Spring April 28th, 2016

The Role of Emotional Distress in Predicting Opiate Analgesic Medication Use in Chronic Pain Patients

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Chronic Pain Patients

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A dissertation submitted in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

In

Clinical Psychology

Seattle Pacific University

School of Psychology, Family & Community

April 2016

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Table of Contents

List of Tables

List of Figures

Amy E. Kupper, 333 words

Abstract

Chronic pain is a common, costly, and debilitating problem. The biopsychosocial model purports that biological, psychological, and social factors are involved in the experience of chronic pain. Multidisciplinary pain management programs adhere to the biopsychosocial model and successfully treat and manage chronic pain. Depression, anxiety, and opiate analgesic medication misuse and abuse are significant problems faced by many individuals with chronic pain, however these relationships are not well understood. This study examined a sample of 248 chronic pain patients who completed a multidisciplinary pain management program. Two hypotheses were tested. First, it was hypothesized that the relationships amongst change in pain, pain-related anxiety, depression, and change in opiate analgesic medication use would be significantly correlated. Second, it was predicted that change in emotional distress would mediate the relationship between change in pain and change in opiate analgesic medication use. Structural equation modeling and residualized change scores were used to examine the hypothesized relationships. Participants ranged from 24 to 81-years-old ($M = 44.4$, $SD = 9.67$), 65% of the participants were male, and they were primarily Caucasian (86.0%). The first hypothesis was largely supported, as there were significant correlations among change in pain and change in anxiety ($r = .202$), change in pain and change in depression ($r = .310$), change in anxiety and change in depression ($r = .587$), change in opioid use and change in anxiety ($r = .188$), and change in opioid use and change in depression ($r = .178$) . The second hypothesis was also supported, as change in emotional distress indirectly affected the relationship between change in pain and change in opiate analgesic

medication use (β = .050; 95% CI = .017 to .099, p = .003). Our findings suggest that emotional distress is a critical variable to address not only when treating chronic pain but also when working with patients with problematic opioid use. These findings have important treatment implications, and suggest that interventions focusing on treating emotional distress may help decrease problems associated with opioid use.

A. CHAPTER I: Introduction and Literature Review

I. Introduction

Chronic pain (CP) is the most common, costly, and problematic medical disorder in the United States among both general and clinical populations (Katz, 2002; Turk & Burwinkle, 2005). Within a three-month period, over 200 million Americans experience some type of persistent pain problem (Lethbridge-Cejku, Schiller, & Bernadel, 2004), and over 17% of primary care doctor visits are due to chronic problems with pain (Gureje, 1998). The estimated prevalence of CP ranges from 7% to 30% in the U.S. population, and 60% to 80% of office visits to physicians involve some sort of pain complaint (Cosser, 2002; Frischenschlager & Pucher, 2002; Loeser, 2001). Most physical injuries and many medical illnesses are painful; however, this pain typically subsides once an injury heals or the illness resolves. However, in some cases, painful conditions may develop without any injury or they may persist even after injuries have completely healed. Further, for some individuals, their pain may persist due to physical damage or impairment. While medical treatments such as anesthetics, narcotics, anxiolytics, or other drugs may reduce the intensity of pain symptoms, many individuals still find that some pain remains. Thus, some people may be stuck with a degree of CP that persists or recurs indefinitely. Common examples range from persistent chronic low back pain to fibromyalgia pain to cancer-related pain. Not only does this pain create significant discomfort and distress for the individual, but because these individuals often continuously seek treatment for their painful condition and because they often become unemployed or disabled as a result of their pain, it creates a costly problem for the healthcare system and society. In order to better understand CP and improve treatments

for these individuals, it is important for clinicians to better comprehend factors that may be predictive of recovery.

Given the complex problems resulting from CP, patients may be referred to a multidisciplinary comprehensive pain rehabilitation program. Such pain management programs attempt to address the multiple difficulties that these patients face simultaneously. They combine intensive physical therapy, occupational rehabilitation, cognitive-behavioral therapy, and coordinated medical management. Comprehensive pain management centers have demonstrated promising results for reducing the negative effects that CP may have for CP patients (Cohen & Campbell, 1996; Turk & Gatchel, 2002), but there is a need to improve our understanding of the patients presenting to such treatment programs and to examine how change may occur over the course of treatment. Multidisciplinary rehabilitation programs for CP aim to address the emotional consequences of pain by challenging patients to make substantial changes in their beliefs about pain and their coping strategies toward pain (Van Tulder, Ostelo, Vlaeyen, Linton, Morley, & Assendelft, 2001). The psychological aspects of CP are very closely related to the physical experience of pain (Osborne, Jensen, Ehde, Hanley, & Kraft, 2007; Raichle, Hanley, Jensen, & Cardenas, 2007). Therefore, it is important to consider both physical and psychological aspects of pain to better understand and manage the CP experience.

Individuals with CP experience extremely high rates of emotional distress. For example, research has documented that depressive symptoms and pain related anxiety frequently co-occur with CP, which results in a difficult combination of symptoms to treat (Banks & Kerns, 1996; Fishbain, Goldberg, Meagher, Steele, & Rosomoff, 1986; Romano & Turner, 1985; Sullivan & Brennan Braden, 2011; Wilson, Mikail, D'Eon, &

Minns, 2001). Pain-related anxiety refers to the cognitions, behaviors, and emotional

responses that reflect specific anxieties and fears associated with pain (McCracken,

Zayfert, & Gross, 1993). Depression refers to combinations of affective distress,

withdrawal from pleasurable activities, problems with sleep and appetite, and cognitive

problems. Research has indicated that as perception of CP intensity increases, depressive

and anxiety symptoms increase as well (Von Korff, Deyo, Cherkin, & Barlow, 1993).

Opiate analgesic pain medications are frequently a component of treatment

approaches for CP. Although they can be effective in reducing pain, particularly acute

pain, prolonged use can become problematic (Sullivan & Brennan Braden, 2011). This is

primarily because research has shown that continued reliance upon analgesic medications

results in a loss of pain-relief efficacy over time, and can exacerbate or maintain pain

problems (Cicero, Lynskey, Todorov, Inciardi, & Surratt, 2008; Fishbain, Cole, Lewis,

Rosomoff, & Rosomoff, 2008; Novak, Herman-Stahl, Flannery, & Zimmerman, 2009).

Although estimates vary considerably, it has been estimated that 55% of CP sufferers use

opiate analgesic medications as a component of their pain treatment, which is

problematic for the several reasons mentioned previously (Cowan, Wilson-Barnett,

Griffiths, & Allan, 2003).

The aim of the present study is to examine how change in self-reported pain

relates to changes in depression and pain-related anxiety over the course of a

multidisciplinary pain management program, and whether or not depression and pain-

related anxiety mediate the relationship between change in self-reported pain and change

in opiate analgesic medication use. It is hypothesized that change in opiate analgesic

medication use will be predicted by pain intensity, but actually will be more strongly

predicted by emotional distress, a variable comprised of anxiety and depression, than by the pain itself.

The present study used data from a sample of CP patients who completed a comprehensive multidisciplinary pain treatment program to examine whether changes in self-reported pain from intake to discharge predicted changes in opiate medication use. Additionally, changes in depression and pain-related anxiety symptoms from intake to discharge will be examined to test for partially mediated relationships. As illustrated by Figure 1, several hypotheses will be evaluated. First, it is predicted that change in self-reported pain over the course of treatment would predict change in a) depressive symptoms, b) pain-related anxiety symptoms, and c) opiate analgesic medication use. Secondly, it is hypothesized that change in depression and pain-related anxiety symptoms partially mediate the relationships between self-reported pain and opiate analgesic medication use. The CP patients that provided the data used in the present study completed treatment between 2006 and 2010, and at intake and discharge they completed measures of pain-related anxiety, self-reported pain, depressive symptoms, and opiate analgesic medication use.

There has been a longstanding debate about the most appropriate statistical method for evaluating change over time. Rather than using simple difference scores, which are subject to a number of problems when used with inferential statistics (MacKinnon, 2008), residualized change score method was used, as described by MacKinnon (2008). This allows regression analyses to predict the discharge scores from the admission scores, and saving the residual values. The residual values represent the difference between the predicted discharge scores and the actual discharge scores, serving

as an index of change for each measure. Using these values, the hypothesized

relationships will be evaluated using structural equation modeling (SEM).

2. Literature Review

2.1. The problem of CP.

Pain has been described by the International Association for the Study of Pain

Subcommittee on Taxonomy as an unpleasant sensory or emotional experience associated

with actual or potential tissue damage, or described in terms of such damage (Mersky,

1979). CP persists for an extended period of time, generally more than six months, and is

usually associated with tissue damage. In some cases, CP can be traced to a specific

injury that has long since healed, such as a serious infection or even a surgical incision.

However, in other cases, there does not appear to be an apparent cause, with no prior

injury and an absence of underlying tissue damage. Often, CP is related to several

conditions, such as low back pain, osteoarthritis, headache, multiple sclerosis,

fibromyalgia, shingles, or nerve damage (neuropathy).

CP is the most common medical disorder in the United States among both general

and clinical populations (Katz, 2002; Turk & Burwinkle, 2005). Exact estimates of the

prevalence of CP ranges, though many researchers believe that CP affects 10%–20% of

adults in the general population (Blyth et al., 2001; Gureje, Von Korff, Simon, & Gater,

1998; Verhaak, Kerssens, Dekker, Sorbi, & Bensing, 1998). Furthermore, in a review of

the literature, Von Korff et al. (2005) estimated a 19% prevalence rate for chronic spinal

pain (neck and back) in the United States in the previous year and a 29% lifetime rate.

Other reports report that 57% of all adult Americans reported experiencing recurrent or

CP in the past year (American Academy of Pain Management, 2003), and of that

percentage, 62% of those individuals reported being in pain for more than 1 year, and 40% reported that they were constantly in pain. Furthermore, CP accounts for more than 80% of all physician visits (Gatchel, 2004a, 2004b).

Due to population increases and the longer lifespans of Americans, CP has inevitably become a larger problem. Individuals 50 years of age and older are twice as likely to have been diagnosed with CP (Gatchel, 2004, 2005). Currently, there are approximately 35 million Americans aged 65 years or older, accounting for 12.4% of the total population. The proportion of the population aged 65 and over is expected to increase by 57% by the year 2030, with Americans now having an average life expectancy of 77 years (Social Security Administration, n.d.). Due to these population trends, there is an increased concern about health care issues of older Americans, including CP problems. As such, the U.S. Congress designated 2001–2010 as the Decade of Pain Control and Research and the Joint Commission on Accreditation of Healthcare Organizations now requires physicians to consider pain as the fifth vital sign

In addition to being the most common medical condition, CP is associated with high financial costs to patients and their families, and society as a whole. In a recent review of the literature, researchers found that CP affects over 50 million Americans and costs more than $70 billion annually in health care costs and lost productivity. Researchers used data from the American Productivity Audit, from August 2001 to July 2002, and discovered that 13% of the work force lost productive work time due to a pain condition, and cost employers $61.2 billion a year (Stewart, Ricci, Chee, Morganstein, & Lipton, 2003). Another report estimated that absenteeism from work due to pain costs European economies €34 billion every year (Beubler et al., 2006). It is therefore clear

that CP represents a substantial burden on society.

CP is often associated with major comorbid psychiatric disorders and emotional suffering. Specifically, rates of depression, anxiety, and substance use are especially high in CP patients. Before the common psychological comorbidities are discussed, it is important to understand the biopsychosocial model of CP.

2.2. The biopsychosocial experience of CP.

The biopsychosocial model is the most widely accepted and heuristic perspective on CP. Specifically, proponents of the biopsychosocial model view physical illnesses, such as pain, as the result of the dynamic interaction among physiologic, psychological, and social factors, which perpetuates and may even worsen the clinical presentation of the illness (Gatchel et al., 2007). Proponents of biopsychosocial model acknowledge the biological bases that underlie most pain conditions, but also note that psychosocial factors may contribute to the experience and impact of pain. Models that only include one or two of these constructs are thought to be incomplete and inadequate (Gatchel et al., 2007). Biopsychosocial conceptualizations of CP have received increasing support in the broader pain literature. In support of these models in populations of individuals with disabilities, factors, such as pain-related cognitions or attributions, coping, and social support have been shown to be associated with pain and functioning in individuals with MS (Osborne, Jensen, Ehde, Hanley, & Kraft, 2007), spinal cord injury (Raichle, Hanley, Jensen, & Cardenas, 2007), acquired limb loss (Hanley et al., 2004), chronic low back pain (Koenig, Kupper, Skidmore, & Murphy, 2014; Skidmore et al., 2015), postpolio

syndrome (Hirsh, Kupper, Carter, Jensen, 2010), and muscular dystrophy (Miro et al., 2009).

Treatment programs, such as the multidisciplinary pain treatment in present study, typically utilize the biopsychosocial model of CP, and address the emotional disorders, such as anxiety, depression, maladaptive cognitions and poor coping skills, physical deconditioning, and other aspects of physical health. Multidisciplinary pain management embraces the fact that the comprehensive assessment-treatment of all these dimensions is needed in order to be effective (Gatchel et al., 2007).

2.3. Emotional Distress in CP.

2.3.1. Pain-related anxiety.

Pain-related anxiety has been described as a cognitive factor that promotes anxious and fearful responses to pain or pain-related events (McCracken, Zayfert, & Gross, 1992). Individuals with CP tend to have higher rates of pain-related anxiety than those who do not have CP (Ditre, Zale, Kosiba, & Zvolensky, 2013). Additionally, individuals with CP and pain- related anxiety have been found to over-estimate their pain intensity, use maladaptive pain-coping responses, and have higher rates of physiological reactivity in anticipation of pain-eliciting physical activity (McCracken, Gross, Sorg, & Edmands, 1993). High rates of pain-related anxiety also contributes to avoidance of activities that are perceived to promote pain, which in turn, often leads to physical deconditioning, secondary behavioral problems, like weight gain, and reduced social contact (Hadjistavropoulos & LaChapelle, 2000). As described in avoidance models of pain, CP patients often avoid activities that they anticipate may cause or increase their

pain. Underlying this avoidance is typically a component of fear or anxiety about experiencing a painful sensation. Kronshage, Kroener-Herwig, and Pfingsten (2001) described this problem as a fear of movement that they referred to as kinesiophobia, which develops as individuals begin to associate movement with acute pain, which they subsequently begin to fear. For CP patients, this pattern causes the individual to systematically avoid the feared stimuli (movement), which reduces fear. The end result is that the avoidance behavior is negatively reinforced (Kronshage, et al., 2001). McCracken and colleagues describe pain-related anxiety as a set of (a) cognitions and ruminations about the consequences of pain, (b) physiological symptoms of fear that are associated with pain, and (c) avoidance or escape behaviors that occur in attempt to evade or reduce pain (McCracken et al., 1993b). There is an element of fear and anxiety underlying avoidance behaviors in CP patients, and pain-related anxiety has been associated with other problematic behaviors, cognitions, and emotions in CP patients. Researchers have found that this pattern of responding is likely to become cyclical in nature, such that emotional responsivity and physical deconditioning lead to greater levels of severe pain, behavioral interference, perceived lack of control over life activities, and affective distress (Asmundson, 1999;; McCracken, 1997; Vowles, Zvolensky, Gross, & Sperry, 2004).

Additional research has demonstrated that pain-related anxiety is associated with a variety of other problems, such as nonspecific physical complaints (McCracken, Faber, & Janeck, 1998), cognitive problems (McCracken & Iverson, 2001), sleep disturbance (Ashworth, Davidson, & Espie, 2010), and reliance on medications (Keogh et al., 2006), all of which can be expected to make it more challenging for the individual to cope with

pain or make improvements in rehabilitation. Carleton et al., (2009) also found that pain-related anxiety and depressive symptoms are related both in CP samples and in other clinical samples, suggesting that these constructs are linked at a fundamental level.

Several studies have found that reductions in pain-related anxiety over the course of rehabilitation are predictive other positive outcomes for CP patients. For instance, McCracken and Gross (1998) found that reductions in pain-related anxiety over the course of a three-week comprehensive rehabilitation program predicted improvement in the areas of pain severity, pain-related interference with activity, and affective distress. Similarly, Burns, Glenn, Bruehl, Harden, and Lofland (2003) found that early reductions in pain-related anxiety predicted decreases in pain severity later in treatment. Further, McCracken, Evon, and Karapas (2002) found that patients who experienced a decrease in pain-related anxiety also reported significantly greater satisfaction with comprehensive rehabilitation programs overall. McCracken, Gross, and Eccleston (2002) found that over the course of a cognitive-behavioral CP treatment program, changes in pain-related anxiety predicted improvements in pain severity, affective distress, activity level, and depression.

2.3.2. Depression.

Depression frequently co-occurs with CP, and this combination of symptoms can be especially challenging to treat (Banks & Kerns, 1996; Fishbain, Goldberg, Meagher, Steele, & Rosomoff, 1986; Romano & Turner, 1985; Sullivan & Brennan Braden, 2011; Wilson, Mikail, D'Eon, & Minns, 2001). Research has indicated that as self-rated pain intensity increases, depressive symptoms increase as well (Von Korff, Deyo, Cherkin, & Barlow, 1993). Similarly, Von Korff et al. (1993) found that when pain intensity is

reduced, depressive symptoms improve.

In the Diagnostic and Statistical Manual of Mental Disorders, (4th ed., text rev.*)*, symptoms of a Major Depressive Episode include depressed mood, anhedonia (markedly diminished interest or pleasure in almost all activities), feelings of guilt or worthlessness, recurring thoughts of death or suicide, fatigue or low energy, impaired concentration or indecisiveness, insomnia or hypersomnia, significant weight loss, and psychomotor agitation or retardation (American Psychiatric Association, 2000). To meet criteria for a major depressive episode, one must have either depressed mood or anhedonia for most of the day nearly every day for a period of at least two weeks in addition to four other depressive symptoms. To qualify to a diagnosis of Major Depressive Disorder, one must have had at least one Major Depressive Episode. Dysthymic Disorder refers to depressed mood that occurs for a period of two years or more on more days than not, in addition to other depressive symptoms that do not meet criteria for a Major Depressive Episode.

Individuals suffering from mood disorders not only struggle with affective distress, withdrawal from pleasurable activities, problems with sleep and appetite, and cognitive problems, but they also often experience increased likelihood of somatic symptoms and pain (Kapfhammer, 2006; Lee, & Tso, 2006; Vaccarino, Sills, Evans, Kalali, & 2008). CP patients often suffer from Major Depressive Disorder and/or Dysthymia (Poole, White, Blake, Murphy, & Bramwell, 2009), and rates of subclinical depression are still problematic for these individuals. Additionally, sleep and fatigue, symptoms of depression but also common problems for individuals suffering from CP, may also contribute to the development and maintenance of both depressive symptoms (Ferentinos et al., 2009; Valentine et al., 2009; Wilson, Eriksson, D'Eon, Mikail, &

Emery, 2002) and CP (Heffner, France, Trost, Ng, & Pigeon, 2011; Kelly, Blake, Power, O'Keeffe, & Fullen, 2011; Zhao, Liu, Yang, Tan, & Yao, 2009).

Several studies have illustrated the relationship between depression and pain severity in individuals with CP. Turner and Jensen (1993) found that group cognitive therapy reduced both pain intensity and depressive symptoms in chronic low back pain patients, suggesting that maladaptive cognitive patterns may be a common maintaining mechanism for both depressive symptoms and pain. Glombiewski, Hartwich-Tersek, and Rief (2010) examined a cognitive-behavioral treatment for CLBP patients and found that it was effective not only in reducing depressive symptoms, but that this reduction in depression was predictive of decreased pain intensity and pain disability

Individuals who experience depressive symptoms are often isolated socially either because they no longer experience social interactions as pleasurable or worthwhile, or because they anticipate rejection or negative outcomes to such experiences (Isaac, Stewart, Artero, Ancelin, & Ritchie, 2009; Steger & Kashdan, 2009). CP patients often limit their social activity, which likely perpetuates depressive symptoms (Melzack, & Wall, 1995; Naliboff, 1985; Ong, Dunn, & Croft, 2006; Turk & Gatchel, 2002; Walker, Sofaer, & Holloway, 2006).

The relationship among depression and pain is complex. The majority of the empirical evidence supports the notion that pain precedes depression (Brown, 1990; Fishbain, Cutler, Rosomoff, & Rosomoff, 1997; Lerman, Rudich, Brill, Shalev, & Shahar, 2015) while few studies suggest that depression may precede pain (Atkinson, Slater, Patterson, Grant, & Garfin, 1991; Katon, Egan, & Miller, 1985; Magni Moreschi, Rigatti-Luchini, & Merskey, 1994). Nonetheless, it is clear that CP and depressive

symptoms are significantly related by nature, which complicates treatment by providing additional barriers to progress (Rudy, Kerns, & Turk, 1988; Von Korff & Simon, 1996).

2.3.3 Comorbid Anxiety and Depression in CP

As mentioned above, depression and anxiety are common disorders experienced by chronic pain patients. Depression and anxiety frequently co-occur and have been found to mutually reinforce each other, suggesting that these constructs are linked at a fundamental level (Carleton et al., 2009). CP patients with higher pain severity ratings usually experience clinically significant symptoms of both depression and anxiety (Brown, 1990; Fishbain, Cutler, Rosomoff, & Rosomoff, 1997; Lerman, Rudich, Brill, Shalev, & Shahar, 2015; McCracken, Gross, and Eccleston, 2002). Due to the comorbidity of anxiety and depression in CP patients, these variables were combined in this study to create a summative variable called emotional distress.

Existing literature supports the rationale that anxiety and depression make up the concept of emotional distress. For example, in a study by Kessler, Nelson, McGonagle, Liu, Swartz, and Blazer (1997), researchers administered the US National Comorbidity Survey, a large general population survey of persons aged 15-54 years in the non-institutionalized civilian population, and found that anxiety disorders and major depressive disorder were the most common comorbidity amongst all individuals. Furthermore, they discovered that the anxiety/depression comorbidity was even more prevalent in chronic pain patients, and that grouping these disorders together into the concept of emotional distress is warranted.

In a large study by Tsang et al., (2008), the authors recommended that emerging clinical reports and research focus on the comorbidity of depression and anxiety in CP

patients opposed to addressing each disorder individually, as the comorbidity between anxiety and depression is so high in this population. Additional researchers are similarly recommended that research studies consider depression and anxiety to be considered as a collective construct of emotional distress (Kathol & Clarke, 2005; Lepine & Briley, 2004; Ohayon, 2004). Researchers have found this to be across different chronic pain conditions. For example, in a study by Bernik, Sampaio, and Gandarela, (2013), researchers found that fibromyalgia, anxiety disorders, and depression tend to occur as comorbid conditions. These researchers elaborated that anxiety disorders and depression share some common neurochemical dysfunctions and central nervous system alterations such as hypo-functional serotonergic system and altered reactivity of the hypothalamic-pituitary-adrenal axis, and therefore should be considered collectively. In a separate study by Donavan, Thompson, and Jacobsen, researchers reported that chronic pain is associated with higher rates of depression and anxiety in cancer pain patients at all points along the cancer trajectory. The researchers further recommended that CP treatment focus on addressing depression and anxiety concurrently (Donavan, Thompson, & Jacobsen, 2012). It is clear that emotional distress is a serious problem in CP patients and should be addressed holistically, opposed to parsing out the individual symptoms of depression and anxiety (Kathol & Clarke, 2005; Lepine & Briley, 2004; Ohayon, 2004, Bernik, Sampai, & Ganarela, 2013; Donavan, Thompson, & Jacobsen, 2012).

2.4. Opiate analgesic medication use

Opioid therapy is the most common approach for the treatment of moderate to severe pain (Max, 1996; World Health Organization, 1996). While the use of opioid analgesics for the treatment of CP has been increasing in recent years (Joranson, et al.,

2002) and has been endorsed by numerous professional societies, the use of opioids remains controversial due to concerns about side effects, long-term efficacy, functional outcomes, and the potential for drug abuse and addiction. About 55% of CP patient use opiate analgesic medications as a component of their pain treatment, and this can be problematic for several reasons (Cowan, Wilson-Barnett, Griffiths, & Allan, 2003).

Surprisingly, there does not seem to be a consensus in the literature on the efficacy of opiate analgesic medications for long-term CP patients (Max, 1996). However, current research suggests that while opiate analgesics provide temporary pain relief so the individual can avoid dealing with pain, long-term use will not improve pain management over time unless it is combined with other pain rehabilitation approaches (Harden, 2002; Naliboff, Wu, & Pham, 2006). Furthermore, long-term reliance on opiate analgesic pain medications is part of the avoidance cycle that maintains and exacerbates CP problems (Lethem et al., 1983). This avoidance cycle is highly reinforcing due to the intrinsic nature of opiate analgesics (Cowan et al., 2003; Jonasson, Jonasson, Wickström, Andersson, & Saldeen, 1998), and CP patients often solely rely on this strategy of pain-relief, and may not engage in other empirically supported pain management treatments (Lethem et al., 1983; Sullivan & Ferrell, 2005). Specifically, CP patients likely will continue their opiate analgesic use and not utilize more active treatments like physical and occupational therapy, relaxation training, and cognitive-behavioral treatments because they require more effort. Furthermore, more active treatments require the individual to face their pain instead of avoiding it (Naliboff et al., 2006).

In addition to their passively reinforcing nature, long-term reliance on opiate analgesics has been found to lead to less pain-relief efficacy, and contributes to the

maintenance and possible exacerbation of pain (Cicero, Lynskey, Todorov, Inciardi, & Surratt, 2008; Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008; Novak, Herman-Stahl, Flannery, & Zimmerman, 2009). Specifically, CP patients who take opioids regularly may build a tolerance for the medication. Thus, CP patients ultimately need to increase the dosage and/or the frequency with which they take opiate analgesic medications to receive the same effect, leading to a problematic cycle of increased medication use and tolerance.

An additional concern about opiate analgesic medication use is the risk drug abuse and dependence, as research has shown that substance use disorders are common among CP patients and society as a whole. Nearly 5% of Americans aged 12 years or older used opioids non-medically in 2010, and the number of deaths from opioids tripled from 1999 to 2008 (Paulozzi et al., 2011) exceeding the number of deaths from heroin and cocaine combined (Substance Abuse and Mental Health Services Administration, 2010). Additionally, about 2.8% of CP patients experience opiate addiction during their pain treatment (Cowan et al., 2003), found that 18.5% of CP patients meet for an analgesic use disorder (Jonasson et al., 1998). CP patients are especially at risk for developing substance use disorders, as opiate analgesic medications are negatively reinforcing (Naliboff et al., 2006). Not only do opioids provide pain relief, but they also can have effects such as euphoria and sedation that often make taking the medication a pleasant experience (Preston, O'Neal, & Talaga, 2008), making them highly reinforcing.

Another reason long-term opiate analgesic medication use is problematic is that increased use is associated with greater prevalence of depressive symptoms and pain-related anxiety in CP patients (Keogh et al., 2006). Furthermore, Hooten et al. (2007)

found that for a reduction in analgesic medication use was associated with simultaneous improvements in pain, somatic symptoms, coping strategies, depressive symptoms, and cognitive patterns in fibromyalgia patients enrolled in a pain rehabilitation program. Interestingly, Sullivan et al., (2006) discovered that the CP patients who are most likely to receive opioid medications to treat their pain are also more likely to be suffering from other co-occurring problems, such as depression, anxiety, and substance use disorders. While the reason for this relationship remains unclear, it suggests that prescribers should be aware for the potential of co-occurring psychological issues that may complicate treatment.

Lastly, individuals who take opiate analgesic medication often suffer from a variety of side effects such as constipation, somnolence, and nausea (Cowan et al., 2003; Naliboff et al., 2006). Additionally, research has demonstrated that long-term, regular opiate analgesic medication use can cause psychomotor impairment and additional chronic health problems (Strumf, Dertwinkel, Wiebalck, Bading, & Zenz, 2000; Sullivan et al., 2006). And CP patients who take opioids regularly and subsequently cease to take this medication can also suffer from severe withdrawal symptoms, such as nausea, vomiting, abdominal pain, perspiration, cramps, insomnia, tremors, irritability, anxiety, insomnia, diarrhea, hot/cold flashes, and fever (APA, 2000; Cowan et al., 2003; Preston et al., 2008). Despite the wide use of opioids for treating CP, there remain a number of reasons (as described above) to suggest this may be problematic and dangerous.

2.5. Summary of literature review.

In summary, CP patients face a large set of challenges beyond pain, including depression, anxiety, and substance abuse. Because these patients experience pain when

engaging in physical, social, and daily productive activities, they tend to avoid participating in such activities and develop anxiety about their pain. This avoidance of activity is negatively reinforced by their evasion of pain, and this cycle continues. All the while, their physical condition deteriorates due to lack of activity, and they often suffer adverse psychosocial stressors such as relationship difficulties and occupational disability, and they begin to suffer from depressive symptoms. Many begin to find that opiate analgesic medications provide their only source of pain relief, and overreliance on such medications and taking opiates in high amounts may begin to have an additional set of adverse physical and psychosocial consequences. Patients are often left feeling as though there is no solution to their circumstance and they begin to feel defined by their pain.

Research has yet to clarify exactly how these various factors involved in the cycle of pain affect one another, but evidence suggests self-rated pain is predictive of emotional distress and opiate analgesic medication use in CP patients. Studies have also found that as pain severity increases, levels of emotional distress also increase. It may be that pain severity leads to emotional distress, and this is the primary reason why high rates of self-rated pain are related to higher and problematic opiate analgesic medication use in CP patients. The present study will to measure how change in pain severity relates to changes emotional distress over the course of a multidisciplinary pain rehabilitation program and whether or not this partially accounted for relationship between change in pain severity and change in opiate-analgesic medication use.

3. Hypotheses

The present study evaluated three hypotheses: 1) change in pain-related anxiety,

self-reported pain, depressive symptoms, and opiate analgesic medication use would each significantly be correlated with one another, 2) change in self-rated pain over the course of treatment would predict change in emotional distress (a variable composed of pain-related anxiety and depressive symptoms), and opiate analgesic medication use, and 3) change in emotional distress would partially mediate the relationships between change in self-rated pain and change in opiate analgesic medication use. The hypothesized model is shown in Figure 1. Data from CP patients who completed a comprehensive pain management program between 2006 and 2010 was used to examine these hypotheses. These patients completed measures of pain-related anxiety, physical activity, self-reported pain, depressive symptoms, and opiate analgesic medication use at intake and again at discharge.

Residualized change score method was used to evaluate these hypotheses, in which I regressed the admission variable scores onto the discharge for the same variable, saving the residual values as new variables (MacKinnon, 2008). These residual scores serve as indices of change over time in each variable, change in pain, pain-related anxiety, depression, and opioid use. The hypothesized relationships were evaluated using SEM, which allows for examination of direct and indirect relationships among variables.
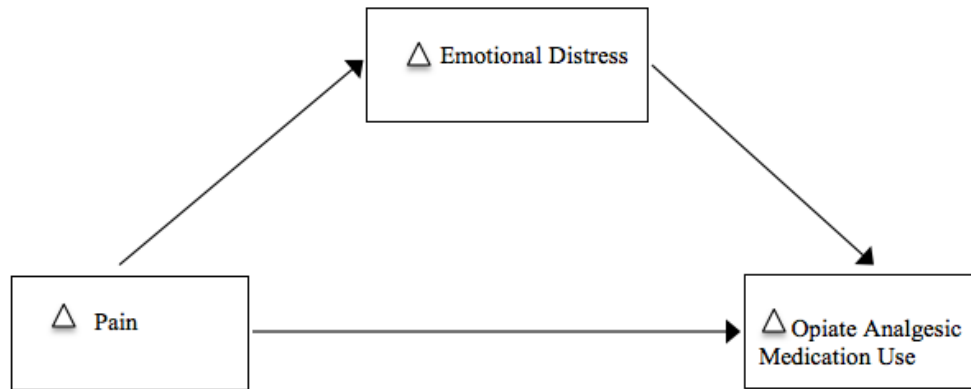
Figure 1. Hypothesized model of relationships between change in self-reported pain, change in emotional distress, and change in opiate analgesic medication use.

B. CHAPTER II: Method

1. Participants

Participants in this study were 276 CP patients who completed treatment at a multidisciplinary pain rehabilitation center in Portland, Oregon between January 2006 and December 2010. These CP patients included all those referred and eligible for rehabilitation. Primary care physicians referred patients to this multidisciplinary pain rehabilitation center once it was determined that these patients have exhausted all surgical CP treatments (i.e. laminectomy, spinal cord stimulator, intrathecal pump) and their pain symptoms required specialized and multidisciplinary treatment. The majority of patients in this sample suffered from chronic back pain (57.4%), with less patients suffering from chronic widespread/fibromyalgia pain (10%), chronic neck pain (9.2%), and chronic shoulder pain (8.2%). The remaining patients reported suffering from other pain locations, such as ankle, arm, hand/finger, foot, leg, head, groin, hip, knee, and chest

pain. All patients included in this study completed measures of each construct, as part of intake before treatment and when discharged from treatment. Specifically, research staff administered the intake interview (consisting of the VRS, BDI-II, and PASS) once when patients first arrived at the rehabilitation center. Once a patient had completed their individualized treatment plan, research staff again administered the same measures at discharge. At this rehabilitation center, these CP patients spent about three to four weeks at the center, with patients attending rehabilitation five days per week, at least six hours per day, and going home on the weekend. Variability in treatment time was determined for each patient individually by the clinical multidisciplinary team. In the present analysis, the average number of days patients received treatment (not including weekends) was 19.58 days (range = 10.5 - 28; SD=1.66). Patients who did not complete discharge evaluations were not included in the analysis, and of the 276 patients who completed treatment, 248 completed discharge measures. Therefore, 28 patients did not have sufficient data for analyses and were removed from the dataset. It is believed that these 28 patients were not explicitly told by the clinical staff to complete the discharge measures and left the rehabilitation center before these measured could be collected. The 28 patients who dropped out showed no significant differences on intake measures, and independent sample t-tests on intake measure were conducted comparing the 248 patients with complete discharge data, and suggested no significant differences (all p-values > .20).

The average age of the 248 study participants was 44.4 years (range = 24–81; SD = 9.67). Consistent with the demographic make-up of individuals attending multidisciplinary pain management programs, the majority (162; 65%) of participants

were men, and 86 (35%) were female. Most participants were Caucasian (214; 86%), 28

participants identified as Hispanic (11%), three were African American (1.2%), and two

were Asian (0.8%), and one participant chose to not disclose their race (0.4%). Almost

all (236; 95%) participants reported current use of opioid medication at intake.

2. Measures

2.1. Self-rated pain.

Patient's self-reported pain was measured using a rating scale, often referred to as a

Verbal Rating Scale (VRS; Jensen & Karoly, 2011) or Numeric Rating Scale (NRS;

Williams, 2010). In this scale, patients are asked to rate the average severity of their

pain, considering the last seven days, on a scale from 0 to 10. On this scale, 0 represents

no pain and 10 represents the highest level of pain. This simple rating scale is used

frequently in research and for clinical purposes and research suggests that this measure is

valid and reliable.

Researchers Jensen and McFarland (1993) examined pain ratings in a sample of

200 CP patients over a period of two weeks, and discovered that single assessments of

current pain tend to be unreliable since typical CP patients experience variability in the

severity of their pain. In contrast, they found that the average of multiple pain ratings

over a period of time demonstrate adequate reliability and validity in CP patients.

Furthermore, Jensen and McFarland (1993) asserted that a patient's average pain ratings

over a specified period of time are likely as reliable and valid as other measures that

compute the average pain rating after collecting multiple pain ratings at different times,

and that measures of average pain are superior to those which only ask about current

pain, worst pain, and least pain (Jensen, 1994). Research has confirmed this hypothesis

(e.g., VonKorff & Saunders, 1996). According to Jensen et al. (1996), the general consensus in the pain research community is that such average measures are more meaningful to the majority of research and clinical work than are snapshots of pain intensity levels (Bolton & Wilkinson, 1998; Bolton, 1999).

Further evidence of the validity of the VRS and NRS is that they are significantly and positively correlated to other measures of pain intensity (Jensen, Karoly, & Braver, 1986; Kremer, Atkinson, & Ignelzi, 1981; Ohnhaus, & Adler, 1975; Paice & Cohen, 1997). In addition to their validity and reliability, these scales are also beneficial and practical, as they are quick, simple to use, and typically well understood by patients (Jensen & Karoly; 2011). In the present study, patients were administered the VRS once at intake and once again at discharge.

2.2. Emotional distress.

2.2.1 Pain-related anxiety.

Pain-related anxiety refers to the cognitions, behaviors, and emotional responses that reflect specific anxieties and fears associated with pain (McCracken, Zayfert, & Gross, 1993).

The Pain Anxiety Symptoms Scale (PASS; McCracken et al., 1992) measures pain-related anxiety. Respondents are asked to read and respond to each question about the frequency of their different pain-related experiences across four domains: cognitive, emotional, physiological, and behavioral. Each item is rated on a 6-point Likert scale ranging from 0 (*never*) to 5 (*always*). The measure has four subscales: Cognitive, (e.g., "I can't think straight when I am in pain"); Escape and Avoidance, (e.g., "I go immediately to bed when I feel severe pain"); Physiological Anxiety, (e.g., "Pain seems

to cause my heart to pound or race"); and Fear, (e.g.," When I feel pain, I think that I may be seriously ill"). Each subscale includes 10 items, and the total measure includes 40 items. To score the measure, items are summed to obtain the total score, which ranges from 0 to 200. To score each subscale, all items on a given scale are summed to obtain a subscale score. Higher scores on the PASS indicate greater levels of pain-related anxiety. A number of studies have assessed the reliability, validity, and factor structure of the PASS and found it to be psychometrically sound (McCracken & Dhingra, 2002; McCracken et al., 1996; McCracken et al.,1993).

The PASS was originally developed using data from 104 CP patients who sought treatment at a multidisciplinary pain treatment center. The original version of the PASS contained 62 items derived using patient's descriptions of pain-related anxiety and fears related to their pain within physiological, motoric, emotional, and cognitive domains. These four domains became the subscales of the PASS.

In these initial validation studies, participants completed the original version of the PASS, the Beck Depression Inventory (BDI; Beck et al., 1961), and measures of pain, cognitive-somatic anxiety, cognitive and behavioral pain coping, pain disability, and trait anxiety. Due to cross-loadings of several items, seven items were removed. Two additional items were also deleted due to weak correlations and skewedness. Of the remaining 53 items, 14 items were in the Physiological Anxiety subscale, 10 items were in the Cognitive subscale, 14 were in the Fear subscale, and 15 were in the Escape and Avoidance subscale. Further analyses of these 53 items revealed Cronbach's alpha values ranging from .81 to .89 for the subscales. Cronbach's alpha for the total score was .94. Intercorrelations for the subscales were significant indicating that the scales are

related to one another; however, overlapping variance values ranged from .20 to .45 suggesting that each subscale also provides unique information about the underlying construct. Within this study, analyses also provided evidence of concurrent validity with the corresponding subscales of the Cognitive Somatic Anxiety Questionnaire (Schwartz, Davidson, & Goleman, 1978). Furthermore, PASS scores were correlated with measures of trait anxiety, pain severity, and catastophizing, which provide further evidence of construct validity. PASS scores were also found to be better predictors of disability and pain interference than the majority of other measures included in these analyses.

The PASS was later shortened so that each subscale contained 10 items, with a total of 40 items (McCracken, Zayfert, & Gross, 1993a). Several factor analysis studies have confirmed that their four-factor solution is a good fit to the data (McCracken, Gross, Hexum, & Semenchuk, 1993; McCracken, Zayfert, & Gross, 1993b), while Osman et al. (1994) found evidence of a five-factor structure, although items partially mapped onto the previously established four-factor solution. Despite the varying reports of the underlying factor structure of the PASS, researchers have consistently found that PASS scores were related to important pain-related outcomes, such as pain severity, opioid analgesic medication use, pain related distress, anxiety, and depression, further supporting the validity of the measure for this sample (McCracken & Dhingra, 2002; McCracken & Gross, 1996). In the present study, patients were administered the PASS once at intake and once again at discharge.

2.2.2 Depression.

Depression was measured by the Beck Depression Inventory (BDI), a self-report measure that was originally developed by Beck et al. (1961). The BDI was revised in

1996 by Beck et al. to the BDI-II in order to reflect the diagnostic criteria present in the

Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV;

American Psychiatric Association, 1994) and this version was used in the present study.

The BDI-II has 21 items, in which respondents are asked to rate each item on a scale

from 0 (*not present*) to 3 (*present*) according to how they have been feeling during the

past two weeks. The BDI-II yields a total score indicating depressive symptomatology,

with scores ranging from 0 to 63 wherein higher scores indicate greater depressive

symptoms.

The BDI-II has been found to have excellent internal reliability, as measured by

Cronbach's alpha, which has been reported at 0.90 to 0.92 in the general population as

well as in clinical populations (Beck et al., 1996; Carmody, 2005; Krefetz, Steer, Gulab,

& Beck, 2002; Storch, Roberti, & Roth, 2004). Additional research has measured the

internal reliability in other populations, including adolescents (Steer et al., 1998), medical

patients (Arnau et al., 2001), and substance users (Buckley, Parker, & Heggie, 2001), and

all studies have found consistent results regarding internal reliability values. Research

has also suggested that the BDI-II has adequate test-retest reliability in general

populations and clinical populations (Beck et al., 1996; Sprinkle et al., 2002).

The BDI-II is widely used in CP research and is generally regarded as a

psychometrically sound measure for this population (Harris & D'Eon, 2007). Poole et al.

(2006) and Harris and D'Eon (2007) found that Cronbach's alpha to be .92 in a CP

samples, suggesting that it a reliable measure of depressive symptoms with CP patients.

For the most part, studies examining the factors present for the BDI-II in CP

samples have suggested a two-factor structure is most appropriate. Specifically, Morely,

Williams, and Black (2002) named the two factors: negative view of the self and somatic and physical functioning. Poole et al. (2006) also found two factors, but the first factor was oriented toward mood and cognitive symptoms and the second was related to mood symptoms and changes in activity and behavior. However, in another study by Harris and D'Eon (2008), the researchers found support for a one latent second-order factor of depression, and three additional first order factors: Negative Attitude, Performance Difficulty, and Somatic Elements, which has been supported by other researchers (Novy, Nelson, Berry, & Averill, 1995). While the exact factor structure of the BDI-II in CP patients has been debated, it is commonly used in CP samples and is largely considered to be an appropriate measure of depressive symptoms within this population (Harris & D'Eon, 2008; Wilson et al., 2001). In addition, BDI-II scores have demonstrated concurrent validity through correlations with other measures of depression (Poole et al., 2009) and measures of pain (Harris & D'Eon, 2008), pain-related anxiety (Keogh et al., 2006), and disability (Poole et al., 2006) in CP patients. In the present study, patients were asked to complete the BDI-II once at intake, and once at discharge.

2.2.3 Emotional Distress

Emotional distress was measured by summing the total scores from an anxiety measure and a depression measure. Specifically, depression total scores from the BDI-II and anxiety total scores from the PASS were summed to create the new variable, emotional distress. Previous research supports the combination of depression and anxiety measures to create an emotional distress measure. Not only is there theoretical rationale for measuring emotional distress opposed to anxiety and depression individually, a number of studies have combined these measures in the existing literature.

For example, in a study of emotional distress, pain and disability in CP patients, researchers summed an anxiety measure (the State-Trait Anxiety Inventory) and a depression measure (the Center for Epidemiologic Studies Depression Scale) to create a combined measure to represent overall psychological distress (Lerman, Rudich, Brill, Shalev, & Shahar, 2015). In another study examining coping, emotional distress, and somatic symptoms in adolescents with CP, researchers created a latent variable composed of depression and anxiety subscales of the Child Behavior Checklist and the Youth Self Report measures (Compas, Boyer, Stanger, Colletti, Thomsen, Dufton, & Cole (2006). In both studies, researchers argued that it makes more sense to consider depression and anxiety together in CP patients as these disorders so frequently occur in this population. In the present study, intake total scores from the BDI-II and the PASS were summed to create the variable emotional distress at admission. Similarly, discharge total scores from the BDI-II and the PASS were summed to create the variable emotional distress at discharge.

2.4. Opioid analgesic medication

Opioid analgesic pain medication use was measured by computing patient's daily dose of morphine sulfate using morphine sulfate equivalencies. Daily value of morphine sulfate (in milligrams) was measured by asking patients to complete a form requiring them to list all of the medications they are currently taking, including any opiate analgesics. Patients were additionally asked to list the dose of each medication, and how often they take each medication. Next, to calculate the morphine sulfate equivalence for the given daily values, research staff multiplied the daily intake of all opiate medications by the ratio given in an equivalency table for the appropriate medication. Morphine

sulfate equivalency is useful for clinical purposes when evaluating opiate analgesic medication use (Vieweg, Lipps, & Fernandez; 2005), and it is the most common way that opiate medication use is measured in recent pain research (Kapural et al., 2010; Morrison, Flanagan, Fischberg, Cintron, & Siu, 2009; Morrison et al., 2003). To complete the morphine sulfate equivalence, research staff used an equivalency table that combined information from several drug manufacturers in addition to other published tables, such as the one included in Vieweg et al. (2005). Specifically, staff computed morphine sulfate equivalence at intake, and again upon discharge.

2.5. Demographic information

Participants were asked to answer several general demographic questions including age, ethnicity, gender, mechanism of injury, and date of injury as part of the intake interview.

3. Procedures

The present study used archived data, and the data used in this analysis was collected between January of 2006 and December of 2010. Patients were typically referred to this pain clinic by their primary care physicians for rehabilitation related to their pain condition. The data were collected with the understanding that de-identified data could be used for further research, and informed consent was obtained from all patients prior to admission. Patients were required to complete measures of all clinical research variables as a part of an intake evaluation prior to beginning treatment and again upon discharge from treatment. Once patients were discharged from this clinic, staff members at the research center entered their data into a database, including the data from

the intake and discharge evaluations that will be used in the present study. In the database, each patient's data was only connected to their identifying information by a subject identification number, which was assigned to them upon admission to the program. Thus, there was no identifying information in the database provided to the investigators of the present study, nor can any research investigators access identifying information. Measures of pain-related anxiety, self-rated pain severity, depression, opiate analgesic medication use, and demographic information were administered by a psychologist at the treatment center. Data from 2006, 2007, 2008, 2009, and 2010 were entered into separate databases by staff at the treatment center and sent from the database coordinator to the primary investigator of this study. The information needed for this study was combined from each year into a single database.

4. Data analysis

Missing data was managed using multiple imputation and cases missing more than 21% of data were removed. Preliminary analyses assessed the normality of the data, and included an examination of means and standard deviations for measures in the study. SEM was used to test the indirect effects of emotional distress, a variable composed of depressive symptoms and pain-related anxiety symptoms, on the relationship between pain severity and opiate analgesic medication use. In order to test the indirect effect of emotional distress in the hypothesized model (see Figure 1), bootstrap sampling procedure was used. Researchers (e.g., Mallinckrodt, Abraham, Wei, & Russell, 2006; Shrout & Bolger, 2002) have recommended using bootstrap resampling methods to test for the significance of indirect effects in mediated models. One strength of the

bootstrapping technique is that it maximizes the statistical power, reducing the chance of type II error (Mallinckrodt et al., 2006). AMOS 19.0 was used to evaluate the indirect effects of pain emotional distress in the relationship between pain severity and opiate analgesic medication use.

Power refers to the probability of accurately rejecting a false null hypothesis. Therefore, in order to increase confidence in findings, it is necessary to consider whether or not a study is adequately powered. Researchers experienced in SEM have offered suggestions regarding a priori power analysis. Klem (2000) suggested that researchers include 5-10 participants per estimated parameter. However many consider that too be too few, and Thompson (2000) suggested 10-20 participants per observed variable, or 100-200 participants for a full analysis. Kline (2005) also reported that 100-200 participants would be an adequate medium sample size for a full SEM analysis. Our model contained three observed variables. Therefore, following the guidelines above, there should be sufficient power to adequately complete analyses.

C: CHAPTER III: Results

1. Preliminary Analysis

All databases were combined into one, and were entered into the Statistical Package for the Social Sciences Version 22.0 (SPSS, 2014). Cases that did not meet the inclusion criteria described above were removed from the database. Specifically, 28 patients did not complete discharge evaluations after completing treatment, and therefore were not included in the final dataset. Preliminary analyses included assessment and imputation of missing data, normality, outlier analysis, and descriptive statistics, and

which are described in more detail below.

1.1. Normality and outlier analysis.

An ample amount of data for analysis was present, with a total of 248 participants. Any cases that did not meet inclusion criteria, or cases that were missing more than 21% of the data were eliminated. All 248 cases were found to meet inclusion criteria and no cases (0%) were found to be missing more than 21% of data. Due to the fact that the AMOS software does not allow for missing data, multiple imputation (MI; Enders, 2010) was used. Scale level imputation data was used as item-level scores were not available. All variables were constrained to their scale-appropriate minimum and maximum values, and all variables were included in the imputation model. Measures that did not have a scale-determined minimum and maximum were constrained by including the most extreme values in the sample. Five imputed datasets were computed, and the pooled values from the five datasets were used for preliminary data analysis. However, only the first imputed dataset was used for SEM analysis, as AMOS programming only allows for one imputed dataset.

According to Field (2009), as sample sizes approach and pass 200, it is unlikely that distributions will be normal. Therefore, normality was assessed in several ways. First, data was reviewed using frequency histograms, normal curves, P-P plots, Q-Q plots, and box plots. Second, z-scores were examined to test for the skewness and kurtosis of variables. Third, descriptive data (see below) was reviewed to verify that data points did not fall outside of expected parameters. Cases that were not normally distributed were closely inspected, and there was no sufficient evidence to support deleting any outliers.

1.2 Descriptive statistics.

Descriptive statistics including the ranges, means, standard deviations, and bivariate correlations for each of the measures used in this study are shown in Tables 1, 2, and 3. Rates of depression, pain-related anxiety, pain, and opioid use at admission and discharge are consistent with what would be expected from individuals before and after multidisciplinary treatment (Hooten, Townsend, Sletten, Bruce, & Rome, 2007; McCracken & Gross, 1998; Zheng, Tepper, Covington, Matthews, & Scheman, 2014). Furthermore, paired sample t-tests showed that all study constructs decreased significantly from intake to discharge. Specifically, pain significantly decreased from intake to discharge, $t(247) = 5.49$, $p < .001$, as did depression (BDI-II), $t(247) = 12.71$, $p < .001$, pain related anxiety (PASS), $t(247) = 9.69$, $p < .001$, and opioid use (MSEQ), $t(247) = 11.70$, $p < .001$. Tables 3 and 4 reflect correlations and regressions after controlling for the effects of age, gender, ethnicity, and days in treatment.

Table 1
Possible Range of Values Compared to Range of Values in the Present Sample (Admission)

	Possible Range		Sample Range	
	Minimum	Maximum	Minimum	Maximum
PASS	0	200	3	132
Pain	0	10	3	10
BDI-II	0	63	1	53
MSEQ	0	N/A	0	368

PASS = Pain Anxiety Symptom Scale
BDI-II = Beck Depression Inventory - II
MSEQ = Morphine Sulfate Equivalency score

Table 2

Possible Range of Values Compared to Range of Values in the Present Sample (Discharge)

| | Possible Range | | Sample Range | |
	Minimum	Maximum	Minimum	Maximum
PASS	0	200	0	129
Pain	0	10	1	10
BDI-II	0	63	0	48
MSEQ	0	N/A	0	354

Table 3

Means (Standard Deviations) and Pearson Correlation Values for the PASS, Pain, BDI-II, MSEQ, & Emotional Distress

Measure		1	2	3	4	5	6	7	8	9	10	11	12	13	M	SD
1.	Pass T1	-	.017	.547**	.044	.880**	.734**	.026	.371**	.069	.614**	.019	.057	.037	49.88	28.38
2.	Pain T1		-	.008	-.017	.015	-.047	.493**	.001	-.009	-.031	-.013	.021	-.059	6.49	1.40
3.	BDI-II T1			-	.036	.879**	.440**	.086	.595**	.067	.577**	.094	.065	.04	21.29	10.36
4.	MSEQ T1				-	.045	.086	-.037	.023	.827**	.06	-.033	-.039	.045	81.55	78.57
5.	Emotional Distress T1					-	.668**	.063	.549**	.078	.677**	.064	.069	.044	0	1.76
6.	Pass T2						-	.088	.611**	.155*	.896**	.129*	.146*	.628**	37.12	27.48
7.	Pain T2							-	.248**	-.004	.188**	.863**	.049	.197**	5.96	1.63
8.	BDI-II T2								-	.112	.899**	.290**	.163*	.740**	13.90	9.80
9.	MSEQ T2									-	.149*	-.003	.531**	.137*	48.77	59.97
10.	Emotional Distress T2										-	.234**	.173*	.763**	0	1.79
11.	Pain Change											-	.044	.261**	0	1.0
12.	MSEQ Change												-	.174*	0	1.0
13.	Emotional Change													-	0	1.78

*Note: PASS = Pain Anxiety Symptoms Scale, BDI-II = Beck Depression Inventory – II, MSEQ = Morphine Sulfate Equivalency score (opiate analgesic medication use), * p < .05, ** p < .01 (2-tailed)*

2. Primary Analysis

2.1 Calculation of residualized change scores.

Linear regression was used to create residualized change scores. Specifically, linear regression was used to predict discharge scores from the admission scores for the same variable, saving the standardized and unstandardized residual values as new variables. Residualized change scores represent an index of change for each variable, and are equivalent to the variability in the discharge scores after accounting for the portion of their variability that is predicted by the admission scores (MacKinnon, 2008). Descriptive data for the residualized change scores and correlations are shown in Table 3.

2.2 Tests of direct and indirect effects.

To test for mediation, bootstrap resampling procedures were used (Mallinckrodt et al., 2006), as the original methods put forth by Baron and Kenny (1986) tend to result in underpowered confidence intervals. Bootstrap resampling involves using the sample as a population reservoir from which a large number of random samples are drawn and continuously replaced so that they have an equal likelihood of being randomly selected on all subsequent drawings (Mallinckrodt et al., 2006). Bootstrap procedure increases power by providing non-symmetric confidence intervals, which reduce the chance of making a Type II error. In the present study, 2,000 bootstrap iterations were specified and used 95% bias-corrected confidence intervals and bootstrap estimates of indirect, direct, and total effects were used, as recommended by Mallinckrodt et al. (2006).

In the model (see Figure 2), standardized residualized change scores were used in

place of each variable to represent indices of change over treatment. The bivariate *a, b,* and *c'* paths of the mediated model were examined, as well as the *c* (total effect) paths and indirect effects. A relationship is considered to be mediated when the indirect effect is 1) statistically significant and 2) the direct effect decreases when the mediator is included in the model (i.e., when there is a decrease from the total effect, *c*, to *c'*, which includes the mediator). According to MacKinnon, an indirect effect can be found even if there is no significant direct effect (MacKinnon, 2008).

The main effect between pain severity and emotional distress was statistically significant, $(\beta = .257; 95\% \text{ CI} = .122 \text{ to } .377, p = .003)$. Similarly, the main effect between emotional distress and opiate analgesic medication use was also significant $(\beta = .199; 95\% \text{ CI} = .078 \text{ to } .316, p = .003)$. The total effect between pain severity and opiate analgesic medication use was not significant, $(\beta = .012; 95\% \text{ CI} = -.135 \text{ to } .126, p = .931)$. However, there was a significant indirect effect of emotional distress $(\beta = .050; 95\% \text{ CI} = .017 \text{ to } .099, p = .003)$. These results suggest that pain predicts emotional distress, emotional distress predicts opiate analgesic use, and emotional distress indirectly affects the relationship between pain severity and opiate analgesic medication use.
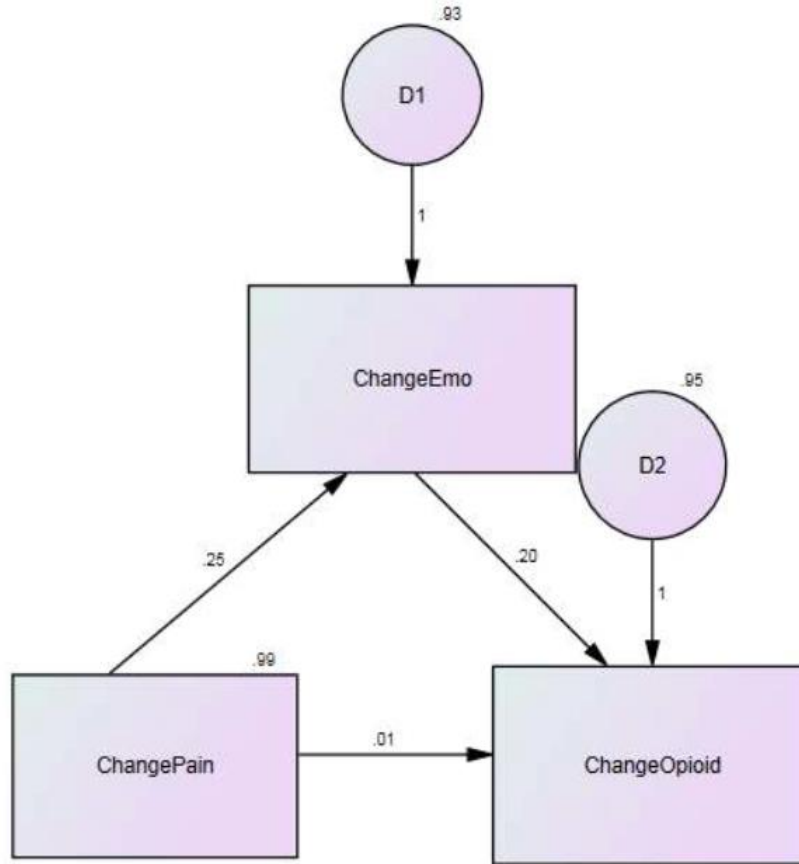
Figure 2. Structural equation modeling strategy used in the present analysis.

Table 4
Bootstrap Results to Test Significance of Mediation Effects

Path/effect	Unstandardized				Standardized				p
	B	*SE*	95% CI		β	SE	95% CI		
			Lower	Upper			Lower	Upper	
c	.060	.060	-.059	.171	.060	.059	-.068	.168	.389
a CP→CE	.258	.065	.120	.378	.257	.064	.122	.377	.003
b CE→CO	.199	.064	.074	.324	.199	.063	.078	.316	.003
c' CP→CO	.012	.063	-.130	.125	.012	.063	-.135	.126	.931
a x b (indirect effect)	.050	.021	.020	.104	.050	.020	.017	.099	.003

Note. The 95% confidence intervals for both the unstandardized and standardized results were produced with the bias-corrected option in the bootstrap dialogue box.

D: CHAPTER IV: Discussion

1. Chronic Pain

CP conditions are major physical and mental health care problems (Melzack, 2005; Turk & Gatchel, 2002; Turk, Meichenbaum, & Genest, 1983). The number of CP patients is continuing to rise, and therefore, a more thorough understanding of these patients and their symptoms is crucial. The biopsychosocial perspective of chronic pain is the most widely accepted approach to treating CP, and the myriad of symptoms that make up the experience of CP is complex. Emotional distress and use of opioid medications are key elements of the biopsychosocial model, and understanding the relationships between these variables will help to best address the needs of the CP patient.

Using a sample of CP patients who completed a four week multidisciplinary pain management program, three hypotheses were evaluated: 1) the variables that represent change in pain-related anxiety, self-reported pain, depressive symptoms, and opiate analgesic medication use will each be significantly correlated with one another, 2) change in self-rated pain over the course of treatment will predict change in emotional distress (a variable composed of pain-related anxiety and depressive symptoms), and opiate analgesic medication use, and 3) change in emotional distress will partially mediate the relationships between self-rated pain and opiate analgesic medication use.

2. Pain is Significantly Correlated with Pain-Related Anxiety and Depression

The first hypothesis that all variables would be significantly correlated, was largely supported. All relationships were significantly correlated with the exception of the relationship between change in opiate analgesic medication use and change in pain.

The finding that change in depression and change in pain-related anxiety would be related has been established previously (Burns et al., 2003; McCracken et al., 2002; McCracken and Gross, 1998), as well as the relationship between change in pain and change in depression (McCracken et al., 2002; McCracken and Gross, 1998). Additionally, the finding that change in pain would be correlated with change in pain-related anxiety is well documented in the literature (Burns et al., 2003; McCracken & Dhingra, 2002; McCracken & Gross, 1998).

However, the finding that both change in depression and change in pain-related anxiety would be significantly correlated with change in opiate analgesic medication use is an important contribution to the literature. Some research has begun to study the relationships between depression and opiate analgesic medication use in CP patients (Merrill, et al., 2012; Grattan, et al., 2012), however, there is a shortage of research that examines this relationship. Furthermore, the finding that pain-related anxiety would be significantly correlated with opiate analgesic medication use, to our knowledge, has not been reported in previous literature. The relationships between pain-related anxiety and opiate analgesic medication use, and depression and opiate analgesic medication use should be closely explored in future research to better understand these relationships.

The finding that change in pain is not significantly related to change in opiate use is surprising. This finding is counter-intuitive, as one would assume that the amount of pain an individual experiences should be related to the amount of pain medications they are taking. A recent study (Goesling et al., 2015) found that pain severity did not significantly predict opiate analgesic medication use, and that depression instead was a better predictor. However, there is a scarcity of research examining this question, and

further research is necessary to disentangle these relationships.

While the exact reason change in pain did not significantly correlate with change in opioid use is unknown, several possible explanations can be generated. First, this study followed patients for three to four weeks. While pain scores from intake to discharge did significantly decrease, this change was smaller in comparison to changes in opioid use and emotional distress throughout treatment, as can be seen by repeated measures *t*-scores. It is possible that within this time period, patients noticed greater changes in pain interference or pain bothersomeness rather than pain severity. Future research should exam whether these unmeasured variables, pain interference and pain bothersomeness, are significantly related to both pain severity and opioid use. Second, it may be that opioid use was decreased over the course of the study, but due to issues of dependence and tolerance, patients did not notice a large decrease in their pain (Cicero, Lynskey, Todorov, Inciardi, & Surratt, 2008; Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008; Novak, Herman-Stahl, Flannery, & Zimmerman, 2009). Instead, these patients may have noticed increased pain or that their pain level did not changes. Third, due to the passive nature of opioid use, it is possible that engaging in comparatively more strenuous activities, such as physical and occupational therapy, initially caused an increase in pain, even though long-term physical and occupational therapy are related to better outcomes (Cicero, Lynskey, Todorov, Inciardi, & Surratt, 2008; Harden, 2002; Naliboff, Wu, & Pham, 2006). Thus, patients may have noticed an increase in their pain, or may not have noticed a difference in pain severity, regardless of change in opioid use (Lethem et al., 1983; Sullivan & Ferrell, 2005). Fourth, patients who did decrease their opioid use over the course of the study may have anticipated that their lower dose would lead to more

pain. Due to their anticipation of continued or increased pain, those who reduced their opioid use would have more difficulty noticing subtle differences in their pain level. While conclusions cannot be draw about these speculations using the present study, future research should seek to evaluate these ideas.

3. Emotional Distress Indirectly Affects the Relationship between Pain and Opiate Analgesic Medication Use

Change in emotional distress was found to indirectly affect the predictive relationship between change in pain severity and change in opiate analgesic medication use. No total effect was detected between change in pain and change in opioid use, but when emotional distress was added to the model, a significant indirect effect was observed. This finding is novel and adds to the understanding of the relationships amongst these variables. Finding a significant main effect between pain severity and emotional distress is consistent with the literature (Goesling et al., 2015). Similarly, finding a significant main effect between emotional distress and opioid use has been found in recent studies (Merrill, et al., 2012; Grattan, et al., 2012). It is surprising that no significant total effect was found between pain severity and opioid use, and while this finding is contrary to what one would expect, it has also been found in other emerging research (Keogh et al., 2006; Grattan, et al., 2012).

As mentioned above, once emotional distress was added toThese findings help to explain the underlying mechanism that may exist in the relationship between pain severity and opioid use. It may be that change in pain alone does not significantly predict opioid use, and only once a patient's level of emotional distress is taken into the equation, will a change in opioid use be detected. Thus, targeting pain alone without considering

emotional distress will likely not address the quantity of opioids an individual is using each day. It is clear that treating emotional distress is essential in order to address pain severity and opiate analgesic medication use. These findings also have a number of important treatment implications. For example, in the context of multidisciplinary pain management programs, when treating CP patients who have higher rates of pain, emotional distress, and opioid use, it is crucial to address the patient holistically and ensure that symptoms of depression and anxiety are being treated.

It may be possible that opiate analgesic medication use at one time can predict future emotional distress and vice versa. However, due to a limited amount of time points (admission and discharge), longitudinal relationships could not be assessed. Future research should further examine the relationships amongst pain severity, emotional distress, and opiate analgesic medication use.

4. Study Limitations

There are several limitations of the current study that are important to consider. First, our study did not include a control group. Second, while using residualized change scores allowed us to study index of change, additional data points would enable us to perform more statistically sensitive analyses and examine our data more longitudinally. Third, the study only looked at total scores of the study measures and did not examine item-level differences. Examining item-level scores could provide additional information including internal consistency. Fourth, the majority of our measures were self-report, and as such, there may be threats to reliability. Fifth, we can only generalize our results to adults with chronic pain who complete multidisciplinary pain management programs.

5. Conclusions

In a sample of 248 individuals with chronic pain who were enrolled in a multidisciplinary pain management program, significant relationships amongst all study variables were found, with the exception of change in pain severity and change in opiate analgesic medication use. The finding that change in depression is significantly related to opiate analgesic use is consistent with emerging literature. Furthermore, the finding that change in pain-related anxiety is significantly related to opiate analgesic use is a novel one and serves as an important addition to the literature. The most important finding was that the change in emotional distress significantly mediated the relationship between change in pain and change in opiate analgesic medication use. This finding is the first of it's kind, and has important treatment implications. This suggests that emotional distress plays an integral role in chronic pain patients who use opioids, and emotional distress could be targeted as a way to decrease the amount of opioids an individual is taking. Due to the increased effort to regulate opiate analgesic medication use and decrease overall prescribing rates, this finding provides a critically important additional to the literature. Future research should continue to examine the relationship between emotional distress and opiate analgesic medication use.

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