnold et al., 2004). The co-occurrence odds ratio (OR)s for psychiatric disorders in individuals with and without fibromyalgia were 153 (95% CI = 26 to 902) for bipolar disorder, 2.7 (95% CI = 1.2 to 6.0) for major depressive disorder, 6.7 (95% CI = 2.3 to 20) for any anxiety disorder, 2.4 (95% CI = 0.36 to 17), and any substance use disorder for 3.3 (95% CI = 1.1 to 10) (Arnold et al., 2006). These results suggested the possibility that fibromyalgia might share underlying pathophysiologic links with some psychiatric disorders (Arnold et al., 2006). However, there is less agreement concerning whether psychiatric disorders should be classified as a member of CSS (Yunus, 2007a). Furthermore, a study examining the relationship between CSS (described as functional somatic syndromes) and depression/anxiety demonstrated that CSSs have an independent latent trait that is different than psychiatric conditions, such as depression and anxiety (Kato, Sullivan, Evengard, & Pedersen, 2009). Nevertheless, mounting data supporting the comorbidity of CSS and psychiatric conditions suggest that recognition of comorbid psychiatric disorders

in CSS patients is a critical component in managing both physical and emotional aspects of CSS (Buskila & Cohen, 2007).

Due to a high comorbidity among CSS members, patients with a CSS condition tend to have multiple CSS diagnoses and/or psychological disturbance (Yunus, 2008). For example, an empirical study of the comorbidty among CSS members in each individual found that half of CSS patients (51%) were diagnosed with more than 1 CSS (Neblett, et al., 2013). The coexistence of comorbidiites has facilitated our understanding of relevant etiological factors common to all other CSSs. Two major phenomena, temporal summation of second pain (wind-up) and dysfunction of descending inhibition mechanism, are known to be involved in development of CSS.

The Mechanism of CSS

Pain receptors, called nociceptors, are located in the skin and viscera, and respond to various types of stimulation such as heat, cold, pressure, and mechanical injury. These receptors change physical energy into electrical signals; these electrical signals are changed into neural impulses that travel toward the spinal cord and brain. Recent advances in our understanding of pain physiopathology and pain pathways have allowed us to explore the role of aberrant central nervous system in a CSS condition.

Peripheral Sensitization and Central Sensitization

The pain signals are generated most often by activation of primary afferent nociceptors located on the terminal branches of primary afferent nerves, A-δ fibers and C fibers. Myelinated afferent neurons, A-δ fibers facilitate fast conduction of information to the spinal cord and brain. Some A-δ afferents respond specifically to noxious mechanical stimuli and/or thermal stimuli. Small and unmyelinated C fibers have larger receptive fields, and are associated with secondary nociceptive sensation. Most C fiber afferents respond to range of noxious mechanical, thermal, and chemical stimuli, and produce a

feeling of aching or burning. Noxious stimulation of the receptive field of C fibers evokes sensitization of nociceptive afferent neurons (Perl, Kumazawa, Lynn, & Kenins, 1976). This enhanced responsiveness reflects a so-called peripheral sensitization. Peripheral sensitization occurs within the site of tissue where the nerve terminal is exposed to noxious stimuli, and contributes to inflammation. This phenomenon explains well the presence of post-injury pain hypersensitivity, but it does not account for the spread of pain hypersensitivity beyond an area of tissue damage. In 1983, Woolf published a study indicating that pain hypersensitivity after peripheral tissue damage in part results from changes in the activity of the spinal cord (Woolf, 1983). Nociceptive afferent neurons carry the neural impulse to dorsal horn neurons in the spinal cord. Some of these neurons in the dorsal horn are multimodal (wide dynamic range: WDR), and respond to the wide range of non-noxious (e.g., gentle touch) and noxious stimuli, as well as nociceptive-specific neurons that respond to nociceptive stimuli. Some of the second neurons in the dorsal horn become hypersensitive because of repetitive firing from nociceptors. These sensitized dorsal horn neurons can respond to lower levels of nociceptive stimuli (i.e., hyperalgesia) as well as some non-noxious stimuli (i.e., allodynia) (Woolf, 1983). In addition, prolonged excitation of dorsal horn neurons activates adjacent neurons, resulting in the expansion of receptive fields beyond the injury site (Cook, Woolf, Wall, & McMahon, 1987). This pain amplification in the dorsal horn neurons of the spinal cord is related to temporal summation of second pain or wind-up. Neural responses related to wind-up are also observed in multiple higher brain areas through ascending pathways from the dorsal horn neurons. The structural and functional mechanisms of ascending pain pathways are well documented in three review papers (Price, 2000, 2002; Staud, 2005). The direct spinal pathways to limbic structures (e.g., hypothalamus and amygdala) and medial thalamic nuclei provide direct inputs to brain areas involved in pain

affect (Bernard & Besson, 1990; Burstein, Cliffer, & Giesler, 1987). Thus, this pathway is associated with immediate affective-motivational responses related to acute pain, such as fear and arousal. The spinothalamic pathway projects to primary and secondary somatosensory cerebral cortical areas. This pathway is also interconnected with a cortico-limbic somatosensory pathway that integrates somatosensory input with other sensory modalities such as vision, audition, and with learning and memory over posterior parietal cortex (Friedman, Murray, O'Neill, & Mishkin, 1986). It later converges on to the same limbic and subcortical structures (e.g., anterior cingulated cortex: ACC, insular cortex, and amygdala) that are directly associated with other ascending pain pathways. On the basis of evidence, the ACC is known to play a complex role in interrelating attentional and evaluative functions, and the activation of ACC is commonly detected during pain processing in brain imaging studies (Price, 2000, 2002). Although pain research has traditionally focused on altered pain transmission via ascending pain pathways, much progress has recently been made toward descending modulation on the generation and maintenance of sensitization (Heinricher, Tavares, Leith, & Lumb, 2009; Millan, 2002; Ren & Dubner, 2002).

Endogenous Pain Modulation

Pain modulation refers to the neural plasticity that facilitates or inhibits pain transmission. The modulation of neural impulses in the central nervous system substantially influences the perception of pain. The role of descending pain facilitatory mechanisms has been more recently studied because it was often masked by the more intense stimuli or higher drug doses used to induce descending pain inhibition (Ren & Dubner, 2002). The periaqueductal gray (PAG)- rostral ventromedial medulla (RVM) system is known to play a critical role in the processing of descending modulation of pain involving both inhibition and facilitation (Gebhart, 2004; Porreca, Ossipov, & Gebhart,

2002). For example, the PAG is interconnected with the hypothalamus and limbic forebrain structures including the amygdala, which influence affective processes described earlier. Pain modulatory signals from the PAG project to dorsal horn neurons of the spinal cord either directly or indirectly via the RVM. Neurons in the RVM are classified into ‘‘ON-cells,’’ ‘‘OFF-cells,’’ and ‘‘NEUTRAL-cells’’. ON-cells play a role in descending facilitation (pro-nociceptive), whereas OFF-cells act to inhibit nociception (anti-nociception) (Fields, Heinricher, & Mason, 1991; Tracey & Dunckley, 2004). Thus, augmented pain processing is associated with increased activity of On-cells and suppression of OFF-cell firing. The role of NEUTRAL-cells is less clear, but they appear to play a role in the shifting balance between RVM inhibition and facilitation (Heinricher et al., 2009). The function of descending pain modulation pathway can be often measured by diffuse noxious inhibitory control (DNIC) mechanism, in which one pain inhibits another in a form of counter-irritation (Le Bars, Dickenson, & Besson, 1979; Tracey & Dunckley, 2004). DNIC is normally triggered by an acute noxious stimulus, and induces inhibition of pain sensation to another painful stimulus. In the situation of patients with CSSs, an imbalance of descending pain modulatory systems contributes to the maintenance of the hyperalgesia and/or an increase in endogenous pain facilitation (Ren & Dubner, 2002).

In many studies, this analgesic DNIC effect has been found to be reduced or absent in groups of CSS patients, such as fibromyalgia (Lautenbacher & Rollman, 1997), chronic tension-type headache, (Pielsticker, Haag, Zaudig, & Lautenbacher, 2005), IBS, and TMD (King, Wong, Currie, Mauderli, & Fillingim, 2009). Furthermore, impaired DNIC was associated with a higher chance for development of chronic pain among patients who underwent thoracotomy surgery (Yarnitsky et al., 2008). The descending modulation pathway also partly explains individual difference in pain perception, including

demographic (e.g., sex, age, and ethnic), genetic, and psychological mediators (e.g., attention, expectation, and pain catastrophizing) (van Wijk & Veldhuijzen, 2010). For example, females, old adults, and African Americans are shown to have a less efficient DNIC response, reflecting less effective pain inhibition. Emotional and psychological state, such as distraction, expectations, pain catastrophizing, and perceptual adaptation levels have also been suggested to influence DNIC effects, particularly in patients with a CSS (van Wijk & Veldhuijzen, 2010). Taken together, these results suggest that DNIC is involved in a central pain modulation system for CSS patients at the spinal and supraspinal level that requires the integration of sensory, cognitive, and affective information. Although central sensitization, which represented is by temporal summation and dysfunction of DNIC, is widely known to be a demonstrable pathophysiology of CSS disorders, other factors such as genetics, poor sleep, trauma, endocrine dysfunction, sympathetic overactivity, psychosocial distress were also proposed to contribute to the presence of CSS (Yunus, 2007a).

Risk Factors of CSS

Genetic Factors

Genetic factors in CSS are often present in genetic markers and family studies. Current evidence suggests that a specific polymorphism of the serotonin transporter and 5-HT2a receptor are present in fibromyalgia (Bondy et al, 1999; Offenbaecher et al., 1999), IBS (Pata et al., 2004; Yeo et al., 2004), Chronic fatigue syndrome, (Narita et al., 2003), TMD (Mutlu, Erdal, Herken, Oz, & Bayazıt, 2004), migraine (Borroni et al., 2005; Juhasz et al., 2002; Szilagyi et al., 2006), and PTSD (Lee et al., 2005). For example, the S/S genotype of 5-HTT was found be higher in fibromyalgia, and this type was also associated with higher levels of depression and psychological distress (Offenbaecher et al., 1999). A silent T102C polymorphism of the 5-HT2a receptor was identified in patients

with various groups of central sensitization. Polymorphisms in the D2 / D4 dopamine receptor gene were also associated with patients with fibromyalgia (Buskila, Cohen, & Neumann, 2004; Malt, Olafsson, Aakvaag, Lund, & Ursin, 2003), migraine (Mochi et al., 2003), and PTSD (Lawford et al., 2003). Finally, the less efficacy of Catechol-O-methyltransferase (COMT) enzyme activity and polymorphisms of COMT (Val158Met) were found to be related to increased sympathetic function and pain sensitivity in patients with fibromyalgia (Littlejohn, 2010). The similarities of genetic factors among patients with CSSs were consistent with the studies demonstrating family aggregation in patients with fibromyalgia and overlapping conditions. Family members of individuals with fibromyalgia were much more likely to have other pain conditions, such as IBS, TMD, headaches, and other regional pain syndromes (Hudson et al., 2003; Kato, Sullivan, Evengard, & Pedersen, 2006). CSSs (previously termed affective spectrum disorders) aggregated strongly in families, and major depressive disorder also showed a significant familial aggregation with other forms of pain conditions. In another study of twins, the odds ratios were calculated to assess the effect of familial aggregation in patients with chronic widespread pain and other conditions. The odds ratios of co-occurrence of chronic fatigue syndrome in chronic widespread pain were 23.5, followed by joint pain (5.3), and IBS (5.2) (Kato et al., 2006). Moreover, the identical twins with and without symptoms of fibromyalgia or chronic fatigue syndromes were found to share abnormalities in sleep or immune function (Smith, Strachan, & Buchwald, 2009). This evidence suggests that genetic factors are partly associated with increased pain sensitivity and higher chance of developing one or more CSSs. Although genetic factors underpin pain processing, psychological and environmental factors (e.g., stress, trauma, coping styles, and pain catastrophizing) also appear to play role in the development and maintenance of central sensitization (Yunus, 2007a).

Psychological and Environmental Factors

In an internet survey of 2,596 patients with fibromyalgia, individuals were asked to indicate any potential triggering events occurred around onset of fibromyalgia. Over 73% of individuals reported perceived triggering events that were attributed to emotional trauma or chronic stress. The next common attributions were acute illness and physical stressors (e.g., surgery, motor vehicle collision, and other injuries; Bennett, Jones, Turk, Russell, & Matallana, 2007). Being exposed to multiple stressors simultaneously or consecutively has often been a significant risk factor for later fibromyalgia and related pain conditions, leading to neural plasticity (Harris & Clauw, 2008). Hypothalamic-Pituitary-Adrenal (HPA) axis dysfunction with a persistent lack of cortisol availability was common to many CSS such as fibromyalgia, chronic fatigue syndrome, as well as stress-related disorders (Heim, Ehlert, & Hellhammer, 2000).

This link between stress, HPA axis dysfunction, and subsequent susceptibility to develop and promote ongoing central sensitization is also supported by studies showing that patients with CSS were more likely to have experienced physical or sexual abuse (Häuser, Kosseva, Űceyler, Kolse, & Sommer, 2011; Heitkemper, Cain, Burr, Jun, & Jarrett, 2011; Kindler, Jones, Perrin, & Bennett, 2010; Ringel et al., 2008). A systematic review with meta-analysis using 18 studies with 13,095 fibromyalgia patients confirmed significant associations between fibromyalgia and physical and sexual abuse in both childhood and adulthood (Häuser et al., 2011). Among chronic low back or neck pain patients, individuals who had a history of abuse in adulthood were 2.5 times more likely to develop chronic widespread pain (Kindler et al., 2010). When they had a history of abuse in childhood, the likelihood of developing chronic widespread pain was increased by 73% (Kindler et al., 2010). Furthermore, patients with IBS and abuse history were

more likely to reported more pain, disturbed sleep, somatic symptoms, and psychological distress (Heitkemper et al., 2008).

Unsuccessful adaptation to such stressful events that produce psychological distress, may often lead to an adverse long-term course of central sensitization pain. A patient's exaggerated negative appraisal of pain conditions (i.e., pain catastrophizing) has been shown to positively correlate with perceived pain intensities (Sullivan et al., 2001), and was associated with increased activity in brain areas related to anticipation of pain, attention to pain, emotional aspects of pain, and motor control (Gracely et al., 2004). Moreover, individuals with high catastrophzing levels showed higher pain intensities and lower DNIC effects, implicating its association with descending pain modulation (Weissman-Fogel, Sprecher, & Pud, 2008). These results supported the notion that maladaptive coping beliefs and behaviors have an impact on central mechanisms of pain control and symptoms associated with central sensitivity syndromes.

Many researchers now view the central sensitivity syndrome within the biopsychosocial model that integrates all factors relevant to pain perception, including genes, environmental stressors, cognitive/affective pain processing (e.g., pain catastrophizing and coping styles), and social support (Winfield, 2007; Yunus, 2008). Therefore, comprehensive assessment of a patient's experience of pain is an important component in understanding each patient, and in providing effective pain management. Brain imaging studies and pain sensory tests allow for more thorough evaluation of patients with CSSs along with self-reported measures.

Assessment of Central Sensitization

Neuroimaing

Advanced brain imaging techniques are now being applied in patients with central sensitization to assess the excitability of brain areas and to evaluate how they

react to specific pain modalities. Numerous brain imaging studies, using functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and single photon emission computed tomography (SPECT), have found the existence of central pain augmentation in fibromyalgia, chronic fatigue syndrome, IBS, and idiopathic low back pain (Cook et al. 2004; de Lange et al., 2004; Giesecke et al., 2004; Gracely, Petzke, Wolf, & Clauw, 2002; Kwiatek et al., 2000; Mountz et al., 1995; Yuan et al., 2003). Altered pain sensory processing systems and reduced affect/attentional regulation of central pain processing in brain structures were detected in CSS patients, including the ACC, insular cortex, amygdala, thalamus, and caudate nucleus. Although activated brain sites across studies vary to some degree, depending on experimental paradigm and pain stimulus, many fMRI studies showing pain-relative brain activity generally agreed with SPECT and PET studies (Goldenberg et al., 2011). Although brain imaging techniques provide the most objective evaluation of central sensitization among CSS patients, the psychophysical assessments of central sensitization have recently been suggested as another useful tool to measure pain modulation processes in healthy subjects and altered pain modulation processes in patients with CSSs.

Quantitative Sensory Testing (QST)

Quantitative Sensory Testing (QST) refers to a method that quantifies the magnitude of physical stimuli that is required to determine a pain perception such as pain threshold, pain tolerance, temporal summation, and pain magnitude rating (Arendt-Nielsen & Yarnitsky, 2009). The QST provides psychophysical methods to systemically examine which pain pathways are involved, impaired or affected (Arendt-Nielsen & Yarnitsky, 2009). The application of experimental pain stimuli (e.g., chemical, mechanical, thermal, and electrical methods) to healthy subjects or patients with CSSs can be performed to assess threshold determination or pain-magnitude rating for a given

stimulus, so called the static QST set (Arendt-Nielsen & Yarnitsky, 2009). The dynamic QST includes tests of central integration (e.g., temporal summation) and tests of descending control (e.g., DNIC) (Arendt-Nielsen & Yarnitsky, 2009). For example, a degree of endogenous analgesia, assessed by the DNIC paradigm (e.g., "pain inhibits pain"), is often measured in human experiments by calculating the difference in the perceived pain levels of the test stimuli (first) before and after the conditioning stimuli (second) (Granot et al., 2008). A deficiency in DNIC has been found in CSS patients with fibromyalgia (Julien, Goffaux, Arsenault, & Marchand, 2005) and IBS and TMJ disorder (King et al., 2009). Furthermore, fibromyalgia patients with comorbid depression showed less efficient DNIC, relative to those without depression (de Souza, Potvin, Goffaux, Chrest, & Marchand, 2009). However, the sensitivity of accuracy of the QSTs on measuring DNIC among CSS patients has not been formally assessed. Along with brain imaging techniques and psychophysiological tests, the clinical signs and symptoms of pain patients can also be evaluated by self-report questionnaires. It has been well documented that patients with central sensitization syndromes commonly experience overlapping pain-related symptoms such as fatigue, insomnia, and memory difficulties, in addition to regional and/or widespread pain augmentation (Yunus, 2007a; Yunus 2008). Self-report measures may provide the most direct measure of pain and pain-related symptoms among these patients. These measures are often used for identifying central sensitization related symptoms, and evaluating pharmacological and non-pharmacological treatment efficacy as outcomes.

Patient Report Assessment

A variety of patient-reported outcomes (PROs) have been designed to capture a sensory experience and additional emotional or affective aspects of pain experience. Since pain is subjective, many PROs have been completed as a self-report form. Most

pain assessments contains only one-item or multiple items, and are used in a form of a visual analogue scale (VAS), numerical rating scale (NRS), or Likert rating scale. Although unidimensional measures of pain intensity have traditionally been used for pain related conditions, the multifactorial nature of fibromyalgia and other CSSs has the use of a number of mutidemensional measures.

To date, there is no gold standard self-report measure of identifying the concept of central sensitivity syndrome. Various self-report measures have been developed to evaluate the disease-specific symptoms and disability such as fibromyalgia (e.g., Fibromyalgia Impact Questionnaire (FIQ; Burckhardt, Clark, & Bennett, 1991); The London Fibromyalgia Epidemiology Study Screening Questionnaire (LFESQ; White, Harth, Speechley, & Østbye, 1999); Fibromyalgia Rapid Screening Tool (FIRST; Perrot, Bouhassira, & Fermanian, 2010)), IBS (e.g., Functional Bowel Disorder Severity Index (FBDSI; Drossman, Talley, Leserman, Olden, & Barreiro, 1995); IBS-Behavioral Responses Questionnaire (IBS-BRQ; Reme, Darnley, Kennedy, & Chalder, 2010)), TMD/TMJ (e.g., TMJ Scale; Levitt & McKinney, 1993), and chronic fatigue syndrome (e.g., CFS Questionnaire; Hawk, Jason, & Torres-Harding, 2006). However, none of these scales measure a variety of key comorbid symptoms associated with central sensitization and CSS. Two symptom scales, Symptom Intensity Scale (SIS) and Patient Health Questionnaire (PHQ)-Somatization are assumed to be associated with a component of central sensitization and CSS.

The Symptom Intensity Scale (SIS) was originally developed from Survey Criteria created in 2003 (Wolfe, 2003). The Survey Criteria consists of two parts; regional pain scale and fatigue visual analogue scale. The regional pain scale score indicates the number of areas (0-19) in which the patient feels pain. The fatigue visual analogue scale indicates how tired an individual feels along with a 10 cm line. A combination of a score

of at least 8 on the regional pain scale and a score of at least 6 on the fatigue visual analogue scale was proposed as a self-report criterion for fibromyalgia diagnosis (Wolfe, 2003). In the later study, Wolfe and Rasker (2006) developed the Symptom Intensity Scale (SIS) by combining half of the regional pain scale score with the fatigue visual analogue scale score. A score of 5.75 or higher differentiated fibromyalgia from other rheumatic disease, and higher scores on the SIS were associated with more severe medical illness and greater mortality (Wolfe & Rasker, 2006). Therefore, the SIS was proposed as a diagnostic tool for fibromyalgia, as well as an useful measure of general health among all rheumatic disease patients (Wilke, 2009). More recently, Smith, Harris, and Clauw (2011) suggested using the SIS to identify individuals who have fibromyalgia and other related coniditons (Smith et al., 2011). However, the SIS does not account for other overlapped symptoms associated with central sensitization and CSSs.

Patient Health Questionnaire (PHQ)- Somatization is a self report version of the PRIME-MD diagnosis instrument developed based on DSM-IV somatization disorder (Kroenke, Spitzer, & Williams, 2002). The PHQ- Somatization consists of 15 somatic symptoms (e.g., stomach, back pain, pain in joints, headaches, constipation/diarrhea, low energy, and trouble sleeping) with a scale from 0 (not bothered at all) to 2 (bothered a lot). PHQ-Somatization scores of 5, 10, 15, represent low, medium, and high somatic symptoms severity, respectively. Total symptom counts were shown to be associated with psychological distress, functional impairment, and healthcare utilization (Kroenke et al., 2002). Although the PHQ- Somatization covers many somatic symptoms associated with central sensitization, it does not ask for emotional and cognitive impairment symptoms that are often characterized among CSS patients. Therefore, there has been a great need for a new self-report instrument to help health professionals recognize and respond to a patient's multiple symptoms that are related to central sensitization.

Chapter 4

Central Sensitization Inventory (CSI)

A new self-report screening instrument, the central sensitization inventory (CSI), was developed to assess the full array of somatic and emotional symptoms associated with central sensitization (Mayer et al., 2012). Part A of the CSI assesses 25 symptoms common to CSS with a Likert scale from 0 (never) to 4 (always). A total score ranges from 0 to 100, and higher scores indicate a greater degree of symptomology related to CSSs. Part B of the CSI asks if subjects have previously been diagnosed with one or more specific CSS diagnoses. The CSI is presented in Appendices A and B. The factor analysis yielded 4 factors (physical symptoms, emotional distress, headache/jaw symptoms, urological symptoms) that accounted for 53.4% of the variance of the dataset. The test-retest reliability and inter-item reliability of the CSI was 0.82, and 0.88, respectively. In the validity study, the patients with fibromyalgia reported the highest scores (Mean/SD = 58.2/10.5) and non-patient samples the lowest (Mean/SD = 28.9/13.5). The subsequent study found that a CSI score of 40 out of 100 best distinguished between the CSS patients and non-patient samples (Neblett et al., 2013), with a sensitivity of 81% and a specificity of 75%. Furthermore, self-reported CSS diagnosis history from the CSI part B, particularly with fibromyalgia, tension headache/migraines, IBS, showed a good agreement with the physician's diagnosis of CSS. However, these findings have not been validated in different samples of chronic pain patients. Furthermore, although the CSI was originally developed as a screener, a single cut-off value may be less adequate to detect treatment outcomes. Therefore, there has been a need to establish "severity categories" for the CSI, like other health-related self-reported measures. More importantly, its concurrent validity with existing CSS-related measures has not been yet examined.

Purpose and Scope of the Current Study

Thus, the present study was designed to respond to a call for additional research on the CSI. This study focused specifically on a large cohort of patients with a CDOMD who were referred to a FRP for tertiary care. The risk factors of having CSS-related symptoms in CDOMD patients at FRP admission were identified. The concurrent validity of the CSI was examined by comparing it to other pain-related psychosocial measures that are widely used in central sensitization pain research, including somatization, perceived pain and disability, depression, sleep disturbance, and fear-avoidance. Instruments such as the somatization module of the Patient Health Questionnaire (PHQ; Spitzer, Kroenke, & Willams, 1999), the pain intensity analogue (Pain VAS; Capra, Mayer, & Gatchel, 1985), the Oswestry Disability Index (ODI; Fairbank et al., 1980), the Pain Disability Questionnaire (PDQ; Anagnostis, Gatchel, & Mayer, 2004), the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), the Insomnia Severity Index (ISI; Morin, 1993), and the Pain Anxiety Symptoms Scales (PASS; McCracken & Dhingra, 2002). The predictive validity of the CSI in response to treatment, and the relationship to 1-year post-treatment outcomes was also examined. Finally, the clinically relevant cutoff values of the CSI were derived, and were analyzed in the same way as described above.

The total CSI scores and clinically relevant levels were compared across four baseline dimensions: 1) demographic and occupational related variables; 2) post-injury psychiatric disorders (DSM-IV diagnoses); 3) abuse history; 4) the previous history of CSS. Furthermore, a series of multivariate analysis were conducted in order to determine whether the CSI is a significant prognostic factor in predicting non-completion of treatment and 1-year socioeconomic outcomes, after controlling all other significant baseline variables.

Hypotheses

The following hypotheses for this study were proposed:

- Hypothesis #1 A high CSI score would be associated with various baseline variables:
  - 1-a. Female patients would report a higher CSI score
  - 1-b. Elderly patients would report a higher CSI score
  - 1-c. Patients with multiple injury sites would report a higher CSI score
  - 1-d Patients with neck/back injuries would report a higher CSI score
  - 1-e. Patients with a longer duration of disability would report a higher CSI score
  - 1-f Patients with comorbid MDD and GAD would report a higher CSI score
  - 1-g. Patients with an abuse history would report a higher CSI score
  - 1-h. Patients with a history of CSS diagnosis would report a higher CSI score
- Hypothesis #2. The concurrent validity of the CSI, as measured by a correlation coefficient, would reveal a moderate association with a measure of Somatization, the PHQ-Somatization as well as psychosocial measures.
- Hypothesis #3. A higher CSI score would be associated with a lower rate of FRP completion.
- Hypothesis #4. The CSI scores would be decreased over the course of the multidisciplinary rehabilitation program.
- Hypothesis #5. A higher CSI score at program discharge would be associated with poorer one-year treatment outcomes, demonstrated by return-to-work, work retention, and health care utilization.
- Hypothesis #6. A single cut-off point of 40 on the CSI would have a predictive ability to identify the high risk of program non-completion and poorer outcomes at 1year post-treatment.

- Hypothesis #7. The proposed CSI severity categories would be effective in measuring the treatment responsive and in detecting poorer outcomes at one-year post treatment.

Chapter 5

Methods

Participants

The present study utilized a consecutive cohort of 724 patients presenting with a chronic disabling occupational musculoskeletal disorders (CDOMD). These patients were referred, and consented to treatment, at a regional functional restoration program (FPR) -- Productive Rehabilitation Institute of Dallas for Ergonomics (PRIDE). All patients were discharged from the FRP during the period from February 2010 to July 2013. The majority of the CDOMD group had cervical, thoracic/lumbar, extremities, and/or multiple musculoskeletal injuries that were compensable under state or federal worker's compensation. Program participation criteria included: 1) work-related injury claim occurred at least four months prior to entry into the program; 2) chronic disability remained following acute conservative care and/or secondary care; 3) surgery was not a clear option or had not provided resolution; 4) severe pain and functional limitations persisted; and 5) ability to communicate in English or Spanish. Of the initial sample of 724 patients, 43 patients were excluded because they did not complete items on the Central Sensitization Inventory (CSI), leaving 681 patients for the baseline assessments. Patients who did, and who did not, complete the CSI, were not significantly different in demographic characteristics, including gender, age, race, marital status, type of injury, or length of disability. Demographic characteristics of the sample of n = 681 are shown in Table 5-1.

Table 5-1 Demographic Characteristics of Sample

Demographic Variables	All patient (n = 681)
Gender (*n*, *%* Male)	443 (65.1%)
Age Mean *yr*/(*SD*)	45.1 (10.6)
Range n (%)	
≤30	74 (10.9)
31-40	158 (23.2)
41-50	217 (31.9)
51-60	189 (27.9)
>60	43 (6.3)
Ethnicity (*n*, %)	
African American	149 (21.9)
Caucasian	374 (54.9)
Hispanic	148 (21.7)
Others/Unknown	10 (1.5)
Marital Status (*n*, %)	
Single	88 (12.9)
Married/Significant Other	379 (55.7)
Separated/Divorced	202 (29.7)
Widowed	12 (1.8)
Type of Injury (*n*, *%*)	
Cervical Spine Only	14 (2.1)
Thoracic/Lumbar Spine Only	234 (34.4)
Multiple Spinal	59 (8.7)
Extremity Only	207 (30.4)
Multiple Musculoskeletal	167 (24.5)
Other	
Length of Disability Mean *month*/(*SD*)	25.2 (40.8)

Procedures

All participants were enrolled in the FRP at PRIDE, and consented to collection of information for treatment management and research purposes. The FRP is a 4-6 week intensive interdisciplinary program, combining a quantitatively-directed exercise protocol with a multimodal disability management team. The major treatment components of the FPR consisted of 1) a comprehensive evaluation; 2) a structured exercise program; 3) a disability management program; 4) a medication management program. Patients

admitted to the program underwent a comprehensive history, physical examination, and psychosocial evaluation, including functional capacity and psychosocial assessment. Patients then participated in a structured exercise program, administered by physical and occupational therapists. The goal of exercise was guided by repeated objective physical measurements, placing the patient into a stepwise computerized progression program that was normalized to age, gender and body mass. The disability management program contained: cognitive-behavioral therapy to promote pain coping skills; medical case management to facilitate vocational reintegration; biofeedback and relaxation training to assist stress management; and educational sessions to improve knowledge of musculoskeletal disorders and to encourage health and fitness maintenance after FRP discharge.

At the initial interview, demographic data were collected and physical and functional capacity measurements were performed by appropriate staff members. The psychosocial instruments were administered at admission to program and at discharge. Follow-up interviews were conducted one-year post FRP. All data used in the present study were part of the patients' standard medical files, and therefore the study was granted exemption status by the Institutional Review Board of the University of Texas at Arlington. All patients also signed a Health Insurance Portability and Accountability Act (HIPPA) authorization prior to program participation. All information was protected by this HIPPA rule, and was confidentially maintained in the institute's database as part of ongoing quality assurance procedures.

Materials and Measures

Baseline Assessments

Baseline assessments, including demographic information, occupational characteristics, a history of abuse, a previous history of CSS, and post-injury psychiatric

disorders (Axis I and Axis II), were collected at admission to the FRP in a structured format. Demographic and injury-related variables collected included: gender, age, ethnicity, type of injury, number of compensable injury parts (i.e., those body parts that were treated as a result of the work-related injury), length of disability, surgery to the injured area, attorney retention rate. Work-related rehabilitation management variables upon admission to the program included: current work status, a sense of job availability, type of occupation, and the level of job demand. Three types of abuse history (physical, sexual, psychological) were collected and recorded as 1 “being reported” and 0 “being denied”). A previous history of CSS diagnosis was collected from a self-report form of the CSI Part B. Due to the overlapping nature of CSS diagnosis, patients who reported that they were previously diagnosed with one or more any CSS were coded as 1, whereas no history was coded as 0. Post-injury Axis I diagnoses (Major Depressive Disorder (MDD); Generalized Anxiety Disorder (GAD); substance use disorder) and Axis II diagnosis (Cluster A: odd, eccentric and suspicious individuals with Paranoid, Schizoid, and Schizotypal Personality Disorder; Cluster B: dramatic, emotional and erratic individuals with Antisocial, Borderline, Histrionic, and Narcissistic Personality; Cluster C: anxious and fearful individuals with Avoidant, Dependent, and Obsessive-Compulsive Personality Disorder) were assessed by a clinician based on the clinical interview and Structured Clinical Interview for DSM-IV Personality Disorder (SCID-II) (First, Spitzer, Gibbon, Willams, & Lorna, 1994), respectively.

Psychosocial and Pain Assessments

The psychosocial and pain assessments, measured at both admission and discharge of the FRP included: the Patient Health Questionnaire (PHQ-Somatization; Spitzer et al., 1999), the pain intensity visual analogue (Pain VAS; Capra et al., 1985), the Oswestry Disability Index (ODI; Fairbank et al., 1980), the Pain Disability

Questionnaire (PDQ; Anagnostis et al., 2004), the Beck Depression Inventory (BDI; Beck et al., 1961), Insomnia Severity Index (ISI; Morin, 1993), the short version of the Pain Anxiety Symptoms Scales (PASS; McCracken & Dhingra, 2002).

Patient Health Questionnaire (PHQ)-Somatization

The PHQ- Somatization is a sub-module of the PRIME-MD Patient Health Questionnaire (PHQ) developed to capture somatization symptoms in a primary care setting (Spitzer et al. 1999). It measures 15 common somatic symptoms in the last four weeks on a scale of 0 (not bothered at all) and 2 (bothered a lot), with a total score of 30. The cut-off points determined to interpret the severity of Somatization are followed as: 0-6 for low somatization, 7–14 for moderate somatization, and greater than 15 for high somatization (Hartzell et al., 2013).

Pain intensity visual analog (PainVAS)

Pain Intensity is one type of visual analog assessment (Capra et al., 1985). The patient is asked to rate the severity of pain along an unmarked 10cm line ranging from no pain to worst possible pain. It evaluates pain levels, with 0 being no pain, and 10 being the highest level of pain. Cut-off points for interpretation of this measure are as follows: less than four indicates “mild pain”; four to five indicates “moderate pain”; six to seven indicates “severe pain”; and scores greater than seven indicate “extreme pain” (McGeary et al., 2006).

Oswestry Disability Index (ODI)

The ODI is a 10-item, self-rated measure that assesses limitations of various activities of daily living secondary to pain, specifically designed for assessment of low back pain (Fairbank et al., 1980). Each item is scored on a 0-5 point scale, with a potential range of total scores from 0 to 50. The total score is doubled and then expressed as a percentage from 0 to 100. Established cut-off points for interpretation of

this measure are as follows: 0-20 % for minimal disability; 20-40% for moderate disability; 40-60% for severe disability; 60-80% for crippled; 80-100% for bed-bound or exaggerating (Fairbank et al., 1980).

Pain Disability Questionnaire (PDQ)

The PDQ is a 15-item questionnaire developed by incorporating various dimensions of other pain disability instruments based on the biopsychosocial aspects of disability (Anagnostis et al., 2004). The PDQ contains a functional status component, psychosocial component, and a total component score. The patients are asked to indicate pain-related functional limitation associated with each domain. Each item was scored from 0 – 10, with a total possible score of 150. Higher scores indicate greater levels of pain and disability. The following cut-off scores for interpretation of this measure are: 0-70 for mild and moderate disability; 71-100 for severe disability; 101-150 for extreme disability (Gatchel, Mayer, & Theodore, 2006).

Beck Depression Inventory (BDI)

The BDI is a 21-item self-report tool designed to assess the severity of depressive symptoms (Beck et al., 1961). Each item was scored from 0 to 3, with a potential range of total scores from 0 to 63. Total scores ranged with cut-off scores of 0-9 for no depression; 10-18 for mild to moderate depression; 19-29 for moderate to severe depression; and greater than 30 for severe depression.

Insomnia Severity Index (ISI)

The ISI is a 7-item patient-report that measures the severity of insomnia, using a 0- 4 scale with a total possible score of 28 (Morin, 1993). Cut-off points established to interpret scores as follows: 0-7 for no insomnia; 8-14 for sub-threshold insomnia; 15-20 for moderate clinical insomnia; 22-28 for severe clinical insomnia (Bastien, Vallieres, & Morin, 2001).

Pain Anxiety Symptom Scale (PASS)

The short-version of PASS is a 20 item self-report measure developed to evaluate pain-related anxiety and fear in individuals with chronic pain conditions (McCracken & Dhingra, 2002). It consists of four subscales measuring dimensions of fear of pain, including escape and avoidance behavior; fear of pain; cognitive anxiety; and somatic anxiety. A 6-point scale ranges from 0 (never) to 5 (always), with a total score of 100. Higher scores on the PASS indicate higher levels of pain-related anxiety. The following cut-off points were established for clinical interpretation in chronic pain population: 0-34 for mild pain anxiety; 34-67 for moderate pain anxiety; 68-100 for severe pain anxiety (Brede, Mayer, Neblett, Willams, & Gatchel, 2011).

One-Year Post-FRP Socioeconomic Outcome Assessments

The socioeconomic outcomes were assessed one-year after treatment. A face-to-face or telephonic structured interview was conducted to determine whether the individual had recovered from the disability phase and returned to normal daily activities. The structured interview examined socioeconomically-relevant outcomes, such as work status and additional health utilization. Work status was measured by whether the patient returned to work at any time during the year after treatment, and whether the patient retained employment by being at work through the 1-year interview. Additional health care utilization assessed seeking healthcare from a new provider, the associated number of visits to a new provider, a new surgery to the original site of injury, and case settlement.

Statistical Analysis

Data Analysis

Table 5-2 details all statistical analysis methods performed for investigating the relationship among various types of variables. The initial univariate models of linear, binary logistic and ordinal regression were used to identify significant baseline factors

that influence the total CSI scores (linear) and clinically relevant groups (binary or ordinal) based on its scores. Following this, a multivariate linear, binary, and ordinal logistic regression model was created to identify an independent predictor, by controlling for other significant contributors found to be associated with the total CSI and/or CSI groups at the univariate level. In some cases, an interaction term between centered variables was also entered to the model to examine the interaction effects. The same analyses were used to determine whether the CSI and/or CSI groups predict the non-completion rate or one-year post-treatment outcomes. The Pearson's correlation *r*, Spearman's Rho, and Gamma were used to examine the construct and concurrent relationship between the CSI and the PHQ-Somatization, as well as other psychosocial measures. For repeated measures designs, the Paired-samples *t*-test (CSI total scores), McNemar's test (dichotomous CSI groups), and Wilcoxon Signed-rank test (ordinal CSI groups) were conducted to investigate the treatment efficacy over time. Finally, Analysis of Covariance (ANCOVA) was performed to examine the CSI group difference in psychosocial improvement while controlling for the initial level of psychosocial functioning. The significant criterion for all above analyses was defined as $p < .05$. The assumption of statistical tests was evaluated and ensured, in terms of outliers, normality, homoscedasticity, independence of errors, linearity, and multicollinearity. In order to reduce bias and obtain more accurate results, bootstrapping of 1000 samples with 95% interval was utilized in some contexts.

Table 5-2 Statistical Methods Used in the Study

Type of Variables		Test	Effect size
Independent Variable	Dependent Variable		
Univariate/Multivariate Regression Analysis			
Categorical /Continuous	Continuous	Linear Regression: *t*-test R^2	Standardized regression slope coefficient (β)
Categorical /Continuous	Dichotomous	Binary Logistic Regression: Wald's Z test, R^2	Exp (B) Odds Ratios
Categorical /Continuous	Categorical (Ordinal)	Ordinal Regression Wald's Z test, R^2	Exp (B) Odds Ratios
Univariate /Multivariate Correlation Analysis			
Continuous	Continuous	Bivariate Correlation Partial Correlation	Pearson's *r*
Categorical /Continuous	Dichotomous	Binary Logistic Regression	
Continuous	Categorical (Ordinal)	Spearman's Rho	
Categorical		Gamma	
Repeated Measures Analysis (Within-Group Comparison)			
Categorical	Continuous	Paired samples *t*-test	Cohen's *d*
Categorical	Dichotomous	McNemar's test	
Categorical	Categorical (Ordinal)	Wilcoxon Signed-rank test	
Between-Group Comparison Analysis (Covariate adjustments)			
Categorical	Continuous	Analysis of Covariance (ANCOVA): *F*-test	

Chapter 6

Results

CSI: Descriptive Information

The distribution of the CSI total scores at FRP admission was normal, and it was supported by a non-significant result of the Kolmogorov-Smirnov test, D (681) = 0.033, p = .078. The histogram of the CSI total scores is presented in Figure 6-1, with scores ranging from 1 to 86, and a mean of 42.7 (SD= 15.3).

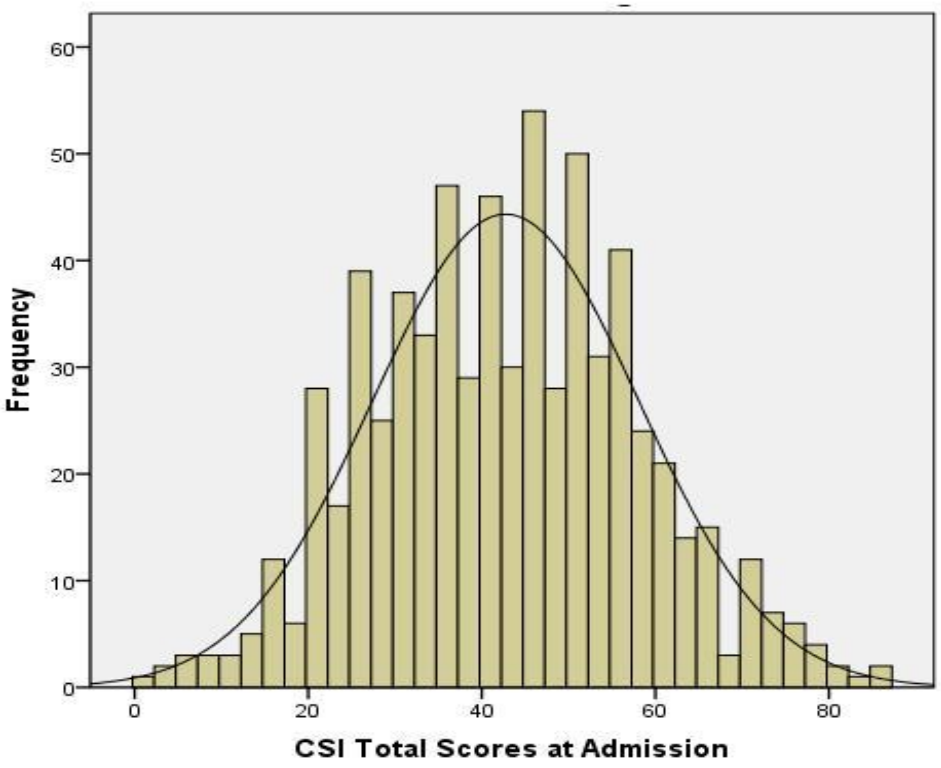


Figure 6-1 Histogram of the CSI Total Scores

CSI Total Scores

Continuous Analysis: Baseline Variables

Tables 6-1 through 6-4 present the data and statistical analyses of the baseline variables (demographic/occupational variables, history of abuse, history of CSS, psychiatric disorders) with regard to mean CSI scores. The univariate linear regression model was used (for each variable) for easy comparison of the standardized effect size. Table 6-1 details the demographic differences based on the mean CSI score. There was a difference between female (CSI mean= 44.5) and male patients (CSI mean= 41.8) regarding the total CSI scores at admission. Type of injury was found to be significantly associated with different CSI scores, with patients with extreme injuries scoring the lowest CSI score (CSI mean = 36.8), relative to those with other injuries. The number of compensable injuries and the length of disability were positively associated with the CSI scores. There were no differences in the CSI scores in terms of age, race, and marital status. There were significant differences found in the sense of job availability and occupation type in relation to the CSI scores. Patients who reported that their original job was not available showed higher scores on the CSI (CSI mean = 45.8), compared to those who reported that their original job was still available (CSI mean = 41.1). Job type (blue vs. white collar occupations) was associated with the CSI scores, such that white collar patients reported higher CSI scores (CSI mean = 45.8) as compared to blue collar patients (CSI mean = 42.2). However, pre-FRP CSI scores did not significantly differ, with respect to pre-FRP surgery, attorney retention, working status at admission, and the level of job demand.

Table 6-2 displays the data and statistical analyses of history of abuse with regard to mean CSI scores. Pre-FRP CSI scores were found to differ between patients with any abuse history (CSI mean = 47.7) and without any abuse history (CSI mean =

41.6). When the type of abuse was considered, the presence of physical abuse show the largest effect (β= .199) on the CSI scores, followed by psychological abuse (β= .166) and sexual abuse (β= .145).

Table 6-3 presents the data and statistical analyses of CSS history with regard to mean CSI scores. Pre-FRP CSI scores were found to significantly differ according to the presence of a previous diagnosis of CSS, endorsed on the CSI-Part B. Patients who reported any previous history of CSS diagnosis showed a higher CSI scores (CSI mean = 46.7) as compared to those who did not report any CSS history (CSI mean = 39.8). When the type of CSS diagnosis was analyzed, the higher score of the CSI was associated with patients with a history of tension headache/migraines (*β*= .232), fibromyalgia (β= .230), IBS (*β*= .225), chronic fatigue syndrome (*β*= .207), restless leg syndrome (*β*= .157),TMJ (*β*= .116), multiple chemical sensitivity (*β*= .115).

Table 6-4 displays the data and statistical analyses for psychiatric disorder differences regarding FRP-admission CSI scores. CSI scores were found to be statistically different according to the diagnosis of Axis I and/or Axis II disorders. Patients with major depressive disorder reported higher CSI scores (CSI mean = 46.2) than those without major depressive disorder (CSI mean = 35.5). Patients with generalized anxiety disorder also showed a higher level of the CSI score (CSI mean = 46.5) as compared to those without generalized anxiety disorder (CSI mean = 41.6). The diagnosis of substance abuse disorder was not associated with the mean CSI scores. The comorbid diagnosis of Axis II disorders (Cluster A: odd or eccentric; Cluster B: dramatic, emotional, or erratic; Cluster C: anxious or fearful) influenced the higher mean CSI scores. Patients with Cluster A, B, or C personality disorders reported higher CSI scores (CSI mean = 53.1, 50.0, and 46.2) than those without personality disorders (CSI mean =42.4, 41.5, and 42.3), respectively.

Table 6-1 Demographic and Occupational Comparisons Based on the Total CSI Scores at Admission

Demographic/Occupational Variables	CSI Scores at Admission	Test Statistics*	*p*-value	Standardized Coefficients (β)*
Gender				
Female	44.5 (15.8)	*t* = 2.24	.025	.086
Male	41.8 (15.0)			
Valid n = 681				
Age				
mean yr (*SD*)	42.7 (15.3)	*t* = 0.29	.773	
Valid n = 681				
Ethnicity, *n* (%)				
African American	42.8 (16.0)	*t* = 0.04	.965	
Caucasian	43.5 (14.7)	*t* = 1.40	.163	
Hispanic	40.8 (15.5)	*t* = -1.75	.081	
Others/Unknown	43.0 (22.8)	*t* = 0.05	.958	
Valid n = 681				
Marital Status, *n* (%)				
Single	41.3 (17.2)	*t* = -0.92	.358	
Married/Significant Other	42.2 (14.9)	*t* = -1.07	.287	
Separated/Divorced	44.5 (14.9)	*t* = 1.97	.050	
Widowed	40.8 (20.6)	*t* = -0.44	.663	
Valid n = 681				
Type of Injury, *n* (%)				
Cervical Spine	50.7 (16.1)	*t* = 1.97	.049	.075
Thoracic/Lumbar Spine	43.2 (14.5)	*t* = 0.58	.563	
Multiple Spinal	47.5 (12.7)	*t* = 2.53	.012	.097
Extremity Only	36.8 (15.2)	*t* = -6.91	<.001	-.256
Multiple Musculoskeletal	47.1 (15.1)	*t* = 4.26	<.001	.161
Valid n = 681				
Number of Compensable Injuries mean (*SD*)	42.7 (15.3)	*t* = 4.19	<.001	.159
Valid n = 681				
Length of Disability mean month (*SD*)	42.7 (15.3)	*t* = 4.20	<.001	.159
Valid n = 681				
Pre-treatment Surgeries, *n* (%)		*t* = 0.04	.677	
No	42.5 (13.8)			
Yes	43.0 (16.2)			
Valid n = 638				
Attorney Retained, *n* (%)		*t* = 1.84	.067	
No	41.9 (15.1)			
Yes	44.7 (15.8)			
Valid n = 581				

Table 6-1 *Continued*

Work Status at Admission, *n* (%)	43.0 (15.2) 41.9 (15.6)	*t* = 0.79	.428	
No				
Yes				
Valid n = 667				
Original Job Available (% yes)		*t* = -3.55	<.001	-.138
No	45.6 (15.7)			
Yes	41.1 (14.9)			
Valid n = 651				
Job Code (*n*, % Blue Collar)				
White	45.8 (15.2)	*t* = -2.23	.026	-.087
Blue	42.2 (15.3)			
Valid n = 662				
Job Demand				
Sedentary/Light	43.8 (15.8)	*t* = 0.61	.544	
Light/Medium	43.8 (15.4)	*t* = 0.90	.370	
Medium/Heavy	42.6 (14.9)	*t* = -0.23	.822	
Heavy/Heavy	42.1 (15.4)	*t* = -0.74	.458	
Valid n = 648				

* A negative value indicates a negative relationship.

Table 6-2 Abuse History Comparisons Based on the Total CSI Scores at Admission

Abuse History	CSI Scores at Admission	Test Statistics	*p*-value	Standardized Coefficients (β)
Any				
No	41.6 (15.0)	*t* = 3.47	.001	.156
Yes	47.7 (15.7)			
Valid n = 487				
Physical	41.7 (14.9)	*t* = 4.60	<.001	.199
No	49.9 (15.1)			
Yes				
Valid n = 513				
Sexual	42.1 (15.1)	*t* = 3.26	.001	.145
No	48.6 (15.2)			
Yes				
Valid n = 498				
Psychological	41.8 (15.0)	*t* = 3.63	<.001	.166
No	48.9 (15.5)			
Yes				
Valid n = 494				

Table 6-3 A History of CSS Diagnosis Comparisons Based on the Total CSI Scores at Admission

CSS History on CSI Part B	CSI Scores at Admission	Test Statistics	*p*-value	Standardized Coefficients (β)
Any				
No	39.8 (14.8)	$t = 7.38$	<.001	.284
Yes	49.5 (15.0)			
Valid n = 624				
Fibromyalgia				
No	41.9 (15.0)	$t = 5.96$	<.001	.230
Yes	56.2 (15.5)			
Valid n = 635				
IBS	41.8 (15.1)	$t = 5.84$	<.001	.225
No	54.8 (14.5)			
Yes				
Valid n = 639				
Tension headaches/migraines	40.8 (15.1)	$t = 6.05$	<.001	.232
No	49.4 (14.8)			
Yes				
Valid n = 637				
TMJ	42.4 (15.4)	$t = 2.94$	.003	.116
No	51.4 (15.4)			
Yes				
Restless Leg Syndrome	42.2 (15.4)	$t = 4.03$	<.001	.157
No	51.9 (13.3)			
Yes				
Valid n = 645				
Chronic Fatigue Syndrome	42.1 (15.2)	$t = 5.35$	<.001	.207
No	57.5 (13.2)			
Yes				
Valid n = 642				
Multiple Chemical Sensitivities	42.6 (15.4)	$t = 2.93$	.004	.115
No	57.7 (14.6)			
Yes				
Valid n = 638				

Table 6-4 Axis I and Axis II Disorder Comparisons Based on the Total CSI Scores at Admission

DSM-IV Psychiatric Disorder	CSI Scores at Admission	Test Statistics	*p*-value	Standardized Coefficients (β)
Axis I Disorder				
Major Depressive Disorder	35.5 (14.5)	$t = 8.93$	<.001	.324
No	46.2 (14.5)			
Yes				
Valid n = 681				
Generalized Anxiety Disorder	41.6 (15.6)	$t = 3.63$	<.001	.138
No	46.5 (13.7)			
Yes				
Valid n = 681				
Substance Use Disorder	42.5 (15.3)	$t = 1.49$	.136	.057
No	45.3 (15.6)			
Yes				
Valid n = 681				
Axis II Disorder				
Cluster A Personality Disorder	42.4 (15.2)	$t = 3.32$	.001	.126
No	53.1 (14.3)			
Yes				
Valid n = 681				
Cluster B Personality Disorder	41.5 (15.1)	$t = 5.26$	<.001	.198
No	50.0 (15.1)			
Yes				
Valid n = 681				
Cluster C Personality Disorder	42.3 (15.6)	$t = 2.01$	.045	.077
No	46.2 (12.1)			
Yes				
Valid n = 681				

Continuous Analysis: Predicting the Total CSI Scores

Univariate analysis results revealed that six demographic and occupational variables (gender, type of injury, number of compensable body parts, length of disability, a sense of job availability, job code), abuse history, a previous history of CSS diagnosis, MDD, GAD, and three Axis II disorders (Cluster A, Cluster B, Cluster C) were significantly related to the CSI scores at admission. Multivariate linear regression analysis was utilized to determine which of the baseline indicators were more associated with higher FRP-

admission CSI scores in a model. All predictors were forced into the model simultaneously without the decision about the order of entered variables, and were later hierarchically entered into the model according to the order of importance.

Before the predictors were entered into the model, the types of injury were re-coded to avoid the issue of collinearity. A dummy code (coded as 0 for extremity injuries; lower and upper and 1 for spinal injuries; cervical, thoracic/lumbar, or both) was used based on the findings from the univariate regressions. The injury type with multiple musculoskeletal systems was not included in the model because, it was highly correlated with the number of compensable body parts, $r = .68$.

Multivariate linear regression revealed that the following five factors were independently associated with higher scores of the CSI: MDD, a history of CSS, spine-related injury, abuse history, and GAD, $F = 8.47$, $p < .001$, Adjusted $R^2 = 0.23$. Following linear regression model with the hierarchical enter method was utilized in order to identify which of five predictors explained most of variations in the CSI scores. The first block contained MDD, indicating that it explained 12% of variance of the CSI scores. Addition of the previous history of CSS diagnoses (endorsed on the CSI Part B) accounted for 4 % of the variance. Abuse history and comorbid GAD accounted for each of 1% of the variance of the CSI scores, respectively. Table 6-5 displays the final model of the baseline predictors with coefficients and 95% of confidence interval. A total of five baseline predictors accounted 22% of the variance of the total CSI scores, $F = 19.96$, $p < .001$, Adjusted $R^2 = 0.22$. All assumptions (i.e., independence of errors, no multicollinearity, homoscedasticity, no significantly influencing outliers) were met for this final multiple regression model.

Table 6-5 Multiple Regression Analysis of the CSI Scores at Admission

Final Model	*B* (95% CI)	*SE B*	*B*	*p*
Constant	28.02 (24.90-31.15)	1.59		<.001
MDD	9.39 (6.26-12.52)	1.59	.292	<.001
A history of CSS	6.20 (2.82-9.58)	1.72	.177	<.001
Spinal Injury*	6.15(3.11-9.19)	1.55	.193	<.001
Abuse History	5.56 (1.74-9.38)	1.94	.140	.004
GAD	4.07 (0.65-7.48)	1.73	.116	.020

Note: $R^2 = 0.22$, $F = 19.96$, $p < .001$
* Extremity injury was used as a reference group

Continuous Analysis: Concurrent Validity of the CSI with Existing Psychosocial Measures

Table 6-6 details the Person's Correlation Coefficients of the association between FRP-admission CSI scores and other FRP-admission psychosocial measures. The CSI demonstrated a significant correlation with a measure of Somatization (PHQ-Somatization), $r = .63$, $p < .001$. Furthermore, the CSI appears to moderately correlate with all aspects along the psychosocial spectrum: the Pain VAS ($r = .33$, $p < .001$), the ODI ($r = .43$, $p < .001$), PDQ ($r = .52$, $p < .001$), BDI ($r = .61$, $p < .001$), ISI ($r = .41$, $p < .001$), and PASS ($r = .43$, $p < .001$). The CSI was better correlated with other CSS-relevant domains (such as depression and sleep disturbance) than the somatization module of the PHQ. The partial correlations were calculated to examine the unique associations among measures. The measures of PHQ-somatization and ODI were excluded from these analyses, because they tap into the similar construct, measured by the CSI and PDQ, respectively. The PDQ was chosen over the ODI because it had better correlations with other psychosocial measures. Partial correlations between the CSI and pain intensity (Pain VAS, $p = .253$) and pain-related anxiety (PASS, $p = .930$), respectively, were not significant after controlling for other psychosocial scores. The level of pain was indirectly associated with the CSI through the perceived disability (after controlling for the PDQ, $p =$

424), while the pain-related anxiety was indirectly associated with the CSI through the depressive symptoms (after controlling for the BDI, $p = .072$).

Table 6-6 Correlation Matrix Comparing the Association Between the FRP-Admission CSI Scores and Other FRP-Admission Psychosocial Scores

	CSI n = 681	PHQ n = 667	Pain VAS n = 649	ODI n = 677	PDQ n = 677	BDI n = 677	ISI n = 561	PASS n = 240
CSI	1	.63**	.33**	.43**	.52**	.61**	.41**	.43**
PHQ		1	.26**	.34**	.35**	.45**	.35**	.41**
Pain VAS			1	.41**	.54**	.31**	.28**	.36**
ODI				1	.57**	.38**	.39**	.31**
PDQ					1	.50**	.39**	.45**
BDI						1	.39**	.59**
ISI							1	.41**
PASS								1

Note. ** p <.001 * p<.05

Continuous Analysis: Predictive Validity Associated with Program Non-Completion

Out of 681 patients, 78.1% (n = 532) of patients completed the FRP. Program completion was associated with different mean CSI scores, such that the patients who failed to complete the FRP reported higher CSI scores (CSI mean = 48.6) than those who completed the FRP (CSI mean = 41.1), $\chi^2 = 26.81$, $p < .001$

Besides the CSI scores, univariate binary logistic regression results revealed the following baseline variables that were associated with the program completion rates: a sense of job availability ($\chi^2 = 27.26$, $p < .001$); working status at admission ($\chi^2 = 11.83$, $p = .001$); length of disability ($\chi^2 = 26.92$, $p < .001$); substance use disorder ($\chi^2 = 25.43$, $p < .001$); MDD ($\chi^2 = 9.74$, $p = .002$); Cluster B personality disorder ($\chi^2 = 6.87$, $p = .009$); a previous history of CSS ($\chi^2 = 5.95$, $p = .015$). Multivariate binary regression model with the hierarchical entry method finalized a better-fit model ($\chi^2 = 78.31$, $p < .001$), including five baseline variables such as the CSI scores, length of disability, working status at admission, substance use disorder, and a sense of job availability. The overall accuracy of classification for the program non-completion was increased to 80.6% with the inclusion of five baseline variables (from 78.2%), Nagelkerke's $R^2 = 0.17$. A details for the binary regression modal for program non-completion is in Table 6-7. The results indicated that the CSI scores at admission was the most significant independent predictor of whether the patient completed the program, $\chi^2 = 25.81$, $p = .001$, Nagelkerke's $R^2 = 0.06$. Finally, the bootstrapped model with 1000 samples confirmed the same results, and no outliers or influential cases were found in this binary regression model.

Table 6-7 Binary Logistic Regression Analysis of Program Non-Completion

Variable	B	*SE*	Wald (χ^2)	*p*	Exp B (95% CI)
Constant	-3.787	.437	75.01	.000	
CSI Scores at Admission	.027	.007	15.53	.000	1.03 (1.01-1.04)
Length of Disability	.008	.002	10.86	.001	1.01 (1.00-1.01)
Working Status at Admission*	.923	.309	8.89	.003	2.51 (1.37-4.61)
Substance Use Disorder	.828	.289	8.21	.004	2.29 (1.30-4.03)
Original Job Availability*	.459	.222	4.28	.039	1.58 (1.02-2.44)

Note: Nagelkerke's $R^2 = 0.17$, $\chi^2 = 78.31$, $p < .001$

* Not working status at admission and no job availability were used as a reference group

Continuous Analysis: Responsiveness to Treatment

The paired samples *t*-test was conducted to examine the responsiveness of the CSI over the FRP. A total of 485 patients completed the CSI at both admission and discharge. The responsiveness of the CSI was found to be significant, with a FRP-admission mean score of 41.2 (*SD* = 14.9), and a FRP-discharge mean score of 32.0 (*SD* = 16.3), $t = 14.6$, $p < .001$, Cohen's $d = .67$.

Continuous Analysis: Predictive Validity Associated with One-Year Socioeconomic Outcomes

Out of 475 cases of program completers between February 2010 and July 2013, 1-year socioeconomic information for the cases after June 2012 has not been tracked at data analysis point. The sample size of 299-309 was analyzed for 1-year post FRP outcomes, depending on the variables under investigation. The CSI scores at discharge were associated with work retention, such that patients who failed to retain work reported higher CSI scores at discharge (CSI mean at discharge = 38.2) as compared to those who retained work (CSI mean at discharge = 29.6), $\chi^2 = 12.72$, $p < .001$. However, CSI scores at discharge did not differ according to return to work, treatment seeking, and new surgery to original injury sites, all $p < .005$ (See Table 6-8). Univariate binary regression test results revealed that three other baseline variables were significantly related to work

retention status at one-year FRP-discharge: Hispanic race (χ^2 = 7.04, p =.008), sedentary-to-light job demand (χ^2 = 8.94, p =.003), and number of compensable body injures (t = 2.52, p =.014). Multivariate binary regression model with the hierarchical entry method finalized a better-fit model (χ^2 = 31.40, p <.001), including all four baseline variables, race (non-Hispanic), job demand (sedentary-light), number of compensable body injuries, and CSI scores at discharge, Nagelkerke's R^2 = 0.16. Table 6-9 details the final binary regression modal for non-work retention at 1 year post FRP. Again, the CSI score at discharge was a significant independent predictor of whether the patient retained work, χ^2 = 13.24, p <.001, Nagelkerke's R^2 = 0.11. Finally, the bootstrapped model with 1000 samples confirmed the same results, and no outliers or influential cases were found in this binary regression model.

Table 6-8 One-Year Outcome Comparisons Based on the Total CSI Scores

One-Year Outcome Measures	CSI Scores at Discharge	Statistical Test	*p*-value	Exp B (95% CI)
Return to Work				
No	36.7 (18.0)	χ^2 = 2.42	.120	
Yes	31.0 (16.1)			
Valid n = 300				
Work Retention*				
No	38.2 (16.9)	χ^2 =12.72	<.001	1.03
Yes	29.6 (15.4)			(1.02-1.05)
Valid n = 298				
Seeking Health Care from a New Provider				
No	31.6 (16.4)	t = 2.17	.141	
Yes	37.9 (16.9)			
Valid n = = 309				
Visit to New Provider, Mean (SD)				
Valid n = 309	31.9 (16.3)	t = .763	.446	
New Surgery to Original Site				
No	31.6 (16.4)	χ^2 = 2.34		
Yes	41.3 (16.2)			
Valid n = 299				

* Non-work retention was used as a reference group

Table 6-9 Binary Logistic Regression Analysis of Non-Work Retention

Variable	B	SE	Wald	*p*	Exp B (95% CI)
Constant	-3.772	.563	44.84	.000	
Sedentary-Light Job Demand	1.240	.455	7.44	.006	3.45 (1.42-8.42)
CSI Scores at Discharge	.026	.010	7.39	.007	1.03 (1.01-1.05)
Number of Compensable Injuries	.232	.102	5.19	.023	1.26 (1.00-1.54)
Non-Hispanic*	.984	.471	4.36	.037	2.67 (1.06-6.73)

Note: Nagelkerke's $R^2 = 0.16$, $\chi^2 = 31.40$, $p < .001$
* Hispanic Race was used as a reference group

Summary of Continuous Analysis

The CSI scores among CDOMD patients were normally distributed from 1 to 86 (out of 100), with a mean of 42.7 (*SD* = 15.3). In terms of the analyses of CSI scores at admission, scores differed according to gender, type of injury, number of compensable injuries, length of disability, a sense of job availability, type of occupation, abuse history and a previous diagnosis of CSS, MDD, and GAD. A multiple linear regression model revealed that MDD, a history of CSS, spinal injury, abuse history, and GAD accounted 22% of the variance of the total CSI scores at admission. Concurrent validity of the CSI ascertained that the correlation between CSI and PHQ-Somatization was moderate (*r* =.63). The CSI also showed medium-to-moderate concurrent validity correlations (*r* =.33 - .61) with other psychosoical measures, such as depression, perceived disability related to chronic pain condition, sleep disturbance, pain-related anxiety, and pain intensity. The measure of pain intensity and pain-related anxiety had indirect associations with the CSI. The higher CSI scores at admission predicted the program non-completion rate with an overall accuracy of 80.6%, along with other four significant baseline predictors (i.e., working status at admission, a sense of job availability, length of disability and substance use disorder). After controlling for the four variables, the CSI score was the most significant predictor of whether the patient completed the program. For the program completers, the mean score of the CSI was decreased from 41.2 to 32.0 after FRP.

Finally, the CSI score at discharge was also the significant predictor of non- work retention after controlling for other contributors that are, non-Hispanic ethnicity, sedentary-light job demand, and number of compensable body injuries.

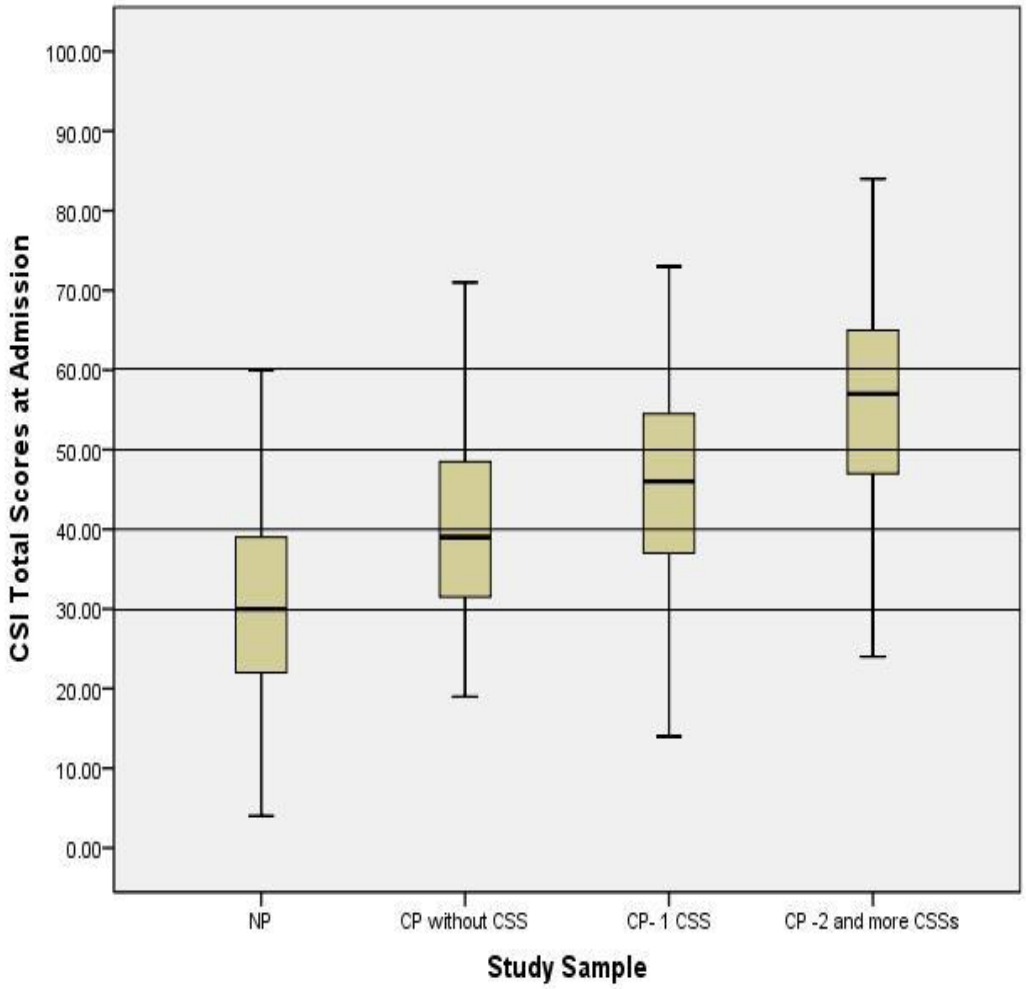
Categorical Classification

In order to provide the cut-off point identifying patients who are at risk of having a CSS, a pre-determined score of CSI 40 was used for a group comparison. Two groups were formed based on the CSI total score collected upon FRP admission: a low risk of CSS (scored less than 40 on the CSI, n = 290, 42.6%) and a high risk of CSS (scored greater than 40 on the CSI, n =391, 57.4%). Although a single cutoff score might be useful in screening patients who are at high risk of CSS, it may be unsuitable for measuring the symptom severity and detecting clinically significant symptom reduction. Many other health-related psychosocial measures have clinically-relevant values or cutoffs that indicate a degree of symptom severity, such as mild, moderate, and severe. Compared to continuous total scores or dichotomous ratings, these categorical rating scales have better clinical utility in making initial treatment decisions and monitoring treatment outcomes (Gatchel et al., 2006). Therefore, severity cut-off levels were established and proposed based on empirical and pragmatic considerations.

In order to define the clinically relevant cutoffs for the CSI, the total mean CSI scores from non-patient and CSS patient groups were obtained from the early publication of CSI (Neblett et al., 2013). Three goals were set up by an interdisciplinary team (including a physician, psychologist, psychophysiological specialist, and statistical expert) with extensive treatment and research experience with chronic pain conditions: 1) ensuring that the majority of the non-patient comparison subjects fell within the lower severity level and the majority of the multiple CSS subjects fell within the higher severity levels; 2) using the previously derived 40 point cutoff within the severity level gradient; 3)

maintaining face validity and ease of interpretation. With these goals in mind, the CSI score was divided into five categories with increasing severity: 0-29 (Minimal), 30-39 (Mild), 40-49 (Moderate), 50-59 (Severe), and 60 and greater (Extreme). A 10 point interval was chosen to define symptom severity because it is easy to remember and use. Also it has widely been used by other self-report measures. These proposed severity levels were supported by empirical evidence and theoretical reasoning. The moderate level cutoff (score of 40) was found to best distinguish CSS patients and non-patient individuals (Neblett et al., 2013). The severe level cutoff (score of 50) equals to the maximum score that the responders will obtain when they indicate "sometimes" on all 25 CSS-related symptoms represented on the CSI.

Figure 6-2 and Table 6-10 show the CSI score distribution from four earlier subject samples (non-patients comparison subjects, chronic pain patients without CSS, chronic pain patients with a single CSS diagnosis, and chronic pain patients with multiple CSS diagnoses) and their relationship with the CSI severity levels. About 75% of the non-patient comparison subjects fell below 40, and approximately half fell into "minimal" range. Similarly 67% of patients with one CSS diagnosis, and 93% of patients with multiple CSS's scored above 40. Forty-six percentages of patients with multiple CSSs scored in the extreme severity range. The prevalence of CSI severity groups for the current study sample (n = 681) was 21.1% (n = 144) for minimal, 21.4% (n = 146) for mild, 23.2% (n = 158) for moderate, 21.4% (n = 146) for severe, and 12.8% (n = 87) for extreme, respectively.



Note: NP- Non-Patient; CP – Chronic Patient; CSS- Central Sensitivity Syndrome

Figure 6-2 Mean, SD, Range of the CSI Total Scores Based on Study Sample (Box Plot)

Table 6-10 CSI Severity Levels Based on Different Study Samples

Sample Comparisons from the CSI Validation Study	Minimal 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+
Non-Patient Sample N = 129	61 (47.3%)	36 (27.9%)	23 (17.8%)	8 (6.2%)	1 (0.8%)
Chronic Pain without CSS N = 32	4 (12.5%)	13 (40.6%)	7 (21.9%)	5 (15.6%)	3 (9.4%)
Chronic Pain with 1 CSS N = 43	5 (11.6%)	9 (20.9%)	13 (30.2%)	13 (30.2%)	3 (7.0%)
Chronic Pain with 2 and more CSSs N = 46	1 (2.2%)	2 (4.3%)	12 (26.1%)	10 (21.7%)	21 (45.7%)

Note: NP- Non-Patient; CP – Chronic Patient; CSS- Central Sensitivity Syndrome

Categorical Analysis (A Single Cut-off): Baseline Variables

For screening purpose, a single cut-off score of 40 of the CSI was used to classify the group of patients who were at high risk of CSS from those who were at low risk of CSS. Tables 6-11 through 6-14 compare the low risk-group (CSI scores < 40) to the high-risk group (CSI scores ≥ 40) on baseline variables (demographic/occupational variables, history of abuse, history of CSS, psychiatric disorders). Table 6-11 details the demographic differences between the low-risk and the high risk group classified with regard to the CSI scores at admission. Type of injury was found to significantly differ between groups, such that patients with cervical, multiple spinal, and multiple musculoskeletal injuries were 4.6 (95% CI: 1.0-20.5), 1.9 (95% CI: 1.1-3.5), and 1.8 (95% CI: 1.3-2.7) times were more likely to belong to the CSS high risk group, while extremity-injured patients were 2.6 (95% CI: 1.9-3.7) times less likely to fall into the CSS high risk group. No group difference was found for lumbar/thoracic injuries. The CSS high-risk group had an average of 2.0 compensable injuries, and it was significantly higher than

the low-risk group (mean injuries =1.2). The time between injury and program admission (i.e., length of disability) was significantly longer for the CSS high-risk group (mean disability month = 29.0) as compared to the low-risk group (mean disability month = 20.0). Finally, individuals in the CSS high-risk group were 1.8 (95% CI: 1.3-2.5) times less likely to report that their original jobs were available at FRP admission, compare to those in the low-risk group. There were no group differences regarding gender, age, race, marital status, pre-treatment surgeries, attorney retention rates, work status at admission, job type, and job demand level.

Table 6-12 displays the comparison between the CSS high-risk and CSS low-risk groups with regard to abuse history. Patients classified as the CSS high-risk group were 2.3 times (95% CI: 1.4-3.8) more likely to have had any type of abuse than those in the low-risk group. When the type of abuse was analyzed, 21% of the high risk group reported physical abuse, followed by psychological abuse (17%), and sexual abuse (13%). A likelihood of having abuse these abuse histories was higher for the CSS high risk group, 2.4 times (95% CI: 1.4-4.0), 2.4 times (95% CI: 1.2-4.8), and 2.0 times (95% CI: 1.1-3.4), respectively.

Table 6-13 presents a comparison of a previous CSS history between the CSS high-risk group and low-risk group. Data of a previous diagnosis of CSS was collected from the Part B section of the CSI questionnaire. Results revealed that 29.0% of patients reported the previous history of any type of CSS. The most frequent diagnosis was migraine or tension headaches (22.9%), followed by IBS (7.7%), restless leg syndrome (6.7%), fibromyalgia (6.6%), chronic fatigue syndrome (4.5%), TMJ (4.1%), and multiple chemical sensitivities (1.4%). Patients in the CSS high risk group were 2.7 times (95% CI: 1.9-4.0) more likely to had a previous diagnosis of CSS.

Table 6-14 displays the psychiatric disorder differences (Axis I and Axis II disorders) between the CSS high-risk group and low-risk group. Out of 681 patients, 68% were diagnosed with MDD, followed by GAD (24%) and substance use disorder (10%). Individuals in the CSS high-risk group were 3.5 times (95% CI: 2.4-4.9) more likely to be diagnosed with MDD than were those in the low-risk group. The CSS high-risk group was 1.8 times (95% CI: 1.3-2.7) more likely to have patients with GAD than the low risk group. The proportion of patients with substance use disorder did not differ between two groups. The diagnosis of Axis II personality disorder was also compared between the CSS high-risk group and low-risk groups. Patients in the high risk group were 3.7 (95% CI: 1.2-10.9), 2.7 (95% CI: 1.6-4.4), and 2.4 times (95% CI: 1.4-4.1) more likely to be diagnosed with Cluster A (odd or eccentric), Cluster B (dramatic, emotional, or erratic), and Cluster C (anxious of fearful) personality disorders, respectively, than those in the low-risk group.

Table 6-11 Demographic and Occupational Comparisons Between the CSS High-Risk and Low-Risk Group

Demographic/ Occupational Variables	Low-Risk Group <40	High-Risk Group ≥40	Test Statistic Wald	*p*	Exp (B) 95% CI
Gender					
n (% Female)	93 (32.1%)	145 (37.1%)	X^2= 1.84	.175	
Valid n = 681					
Age					
mean yr (*SD*)	45.0 (10.8)	45.1 (10.4)	X^2 = 0.01	.961	
Valid n = 681					
Ethnicity, *n* (%)					
African American	66 (22.8%)	83 (21.2%)	X^2 = 0.23	.633	
Caucasian	149 (51.4%)	225 (57.5%)	X^2 = 2.55	.110	
Hispanic	69 (23.8%)	79 (20.2%)	X^2 = 1.26	.262	
Others/Unknown	6 (2.1%)	4 (1.0%)	X^2 = 1.21	.272	
Valid n = 681					
Marital Status, *n* (%)					
Single	43 (14.8%)	45 (11.5%)	X^2 = 1.62	.203	
Married/Significant	162 (55.9%)	217 (55.5%)	X^2= 0.01	.925	
Other	78 (26.9%)	124 (31.7%)	X^2 = 1.85	.174	
Separated/Divorced	7 (2.4%)	5 (1.3%)	X^2 = 1.20	.274	
Widowed					
Valid n = 681					
Type of Injury, *n* (%)					
Cervical Spine	2 (0.7%)	12 (3.1%)	X^2 = 1.20	.048	4.6 (1.0-20.5)
Thoracic/Lumbar Spine	96 (33.1%)	138 (35.3%)	X^2 = 0.35	.552	
Multiple Spinal	17 (5.9%)	42 (10.7%)	X^2 = 4.87	.027	1.9 (1.1-3.5)
Extremity Only*	122 (42.1%)	85 (21.7%)	X^2 =31.65	<.001	2.6 (1.9-3.7)
Multiple Musculoskeletal	53 (18.3%)	114 (29.2%)	X^2 =10.49	.001	1.8 (1.3-2.7)
Valid n = 681					

Table 6-11 *Continued*

Number of Compensable Injuries mean (*SD*)	1.7 (1.2)	2.0 (1.4)	X^2= 8.71	.003	1.2 (1.1-1.4)
Length of Disability mean month (*SD*)	20.0 (35.1)	29.0 (44.2)	X^2 = 7.67	.006	1.0 (1.0-1.0)
Pre-treatment Surgeries n (%)	136 (50.2%)	182 (49.6%)	X^2 = *0.02*	.882	
Valid n = 638					
Attorney Retained n (%)	54 (22.0%)	82 (24.5%)	X^2 = *0.51*	.478	
Valid n = 581					
Work Status at Admission n (%)	66 (23.2%)	89 (23.2%)	X^2 = *0.00*	1.00	
Valid n = 667					
Original Job Available(% yes)*	201 (72.3%)	220 (59.0%)	X^2 = *12.24*	<.001	1.8 (1.3-2.5)
Valid n = 651					
Job Code (n, % Blue Collar)	245 (86.9%)	310 (81.6%)	X^2 = *3.33*	.068	
Valid n = 662					
Job Demand					
Sedentary/Light	28 (10.1%)	43 (11.6%)	X^2 = *0.68*	.409	
Light/Medium	52 (18.8%)	80 (21.5%)	X^2 = *0.32*	.571	
Medium/Heavy	105 (38.0%)	133 (35.8%)	X^2 = *0.35*	.553	
Heavy/Heavy	91 (33.0%)	116 (31.2%)	X^2 = *0.23*	.631	
Valid n = 648					

* Extremity only injury and original job availability were used for a reference group

Table 6-12 Abuse History Comparisons Between the CSS High-Risk and Low-Risk Group

Abuse History (Yes)	Low-Risk Group <40	High-Risk Group ≥40	Wald (*p*)	Odds Ratios (95% CI)
Any Abuse Valid n = 487	25 (12.0%)	67 (24.0%)	X^2 = 10.80 (.001)	2.3 (1.4-3.8)
Physical Abuse Valid n = 513	22 (10.2%)	63 (21.2%)	X^2 = 10.57 (.001)	2.4 (1.4-4.0)
Sexual Abuse Valid n = 498	12 (5.6%)	36 (12.6%)	X^2 = 6.51 (.011)	2.4 (1.2-4.8)
Psychological Abuse Valid n = 494	20 (9.5%)	49 (17.3%)	X^2 = 5.85 (.016)	2.0 (1.1-3.4)

Table 6-13 A History of CSS Diagnosis Comparisons Between the CSS High-Risk and Low-Risk Group

CSS History of CSI Part B (Yes)	Low-Risk Group <40	High-Risk Group ≥40	Wald (*p*)	Odds Ratios (95% CI)
Any CSS Valid n = 624	48 (18.0%)	133 (37.3%)	X^2 = 26.57 (<.001)	2.7 (1.9-4.0)
Headache/tension migraine Valid n = 642	38 (14.0%)	109 (29.4%)	X^2 = 20.11 (<.001)	2.6 (1.7-3.8)
IBS Valid n = 639	6 (2.2%)	43 (11.7%)	X^2 = 15.72 (<.001)	5.8 (2.4-13.8)
Restless leg syndrome Valid n = 642	9 (3.3%)	34 (9.1%)	X^2 = 7.65 (.006)	2.9 (1.4-6.1)
Fibromyalgia Valid n = 635	7 (2.6%)	35 (9.6%)	X^2 = 10.62 (.001)	4.0 (1.7-9.1)
Chronic fatigue syndrome Valid n = 642	3 (1.1%)	26 (7.0%)	X^2 = 9.54 (.002)	6.7 (2.0-22.3)
TMJ Valid n = 637	6 (2.2%)	20 (5.5%)	X^2 = 3.93 (.047)	2.6 (1.0-6.4)
Multiple chemical sensitivities Valid n = 638	0 (0.0%)	9 (2.4%)	X^2= .000 (.999)	

Table 6-14 Psychiatric Disorder Comparisons Between the CSS High-Risk and Low-Risk Group

DSM-IV Psychiatric Disorder (Yes)	Low-Risk Group <40	High-Risk Group ≥40	Wald (*p*)	Odds Ratios (95% CI)
Axis I Disorder				
Major Depressive Disorder Valid n = 681	152 (52.4%)	310 (79.3%)	X^2= 52.77 (<.001)	3.5 (2.5-4.9)
Generalized Anxiety Disorder Valid n = 681	52 (17.9%)	112 (28.6%)	X^2= 10.30 (.001)	1.8 (1.3-2.7)
Substance Use Disorder Valid n = 681	29 (10.0%)	42 (10.7%)	X^2= 0.10 (.754)	
Axis II Disorder				
Cluster A Personality Disorder Valid n = 681	4 (1.4%)	19 (4.9%)	X^2= 5.43 (.020)	3.7 (1.2-10.9)
Cluster B Personality Disorder Valid n = 681	24 (8.3%)	76 (19.4%)	X^2= 15.67 (<.001)	2.7 (1.6-4.4)
Cluster C Personality Disorder Valid n =681	18 (6.2%)	53 (13.6%)	X^2= 9.18 (.002)	2.4 (1.4-4.1)

Categorical Analysis (A Single Cut-off): Predicting the CSS High-Risk Group

Univariate analysis results confirmed that four injury and occupational variables (type of injury, number of compensable body injuries, length of disability, and a sense of job availability), along with abuse history, a previous history of CSS diagnosis, MDD, GAD, and three Axis II disorders (Cluster A, Cluster B, Cluster C) were associated with membership in the high CSS risk group. In order to examine the risk factors that predicted the high risk group, a multiple binary regression analysis with entry method was conducted. A final model revealed a total of five high impact risk factors, MDD, spine-

related injury, GAD, a previous history of CSS, and a sense of job availability, X^2=92.53, p <.001. These seven risk factors accounted for 25% of the variance in the CSS high-risk group, Negelkerke adjusted R^2 = 0.25. Another binary regression model with the hierarchical enter method based on both statistical and theoretical rationales was utilized in order to identify which of the baseline indicators had unique relationships with the CSS high-risk group when controlling for other variables. The first block contained MDD and GAD, indicating that two factors explained 16% of variance of the CSS high risk group, X^2= 56.00, p <.001. Addition of spinal injury (i.e., non-extremity injury) accounted for 4 % of the variance of the CSS high risk group, X^2=18.68, p <.001. The previous history of CSS diagnoses, endorsed on the CSI Part B, explained 3% of the variance in the CSS high risk group, X^2=10.00, p =.002. A sense of job availability accounted for 2% of the variance of the CSS high risk group (X^2=7.84, p = .005). Table 6-15 displays the final model of the high CSS risk factors with coefficients and odd ratios. The bootstrapped model with 1000 samples confirmed the same results, and no outliers or influential cases were found in this binary regression model.

Table 6-15 Binary Logistic Regression Analysis of the CSS High Risk Group

Variable	B	*SE*	Wald	*p*	Exp B (95% CI)
Constant	-1.784	.255	49.16	.000	
MDD	1.276	.223	32.68	.000	3.6 (2.3-5.5)
Spine-related Injury*	.847	.215	15.53	.000	2.3 (1.5-3.6)
Previous Diagnosis of CSS	.761	.252	9.10	.003	2.1 (1.3-3.5)
A Sense of Job Non-Availability*	.610	.219	7.74	.005	1.8 (1.2-2.8)
GAD	.860	.255	11.39	.001	2.4 (1.4-3.9)

Note: Nagelkerke R^2 = 0.25, χ^2 = 92.53, p <.001
* Extremity only injury and job availability were used as a reference group

Categorical Analysis (A Single Cut-off): Concurrent Validity of the CSI with Existing Psychosocial Measures

In order to examine the concurrent validity of the CSI, two CSS risk groups (high vs low) were compared on PHQ-Somatization, and the other psychosocial instruments measuring similar components involving CSS. The CSS high-risk group showed higher levels of somatization-related symptoms (measured by the PHQ-Somatization), pain intensity (measured by the PainVAS), perceived pain disability (measured by the ODI and the PDQ), depression (measured by the BDI), sleep disturbance (measured by the ISI), and pain-related anxiety (measured by the PASS) as compared to the low risk group, all *p*s <.001. These psychosocial measures were analyzed both as continuous and categorical variables, using previously established cut-off points. All psychosocial scores were positively associated with the high risk of having a CSS. The multivariate regression model revealed that the measures of depression and sleep disturbance were independently associated with the high CSS risk group. The measures of the pain intensity, pain disability, and pain-related anxiety had mediational indirect associations with the CSS high risk group. Not surprisingly, the CSS high-risk group had a greater number of patients who fell into the moderate through extreme categories of other psychosocial measures as compared to the low-risk group. Table 6-16 details psychosocial score comparisons between the CSS high-risk and low-risk group.

Table 6-16 Psychosocial Score Comparisons Between the CSS High-Risk and Low-Risk Group

Psychosocial Measures	Low-Risk Group <40	High-Risk Group ≥40	Wald (*p*)	Effect Size
PHQ-Somatization				
Mean (SD)	6.0 (3.2)	10.3 (4.2)	χ^2 = 96.60 (<.001)	OR= 1.4 (1.3-1.5)
≥ 7 PHQ-Somatization, n (%)	110 (38.6%)	315 (82.5%)	χ^2= 135.8 (<.001)	OR= 7.5 (5.2-10.7)
Valid n = 667				
Pain VAS				
Mean (SD)	6.6 (2.1)	7.8 (1.6)	χ^2= 35.98 (<.001)	OR=1.4 (1.2-1.5)
≥ 8 Pain VAS, n (%)	117 (40.3%)	220 (56.3%)	χ^2 = 16.88 (<.001)	OR=1.9 (1.4-2.6)
Valid n = 681				
Pain Disability Questionnaire (PDQ)				
Mean (SD)	85.6 (25.3)	106.9 (22.5)	χ^2 = 54.80 (<.001)	OR=1.1 (1.0-1.1)
≥ 71 PDQ, n (%)	209 (72.1%)	367 (95.3%)	χ^2 = 71.48 (<.001)	OR=7.9 (4.6-13.5)
Valid n = 675				
Beck Depression Inventory (BDI)				
Mean (SD)	12.5 (7.8)	22.6 (9.7)	χ^2 = 87.52 (<.001)	OR=1.1 (1.1-1.2)
≥ 20 BDI, n (%)	45 (15.7%)	219 (56.2%)	χ^2 = 113.85 (<.001)	OR=6.9 (4.7-10.0)
Valid n = 677				
Insomnia Severity Index (ISI)				
Mean (SD)	15.1 (8.7)	19.8 (5.5)	χ^2 = 39.34 (<001)	OR=1.1 (1.1-1.1)
≥ 15 ISI, n (%)	131 (53.9%)	256 (81.1%)	χ^2= 48.02 (<001)	OR=3.7 (2.5-5.4)
Valid n = 561				
Pain Anxiety Symptoms Scale (PASS)				
Mean (SD)	37.4 (19.7)	52.2 (22.2)	χ^2 = 18.56 (<001)	OR=1.0 (1.0-1.10)
≥ 34 PASS, n (%)	55 (53.9%)	107 (77.5%)	χ^2= 14.91 (<001)	OR=2.9 (1.7-5.2)
Valid n = 240				

Categorical Analysis (A Single Cut-off): Predictive Validity Associated with Program Non-Completion

Figure 6-3 displays the FRP program non-completion rates between the CSS high-risk group and low-risk group. Program non-completion rate was significantly higher in the CSS high-risk group (27%), compared to those in the low risk group (15%), χ^2= 16.17, p <.001. The individuals in the high-risk group were 2.2 times (95% CI: 1.5-3.3) less likely to complete the FRP. Out of 149 program non-completers, 72% of patients were in the CSS-high risk group, whereas 28% of those were in the low-risk group.

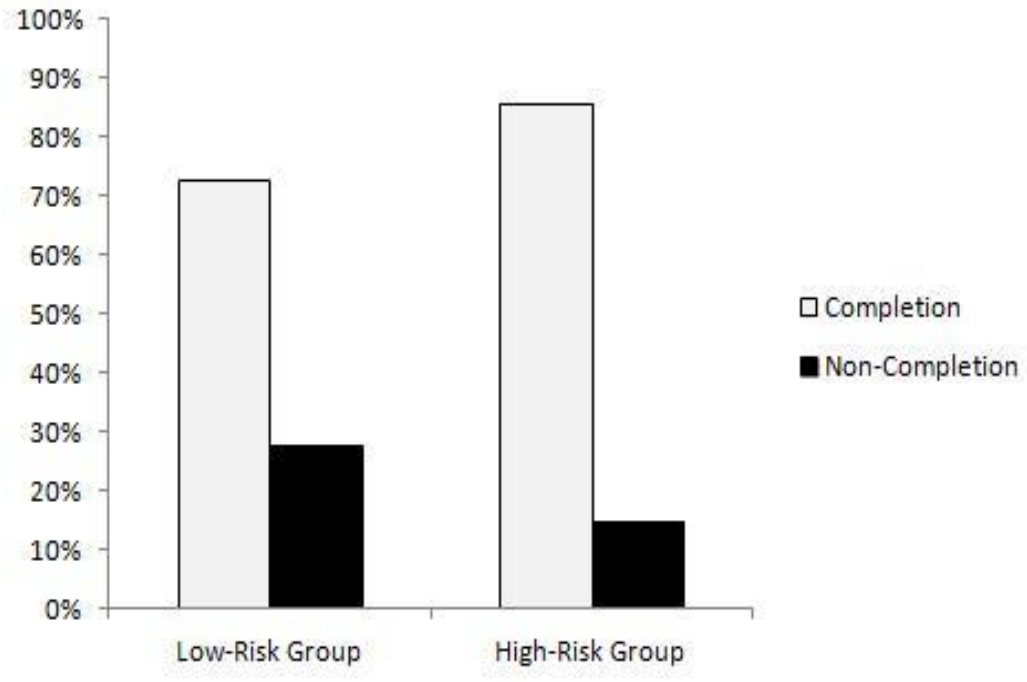


Figure 6-3 Program Non-Completion Rate Between the CSS High-Risk and Low-Risk Group

Categorical Analysis (A Single Cut-off): Responsiveness to Treatment

After finishing the FRP, the proportion of the CSS high-risk group dropped from 53.3 % (n = 253) to 29.7 % (n= 141). Out of 253 patients who classified as the high-risk group at admission, 131 patients (51.8%) were re-classified into the low-risk group after the FRP program. Another 122 patients (48.2%) remained in the high-risk group, McNemar's test (see Figure 6-4). The changed group (high to low) and non changed group (high to high) were compared with regard to baseline variables. Univariate analysis results revealed the following four factors: Caucasian, X^2= 19.91, p <.001; Cluster A personality disorder, X^2 =4.21, p =.053 (marginal); Cluster B personality disorder X^2 =12.81, p <.001; Cluster C personality disorder, X^2 =6.74, p =.009; abuse history, X^2 =3.96, p =.047. Using a multivariate binary regression analysis, two factors (Caucasian and Cluster B personality disorder) were found to successfully explain 13% of the variance in the unchanged high-risk group, X^2 = 26.80, p <.001. Addition of the interaction term of Caucasian and Cluster B personality disorder did not influence the model, X^2 = 0.04, p =.846, indicating that both factors appeared to be independent risk factors for non-responders, after controlling for each other. Results from the Wald analysis revealed a marginal significant level for Cluster B personality disorder (X^2= 3.75, p = .053, B (SE) = 0.89 (0.46) with the odds ratios of 2.4 (95% CI: 1.0-6.0). Caucasian CSS high-risk patients were 2.7 times (95%CI = 1.6-4.7) more likely to remain in the high risk group even after the FRP, X^2 = 24.30, p < .001, B (SE) = 1.01 (0.28).

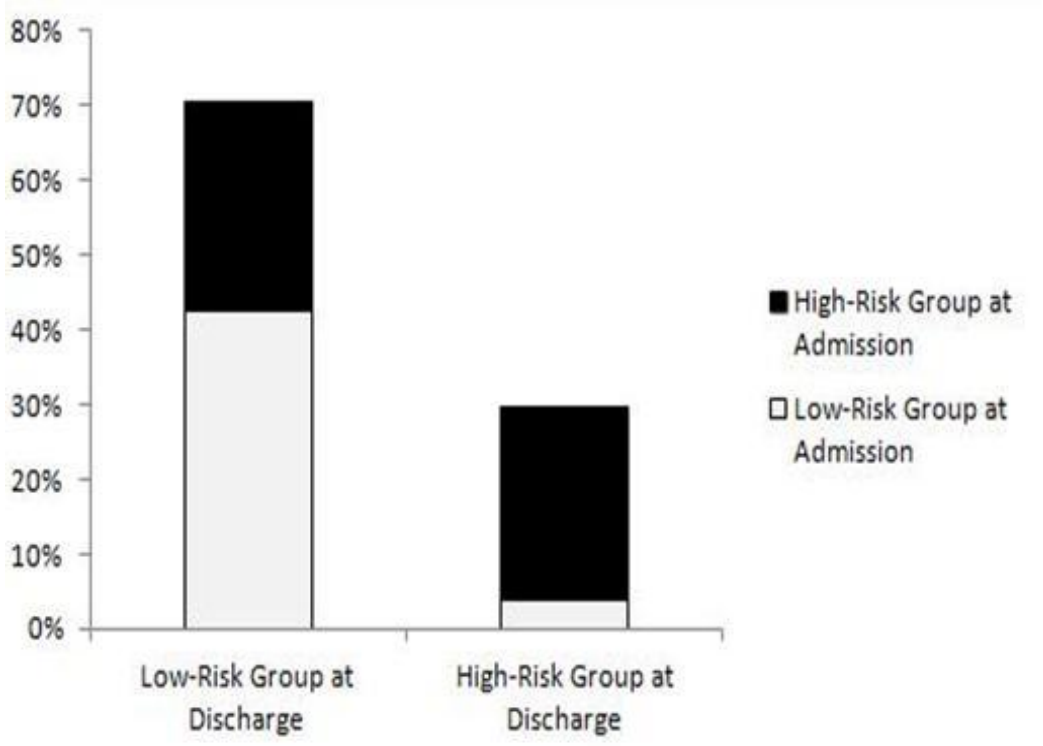


Figure 6-4 CSS Risk Group Changes over FRP

Related to changes over the FPR, the admission- and discharge FRP psychosocial scores were compared between two risk groups (Table 6-17). Within-group comparisons showed that both low- and risk-group significantly improved on psychosocial scores, regardless of the initial classification. The score changes from admission-to-discharge FRP were larger in the high CSS risk group for somatization-related symptoms (PHQ-somatization, $p = .001$), pain intensity (Pain VAS, $p = .020$), perceived pain disability (ODI, $p = .022$), and sleep disturbance (ISI, $p < .001$) while controlling for the initial levels. Individuals in the high risk of having a CSS benefited more from interdisciplinary FRP.

Table 6-17 Psychosocial Score Changes Between the CSS High-Risk and Low-Risk Group

Psychosocial Measures	Low-Risk Group <40	High-Risk Group ≥40	Test Statistic (*p*)
PHQ-Somatization			
Admission	5.9 (3.1)	10.1 (4.1)	
Discharge	4.8 (3.2)	8.2 (5.0)	F_{change} = 11.52
Change	1.1 (3.5)	1.9 (4.8)	(.001)
Within-Group *p* value	<.001	<.001	
Valid n = 477			
Pain Visual Analogue Score			
Admission	6.5 (2.1)	7.4 (1.5)	F_{change} = 5.48
Discharge	4.4 (2.4)	5.2 (2.2)	(.020)
Change	2.0 (2.6)	2.2 (2.5)	
Within-Group *p* value	<.001	<.001	
Valid n = 475			
Oswesty Disability Index			
Admission	32.8 (16.8)	44.9 (15.8)	F_{change} = 5.30
Discharge	20.1 (15.1)	29.6 (16.9)	(.022)
Change	12.8 (14.5)	15.3 (16.3)	
Within-Group *p* value	<.001	<.001	
Valid n= 456			
Pain Disability Questionnaire			
Admission	84.0 (25.6)	104.9 (22.2)	F_{change} = 3.34
Discharge	53.1 (28.5)	72.7 (30.8)	(.068)
Change	32.4 (30.3)	36.9 (33.4)	
Within-Group *p* value	<.001	<.001	
Valid n = 472			
Beck Depression Inventory			
Admission	12.5 (7.9)	21.5 (9.3)	F_{change} = 1.70
Discharge	7.8 (8.0)	13.2 (8.9)	(.193)
Change	4.8 (8.3)	8.4 (9.0)	
Within-Group *p* value	<.001	<.001	
Valid n = 472			
Insomnia Severity Index			
Admission	14.7 (9.1)	19.4 (5.8)	F_{change} = 14.45
Discharge	9.9 (7.1)	14.4 (6.9)	(<.001)
Change	4.8 (8.6)	5.0 (7.6)	
Within-Group *p* value	<.001	<.001	
Valid n = 380			
Pain Anxiety Symptoms Scale			
Admission	33.5 (19.1)	51.8 (23.7)	F_{change} = 2.21
Discharge	19.9 (17.6)	33.3 (23.1)	(.140)
Change	13.8 (21.3)	18.9 (21.9)	
Within-Group *p* value	<.001	<.001	
Valid n = 126			

Categorical Analysis (A Risk Cut-off): Predictive Validity Associated with One-Year Socioeconomic Outcomes

The CSI high-risk group at FRP discharge and the low-risk group at FRP discharge were compared according to socioeconomic outcome variables at 1 year post-program. The CSS risk-groups at FRP discharge were not associated with any of socioeconomic outcome measures (e.g., return to work, work retention, health utilization, surgery to original injury sites) at 1-year post-FRP (See Table 6-18).

Table 6-18 One-Year Socioeconomic Outcome Comparisons Between the CSS High-Risk and Low-Risk Group

One-Year Socioeconomic Measures	Low-Risk Group <40	High-Risk Group ≥40	Test Statistic	*p*-value
Return to Work (Yes) Valid n = 300	201 (93.5%)	78 (91.8%)	$\chi^2 = 0.28$	.598
Work Retention (Yes) Valid n = 298	178 (82.2%)	63 (75.0%)	$\chi^2 = 2.61$	.106
Seeking Health Care from a New Provider (Yes) Valid n = 309	9 (4.1%)	7 (7.6%)	$\chi^2 = 1.58$	.209
Visit to New Provider Yes, Mean (SD) Valid n = 299	0.4 (2.7)	0.7 (3.7)	$t = 0.74$	.461
New Surgery To Original Site (Yes) Valid n = 299	3 (1.4%)	4 (4.5%)	$\chi^2 = 2.65$	.104

Categorical Analysis (Severity Cutoffs): Baseline Variables

Tables 6-19 thru 6-22 details the statistical comparisons of the baseline variables (demographic/occupational variables, history of abuse, history of CSS, psychiatric

disorders) based on five CSS symptom severity levels. Table 6-19 presents the demographic, injury, and occupational differences based on the degree of symptom severity. Univariate ordinal regressions revealed significant associations between the CSS symptom severity levels and the demographic and occupational variables at FRP admission with regard to female gender (p = .036), non-Hispanic race (p = .042), cervical injuries (p = .017), multiple spinal injuries (p = .019), non-extremity injury (p <.001), multiple musculoskeletal injuries (p <.001), a greater number of injuries (p <.001), a longer length of disability (p <.001), a sense of job availability (p <.001), and a white collar occupation (p =.029). However, there were no severity level differences regarding age, marital status, pre-treatment surgeries, and attorney retention rates, work status at admission, and job demand level.

Table 6-20 through 6-22 present the history of abuse and CSS diagnoses, and the diagnosis of psychiatric disorders related to CSS symptom severity levels. A clinician found that 18.9 % of CDOMD patients (responders, n = 487) had a history of abuse (e.g., physical, sexual, and/or psychological), and it was significantly associated with the severity membership (p <.001). Of the responders (n = 624), 29.0% of the CDOMD patients reported that they had previously been diagnosed with one or more CSS diagnosis listed on the CSI-Part B (headache/ tension migraine, IBS, restless leg syndrome, fibromyalgia, chronic fatigue syndrome, TMJ, and/or multiple chemical sensitivities). The presence of self-reported history of one or more CSS diagnoses was positively associated with the CSS symptom severity levels, p <.001. Finally, the structured mental health evaluation identified 67.8%, 24.1%, and 10.4% of MDD, GAD, and Substance use disorder in CDOMD patients. The prevalence of Axis II personality disorders in this study population was 3.4% for Cluster A (odd or eccentric), 14.7% for Cluster B (dramatic, emotional, or erratic), and 10.4% for Cluster C (anxious or fearful),

respectively. The comorbid psychiatric disorders (except the substance use disorder) were associated with the CSS symptom severity levels, all *p*s <.05.

6-19 Demographic and Occupational Comparisons Among CSS-related Symptom Severity Groups

Demographic/ Occupational Variables	Minimal 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+	Wald (*p*)	Exp (B) 95% CI
Gender							
n (% Female)	47 (32.6%)	46 (31.5%)	50 (31.6%)	55 (37.7%)	40 (46.0%)	χ^2 = 4.39 (.036)	1.2 (1.0-1.8)
Valid n = 681							
Age							
mean yr (*SD*)	44.8 (11.6)	45.3 (10.1)	45.5 (11.0)	44.9 (10.0)	44.8 (10.1)	X^2= 0.01 (.933)	
Valid n = 681							
Ethnicity, *n* (%)							
African American	32 (22.2%)	34 (23.3%)	33 (20.9%)	28 (19.2%)	22 (25.3%)	X^2= 0.02 (.898)	
Caucasian	71 (49.3%)	78 (53.4%)	84 (53.2%)	94 (64.4%)	47 (54.0%)	X^2= 3.45 (.063)	
Hispanic		31 (21.2%)	41 (25.9%)	23 (15.8%)	15 (17.2%)	X^2= 4.14 (.042)	1.4 (1.0-1.9)
Others/Unknown	3 (2.1%)	3 (2.1%)	0 (0.0%)	1 (0.7%)	3 (3.4%)	X^2= 0.05 (.820)	
Valid n = 681							
Marital Status, *n* (%)							
Single	25 (17.4%)	18 (12.3%)	18 (11.4%)	13 (8.9%)	14 (16.1%)	X^2= 1.48 (.224)	
Married/Sig Others	79 (54.9%)	83 (56.8%)	94 (59.5%)	81 (55.5%)	42 (48.3%)	X^2= 0.47 (.495)	
Separated/Divorced	37 (25.7%)	41 (28.1%)	45 (28.5%)	50 (34.2%)	29 (33.3%)	X^2= 2.94 (.087)	
Widowed	3 (2.1%)	4 (2.7%)	1 (0.6%)	2 (1.4%)	2 (2.3%)	X^2= 0.27 (.606)	
Valid n = 681							
Type of Injury, *n* (%)							
Cervical	2 (1.4%)	0 (0.0%)	3 (2.7%)	5 (3.4%)	4 (4.6%)	X^2= 5.69 (.017)	3.2 (1.2-8.3)
Thoracic/Lumbar	44 (30.6%)	52 (35.6%)	59 (37.3%)	56 (38.4%)	23 (26.4%)	X^2= 0.03 (.874)	
Multiple Spinal	5 (3.5%)	12 (8.2%)	15 (9.5%)	18 (12.3%)	9 (10.3%)	X^2= 5.50 (.019)	1.8 (1.1-2.8)
Extremity Only	73 (50.7%)	49 (33.6%)	40 (25.3%)	28 (19.2%)	17 (19.5%)	X^2=40.66(<.001)	2.5 (2.0-3.6)
Multiple-Musculoskeletal	20 (13.9%)	33 (22.6%)	41 (25.9%)	39 (26.7%)	34 (39.1%)	X^2=16.69(<.001)	1.9 (1.4-2.6)
Valid n = 681							

Table 6-19 Continued

Number of Compensable Injuries mean (*SD*) Valid n = 681	1.6 (1.1)	1.8 (1.2)	1.8 (1.3)	1.9 (1.2)	2.4 (1.8)	X^2=21.01(<.001)	1.3 (1.2-1.4)
Length of Disability mean month (*SD*) Valid n = 681	17.8 (25.6)	22.2 (42.5)	20.5 (34.6)	33.1 (48.7)	37.7 (49.7)	X^2=17.12(<.001)	1.0 (1.0-1.0)
Pre-treatment Surgeries Yes , *n* (%) Valid n = 638	70 (52.2%)	66 (48.2%)	66 (44.6%)	63 (45.3%)	53 (66.3%)	X^2= 0.67(.414)	
Attorney Retained Yes, *n* (%) Valid n =581	30 (22.1%)	21 (23.9%)	22 (21.8%)	20 (24.4%)	13 (30.2%)	X^2= 1.70 (.193)	
Work Status at Admission Yes , *n* (%) Valid n = 667	36 (25.5%)	24 (21.0%)	24 (23.5%)	25 (23.6%)	13 (22.1%)	X^2= 0.10 (.754)	
Original Job Available Yes, *n* (%) Valid n = 651	101 (72.7%)	100 (71.9%)	95 (66.3 %)	79 (56.4%)	46 (55.4%)	X^2=13.58(<.001)	1.7 (1.3-2.3)
Job Code (*n*, % Blue Collar) Valid n = 662	124 (87.9%)	121 (85.8%)	131 (85.6%)	109 (76.8%)	70 (82.4%)	X^2= 4.75 (.029)	1.5 (1.0-2.2)
Job Demand							
Sedentary/Light	14 (10.2%)	14 (10.1%)	13 (8.8%)	20 (14.1%)	10 (12.0%)	X^2= 0.95(.330)	
Light/Medium	30 (21.9%)	22 (15.8%)	28 (19.0%)	33 (23.2%)	19 (22.9%)	X^2= 0.71(.398)	
Medium/Heavy	45 (32.8%)	60 (43.2%)	56 (38.1%)	46 (32.4%)	31 (37.3%)	X^2= 0.03 (.873)	
Heavy/Heavy	41 (35.0%)	43 (30.9%)	50 (34.0%)	43 (30.3%)	27 (27.7%)	X^2= 0.89 (.346)	
Valid n = 648							

Table 6-20 Abuse History Comparisons Among CSS-related Symptom Severity Groups

Abuse History (Yes)	Minimal 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+	Wald (*p*)	Exp (B) 95% CI
Any Valid n = 487	11 (10.9%)	14 (13.1%)	24 (21.2%)	25 (25.0%)	18 (29.0%)	X^2= 12.25 (<.001)	2.1 (1.4-3.1)
Physical Valid n = 513	9 (8.6%)	13 (11.7%)	14 (12.0%)	28 (25.0%)	21 (30.9%)	X^2= 21.75 (<.001)	2.7 (1.8-4.2)
Sexual Valid n = 498	5 (4.9%)	7 (6.4%)	11 (9.6%)	12 (11.3%)	13 (20.0%)	X^2= 10.95 (.001)	2.5 (1.4-4.2)
Psychological Valid n = 494	8 (7.8%)	12 (11.1%)	14 (12.2%)	18 (17.0%)	17 (27.0%)	X^2= 12.26 (<.001)	2.3 (1.4-3.6)

Table 6-21 A History of CSS Diagnosis Comparisons Among CSS-related Symptom Severity Groups

CSS History of CSI Part B (Yes)	Minimal 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+	Wald (*p*)	Exp (B) 95% CI
Any Valid n = 624	15 (11.0%)	33 (25.2%)	43 (29.5%)	48 (36.6%)	42 (52.5%)	43.59 (<.001)	2.9 (2.1-4.0)
Headache/tension migraine Valid n = 642	12 (8.7%)	26 (19.5%)	34 (22.7%)	39 (28.3%)	36 (43.4%)	34.88 (<.001)	2.7 (2.0-3.8)
IBS Valid n = 639	2 (1.5%)	4 (3.0%)	12 (8.0%)	13 (9.6%)	18 (21.7%)	29.57 (<.001)	4.4 (2.5-7.6)
Restless leg syndrome Valid n = 642	2 (1.4%)	7 (5.3%)	9 (6.0%)	14 (9.9%)	11 (13.1%)	13.17 (<.001)	2.8 (1.6-4.9)
Fibromyalgia Valid n = 635	3 (2.2%)	4 (3.0%)	6 (4.1%)	13 (9.6%)	16 (19.3%)	27.13 (<.001)	4.6 (2.6-8.3)
Chronic fatigue syndrome Valid n = 642	1 (0.7%)	2 (1.5%)	3 (2.0%)	12 (8.6%)	11 (13.3%)	24.15 (<.001)	5.7 (2.8-11.4)
TMJ Valid n = 637	3 (2.2%)	3 (2.3%)	4 (2.7%)	8 (5.9%)	8 (9.6%)	9.29 (.002)	3.0 (1.5-6.1)
Multiple chemical sensitivities Valid n = 638	0 (0.0%)	0 (0.0%)	4 (2.7%)	1 (0.7%)	4 (4.8%)	6.34 (.012)	4.7 (1.4-15.7)

Table 6-22 Psychiatric Disorder Comparisons Between the CSS High-Risk and Low-Risk Group

DSM-IV Psychiatric Disorder (Yes)	Minimal 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+	Wald (*p*)	Exp (B) 95% CI
Axis I Disorder							
Major Depressive Disorder Valid n = 681	65 (45.1%)	87 (59.6%)	115 (72.8%)	117 (80.1%)	78 (89.7%)	67.67 (<.001)	3.5 (2.6-4.7)
Generalized Anxiety Disorder Valid n = 681	19 (13.2%)	33 (22.6%)	47 (29.7%)	37 (25.3%)	28 (32.2%)	10.47 (.001)	1.7 (1.2-2.3)
Substance Use Disorder Valid n = 681	8 (5.6%)	21 (14.4%)	16 (10.1%)	13 (8.9%)	13 (14.9%)	1.50 (.221)	
Axis II Disorder							
Cluster A Personality Disorder Valid n = 681	1 (0.7%)	3 (2.1%)	5 (3.2%)	6 (4.1%)	8 (9.2%)	11.14 (.001)	3.6 (1.7-7.7)
Cluster B Personality Disorder Valid n = 681	12 (8.3%)	12 (8.2%)	20 (12.7%)	33 (22.6%)	23 (26.4%)	24.63 (<.001)	2.6 (1.8-3.9)
Cluster C Personality Disorder Valid n = 681	10 (6.9%)	8 (5.5%)	22 (13.9%)	23 (15.8%)	8 (9.2%)	4.56 (.033)	1.6 (1.0-2.5)

Categorical Analysis (Severity Cut-offs): Predicting the CSI Severity Levels

A multivariate ordinal regression model was conducted to identify significant baseline contributing variables that would predict the CSS symptom severity levels (See Table 6-23). Five predictors were identified and accounted for 22% of the variance in the severity levels, including MDD, abuse history, GAD, self-reported previous CSS diagnoses, and spinal injuries (opposed to non-extremity injuries), $\chi^2 = 80.06$, $p < .001$, Negelkerke pseudo $R^2 = 0.22$. The odds of being classified for a high level of symptom severity increased by 3.3 times (95% CI = 2.1 – 5.1) with the presence of MDD, 2.2 times (95% CI = 1.4-3.4) with the abuse history, 2.1 times (95% CI = 1.2-3.1) with GAD, 2.0 times (95% CI = 1.2-3.2) with self-reported CSS history and 1.6 times (95% CI = 1.0-2.5) with spinal injuries, respectively.

Table 6-23 An Ordinal Regression Analysis of the CSS-related Symptom Severity Levels

Ordinal Regression (Logit Link Function)	Estimate (95% CI)	SE	Exp (Estimate) (95% CI)	Wald	*p*
Intercept					
Threshold (Degree of Symptom= 1)	0.36 (-0.07-0.79)	0.22			.104
Threshold (Degree of Symptom= 2)	1.54 (1.08-1.99)	0.23			<.001
Threshold (Degree of Symptom= 3)	2.61 (2.11-3.12)	0.26			<.001
Threshold (Degree of Symptom= 4)	4.03 (3.42-4.63)	0.31			<.001
MDD	1.19 (0.76-1.61)	0.22	3.3 (2.1-5.0)	30.34	<.001
Spinal Injury*	0.75 (0.34-1.15)	0.21	2.1 (1.2-3.1)	13.22	<.001
A Previous History of CSS	0.77 (0.33- 1.21)	0.23	2.2 (1.4-3.4)	11.69	.001
Abuse History	0.68 (0.18-1.17)	0.25	2.0 (1.2-3.2)	7.09	.008
GAD	0.48 (0.03-0.92)	0.23	1.6 (1.0-2.5)	4.45	.035

Note: Negelkerke pseudo R^2= 0.22, χ^2 = 80.06, p <.001;
* Extreme only injury was used as a reference group

Categorical Analysis (Severity Cut-offs): Concurrent Validity of the CSI with Existing Psychosocial Measures

Table 6-24 presents the associations between the CSS symptom severity levels and the somatization module of the PHQ and other psychosocial measures at FRP admission. As the CSS symptom severity level increased, the scores and levels of somatization-related symptoms (assessed by a sub-module of the PHQ), depressive symptoms (assessed by the BDI), perceived disability (assessed by the ODI and PDQ), sleep disturbance (assessed by the ISI), pain-related anxiety (assessed by the PASS), and pain intensity (assessed by the Pain VAS) were increased, all *p*s <.001. The partial correlations were calculated to examine the unique associations among measures. The results revealed that partial correlations between the CSI and pain intensity (Pain VAS, $p = .156$) and pain-related anxiety (PASS, $p = .989$), respectively, were not significant after controlling for other psychosocial scores. The pain-related anxiety was indirectly associated with the CSS symptom severity levels through the depressive symptoms (after controlling for the BDI, $p = .187$). The level of pain intensity was indirectly associated with the CSS symptom severity levels through the perceived disability (after controlling for the PDQ, $p = 341$) or pain related-anxiety (after controlling for the PASS, $p = .341$).

Table 6-24 Psychosocial Score and Severity Level Comparisons among CSS-related Symptom Severity Groups

Psychosocial Measures	Minimal 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+	Statistical Test Spearman's rho Gamma
PHQ-Somatization						
Mean (SD)	5.1 (2.9)	6.9 (3.3)	8.2 (3.2)	10.7 (3.7)	13.2 (4.5)	.598 (<.001)
0-6 Low	105 (74.5%)	70 (48.6%)	48 (31.6%)	12 (8.4%)	7 (8.0%)	.708 (<.001)
7-14 Moderate	35 (24.8%)	71 (49.3%)	100 (65.8%)	110 (76.9%)	44 (50.6%)	
≥ 15 High	1 (1.5%)	3 (2.1%)	4 (2.6%)	21 (14.7%)	36 (41.4%)	
Valid n = 667						
Pain VAS						
Mean (SD)	6.2 (2.2)	7.0 (1.9)	7.3 (1.6)	7.6 (1.6)	8.0 (1.4)	.264 (<.001)
0-3 Mild	16 (11.1%)	3 (2.1%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	.301 (<.001)
4-5 Moderate	28 (19.4%)	29 (19.9%)	16 (10.1%)	15 (10.3%)	2 (2.3%)	
6-7 Severe	50 (34.7%)	47 (32.2%)	61 (38.6%)	49 (33.6%)	27 (31.0%)	
8-10 Extreme	50 (34.7%)	67 (35.9%)	80 (50.6%)	82 (56.2%)	58 (66.7%)	
Valid n = 681						
Oswestry Disability Index (ODI)						
Mean (SD)						
0-20 Minimal	37 (27.2%)	32 (22.7%)	11 (7.4%)	3 (2.2%)	4 (4.7%)	.389 (<.001)
21-40 Moderate	60 (44.1%)	53 (37.6%)	59 (39.6%)	49 (35.8%)	22 (25.6%)	.407 (.039)
41-60 Severe	32 (23.5%)	48 (34.0%)	62 (41.6%)	62 (45.3%)	25 (29.1%)	
61-80 Crippled	7 (5.1%)	7 (5.0%)	16 (10.7%)	20 (14.6%)	34 (39.5%)	
81-100 Bed Bound/ Exaggerating	0 (0.0%)	1 (0.7%)	1 (0.7%)	3 (2.2%)	1 (1.2%)	
Valid n = 649						
Pain Disability Questionnaire(PDQ)						
Mean (SD)	77.5 (25.1)	93.5 (23.0)	100.6 (23.3)	108.3 (20.6)	115.9 (21.2)	.509 (<.001)
0-70 Mild/Moderate	54 (37.5%)	27 (18.5%)	13 (8.4%)	5 (3.4%)	0 (0.0%)	.573 (<.001)
71-100 Severe	66 (45.8%)	52 (35.6%)	51 (32.9%)	40 (27.4%)	12 (14.5%)	
101-150 Extreme	24 (16.7%)	67 (45.9%)	91 (58.7%)	101 (69.2%)	71 (85.5%)	
Valid n = 675						

Table 6-24 *Continued*

Beck Depression Inventory (BDI)						
Mean (SD)						
0-9 No	10.6 (7.9)	14.4 (7.4)	18.7 (8.1)	23.1 (9.0)	29.0 (10.1)	.589 (<.001)
10-15 Mild	79 (56.0%)	35 (24.0%)	19 (12.1%)	7 (4.8%)	3 (3.4%)	.589 (<.001)
16-19 Mild/Moderate	25 (17.7%)	60 (41.1%)	40 (25.5%)	20 (13.7%)	7 (8.0%)	
20-29 Moderate/Severe	23 (16.3%)	20 (13.7%)	38 (24.2%)	31 (21.2%)	6 (6.9%)	
≥30 Severe	10 (7.1%)	26 (17.8%)	40 (25.5%)	54 (37.0%)	25 (28.7%)	
Valid n = 677	4 (2.8%)	5 (3.4%)	20 (12.7%)	34 (23.3%)	46 (52.9%)	
Insomnia Severity Index (ISI)						
Mean (SD)						
0-7 No Clinically Insomnia(CI)	12.8 (7.0)	17.3 (9.5)	18.6 (5.9)	19.9 (5.0)	21.9 (5.0)	.418 (<.001)
8-14 Sub-threshold CI	26 (21.8%)	13 (10.5%)	4 (3.1%)	2 (1.6%)	1 (1.5%)	.437 (<.001)
15-21 Moderate CI	42 (35.3%)	31 (25.0%)	31 (24.4%)	16 (12.7%)	6 (9.2%)	
≥ 22 Severe CI	39 (32.8%)	49 (39.5%)	46 (36.2%)	60 (47.6%)	19 (29.2%)	
Valid n = 561	12 (10.1%)	31(25.0%)	46 (36.2%)	48 (38.1%)	39 (60.0%)	
Pain Anxiety Symptoms Scale (PASS)						
Mean (SD)	35.6 (20.2)	38.7 (19.5)	44.4 (20.6)	51.1 (19.8)	64.1 (22.8)	.396 (<.001)
< 34 Mild	21 (51.2%)	26 (42.6%)	16 (32.0%)	11 (22.0%)	4 (10.5%)	.427 (<.001)
34-67 Moderate	18 (43.9%)	29 (47.5%)	27 (54.0%)	30 (60.0%)	18 (47.4%)	
> 67 Severe	2 (4.9%)	6 (9.8%)	7 (14.0%)	9 (18.0%)	16 (42.1%)	
Valid n = 240						

Categorical Analysis (Severity Cut-offs): Predictive Validity Associated with Program Non-Completion

Of 681 total patients, 22% (n = 149) of patients failed to complete the program. There was a linear trend for increasing rates of FRP non-completion (10.4%, 18.5%, 20.9%, 28.8%, and 36.8%) associated with the CSS symptom severity levels, $\chi^2 = 27.9$, $p < .001$ (See Figure 6-5). The odds ratios of non-program completers (reference group: "Minimal" group) were 2.3 (95% CI = 1.2-4.4) for moderate, 3.5 (95% CI = 1.8-6.6) for severe, and 5.0 (95% CI =2.5-10.0) for extreme, respectively. There was no difference in the non-completion rates between the minimal and mild groups.

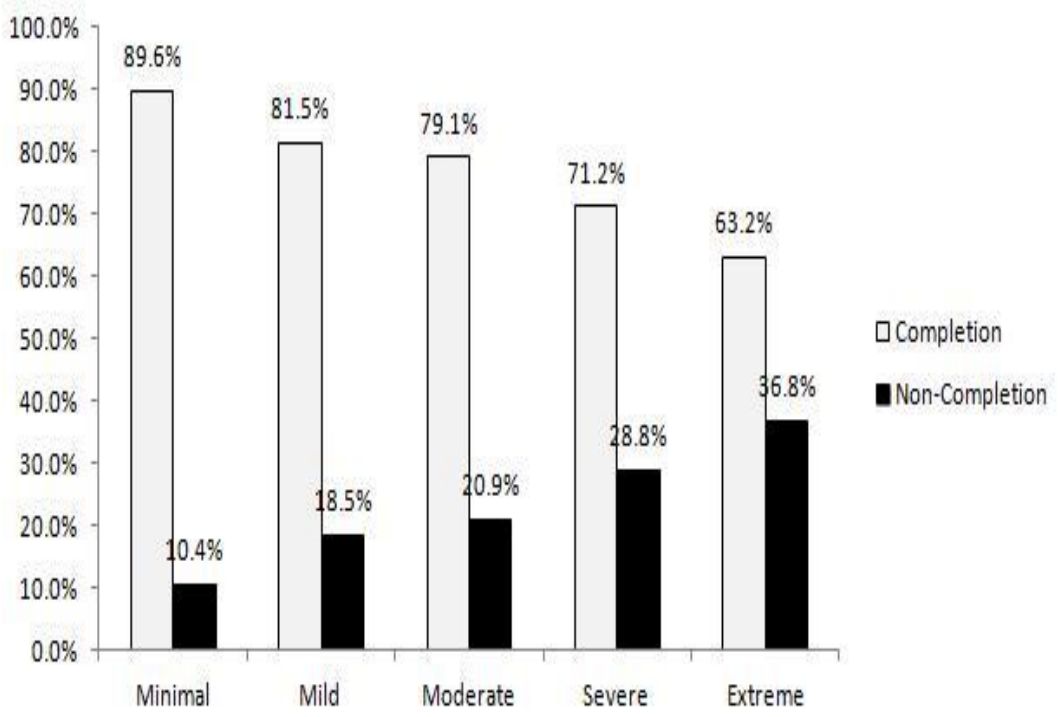


Figure 6-5 Program Non-Completion Rates Across CSI Severity Groups

Categorical Analysis (Severity Cutoffs): Responsiveness to Treatment

A total of 475 patients completed the FRP, and had the CSI scores both at FRP admission and discharge. At FRP admission, 24.2 %, 22.5%, 23.4%, 19.4%, and 10.5% of patients were classified as minimal, mild, moderate, severe, and extreme symptom groups, respectively. After completing FRP, the prevalence of the minimal and mild groups increased by 21.9% and 1.7%, while the prevalence of the moderate, severe, and extreme groups decreased by 10.0%, 9.1%, and 4.6%, respectively (See Figure 6-6). A significant level change from FRP-admission to FPR-discharge was supported by the Wilcoxon signed-rank test. There was a significant decrease in CSS symptom severity levels over FRP with a medium effect size, $z = -10.01$, $p < .001$, $r = -.32$. When within-group changes were considered, 95.7% of "minimal", 86.9% of "mild", 69.3% of "moderate", 43.5% of "severe", and 28% of "extreme" level individuals at FRP admission reported either minimal or mild levels of CSS related symptoms after FRP. Among 253 individuals classified as having moderate and above-moderate level of CSS symptoms at FRP admission, 71.1% (n = 180) reported symptom reduction (one or two levels changes) at FRP discharge. Another 28.9% (n = 73) of patients reported that their symptoms remained (n = 48) or became worse (n = 25) after FRP completion. Two groups were compared with regard to baseline variables. Four baseline variables were associated with treatment resistance: Caucasian Race (Compared to African), abuse history, Cluster A Personality Disorder, and Cluster Personality Disorder, all *p*s <.001. Treatment resistant patients were 3.4 times (95%CI: 1.4-8.2) more likely to be Caucasians, 2.5 times (95% CI: 1.2-5.3) more likely to have a history of abuse, and 3.9 times (95% CI: 1.1-14.4) and 2.2 times (95% CI: 1.1-4.3) were more likely to have comorbid Cluster A and Cluster B Personality Disorders, respectively. A multivariate binary logistic analysis revealed that

only Caucasian Race was an independent predictor of treatment resistance, $\chi^2 = 4.32$, $p = .038$.

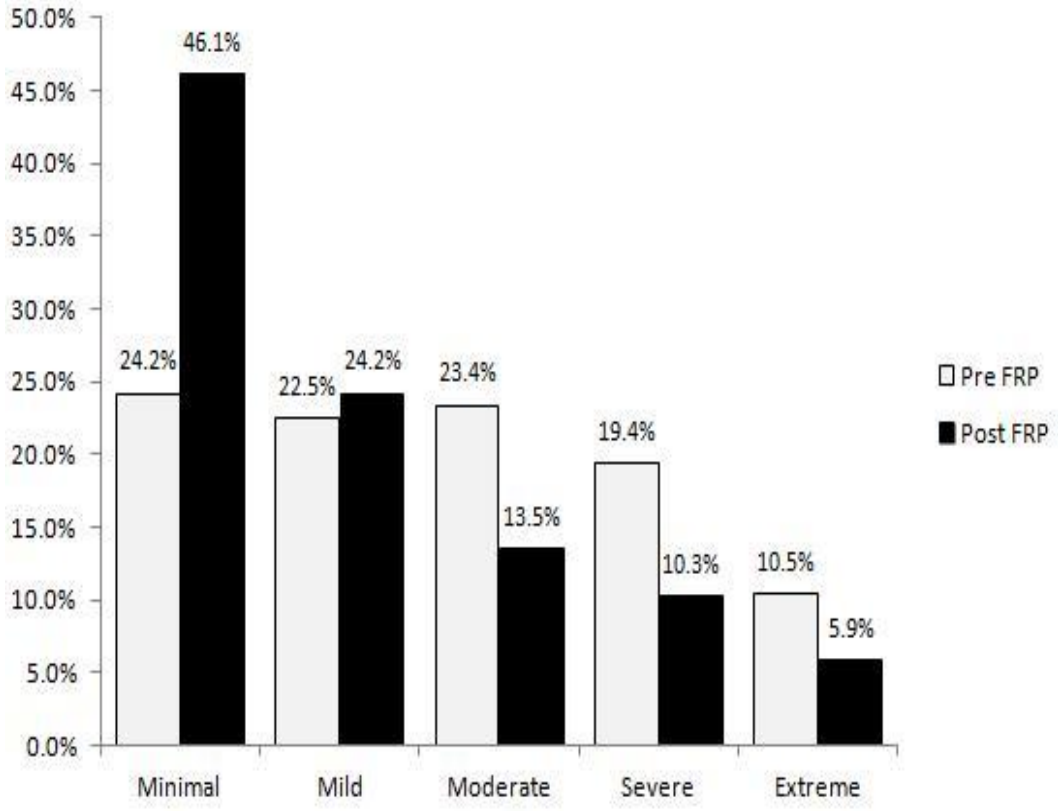


Figure 6-6 CSI Seveiry Group Changes Over FRP

Categorical Analysis (Severity Cut-offs): Predictive Validity Associated with One-Year Socioeconomic Outcomes

The five CSI severity groups were compared on socioeconomic outcome variables 1 year post-FRP (See Table 6-25). The linear associations were found among CSI severity groups for the rates of work retention and seeking treatment from a new health provider. For example, having a high level of CSS related symptoms at FRP discharge was associated with the lower rate of work retention at 1-year post FRP, $\chi^2 =$

9.77, p =.001. The work-retention rates for each severity group were 85.8 % for minimal, 77.3 % for mild, 94.7 % for moderate, 60.7 % for severe, and 55.6 % for extreme, respectively. The severity groups were linearly associated with increased treatment seeking behaviors, $\chi^2 = 4.11$, p =.043.

Table 6-25 One-Year Outcomes Comparisons Among CSS-related Symptom Severity Groups

One-Year Socioeconomic Measures	Minimal 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+	Statistical Test *p*-value
Return to Work (Yes) Valid n = 300	140 (94.0%)	61 (92.4%)	37 (97.4%)	25 (89.4%)	16 (84.2%)	χ^2 = 1.51 (.219)
Work Retention (Yes) Valid n = 298	127 (85.8%)	51 (77.3%)	36 (94.7%)	17 (60.7%)	10 (55.6%)	χ^2 = 9.77 (.001)
Seeking Health Care from a New Provider (Yes) Valid n = 309	3 (2.0%)	6 (8.8%)	2 (4.9%)	3 (9.7%)	2 (10.0%)	χ^2 = 4.11 (.043)
Visit to New Provider Yes, Mean (SD) Valid n = 299	0.3 (2.7)	0.6 (2.5)	0.5 (2.8)	0.3 (0.9)	1.7 (6.7)	Linear= 7.42 (.135)
New Surgery To Original Site (Yes) Valid n = 299	1 (1.5%)	2 (2.9%)	2 (2.9%)	0 (0.0%)	2 (5.9%)	χ^2 = 2.83 (.092)

Chapter 7

Discussion

The purpose of the current study was; 1) to identify the baseline predictors associated with the CSI scores at admission; 2) to assess the concurrent validity of the CSI related to the PHQ-Somatization and other psychosocial measures; and 3) to confirm the predictive value of a pre-determined cut-off point of CSI 40 and the clinically-relevant CSI severity categories with regard to program non-completion, and poorer 1-year socioeconomic outcomes after FRP.

The CSI is a newly developed measure to alert clinicians to various multiple somatic and emotional symptoms associated with CSS (Mayer et al., 2012). However, none of the studies have examined its concurrent validity by comparing it to a measure of somatization and psychosocial measures that are widely used in CSS research. In addition, the present study is the first, to date, investigating the predictive value of the pre-determined single cut off point of CSI 40 and proposed CSI severity categories (cutoffs 30, 40, 50, and 60) in identifying a group of patients who are less likely to complete the rehabilitation program, and who have less successful one-year socioeconomic outcomes after interdisciplinary treatment. Any covariate potential predictors found in univariate analysis were controlled for in the regression analysis. The results of this study provide the comprehensive psychometric properties of the CSI for its clinical use in chronic pain research.

Evaluation of Hypotheses

The first hypothesis, the CSI scores would differ according to baseline predictors, was partially supported. The univariate analysis results supported the relationship of the CSI scores to gender (hypothesis 1-a), multiple injuries (hypothesis 1-c), spinal injury (hypothesis 1-d), longer length of disability (hypothesis 1-e), a diagnosis of depression

and/or anxiety (hypothesis 1-f), the presence of abuse experience (hypothesis 1-g), and the previous history of CSS (hypothesis 1-h). However, the association of the CSI scores and advanced age (hypothesis 1-b) was not supported. One study examining age-related differences in DNIC (a measure of CNS pain inhibition) over a range of age continuum found that DNIC begins declining at middle age (between 40 and 50 years old), and distinguishes at older age (between 60 and 75 years old), compared with younger age (between 20 and 35 years old), (Lariviere, Goffaux, Marchand, & Julien, 2007). A relatively narrow age range in the current study sample can be a possible explanation of insignificant results. For example, the number of patients in younger age (≤ age 30) and older age (> age 60) were 11% and 6%, respectively. Moreover, a different pattern of age effect can be found in healthy individuals and patients with chronic pain conditions. More studies are needed to further examine the association with CSS symptoms and advanced age. No hypothesis was built with regard to the occupational baseline variables and Axis II personality disorders. The univariate comparison results revealed that the CSI score was related to non-availability of a job, which was reported by the patient at program admission. An alternative explanation is that the sense of non-availability of the patient's original job might put him or her under stress, and in turn exacerbate his or her somatic and emotional symptoms. The CSI scores was also positively associated with all types of Axis II personality disorders, Cluster A (odd, eccentric, and suspicious individuals), Cluster B (dramatic, emotional, and erratic individuals), and Cluster C (anxious and fearful individuals). The high prevalence of Axis II personality disorders was found in patients with fibromyalgia (Ross et al., 2009; Uguz et al., 2010) and IBS (Blanchard et al., 2004). Of those with fibromyalgia, 31-47% of patients were diagnosed with any Axis II personality disorders, such as obsessive-compulsive (23% - 30%), borderline (16.7%), and avoidant (10.7%) personality disorders (Ross et al., 2009; Uguz et al., 2010). The

prevalence rates were much higher than in the control subjects (Uguz et al., 2010). Similarly, the most common personality disorder found in patients with IBS, was obsessive-compulsive personality disorder (12%), followed by avoidant personality disorder (5%) (Blanchard et al., 2004).

Multivariate analysis confirmed five significant baseline predictors of the high CSI scores that included: MDD, GAD, spine-related injury, a previous CSS diagnosis, and abuse history. The second hypothesis, that the concurrent validity of the CSI would reveal a moderate association with the PHQ-Somatization as well as other psychosocial measures, was supported. The CSI scores were positively related to scores of somatization-related symptoms, perceived disability, depressive symptoms, sleep disturbance, and pain-related anxiety. Partial correlation revealed that the pain intensity and pain-related anxiety had indirect relationships with the CSI. The third hypothesis stating the high CSI scores would be associated with the lower completion rates was supported. Furthermore, the CSI score at admission was found to be the most significant predictor of the program non-completion, while controlling for other significant baseline predictors such as non-working status at admission, non-availability of job, length of disability, and substance use disorder. The fourth hypothesis, that the CSI scores would be significantly reduced over FRP, was supported. The fifth hypothesis which included the association between the CSI scores at FRP discharge and 1-year socioeconomic outcomes was partially supported. The CSI score at discharge was found to be a significant indicator in predicting the lower work retention, while controlling for other significant factors such as non-Hispanic, number of compensable injuries, and sedentary- and light job demands. However, the scores were not associated with other 1 year socioeconomic outcomes. The sixth hypothesis, that a single cut-off point of 40 would have a predictive ability to identify the high risk of program non-completion and poorer

outcomes at 1 year post-FRP, was also partially supported. Findings using the single-cut off were comparable to those when the CSI was used as a continuous measure. However, the single cut-off point at FPR discharge did not predict the low work retention rates. The proposed CSI severity categories were more sensitive to detect the different treatment outcomes after FRP. It supported the final hypothesis.

Baseline Indicators

Multivariate linear regression models identified five baseline predictors (MDD, GAD, the previous history of CSS, spine-related injury, abuse history) that were associated with higher total CSI scores at admission. Another multivariate binary logistic regression using the CSI risk groups (classified by based on the predetermined single cut-off point of 40 on the CSI) confirmed that four factors, MDD, GAD, the previous history of CSS, spine-related injury, were still valid independent predictors of having high risk of CSS. Whereas abuse history was not a valid predictor for the high CSS risk group, the other predictor, a sense of job availability was additionally identified as a significant indicator for the CSS high risk group. Multivariate ordinal regression using the CSI severity groups (classified by based on the proposed four cut-offs of 30, 40, 50, and 60 on the CSI) showed the same results found in the continuous analysis. This provides evidence that the CSI severity categories successfully captured the characteristic related to the total CSI scores

Previous research has found a high comorbidity of depression and anxiety in patients with CSS, which was reviewed in Chapter 3. The findings that both a diagnosis of depression and anxiety were significant contributors of the CSI scores and the CSI classifications indicated that the CSI well measured the construct of CSS. Having a history of CSS was also a predictor of high CSI score and the CSI groups. This was similar to the previous finding that comorbid history of CSS (e.g., IBS, restless legs

syndrome, and/or migraines) was associated with the development of widespread pain from chronic back of neck pain (Kindler et al., 2010). It also indicates that self-reported CSS diagnosis history (listed in the CSI Part B) can be a reliable source to help identify patient who have a substantial degree of CSS related symptoms. In a previous study, self-reported CSS diagnosis history from the CSI part B, particularly with fibromyalgia, tension headache/migraines, and IBS, showed good agreement with the physician's diagnosis of CSSs (Neblett et al., 2013). Not surprisingly, a single or multiple spinal injuries significantly predicted the CSI scores and the CSI groups. There have not been many studies to investigate the relationship between injury areas and CSS, but neck injury was found to be associated with development of fibromyalgia. In a study comparing patients with neck injury and those with leg fractures, fibromyalgia occurred 13 times more frequently following neck injury than following lower-extremity injury (Buskila, Neumann, & Vaisberg, 1997). Furthermore, CDOMD patients with comorbid fibromyalgia were 4.5 times more likely to be diagnosed with a cervical injury compared with the no chronic widespread pain group (Howard et al., 2010).

Concurrent Validity

The analyses regarding the correlation of the CSI with the PHQ-Somatization and other psychosocial measures confirmed its concurrent validity. The CSI was highly correlated with the somatization measure (r = .63) and depression measure (r = .61), followed by the perceived disability measure (r = .43-.52), pain-related anxiety measure (r= .43), and sleep disturbance measure (r = .41). The correlation between the CSI and pain severity measure was positively significant, but the degree was relatively low (r = .33). Moreover, the CSI showed a better correlation with other psychosocial measures, compared to the somatization module of PHQ. It was interesting to note that the construct of pain intensity and pain-related anxiety, assessed by pain VAS and PASS, was

indirectly associated with the CSI through either pain disability or depression, respectively. This suggests that pain in the context of disability and anxiety associated with depression appear to be associated with CSS related symptoms. When the CSI groups were compared with other psychosocial measures, the CSS high-risk group also successfully contained patients with the moderate through severe levels of somatization-related and psychosocial scores. Again, the established CSS symptom severity levels were positively correlated with the scores and severity levels of the PHQ-Somatization, as well as other psychosocial measures.

Predictive Validity: Program Non-Completion

Multivariate binary logistic regression with the program completion rate revealed that the CSI scores at admission independently predicted the non-completion rate, after controlling for other significant indicators, such as working status at admission, the sense of job availability, length of disability, and substance use disorder. These factors were also proven to be associated with FRP non-completion rates in the previous study (Howard et al., 2009). Individuals in the CSS high risk-group were 2.2 times were less likely to complete the FRP as compared to those in the low-risk group. Again, individuals with the high level of CSS symptoms were less likely to complete the FRP compared to those with no CSS symptoms. For example, the moderate, severe, and extreme CSI severity groups were 2.3 times, 3.5 times, and 5.0 times were less likely to complete the FRP, compared to a group with the minimal level.

Response to Treatment

After FRP completion, the mean score of the CSI was significantly decreased, indicating that treatment components of the FRP relieved patient's somatic and emotional symptoms associated with CSS. Also, regardless of initial CSI score levels, patients showed improvement on psychosocial functioning, measured by other psychosocial

measures. After completing the FPR, almost half of individuals (51.8%) in the CSS high-risk group were re-classified into the low-risk group. A subsequent analysis revealed that patients with Cluster B personality disorder and Caucasian patients were 2.4 and 2.7 times more likely to remain as the high risk group after FRP. Unlike other psychosocial risk factors, personality disorders cannot be easily treated in a short period of time. Identification and recognition of patients with the CSS high-risk group and with comorbid Cluster B diagnosis may help clinicians provide better strategies to these individuals. In analysis with the CSI severity categories, Caucasian race was a sole independent predictor for treatment-resistance. The effect of Caucasian race on treatment resistance with regard to the CSS symptoms has not been studied well. Future studies will be needed to replicate these results, and address the relevance of race in treatment efficacy.

Predictive Validity: One-Year Socioeconomic Outcomes

Out of several one-year socioeconomic outcomes measured after 1 year post-FPR, only work retention rate was associated with the CSI scores at discharge. Work retention was defined as the ability to maintain employment throughout the post-FRP follow-up interval, and therefore has been considered an objective measure of regaining occupational function (Brede et al., 2012). The CSI score at discharge was one of independent predictors of work retention, after controlling for other significant factors affecting work-retention rates, including non-Hispanic, number of compensable injuries, and sedentary-light job demand. Because none of these variables were previously found to significantly impact work retention rate, more studies are needed to examine the potential link. The CSS high-risk group classified at FRP discharge failed to distinguish patients who did not retain work from those who did. In a subsequent study using the CSI severity categories, the CSI severity levels was negatively associated with the work retention rates, such as 85.8 % for minimal (CSI score 0-29), 77.3 % for mild (CSI score

30-39), 94.7 % for moderate (CSI score 40-49), 60.7 % for severe (CSI score 50-59), and 55.6 % for extreme (CSI score 60-100), respectively.

Conclusion

The goal of the present study was to examine the validity of a newly developed self-report measure, the CSI, by comparing it to other psychosocial measures, and by investigating its ability to predict program non-completion rate and unsuccessful 1-year socioeconomic outcomes among CDOMD patients. In spite of growing clinical attention to central sensitization and CSS, there has been no self-report instrument capable of assessing a full array of somatic and emotional symptoms associated with CSSs. As a consequence, the CSI was designed to help clinicians recognize multiple symptoms related to CSS. The current study represents a comprehensive psychometric examination of the CSI in order to make it more clinically useful across broader patient population.

First of all, the CSI successfully captured the characteristics and risk factors of CSSs. Individuals with high CSI scores were more likely to have comorbid psychiatric disorders (e.g., MDD and GAD), and the previous history of CSS diagnosis. The presence of spinal disorders (opposed to extremity disorders) and/or abuse experience also predicted a high score on the CSI. More importantly, the construct validity of the CSI was proven by the comparison with the measure of somatization-related symptoms, depression, and sleep disturbance. In addition to use as a screener, the newly proposed CSI severity levels classification (e.g., minimal, mild, moderate, severe, extreme) showed that the CSI can be a useful measure of treatment responsiveness, and can predict long-term outcomes. The well-known criticism for score categorization is loss of information. However, the findings from the CSI severity levels were almost identical to those from the total CSI scores without losing information of the measure.

Recognition of somatic and emotional symptoms associated with a CSS condition becomes tremendously important in various medical disciplines. The findings support the use of the CSI as a standard clinical treatment outcome measure in the area of chronic pain with structural cause. The proposed CSI severity levels provide a guideline for clinicians in interpreting CSI scores in clinical trials with regard to clinical decision-making. Multidisciplinary approaches have shown to be effective for treating patients with fibromyalgia and other central pain syndromes (Wallace & Clauw, 2005). A recent meta-analysis also revealed that a combination of pharmacological interventions and multimodal non-pharmacological interventions were most promising for managing central pain syndromes (Nüesch, Häuser, Bernardy, Barth, & Jüni, 2013). Therefore, cognitive behavioral treatment, physical therapies, and CSS-specific pharmacotherapy (e.g., anticonvulsants and antidepressants), which have all demonstrated clinical efficacy in treatment of CSSs, might be recommended for patients scoring in the higher CSI severity levels. Clinicians may also want to maintain a watchful attention to the mild severity level (CSI score 30-39), especially for patients with spinal injuries and/or abuse history) before central sensitization become an issue. Treatment efficacy studies of the FRP program revealed that the presence of comorbid CSS conditions (e.g. chronic widespread pain, fibromyalgia) among chronic pain patients did not interfere with effective pain management, as long as they were properly identified and appropriately managed during the treatment process (Hartzell et al., 2012; Mayer, Towns, Neblett, Theodore, & Gatchel, 2008). Viewed in this light, the CSI will provide useful clinical information for identifying patients who may be at risk for treatment failure and may require extra attention to maintain treatment gains and productivity. Certainly further examination will need to replicate and extend the findings of this study for the cut-off 40

of the CSI and the four severity cutoffs (CSI 30, 40, 50, and 60) to gain the clinical importance.

Possible limitation of the present study was that no actual diagnosis of CSS was assessed to distinguish patients with and without CSS. The pre-determined cut-off point of 40 of the CSI was used to determine the CSS high-risk group from the low-risk group. Although the previous study revealed that the cut-off 40 successfully distinguished patients with a diagnosis of CSS from non-patient samples with a sensitivity of 85% and a specificity of 75%, it has not been replicated by other researchers. Furthermore, the previous cut-off study of the CSI was conducted using the patients in one interdisciplinary pain clinic, so cut-off scores may differ depending on CSS patient samples. The same limitation can be applied to the CSI severity categories. Finally, the concept of CSI originally derived from the shared pathopsychological mechanism, called central sensitization. In addition to the overlapping nature of CSS, the presence of central sensitization (e.g., hyperalgesia, allodynia, and expanded receptive field) was one of important components of diagnosing CSS. Therefore, future comparison of the CSI to psychophysical tests of central sensitization will provide another valuable dimension of the CSI. Nevertheless, in conclusion, the current findings support that the CSI is a clinically valid and useful self-report measure for both identifying patients with a high risk of CSS and for assessing the severity their symptoms. Future studies may extend these results by evaluating its utility in other clinical populations.

Appendix A

Central Sensitization Inventory: Part A

Please circle the best response to the right of each statement.						
1	I feel unrefreshed when I wake up in the morning.	Never	Rarely	Sometimes	Often	Always
2	My muscles feel stiff and achy.	Never	Rarely	Sometimes	Often	Always
3	I have anxiety attacks.	Never	Rarely	Sometimes	Often	Always
4	I grind or clench my teeth.	Never	Rarely	Sometimes	Often	Always
5	I have problems with diarrhea and/or constipation.	Never	Rarely	Sometimes	Often	Always
6	I need help in performing my daily activities.	Never	Rarely	Sometimes	Often	Always
7	I am sensitive to bright lights.	Never	Rarely	Sometimes	Often	Always
8	I get tired very easily when I am physically active.	Never	Rarely	Sometimes	Often	Always
9	I feel pain all over my body.	Never	Rarely	Sometimes	Often	Always
10	I have headaches.	Never	Rarely	Sometimes	Often	Always
11	I feel discomfort in my bladder and/or burning when I urinate.	Never	Rarely	Sometimes	Often	Always
12	I do not sleep well.	Never	Rarely	Sometimes	Often	Always
13	I have difficulty concentrating.	Never	Rarely	Sometimes	Often	Always
14	I have skin problems such as dryness, itchiness or rashes.	Never	Rarely	Sometimes	Often	Always
15	Stress makes my physical symptoms get worse.	Never	Rarely	Sometimes	Often	Always
16	I feel sad or depressed.	Never	Rarely	Sometimes	Often	Always

17	I have low energy.	Never	Rarely	Sometimes	Often	Always
18	I have muscle tension in my neck and shoulders.	Never	Rarely	Sometimes	Often	Always
19	I have pain in my jaw.	Never	Rarely	Sometimes	Often	Always
20	Certain smells, such as perfumes, make me feel dizzy and nauseated.	Never	Rarely	Sometimes	Often	Always
21	I have to urinate frequently.	Never	Rarely	Sometimes	Often	Always
22	My legs feel uncomfortable and restless when I am trying to go to sleep at night.	Never	Rarely	Sometimes	Often	Always
23	I have difficulty remembering things.	Never	Rarely	Sometimes	Often	Always
24	I suffered trauma as a child.	Never	Rarely	Sometimes	Often	Always
25	I have pain in my pelvic area.	Never	Rarely	Sometimes	Often	Always
					Total=	

Appendix B

Central Sensitization Inventory: Part B

Have you been diagnosed by a doctor with any of the following disorders?

Please check the box to the right for each diagnosis and write the year of the diagnosis.

		NO	YES	Year Diagnosed
1	Restless Leg Syndrome			
2	Chronic Fatigue Syndrome			
3	Fibromyalgia			
4	Temporomandibular Joint Disorder (TMJ)			
5	Migraine or tension headaches			
6	Irritable Bowel Syndrome			
7	Multiple Chemical Sensitivities			
8	Neck Injury (including whiplash)			
9	Anxiety or Panic Attacks			
10	Depression			

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Biographical Information

YunHee Choi was born in Seoul, South Korea, and grew up in Gangneung until she left for college. She received a Bachelor of Arts degree in Psychology from Duksung Women's University in 2004, and received her Master of Arts degree in Experimental Psychology from Indiana State University in 2007. Ms. Choi's has been involved in numerous interdisciplinary chronic pain research projects using quantitative statistical techniques. A recent research focus is in the assessment of health-related patient reported outcomes, and evaluation of the risk factors for the progression to chronicity, in musculoskeletal pain, using a biopsychosocial approach. Her research expertise includes research design and quantitative research skills, such as questionnaire development, data management, and multivariate statistical analyses.