

Psychological Flexibility, Pain Characteristics and Risk of Opioid Misuse in Noncancerous Chronic Pain Patients

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Abstract

Chronic pain has an estimated annual prevalence rate between 10 and 35%. In the US, first-line treatment for chronic pain is often opioids. Objective: To our knowledge, this is the first study exploring psychological flexibility and its association with pain severity, pain interference and risk of opioid misuse in chronic pain patients. Methods: Data were collected at two outpatient pain clinics in the northeastern United States. Adults (N=99) completed a cross-sectional survey with validated measures. Pain severity and pain interference were hypothesized to uniquely predict the risk of opioid misuse. Pain severity was hypothesized to predict pain interference. Finally, psychological flexibility was hypothesized as an indirect effect in these relationships. Results: Main findings suggest that pain severity predicts risk of opioid misuse, mediated by psychological flexibility. Finally, results suggest pain severity predicts pain interference, mediated by psychological flexibility. Discussion: Implications of findings are discussed in terms of future psychological and medical assessments and interventions for chronic pain patients seeking prescription opioids.

Keywords Chronic pain · Opioids · Pain interference · Pain severity · Psychological flexibility

In the United States, chronic pain has estimated annual prevalence rates from 10 to 35% in adults, plaguing over 100 million Americans (Bonica & Loeser, 2000; Harstall, 2003; Reid et al., 2011). Treatment is costly for chronic pain, averaging \$35,651 per person (Simmons, Avant, Demski, & Parisher, 1988; Turk & Burwinkle, 2005). Aside from the monetary expense of treatment, other costs (e.g., disability compensation, lost productivity, legal fees, lost tax revenue, absenteeism, sleep issues, and increased health care utilization) are common (Mounce, 2002; Peles et al., 2006; Trafton et al., 2004; Turk & Burwinkle, 2005). Furthermore, chronic pain has shown a high comorbidity with a variety of psychological difficulties, especially depression (Barry et al., 2009; Miller & Cano, 2009).

Treatments for chronic pain are many and varied. Medical treatments include analgesics (e.g., opioids, tricyclic antidepressants, anticonvulsants), surgical interventions, spinal cord stimulators (SCS) and implantable drug delivery systems (IDDS). However, medical treatments, as well as other previously conventional treatments (e.g., bed rest, acupuncture, and massage) have costly tradeoffs and questionable efficacy for treating persistent pain (Nachemson, 1998; Turk & Burwinkle, 2005; Vingard & Nachemson, 2000). Conversely, psychological interventions have shown modest benefits for individuals with chronic pain, specifically in regard to daily functioning and health-related quality of life (Hoffman, Papas, Chatkoff, & Kerns, 2007).

Opioid Use

Treatment for chronic pain is often pharmacological (Hylands-White, Duarte, & Raphael, 2017). In the late 1990s, pain medications were the second most prescribed drugs in physicians' offices and emergency rooms, after cardiac-renal drugs (Schappert, 1998). Furthermore, pain medications accounted for 12% of all medications prescribed during ambulatory office visits (National Center for Health Statistics, 1998). Since the 1990s, opioid prescriptions have

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boomed in the United States (Caudill-Slosberg, Schwartz, & Woloshin, 2004; Olsen, Daumit, & Ford, 2006). Opioids, a potent analgesic, are a widely used prescription medication for persistent and recurrent pain that have been used in medical settings for centuries (Yim & Parsa, 2018). According to Substance Abuse and Mental Health Services Administration (2013), there was a dramatic increase in the number of individuals seeking prescription opioids between 2000 and 2011. At the same time, there was a 500% increase in admission for treatment of opioid-related dependency issues. Thus far, however, research on strong opioids (e.g., morphine, hydromorphone, oxycodone, oxymorphone, tapentadol) reveals only modest effectiveness, SMD = -0.43, 95% CI [-0.52, -0.33], with chronic pain (Chaparro et al., 2013). Randomized controlled trials for opioids as treatment for chronic pain have yielded pain reductions from 18 to 66% (Caldwell et al., 2002; Wilder-Smith, Hill, Spargo, & Kalla, 2001). Turk (2002) found that the overall weighted mean for pain reduction across all RCTs for opioid treatment of chronic pain cases was 33%. However, Clark, Young, and Cole (2002) found pain reduction also occurred with inactive (10%) and active (20%) placebos, thereby questioning the relative overall efficacy of opioids as independent from placebo effects.

Opioids have been a controversial topic in medical practice due to adverse side effects, mortality outcome data, and abuse potential. Common opioid-related adverse side effects include constipation, nausea, vomiting, sedation and clouded mentation, hypogonadism and decreased levels of dehydroepiandrosterone sulfate (a hormone related to fatigue and/ or concentration), pruritus (i.e., itchy skin), and myoclonus (i.e., twitching; Chou et al., 2009). Regarding mortality, legally prescribed opioids have directly or indirectly caused more than 100,000 deaths in the United States since regulations were lifted in the 1990s to allow prescription opioid use for noncancerous chronic pain (Johns Hopkins Bloomberg School of Public Health, 2015). For example, in 2010, about half (16,651) of the ~ 38,000 pharmaceutical-related deaths were related to opioids (Jones, Mack, & Paulozzi, 2013).

Furthermore, individuals with chronic noncancerous pain can be prone to opioid misuse and abuse. Varying estimates for opioid misuse and abuse within this population range from 1 to 40% (Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008; Ives et al., 2006; Martell et al., 2007). And, several studies have found a common co-occurrence of prescription opioid use disorder and chronic pain (Cicero et al., 2008; Green et al., 2009). A study by Boscarino, Hoffman, and Han (2015) evaluating diagnostic criteria of the *Diagnostic and Statistical Manual-5* relating to opioid abuse found that 41.3% of 705 patients being treated with chronic opioid therapy (COT) met criteria for opioid use disorder (OUD). Of these individuals, 28.1% met criteria for mild OUD, 9.7% met criteria for moderate OUD and 3.5% met criteria for severe OUD. Vowles and colleagues (2015) conducted a systematic meta-analysis of opioid misuse, abuse, and addiction in chronic pain patients. They used definitions taken from The Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMMPACT) and Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION) in conjunction with weighted means for high and low-quality studies to account for the wide range of methodologies in the 38 included studies. Overall, statistical analyses revealed rates of opioid misuse between 21 and 29%. They found rates of abuse were not reported in the studies, and rates of addiction were between 8 and 12%. At the same time, 42 to 61% patients entering treatment for prescription opioid use disorder reported chronic pain (Cicero et al., 2008; Green et al., 2009, Weiss et al., 2011). Alongside the increasing incidences of opioid misuse and abuse, opioid-related overdoses have also been on the rise in the last several years (Chen, Hedegaard, & Warner, 2014; Jones et al., 2013).

Pain-Related Distress

Pain Severity

Traditionally, pain severity has been the primary target for pain measurement. Pain is often examined through dichotomous variables (i.e., pain or no pain; Chakrabarti et al., 2010; Dhingra et al., 2015; Fox et al., 2012; Ilgen, et al., 2006; Peles et al., 2006; Weiss et al., 2011). However, pain rating scales (e.g., visual-analogue scale, numerical rating scale, verbal rating scale) offer a more extensive assessment of pain with better validity and reliability (Williamson & Hoggart, 2005). Pain rating scales offer unique challenges to the accurate assessment of pain. The visual-analogue scale is statistically the most robust; however, is the most likely to be misunderstood by patients (Williamson & Hoggart, 2005). The verbal rating scale is the easiest to use but is the least sensitive of the three scales and interpretation is often misunderstood by clinicians (Williamson & Hoggart, 2005). Finally, the numeric rating scale overall provides acceptable sensitivity, is easy to administer, and provides interval level data for statistical analyses (Williamson & Hoggart, 2005). Past studies have found no relationship between pain and opioid misuse and abuse during COT (Chakrabarti et al., 2010; Fox et al, 2012) or between pain severity and interference with dichotomously assessed opioid use (i.e., "is currently using" and "is not currently using") in pain rehabilitation contexts cross-sectionally (Rome, Townsend, Bruce, Sletton, Luedtke, & Hodgson, 2004). However, assessment of subjective pain severity has been linked to opioid use in longitudinal studies. Griffin and colleagues

(2016) longitudinally examined the effects of patient-rated pain severity on later prescribed opioid use in chronic pain patients who were in buprenorphine-naloxone treatment for prescription opioid use disorder. The investigators found that greater pain severity reported in one week was significantly associated with increased opioid use in the following week. Further studies have also found associations between singleitem pain severity and risk factors of opioid relapse in SUD (Potter, Shiffman, & Weiss, 2008). However, understanding how pain severity relates to risk factors associated with opioid misuse in patients not yet being treated for SUD is a critical and proactive strategy to combat the opioid epidemic.

Pain Interference

Assessing life functioning is crucial for patients with pain. Although life functioning is considered to be a reactive dimension of pain experience, pain interference is the degree to which subjective levels of pain limits functioning in daily life domains (e.g., mood, walking and other physical activity, work, social activity, relations with others and sleep; Cleeland & Ryan, 1994). Higher levels of pain interference have been associated with intermittent/lower-dose and regular/higher-dose opioid use compared to minimal use or nonuse (Turner, Shortreed, Saunders, LeResche, & Von Korff, 2016).

Psychological Flexibility

Psychological flexibility is a dimensional construct, featuring several interconnected human processes that contribute to health and well-being (Hayes, Strosahl, & Wilson, 2012). It reflects one's willingness to be open, centered, and engaged with the external and internal world. Working together, the open and centered processes of mindfulness and acceptance (i.e., acceptance, defusion, present moment, and self-as-context) interplay with commitment and behavioral engagement (values, committed action) to create psychological flexibility. Psychological flexibility, as a model for psychological health and well-being, captures "the dynamic, fluctuating, and contextually-specific behaviors that people deploy when navigating the challenges of daily life" (Kashdan & Rottenberg, 2010, p. 866). Psychological flexibility has been empirically linked with a growing number of health-related outcomes, including mental and behavioral response shifts in self-regulation and balance among important life domains (Kashdan & Rottenberg, 2010). The psychological flexibility model proposes that pain and suffering is an inherent aspect of human life. With flexibility, humans are more able to adapt to ever-changing internal and external environments. It is with inflexibility and rigidity where behavioral restriction manifests.

A growing interest and research focus within clinical psychology and behavioral medicine is the acceptance of pain, in acceptance-based therapies including mindfulness-based stress reduction (MBSR; Kabat-Zinn, 2003), mindfulnessbased cognitive therapy (MBCT; Day, 2017), and acceptance and commitment therapy (ACT; Dahl, Wilson, Luciano, & Hayes, 2005; McCracken & Vowles, 2014), rather than controlling or fighting the pain, previously explored in traditional cognitive behavioral approaches (Veehof, Oskam, Schreurs, & Bohlmeijer, 2010). Exposure, within an acceptance-based framework, works to increase the willingness of patients to come in direct contact with unpleasant experiences associated with pain. Through exposure to pain sensations, pain thoughts, or memories linked to the pain, the patient is able to alter the relationship he or she has with these experiences and take steps to improving life behaviors. Acceptance-based therapies suggest that neither pain nor the content of pain-related thoughts causes problematic behaviors; instead, it is the patient's relationship to these experiences and thoughts that are problematic. Cognitive defusion is often utilized to deliteralize and provide distance from pain-related language. Finally, values work is emphasized through the process of clarification of and commitment towards values-based behaviors. With pain, acceptancebased psychotherapies help patients understand the ways in which they have moved away from their values as a function of attempts at pain alleviation. Although previous research has examined the contribution of psychological flexibility to both pain severity (e.g., Fish et al., 2013) and pain interference (e.g., Kwok, Chan, Chen, & Lo, 2016; Trompetter, Bohlmeijer, Fox, & Schreurs, 2015), the potential mediating roles of psychological flexibility in the relationships among pain severity, pain interference, and the risk of opioid misuse have not been systematically evaluated in an outpatient sample.

Present Study

Assessing risk for opioid misuse should take a central role for medical and behavioral professionals when examining patients seeking prescription opioids. The present study aims to identify characteristics of patients at risk for opioid misuse as well as provide information about intervention for reducing this risk of misuse. Many studies have examined predictors of opioid-related substance use disorders. However, the present study examines the risk of opioid misuse, specifically important when considering the onset of opioid therapy. By measuring the risk of opioid misuse in non-substance use disorder populations, assessment and intervention becomes proactive in attempts to eliminate the potential for later misuse. These assessment measures can be used in initial or early consultation for pain management. The willingness to be open, centered, and engaged with the external and internal world, known as psychological flexibility, appears to be an important mechanism when predicting opioid misuse risk. By understanding this role of psychological flexibility on the potential for opioid misuse among individuals with noncancerous chronic pain, risk for substance misuse may be better understood and liability for developing opioid addiction may be reduced. Furthermore, clinical interventions may be enhanced through use of information about psychological flexibility and chronic pain characteristics.

The present study evaluates the relationships between pain severity, pain interference, risk for opioid misuse and psychological flexibility in patients with noncancerous chronic pain. Specific hypotheses include: (a) self-reported pain severity and pain interference will each individually predict risk of opioid misuse; (b) self-reported pain severity will predict perceived pain interference; and (c) psychological flexibility will significantly account for the relationships between the predictor and outcome variables in the aforementioned hypotheses.

Materials and Methods

Participants

Participants were recruited from two outpatient pain clinics in the northeastern United States. A priori power analysis for F tests was conducted using G*Power (Faul, Erdfelder, Buchner, & Lang, 2009; Faul, Erdfelder, Lang, & Buchner, 2007), with an anticipated effect size (f^2) set at the 0.15 level, desired statistical power set at 0.80, the probability level set at the 0.05 level, and the number of predictors set at 2. Results indicated that a sample size of at least 77 participants would be necessary. Examination of sample size requirements for tests of indirect effects (Fritz & MacKinnon, 2007) indicated that 78 participants would be needed for percentile bootstrap analyses assuming medium-size effects between the predictor and the intervening variable and between the intervening and criterion variables. Individuals were eligible for participation if they were at least 18 years of age and currently being treated for pain at these pain outpatient clinics. Due to the disparity in experience between cancerous pain and pain related to other conditions, the present study focused on the subset of patients whose pain was not related to a diagnosis of cancer. In addition, only participants fluent in English were eligible to participate due to the English language validated measures used. Therefore, patients identifying pain related to a cancer diagnosis or are not fluent in English were not eligible for participation in the study.

Procedure

The study was approved by an institutional review board. Administration of all materials was in-person, via paper and pencil. All participants provided informed consent acknowledging the voluntary and confidential nature of the study. Participants were invited to participate in the research study only if they approached the research booth set up in the corner of a waiting room at the pain specialist outpatient clinics. Participants were offered the opportunity to enter a raffle for a \$100 Amazon gift card as a gesture of appreciation for their time. After informed consent forms were signed, the participants were administered a battery of measures. Measures are listed below in order of administration.

Demographic Questionnaire

The participants completed a demographic questionnaire pertaining to their self-reported age, gender, weight, race and prescriptions.

The Brief Pain Inventory-Short Form (BPI-SF)

The BPI (Cleeland & Ryan, 1994), an 11-item self-report measure, has been widely used to measure daily pain severity and pain interference in individuals with chronic and persistent pain. The BPI-SF is widely used for nonmalignant acute and chronic pain in both non-opioid use disorder and opioid use disorder patients (Dhingra et al., 2013; Tan, Jensen, Thormby, & Shanti, 2004). Severity of pain is measured using the BPI-SF Pain Severity 4-item subscale. This score is indicated by the mean of the four subscale items: pain at its worst in the last 24 h, pain at its least in the last 24 h, pain on average, and pain right now, with 0 (no pain) to 10 (*pain as bad as you can imagine*). Cronbach's α for the BPI-SF Pain Severity scale has been estimated at 0.87. Interference of pain is measured using the BPI-SF Pain Interference 7-item subscale. These items ask participants to rate the degree to which their pain has caused interference in daily functioning (e.g., general activity, mood, walking, normal work, relationships, sleep and life enjoyment). These items are assessed based on the last week, with 0 (does not inter*fere*) to 10 (*completely interferes*). The mean score for these items is used to measure pain interference. Cronbach's α for the BPI pain interference scale has been assessed at 0.89.

Acceptance and Action Questionnaire-II (AAQ-II)

The AAQ-II (Bond et al., 2011), a 7-item self-report measure, assesses a person's experiential avoidance as well as the acceptance and action of psychological flexibility. The total score is usually evaluated where higher scores reflect greater experiential avoidance and immobility and lower scores reflect greater acceptance and action. The AAQ-II has shown to have adequate internal reliability; Cronbach's α ranges from 0.78 to 0.88 (Fledderus, Voshaar, Klooster, & Bohlmeijer, 2012).

Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)

The SOAPP-R (Butler, Budman, Fernandez, & Jamison, 2004), a 24-item self-report measure, is designed to measure an individual's relative risk for developing long-term opioid use related problems. Items on this measure are answered by a Likert-scale ranging from 0 (never) to 4 (very often). The developers validated that high sensitivity and specificity cutoff scores of 18 points or higher are categorized as "at-risk" and scores of 22 or higher were indicative of "high risk" for predicting abnormal medication-related behaviors in pain clinic patients. In the present study, higher scores reflect a greater risk for opioid misuse. The SOAPP-R has been validated for individuals with chronic pain who are being considered for or are on long-term opioid therapy and shows good reliability and validity. Further, the SOAPP-R exhibits less susceptibility to deception compared to other similar measures (Butler et al., 2004).

Results

Data Analytic Plan

This was a cross-sectional design. Using SPSS version 23.0 for Macintosh (IBM Corp., 2015), a series of correlational, direct effect and indirect effect analyses were planned. Descriptive statistics were reported for all variables in the study. The first aim was to understand any correlations between risk for opioid misuse, pain severity, pain interference, and psychological flexibility. Pearson's r correlations were planned between the SOAP-R, BPI-SF subscales, and AAQ-II. The relationships between these variables were further planned to be explored using direct and total effect analyses. Moreover, analyses for indirect effects were planned to explore if the relationships between these variables could be explained by psychological flexibility. All indirect effect analyses were performed using bootstrapping (10,000 samples) in PROCESS to estimate effects and bias-corrected confidence intervals (BCa CI; Hayes, 2013). These indirect effects were considered to be significant when the BCa CIs did not include zero (Field, 2013).

Preliminary Analyses

One hundred and nine participants completed the study. One participant reported not being fluent in English. Four participants reported that their pain was related to a cancer diagnosis. Five participants did not fill out one or more of the measures. Therefore, those participants were excluded from analyses. After exclusion criteria (e.g., cancerous pain, non-English fluency) were taken into account, 99 participants were included in analyses. For those who missed individual items on the measures, their unique subscale mean was used as a replacement. Missing values analysis revealed that 0.51% of data were missing from the BPI-SF Severity subscale and 0.58% of data were missing from the BPI-II Interference Subscale. There were no missing data from the AAQ-II or the SOAPP-R. Preparatory data analyses were run to determine if there were problems in the data set prior to the main analysis (i.e., missing data, outliers, skewness) and to ensure that the data sample meets the assumptions of parametric statistical analyses. These assumptions include: (a) linearity, (b) homoscedasticity, (c) independence of errors, and (d) multivariate normality. Because assumptions were violated within this sample, robust bootstrapping methods (set at 10,000 samples) were conducted so that correlational, direct, and indirect effect analyses could be run without meeting the assumptions of normally distributed data (Efron & Tibshirani, 1993). No demographic information was shown to predict or be associated with criterion variables, examined through a series of Spearman's p correlations and one-way independent ANOVAs.

Descriptive Statistics

Descriptive statistics for gender, age, weight, and prescription types are included in Table 1. Study participants ranged in age from 26 to 87 years old (M=57, SD=12.9). There were 32 men (32.3%) and 67 women (67.7%). Racial composition of the sample was 64.6% Caucasian, 20.2% African American, 6.1% Hispanic, 3% Asian, 1% Native American, 5% Other or missing data. Means and descriptive statistics of the criterion and outcome measures used in the analyses are presented in Table 2.

Correlations

Zero-order correlations for all study measures are included in Table 3. Table 3 shows Spearman's ρ correlations between all variables examined in the direct and indirect effect models. Spearman's ρ was used in place of Pearson's *r* because the data did not meet assumptions for normal distribution. All study variables were significantly and positively correlated with each other. Scores on the SOAPP-R were strongly correlated with scores on the AAQ-II ($\rho = 0.63$, p < 0.001), moderately correlated with scores on the BPI-SF interference ($\rho = 0.40$, p < 0.001), and weakly correlated with scores on the BPI-SF severity ($\rho = 0.20$, p < 0.05). Subscale scores

Table 1	Demographic	characteristics of	participants	(N = 99)
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Characteristic	п	%	М	SD
Gender				
Female	32	32.3		
Male	67	67.7		
Age (years)	96		57	12.9
Weight (pounds)	94		190.7	42.7
Race				
American Indian or Native American	1	1		
Asian	3	3		
Black or African American	20	20.2		
Hispanic	6	6.1		
White or Caucasian		63.6		
Other		3		
Opioid prescription				
Yes	64	64.6		
No		33.3		
Type of opioid prescription				
Hydrocodone		3.1		
Hydrocodone/acetaminophen		6.3		
Morphine		3.1		
Oxycodone		25		
Oxycodone/acetaminophen		23.4		
Did not know		6.3		
Multiple		23.4		

Percentages of opioid prescriptions are based on the total number of patients who were prescribed opioids, not the total sample

on the BPI-SF (interference and severity) were moderately correlated to each other ($\rho = 0.55$, p < 0.001).

Hypothesis Testing

Pain Severity-Psychological Flexibility-Risk for Opioid Misuse Analyses

Pain severity exerted a significant total effect on risk for opioid misuse, B = 1.55, $R^2 = 0.059$, p = 0.016, 95% BCa CI [0.462, 2.685]. Indirect effect analyses revealed that

Table 2Descriptive statistics ofthe major study variables

psychological flexibility, B = 1.729, 95% CI [0.955, 2.780] significantly accounted for the relationship between pain severity and risk for opioid misuse. The direct effect of pain severity on risk for opioid misuse was nonsignificant in the mediation model, B = -0.175, p > 0.05, 95% BCa CI [-1.295, 0.945]. See Table 4 and Fig. 1 for all direct effect results for variables predicting risk of opioid misuse.

Pain Interference-Psychological Flexibility-Risk for Opioid Misuse Analyses

Pain interference exerted a significant total effect on risk for opioid misuse, B = 2.019, $R^2 = 0.164$, p < 0.001, 95% BCa CI [1.172, 2.889]. Indirect effect analyses revealed that psychological flexibility, B = 1.466, 95% BCa CI [0.754, 2.566] significantly accounted for the relationship between pain interference and risk for opioid misuse. The direct effect of pain severity on risk for opioid misuse was nonsignificant in the mediation model, B = 0.55, p > 0.05, 95% BCa CI [-0.364, 1.468]. See Table 4 and Fig. 1 for all direct effect results for variables predicting risk of opioid misuse.

Pain Severity-Psychological Flexibility-Pain Interference Analyses

Pain severity exerted a significant total effect on pain interference, B = 0.755, $R^2 = 0.344$, p < 0.001, 95% BCa CI [0.567, 0.921]. Indirect effect analyses revealed that psychological flexibility, B = 0.180, 95% BCa CI [0.072, 0.314] significantly accounted for the relationship between pain severity and pain interference. See Table 4 and Fig. 2 for direct effect results for variables predicting pain interference.

Discussion

Reliance on opioid-related medications as a first-line treatment for chronic pain continues despite concerns about opioid misuse (Rubin, 2019). Extensive research has suggested several potential harmful and adverse side effects of opioids. As chronic pain patients seek prescription opioids

Variable	n	М	SD	α	Range		Skew
					Potential	Actual	
BPI-SF							
Severity	99	6.08	1.90	0.86	0–10	1.5 - 10	- 0.273
Interference	99	5.83	2.44	0.91	0-10	0.14-10	-0.477
AAQ-II	99	22.1	11.79	0.91	7–49	7–49	- 0.471
SOAPP-R	99	18.18	12.17	0.89	0–94	0–54	0.754

BPI-SF Brief Pain Inventory-Short Form, AAQ-II Acceptance and Action Questionnaire-II, SOAPP-R Screener and Opioid Assessment for Patients with Pain-Revised

Table 3 Summary of correlations for scores on the SOAPP-R, BPI-SF subscales and AAO-II

Measure	1	2	3	4
1. SOAPP-R	_			
2. BPI-SF (severity)	0.20*	_		
3. BPI-SF (interference)	0.40**	0.55*	-	
4. AAQ-II	0.63**	0.44**	0.58**	_

BPI-SF Brief Pain Inventory-Short Form, AAQ-II Acceptance and Action Questionnaire-II, SOAPP-R Screener and Opioid Assessment for Patients with Pain-Revised

Spearman two-tailed correlations are reported. *p <.05; **Correlation is significant at p < .001

 Table 4
 Summary of linear direct effect analyses

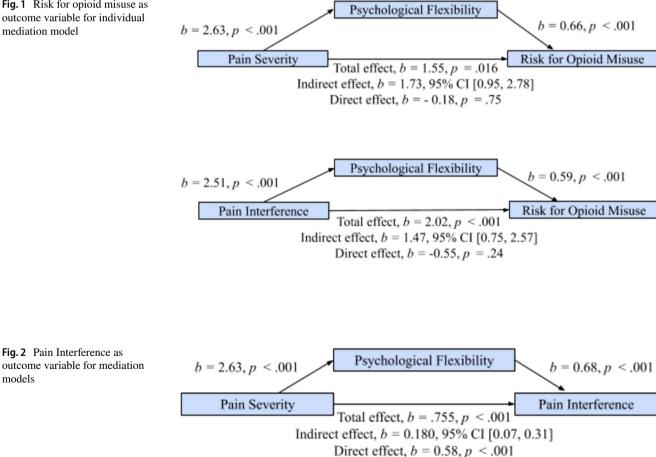
Variable	В	SE	95% BCa CI	р	
	Predicting risk of opioid misuse				
Pain severity	1.554	.591	[0.462, 2.685]	.009	
Pain interference	2.019	.449	[1.172, 2889]	<.001	
	terference				
Pain severity	0.755	.093	[0.567, 0.921]	<.001	

CI 95% bias-corrected accelerated confidence intervals

Fig. 1 Risk for opioid misuse as outcome variable for individual mediation model

models

risk of misuse early in the treatment process. In the sample examined, 65% of patients being treated for chronic pain by medical pain specialists reported receiving opioid prescriptions. The most commonly reported opioid medications taken were oxycodone (24.6%; e.g., OxyContin, Oxecta, Roxicodone), oxycodone and acetaminophen (23.1%; e.g., Percocet, Endocet, Roxicet), morphine (9.2%), and hydrocodone/acetaminophen (6.2%; e.g., Lorcet, Vicodin). In addition, many of the patients in the study's sample reported taking more than one type of opioid concurrently (23.1%). Interestingly, a significant portion of patients reported having an opioid prescription but did not know the details about their medication, indicating the potential of lack of doctor-patient pharmacological education and communication (7.7%). Previous studies have reported rates of opioid misuse and abuse in chronic pain patients ranging from 1 to 40% (Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008; Ives et al., 2006; Martell et al., 2007). A recent study by Boscarino and colleagues (2015) found that 41.3% of patients being treated for pain with COT met criteria for opioid use disorder. Similarly, in our study examining risk factors for opioid misuse (rather than diagnostic criteria for



opioid misuse), we found that 51.3% of the patients being treated for chronic pain were "at-risk" for opioid misuse.

The findings from this study revealed two key predictors of risk for opioid misuse. The findings, as shown in Model 1, suggest that when patients subjectively report higher levels of pain, they are more likely to be at risk of misusing opioid prescriptions. These findings corroborate previous research of a similar nature. Griffin and colleagues (2016), for example, found that pain severity was related to later opioid use, though they did not look at risk for opioid misuse. Model 2 explored the role of pain interference as a predictor of risk for opioid misuse. The findings for this model suggested that when patients report an inability to function in different aspects of daily life due to their pain, they are at higher risk for opioid misuse. Our findings were similar to results found by Turner and colleagues (2016), who reported pain interference was related to later opioid use, though these authors did not examine risk for opioid misuse. Subjective reports of pain severity and interference appear to significantly predict current use, misuse in SUD populations, as well as risk for misuse in medical non-SUD populations (as examined in the current study).

Another crucial finding of the present study is that psychological flexibility appears to account for a significant portion of the associations in these models. The relationships between pain severity and interference with opioid misuse risk were predicated on the patient's overall willingness to be open, centered, and present with external and internal experiences (i.e., psychological flexibility). This indirect effect of psychological flexibility was so significant that neither pain severity nor pain interference significantly predicted risk of opioid misuse when psychological flexibility was included in the model. The finding that psychological flexibility plays an important role in the prediction of both risk for opioid misuse by both severity and interference builds upon previous research examining the association between acceptance and pain tolerance (Masedo & Esteve, 2007; McMullen et al., 2008; Páez-Blarrina et al., 2008; Richardson et al., 2010; Vowles et al., 2007). Patients' reports of pain severity or interference alone may be less informative when predicting risk of opioid misuse than their reports of psychological flexibility. At the least, the relationship patients have to their experience should be assessed in conjunction with assessment of severity and interference. Further, teaching mindfulness- and acceptance-based strategies, which are core processes contributing to psychological flexibility (Dahl, Wilson, Luciano, & Hayes, 2005), may serve to mitigate future risk of opioid misuse when reported pain severity and pain interference are high. In this way, the findings of the present study have important clinical implications for both assessment and treatment of patients with chronic pain. The assessment of psychological flexibility, in addition to pain experience, could assist in identifying patients potentially at risk for opioid misuse, while treatment approaches designed to promote flexible responding to pain experiences may assist in reducing risk for opioid misuse.

Many psychological interventions target values-driven behaviors (i.e., doing what matters most to the patient as a way of regaining functioning), especially approaches informed by contextual behavioral science (e.g., ACT, behavioral activation, compassion-focused therapy). Chronic pain patients, however, often report that their pain interferes with various life domains, leading them to reduce valuesdriven activities in favor of behaviors designed to change their subjective experience of pain or distress. Yet, the results of the present study indicate that sensitivity to pain experience may heighten the degree to which pain interferes with other important life activities. As the findings for Model 2 indicate, patients who reported higher pain severity also reported higher pain interference. Interestingly, psychological flexibility significantly mediated this relationship, suggesting that the patient's responses to, and relationship with, pain-related sensations (i.e., pain stimuli) and painrelated thoughts may have greater impact on functioning than the presence of pain itself.

These findings have implications for the integrated treatment for chronic pain patients. Physicians and other medical professionals considering opioid treatments can use the models presented in Figs. 1 and 2 to better understand both the misuse-related risks of inflexible patient responses to chronic pain and the psychological processes that are addressed by effective behavioral interventions (Probst, Baumeister, McCracken, & Lin, 2019; Scott, Hann, & McCracken, 2016; Vowles & McCracken, 2010). A patient's willingness to be open, centered, and engaged with external and internal experiences appears to play a crucial role in many difficulties associated with chronic pain, including the relationships among pain severity, interference, and opioid abuse risk. Further, these findings regarding psychological flexibility could guide physicians in advocating and explaining mindfulness- and acceptance-based clinical interventions for chronic pain (e.g., ACT, mindfulness-based stress reduction), both as a way of mitigating the risk of prescription misuse and of improving functional outcomes. Finally, other forms of psychological intervention for chronic pain (e.g., CBT, psychodynamic therapies) could be strengthened by integrating techniques targeting psychological flexibility when patients are at risk of aberrant opioid-related behaviors or pain-related interference with values-driven behaviors.

Our findings must be considered in the context of several limitations. First, the cross-sectional design of the study poses several challenges to accurately interpret data including difficulty distinguishing causation from association, assessing for all potentially confounding variables, and susceptibility to bias (e.g., responder bias, recall bias, interviewer bias; Mann, 2003). Second, selection bias may have occurred due to the convenience sample, which is taken from two outpatient clinics in one region of the United States. Generalization to other patient populations and settings may be ill-advised. Also contributing to selection bias is the small percentage of eligible participants that agree to enroll in the study. Data were collected only when an investigator was at the outpatient pain clinic, meaning that many individuals that met eligibility requirements being treated at the clinic at other points in time did not have the opportunity to participate. Response bias may have occurred. Individuals in the waiting room only participated in the study if they approached the investigator. Therefore, the investigator may have possessed characteristics that influenced whether some individuals inquired about the study and why others did not. Furthermore, only individuals who are fluent in English were able to take part in the study, leaving some individuals from minoritized populations and non-English speaking populations excluded. Moreover, patients who were willing to participate in the study may possess characteristics that differ from those who did not. In addition, only some patient variables were examined. Future directions should include other demographic variables such as ethnicity, income, or educational attainment.

Second, the sample is relatively small which may have posed a threat to finding significance and ensuring a representative distribution of the population. Furthermore, limitation stems from the lack of available research concerning psychological flexibility and risk of opioid use, pain severity, and pain interference. This made the foundation of understanding the present research difficult. Future directions should examine these relationships in more depth and with different populations. These models may be explored with patients with pain related to cancer rather than chronic noncancerous pain. A central limitation to this study is the use of measures, specifically the SOAPP-R. The SOAPP-R assesses a person's relative risk of future opioid misuse, not current opioid misuse. The SOAPP-R measures risk by assessing a variety of factors that have been linked to opioid misuse (e.g., mood swings, cravings, trauma). Future studies may address if the present variables (e.g., psychological flexibility) relate to affective measures of opioid risk, as assessed in the SOAPP-R.

Lastly, inherent challenges occur when using self-report measures. This includes the construct validity in assessing the underlying theoretical constructs of interest. Finally, the self-report nature of this study relies on self-awareness and honest answering. Through informed consent, the participants were made aware that their answers were confidential and would not be exposed to their doctors. However, participants may still have answered in fear of medication and/or treatment alterations.

In conclusion, opioid misuse with chronic pain patients is a relevant yet copious topic in current academic and clinical communities. Previous research has suggested that pain severity and pain interference predict opioid use in those with diagnosed SUD. However, the frontline medical offices that are evaluating patients in the beginning of their journey must be able to accurately predict risk of later issues with legally prescribed opioids. Though administering a quick battery of self-report measures (~15 min), medical professionals can gain more information in early assessment for opioid therapy for chronic pain. By adding a measure of psychological flexibility, these medical professionals can immediately identify interventional treatment strategies, if warranted. The present study suggests that psychosocial assessment is an invaluable component of opioid-assisted treatment for chronic pain.

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Compliance with Ethical Standards

Conflict of interest All authors have agreed to identified order of authorship. There are no known conflicts of interest.

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