Does pain catastrophizing and distress intolerance mediate the relationship between PTSD and prescribed opioid misuse in people with chronic noncancer pain?

Alicia E. López-Martínez[1], Gloria Sainero-Tirado[2], Rosa Esteve[1], Ángela Reyes-Pérez[2], Gema T. Ruiz-Párraga[1], Rocío de la Vega[1], Elena R. Serrano-Ibáñez[3], and Carmen Ramírez-Maestre[1].

[1] Faculty of Psychology and Speech Therapy, University of Málaga, Instituto de Investigaciones Biomédicas de Málaga (IBIMA), Campus de Teatinos S/N, 29071 - Málaga, Spain.

[2] Faculty of Psychology and Speech Therapy, University of Málaga, Campus de Teatinos S/N, 29071 - Málaga, Spain.

[3] Área de Psicología. Facultad de Ciencias de la Salud, Universidad Isabel I, Fernán González 76, 0900 - Burgos, Spain. Instituto de Investigaciones Biomédicas de Málaga (IBIMA), Campus de Teatinos S/N, 29071 - Málaga, Spain.

Corresponding author: Rosa Esteve. PhD. Departamento de Personalidad, Evaluación y Tratamiento Psicológico, Facultad de Psicología y Logopedia, Universidad de Málaga, Campus de Teatinos, s/n. 29071-Málaga (Spain). Tel.: +34 952 132405; E-mail: zarazaga@uma.es

Objective: There is an ongoing debate on the use of long-term high-dose medically prescribed opioid analgesics for patients with chronic noncancer pain. Such use is elevated when there is comorbid pain and PTSD, which is quite prevalent. Therefore, it is relevant to investigate the psychological variables that may explain opioid misuse in this population. The purpose of this study was to examine the interaction effect of PTSD severity, distress intolerance, and pain catastrophizing on prescribed opioid misuse in chronic noncancer pain patients. ***Method:*** A total of 168 participants (mean age = 60 years, 74% women) were assessed regarding opioid medication, pain intensity, traumatic psychological events, PTSD, distress intolerance, pain catastrophizing, and current opioid misuse. ***Results:*** Groups were formed according to the level of PTSD severity (no symptoms, moderate symptoms, and severe symptoms). Significant differences were found between the groups in pain intensity, catastrophizing, distress intolerance, and opioid misuse. The severe-symptoms group had the highest scores on all variables. There were no between-group differences in the prescribed medication. Mediation analysis showed that the relationship between PTSD severity and opioid misuse was completely and independently mediated by distress intolerance and pain catastrophizing. ***Conclusions:*** Distress intolerance and pain catastrophizing may be theoretically and clinically relevant constructs in understanding the motivation for opioid misuse in people with concurrent chronic noncancer pain and PTSD.

Keywords: chronic noncancer pain, PTSD, opioid misuse, distress intolerance, catastrophizing.

Clinical Impact Statement

The comorbidity between posttraumatic stress disorder (PTSD) and chronic pain increases the likelihood of prescribed opioid misuse. However, there is very little research aimed at understanding what might explain this misuse. A total of 168 people with PTSD and chronic pain who were prescribed with opioids participated in the study. The results confirmed that those with more severe PTSD showed significantly higher opioid misuse and that this could be due, at least in part, to psychological variables such as pain catastrophizing (i.e., the belief that pain cannot be overcome) and distress intolerance (i.e., the inability to cope with uncomfortable emotions).

It has been shown that the use of opioids to treat chronic noncancer pain leads to limited improvements in pain and physical functioning (Busse et al., 2018). Despite this result, opioids are frequently prescribed to treat people with these conditions (Sola et al., 2020). Unfortunately, there is evidence of opioid misuse in chronic pain patients (Han et al., 2017; Vowles et al., 2015). In addition, previous studies have suggested that more than 60% of individuals with chronic pain and opioid dependence meet criteria for a mood disorder and that this group is more likely to be prescribed opiates for pain management than those without a diagnosed mental health disorder (Ketchen et al., 2016; McHugh et al., 2016). Moreover, opioid use disorder is more common in chronic noncancer pain patients with posttraumatic stress symptoms (PTSD) (Ditre et al., 2019; López-Martínez et al., 2019). This result is not surprising, given the high rates of PTSD among opioid-using populations (Dahlby & Kerr, 2020). In fact, the concurrence of PTSD, pain, and opioid abuse is common (López-Martínez et al., 2019).

People with comorbid PTSD and chronic pain report high levels of intense pain and affective distress and rely more heavily on medication to manage both pain and psychological distress (Ketchen et al., 2016). Chronic pain can be considered a stressor that contributes to substance use as a means of coping, thus hindering the use of other more adaptive strategies and contributing to the maintenance of both pain and addiction (Diltre et al., 2019). Thus, fluctuations in pain or somatic cues that are interpreted as harmful can lead to a cascade of negative emotions and catastrophizing thoughts in people with chronic pain, which would interfere with their ability to regulate emotional distress (Pegram et al., 2017). The avoidance of psychological distress is one of the factors that may explain patterns of substance use in people with PTSD (Miglin et al., 2020). Indeed, there are indications that most patients who have problematic opioid use (i.e., misuse) do so in an attempt to reduce symptoms of anxiety, depression, and even anger (Garland et al., 2015). It has also been suggested that these individuals have difficulties implementing emotional regulation strategies aimed at reducing negative affect, and that these difficulties may lead to the misuse of prescribed medication (Aaron et al., 2020).

There is little research on opioid medication misuse in people with comorbid PTSD and chronic pain: nevertheless, it has been suggested that both disorders may share a vulnerability pathway (Ketchen et al., 2016). Currently, there is a sizeable literature in support of shared pathways between chronic pain and PTSD. Neurobiological, social, emotional, and psychological mechanisms, as well as symptom overlap, have been identified in the comorbidity of these disorders (e.g., Fishbain et al., 2017; Gasperi et al., 2021; Siqveland et al., 2017). In fact, there is empirical evidence relating to how PTSD and chronic pain might mutually maintain each other (see the review by Ravn et al., 2018). This study focuses on cognitive-behavioral pain appraisals (i.e., catastrophizing) and on cognitive-

behavioral emotion regulation skills (i.e. distress intolerance) related to prescribed opioid misuse in chronic noncancer pain patients with concurrent PTSD.

Indeed, there may be common factors related to pain and emotion that could underlie motivations for substance abuse in people with this comorbidity. […]Thus, there may be common factors related to pain and emotion that could underlie motivations for substance abuse in people with this comorbidity. In fact, it has been suggested that a small set of transdiagnostic vulnerability variables may underlie some emotional disorders as well as their comorbidity with pain (Sauer-Zavala et al., 2012). Such variables include distress intolerance and catastrophizing, which have been considered to be related but distinct dispositional factors (Diltre et al., 2019; Linton, 2013; McHugh et al., 2020).

Distress intolerance has been described as the inability to tolerate negative emotional and/or physical states (Leyro et al., 2010). An association has been suggested between more severe PTSD symptoms and low distress tolerance: thus, the latter would be a factor in the maintenance and occurrence of PTSD symptomatology (e.g., Akbari et al., 2021; Boffa et al., 2018; Vujanovic & Zegel, 2020). However, there are few studies on the role of distress intolerance in the experience of pain (Rogers et al., 2018). Nevertheless, previous studies have found a significant association between lower distress tolerance and more severe pain, pain disability, and frequency of pain disability (Rogers et al., 2018), while other studies have found associations between distress intolerance and anxiety as well as between distress intolerance and opioid misuse in response to pain in chronic pain patients (McHugh et al., 2016).

People with low distress tolerance are more likely to use drugs to manage negative emotional states due to their limited ability to tolerate pain and pain-related negative affect (Buckheit et al., 2020; McHugh et al., 2016). Hence, opioid abuse could be a way to escape from distress while increasing the likelihood of generating dependence on this medication. This suggestion would be supported by the findings of Zegel et al. (2020), who found that distress intolerance moderates the association between opioid abuse and alcohol abuse in chronic pain patients, and that there is a significant association between distress intolerance and opioid dependence.

It has been suggested that distress intolerance is a variable that could increase the likelihood of catastrophizing (Linton, 2013). It has also been suggested that when pain sensations are interpreted through catastrophic cognitive appraisals, chronic pain patients may experience impaired emotional regulation, which would be accompanied by a decreased tolerance to distress (McHugh et al., 2016). Similarly, it has been suggested that catastrophic cognitions could be a transdiagnostic cognitive mechanism, which plays a role in a wide variety of disorders (Gellatly & Beck, 2016). The results of previous studies have shown that the tendency to catastrophize about pain mediates the relationship between PTSD symptomatology and both pain severity and pain interference (Gilliam et

al., 2019). Empirical evidence has indicated an association not only between pain catastrophizing and opioid abuse, but also between pain catastrophizing and other substances such as cannabis (Martel et al., 2014; Sterniczuk and Whelan, 2016).

The first steps have been taken towards a transdiagnostic approach in the analysis of the relationship between chronic pain and opioid use. Treatments based on transdiagnostic factors are more efficient when there are comorbid disorders that share common transdiagnostic processes (Aaron et al., 2020; LaRowe et al., 2020). This is the case in such disorders as chronic pain, a previous history of traumatic events, and substance abuse (Riquino et al., 2018). However, there is limited research evidence on the role of transdiagnostic variables in prescribed opioid misuse in people with comorbid chronic pain and PTSD. Therefore, the main purpose of this study was to investigate the mediation effect of PTSD severity, distress intolerance, and pain catastrophizing on prescribed opioid misuse in a sample of individuals with chronic noncancer pain. To this end, we examined two hypotheses:

(a) Three groups were formed according to the level of PTSD severity (no symptoms, moderate symptoms, and severe symptoms). We tested differences between the three groups in pain intensity, distress intolerance, catastrophizing, opioid misuse, and opioid prescriptions. We hypothesised that the severe PTSD symptoms group would have significantly higher levels of pain intensity, distress intolerance, catastrophizing, and opioid misuse, and that more opioid medication would be prescribed to this group than to the others. We predicted that there would be significant differences between groups in relation to opioid prescriptions.

(b) We investigated the mediating effect of both distress intolerance and catastrophizing on the relationship between PTSD severity and opioid misuse. As mentioned, the association between PTSD and distress intolerance is well established (Akbari et al., 2021). In addition, some recent findings have experimentally demonstrated strong correlations between pain catastrophizing and pain variables (McHugh et al., 2020). It was therefore hypothesised that the relationships between PTSD symptoms and opioid misuse would be serially mediated by the inability to tolerate negative states (i.e., distress intolerance) and, subsequently, the tendency to catastrophize about pain.

Method

Participants

A convenience sample of 168 individuals with nononcologic chronic pain (74% women) participated in the study. Their ages ranged from 34 to 84 years (M = 59.8, SD = 10.44).

Participants were recruited through two local associations of people with fibromyalgia and two Pain Units. Individuals were eligible for the study if they met the following criteria: a) continuous or intermittent noncancer pain of at least 3 months; b) pain at an intensity of 3 or more out of 10; c) pain which appears on 5 or more days per week; d) able to understand Spanish; and e) able to

understand spoken instructions and questionnaires. Exclusion criteria were as follows: a) severe injuries that required immediate surgery; b) presence of other chronic diseases involving disability; and c) major psychiatric illness.

Measures

Demographic and clinical history. All participants were asked to provide information on age, primary chronic pain diagnoses, and pain duration. In addition, information was collected on opioid medication intake in relation to dose, duration, frequency, and adherence.

Life Events Checklist for DSM-5 Standard Version. Exposure to past traumatic events was assessed with the Life Events Checklist for DSM-5 Standard Version (LEC-5) (Weathers et al., 2013a). This instrument is a 17-item self-report measure that assesses the experience of various traumatic stressful events related to DSM-5 criterion A for PTSD.

***PTSD Checklist for DSM-5*.** Once they had completed the LEC, participants were asked to complete the PCL-5 by thinking of the event that they considered to be the most severe of those they had experienced. The PTSD Checklist for DSM-5 (PCL-5) (Weathers et al., 2013b) scores 20 symptoms corresponding to the symptomatic dimensions of PTSD (i.e., re-experiencing, avoidance, changes to mood and cognitions, and hyperarousal) on a 4-point scale from 1 (not at all) to 4 (extremely). We used the overall score of this list. Previous studies with the PCL-5 have found a cut-off of 31 to 33 as indicative of probable PTSD across samples (e.g., Ashbaugh et al., 2016; Bovin et al., 2016). Nevertheless, as Weather et al. (2013b) have pointed out, the population and the purpose of the screening may warrant different cut-off scores. In the case of the chronic pain population, we are not aware of studies that have examined the PCL-5 cut-off point for this population. Given that PTSD was assessed with a scale instead of using DSM criteria, we therefore decided to use a more conservative cut-off of score of ≥ 36 to minimize false positives.

Distress Tolerance Scale. The Distress Tolerance Scale (DTS) (Simons & Gaher, 2005) is a 15-item measure to assess the degree to which a person experiences and endures psychological states of emotional distress. Each item is rated on a 5-point scale from 1 (strongly disagree) to 5 (strongly agree). Higher scores indicate lower tolerance. In this study, the scale had a Cronbach's alpha value of .84.

Coping Strategies Questionnaire. We assessed pain catastrophizing using the 2-item Coping Strategies Questionnaire (CSQ) (Jensen et al., 2003). This instrument has been shown to provide a valid and reliable measure of catastrophizing when used with chronic pain patients (Jensen et al., 2003). Respondents indicate the frequency with which they experienced two catastrophizing thoughts and feelings when in pain on a 7-point scale ranging from 0 (never) to 6 (always). In this study, the scale had a Cronbach's alpha value of .87.

Pain Index. Participants were asked to rate their mildest, average, and worst pain during the past 2 weeks and their current pain on a numerical rating scale ranging from 0 (no pain) to 10 (worst pain possible). A composite pain intensity score was calculated for each participant by computing the mean of the mildest, average, worst, and current pain (Jensen & Karoly, 2011). In this study, the scale had a Cronbach's alpha value of .80.

***Current Opioid Misuse Measure*. The Current Opioid Misuse Measure** (COMM) (Butler et al., 2007) is a 17-item self-assessment measure for monitoring chronic pain patients receiving opioid therapy who may be manifesting aberrant medication use suggestive of substance misuse. Each item is rated on a 5-point scale from 0 (never) to 4 (very often). A total score of nine or more indicates positive opioid misuse (i.e., the patient has been identified as misusing his/her medication and is at an increased risk of abuse). In this study, the scale had a Cronbach's alpha value of .79.

Procedure

The project was conducted in accordance with the Declaration of Helsinki and received ethical clearance by the Institutional Ethics Review Board (ERC UMA-66-2019-H) and the Regional Hospital Ethics Committee. All individuals who fulfilled the eligibility criteria were informed by their doctor (in the case of Pain Units) or by the president of the association (in the case of fibromyalgia associations) of the study aims and the possibility of participating. Participants who showed interest were referred by their doctor or by the president of the association and were contacted by telephone to make an appointment for the assessment at their clinic. In total, 201 participants were contacted, of whom 168 agreed to participate and 33 refused to participate.

Participants were fully informed of the aim of the study and were assured of their personal anonymity and the confidentiality of the survey. Subsequently, they provided signed informed consent and had a semi-structured interview with a trained psychologist, who verbally administered the study measures. Average interview time was 75 minutes. Participants were not compensated for their time. Data collection took place from March 2018 to February 2020.

Data Analysis

All analyses were performed using the SPSS statistical package for Windows version 25.0 (SPSS, Chicago, USA). We first estimated the number of participants with PTSD using the PCL-5 cut-off point. We then categorized participants according to their PCL-5 score and analysed the clinical and sociodemographic characteristics of each group.

We conducted chi-squared tests to compare groups by categorical variables (i.e., sex, pain diagnosis, and prescribed opioid medication). Analysis of variance (ANOVA) was computed using the Bonferroni post-hoc test to determine whether there were statistically significant differences

between groups for each dependent variable (i.e., pain intensity, opioid misuse, distress tolerance, and pain catastrophizing).

We conducted a regression-based serial multiple mediation analysis using the PROCESS-macro in SPSS version 3.5.3. This analysis was conducted only with participants whose PCL-5 score was indicative of probable PTSD (i.e., scores ≥ 36). Bivariate correlations were previously calculated using Pearson correlations. We used PROCESS-macro model 6 because the hypothesis formulated can best be tested in this way. The hypothesis posits a mediation model with two mediating variables that operate in sequence. Thus, the analytical strategy was based on this method in order to evaluate the indirect effect of PTSD scores on opioid misuse (i.e. COMM scores) via the mediating processes of distress intolerance and pain catastrophizing, with the two variables operating sequentially. Sex was introduced in the model as a covariate. The indirect effect was calculated using 5,000 bootstrap samples for bias-corrected bootstrap confidence intervals (CIs). An indirect effect is considered statistically significant if the established CI (95% CI) does not include the value 0. If the CI includes the value 0, the null hypothesis cannot be rejected (i.e., that there is no association between the variables involved) (Hayes, 2013).

Results

Patients who had a score equal to or greater than 36 on the PCL-5 were considered to have PTSD symptoms. Participants were divided into three groups: (a) with no-to-mild PTSD symptoms (score less than 35, n = 45), (b) with moderate PTSD symptoms (scores between 36 and 50, n = 61), and (c) with severe PTSD symptoms (scores greater than 50, n = 62). Table 1 shows the demographic and clinical characteristics of the three groups of participants. No significant differences were found between groups in age, sex, pain diagnosis, pain duration, and type of opioid medication prescription.

– PLEASE INSERT TABLE 1 AROUND HERE –

In addition, no significant differences were found between groups in dose, frequency, and duration of opioid intake. However, significant differences were found between groups in their pattern of Tramadol intake. Specifically, significantly more participants (16%) in the severe PTSD symptoms group did not follow the physicians' recommendations regarding Tramadol intake (χ^2 (6) = 17.06, p< .01), which was the most prescribed opioid in this group. No differences were found between the groups with no-to-mild PTSD symptoms and moderate PTSD symptoms.

The mean number of traumas experienced by each group was as follows: the no-to-mild PTSD symptoms group, 1.80 traumas (range = 0-3, SD = 1.04), the moderate PTSD symptoms group, 1.87 traumas (range = 0-3, SD = 1.04), and the severe PTSD symptoms group, 1.89 traumas (range = 0-3, SD = 1.00). No statistically significant differences in the mean numbers of traumas were found between groups (F(2,165) = 0.10, p = .905). Almost half (47%) of the participants in the no-to-mild

PTSD symptoms group had experienced a life-threatening transportation accident and 27% had experienced a natural disaster. In the moderate PTSD symptoms group, the most frequent trauma was a life-threatening vehicle accident (28%) followed by a natural disaster (20%). In the severe PTSD symptoms group, the most frequent traumas were a life-threatening transportation accident (39%) and physical abuse (21%). Of interest, whereas sexual abuse had been experienced by 7% of people in the no-to-mild PTSD symptoms group and the moderate PTSD group, sexual abuse was reported by 13% of people in the severe PTSD group.

Regarding the ANOVA results, main effects were found between groups in pain intensity ($F(2,162) = 4.12$, $p = .02$, $d = 0.72$, $\eta^2_p = .05$), opioid misuse ($F(2,162) = 17.96$, $p < .001$, $d = 0.99$, $\eta^2_p = .18$), distress intolerance ($F(2,162) = 10.44$, $p < .001$, $d = 0.99$, $\eta^2_p = .11$), and pain catastrophizing ($F(2,162) = 6.91$, $p < .01$, $d = 0.92$, $\eta^2_p = .08$). Although the means of all variables were lower in the no-to-mild PTSD symptoms group, post-hoc comparisons only showed statistically significant differences in pain intensity between the severe PTSD symptoms group and the group with no-to-mild PTSD symptoms. In addition, statistically significant differences in opioid misuse, distress intolerance, and pain catastrophizing were found between the severe PTSD symptoms group and the other two groups. Table 2 shows these results.

– PLEASE INSERT TABLE 2 AROUND HERE –

Before testing the mediation hypotheses, we computed Pearson's product-moment correlations between all variables (see Table 3). Pain intensity was significantly correlated only with PTSD symptoms. The remaining variables showed significant correlation coefficients with values between .44 and .27.

– PLEASE INSERT TABLE 3 AROUND HERE –

The results from the serial mediation analysis with two mediators indicated that the total effect of PTSD symptoms on opioid misuse ($c = .41$, $p < .001$) could be explained by significant indirect effects through distress intolerance and catastrophizing independently as well as through both mediators in combination (see Figure 1). However, mediation was partial, because the direct effect of PTSD symptoms on opioid misuse remained significant ($c' = .27$, $p < .01$). Therefore, part of the association between PTSD symptoms and opioid misuse is not explained by distress intolerance and catastrophizing. The effect of sex was not significant (total effect model, $B = -.33$, $SE = 1.63$, $p = .84$). Table 4 shows all the results of the mediation analysis.

– PLEASE INSERT FIGURE 1 AROUND HERE –

– PLEASE INSERT TABLE 4 AROUND HERE –

A 95% bias-corrected CI based on 5,000 bootstrap samples showed that the long-way indirect effects ($a_1 * d_{21} * b_2 = .03$) as well as both shortcut-effects ($a_1 * b_1 = .07$, $a_2 * b_2 = .06$) were above zero. These results indicate with 95% certainty that the indirect effects are indeed positive, thus

confirming the hypothesis. The direct and indirect effects of PTSD symptoms together explain 19% of the proportional variance (R^2) in opioid misuse. In combination with the direct effects of distress intolerance and catastrophizing, this result explains 32% of the proportional variance in opioid misuse.

Discussion

This study had a twofold aim: a) to analyse the differences between chronic nononcologic patients with different levels of PTSD symptoms in pain intensity, distress intolerance, catastrophizing, opioid misuse, and opioids prescription; (b) and to investigate the mediating effect of two psychological transdiagnostic variables (i.e., distress intolerance and catastrophizing) on the relationship between PTSD symptoms and prescribed opioid misuse. To the best of our knowledge, this is the first study to examine these issues.

Regarding the first study aim, we hypothesized that the severe PTSD symptoms group would show higher scores in pain intensity, distress intolerance, catastrophizing, and opioid misuse. The results confirmed the hypothesis. Significant differences were found in opioid misuse, distress intolerance, and pain catastrophizing between the chronic pain patients with more severe PTSD symptoms and the no-to-mild symptoms group and the moderate PTSD symptoms group. Significant differences in pain intensity were also found between the severe PTSD symptoms group and the no-to-mild PTSD symptoms group. However, contrary to our predictions, no differences were found between groups in opioid prescription. Likewise, no differences were found between the moderate PTSD symptoms group and the no-to-mild PTSD symptoms group in any variable. Given that the use of a scale to diagnose PTSD instead of using DSM criteria could inflate the prevalence rates for the disorder, we used a more conservative criterion to categorize participants. Hence, it can be assumed that the severe PTSD symptoms group was the only one that met the diagnostic criteria for PTSD.

Our study, and its results, adds to a growing body of literature regarding the association between chronic pain and PTSD severity. For example, previous empirical evidence has shown that PTSD symptom severity is prospectively associated with more severe clinical presentation in patients with chronic whiplash-associated disorders (Pedler & Sterling, 2013). Thus, the patients who were the most likely to experience more severe PTSD symptoms after a motor vehicle collision were also more likely to report severe neck pain and pain disability 3 months or more after the injury. Similarly, other studies have shown that higher pain interference, higher fear of movement/(re)injury, and more anxiety and depression symptoms are reported by chronic pain patients with more severe PTSD symptoms then either trauma-exposed patients who did not fulfil DSM-IV criteria for a diagnosis of PTSD and patients without PTSD symptoms (Åkerblom et al., 2017). Furthermore, our findings show that participants in the severe PTSD symptoms group were those with significantly high scores in opioid misuse, distress intolerance, and pain catastrophizing. It must be borne in mind that people in

this group had experienced more physical and sexual abuse (i.e., interpersonal traumas). It is well known that interpersonal traumas are more damaging than noninterpersonal forms and that they are significantly and directly related to physical health. PTSD is a significant variable in explaining this association (for a review, see López-Martínez et al., 2018). In addition, higher PTSD severity has been shown to be related to both increased substance abuse and increased difficulties in regulating emotions (Weiss et al., 2019). Moreover, it has been demonstrated that substance use increases as PTSD worsens (Back et al., 2014).

Although the processes underlying the relationship between PTSD and chronic pain remain unclear, specific neurobiological mechanisms have been suggested to underlie their comorbidity. Thus, it has been proposed that the high concurrence of PTSD and chronic pain may be related to shared pathophysiological mechanisms and that the risk of their comorbidity may be increased by interactions between the endocannabinoid and opioid systems that impact opioid sensitivity (Scioli-Salter et al., 2015). These proposals could explain why people with both PTSD and chronic pain are more likely to develop an opioid use disorder (Ditre et al., 2019; López-Martínez et al., 2019). Moreover, previous studies have found that specific types of pain conditions, such as musculoskeletal pain, may impact the nature of the comorbidity and are associated with an increased risk of opioid abuse (Bilevicius et al., 2018). Our results are in line with these findings: the most frequent type of pain was musculoskeletal and significantly higher levels of opioid misuse were found in the severe PTSD symptoms group than in either the no-to-mild PTSD symptoms group or the moderate PTSD symptoms group.

Both PTSD and chronic pain share several psychological characteristics such as distress intolerance and pain catastrophizing, which are related to an increased propensity for opioid misuse and abuse. Distress intolerance has been shown to be related to opioid misuse in response to pain in chronic pain patients (McHugh et al., 2016) and has also been found to be significantly associated with opioid dependence in this population (Zegel et al., 2020). Because people with chronic pain and PTSD are more likely to experience negative emotions, opioid abuse might be a way to avoid psychological distress: such avoidance has been suggested to be a variable that could explain substance abuse in individuals with PTSD (Miglin et al., 2020). Our findings point in this direction, in that the patients with more severe PTSD symptoms were also those with higher scores in both distress intolerance and opioid misuse. Thus, they are at higher risk of opioid abuse. Importantly, although Tramadol had been prescribed to more participants in this group, they were the least adherent to the prescribed intake pattern of this opioid. It is noteworthy that these findings cannot be accounted for by differences in pain intensity, because no differences were found between the moderate PTSD symptoms group and the severe PTSD symptoms group. Moreover, these results cannot be due to increased opioid prescription either, because, as previously mentioned, no

significant differences were found between the groups. These findings may be explained by the fact that PTSD is very common following an accident or injury (Fekadu et al., 2019) and opioids remain the firstline treatment for acute moderate-to-severe pain following injury (Califf et al., 2016). The three groups reported life-threatening transportation accidents as the most frequent traumatic event, which may partly explain why there were no differences between the groups in opioid prescribing. Nevertheless, this speculation deserves future empirical investigation.

Previous results have shown that pain catastrophizing is related to substance abuse, including opioid abuse (Martel et al., 2014), particularly in people with chronic musculoskeletal pain (Martínez-Calderón et al., 2021). Furthermore, in chronic pain patients prescribed opioids in primary care settings, it has been demonstrated that the higher the level of catastrophism, the higher the level of opioid misuse (Lazaridou et al., 2017). However, none of these studies addressed the issue of chronic pain and PTSD comorbidity. There is a dearth of research on this issue, although a recent study has shown that pain catastrophizing fully mediated the relationship between PTSD symptoms and pain outcome (i.e., pain severity and pain interference) in a sample of people with chronic pain (Wesley et al., 2019).

Recent studies have shown that distress intolerance and catastrophizing, despite being distinct factors, are related dispositional variables in individuals with chronic pain (McHugh et al., 2020). Our findings provide additional support to this relationship, in that they show that both these transdiagnostic variables mediated the relationship between PTSD symptoms and prescribed opioid misuse. Therefore, the results suggest that the inability to tolerate negative emotional and physical states (i.e., distress intolerance) combined with the tendency to catastrophize about pain seem to be relevant factors through which PTSD symptoms are related to aberrant opioid medication use. In addition, as hypothesized, the model suggested that higher levels of PTSD symptomatology were related to higher scores on opioid misuse. Hence, part of the association between PTSD symptoms and opioid misuse was a direct effect, whereas another part was the result of the association of PTSD symptoms with the two mediators and their effect on opioid misuse. A comparison of the standardized coefficients suggest that the total indirect effects accounted for by the mediators is relatively small. However, the fact that all effects were significant and positive still supports the validity of the hypothesized model. Future research should investigate other possible factors involved in opioid misuse in people with PTSD and chronic noncancer pain.

It is noteworthy that these results partially support previous recent theoretical models, such as the reciprocal model of pain and substance abuse (Ditre et al., 2019), which attempts to explain the role of psychopathology as a potential mechanism of action. This proposal suggests that a transdiagnostic approach is of particular relevance to the study of comorbid disorders because it can aid in the identification of shared mechanistic processes between pain and substance abuse, which

would include distress intolerance and pain catastrophizing as relevant transdiagnostic mechanisms (Ditre et al., 2019). Moreover, the principle of parsimony would be fulfilled by applying the same underlying principles across disorders to address the factors implicated in comorbid pain, PTSD symptoms, and opioid risk abuse.

As with any study, the conclusions must be considered in light of the study limitations. Firstly, the cross-sectional nature of the research design does not allow us to establish causality between the studied variables. Secondly, the study sample mainly comprised female participants. Even if this ratio was representative of the general population with chronic pain, it may still have biased the results. While sex was controlled for in the mediation analysis, future studies should seek to replicate the results using a more representative sample of the population to generalize the findings. Thirdly, all measures were collected via self-reports and so the results may be biased due to shared method variance. Fourthly, the interpretation of the results could have been substantially affected by possible unaddressed confounders. Finally, most of the study participants reported musculoskeletal pain as their primary pain, suggesting that the results may not be generalizable to people with other pain diagnoses.

Taking into account the high co-occurrence of chronic pain and PTSD, consistent screening practices and coordinated care should be implemented in the treatment of both disorders, particularly in the presence of problems associated with opioid use. To the best of our knowledge, no previous research has investigated associations between the variables considered in the current study in a single model. However, given the paucity of studies, more research is needed to better identify and treat chronic pain patients with mental health problems, such as PTSD, as well as their risk of opioid abuse.

References

Aaron, R. V., Finan, P. H., Wegener, S. T., Keefe, F. J., & Lumley, M. A. (2020). Emotion regulation as a transdiagnostic factor underlying co-occurring chronic pain and problematic opioid use. *American Psychologist*, *75*(6), 796–810. doi:10.1037/amp0000678

Akbari, M., Hosseini, Z. S., Seydavi, M., Zegel, M., Zvolensky, M. J., & Vujanovic, A. A. (2021). Distress tolerance and posttraumatic stress disorder: a systematic review and meta-analysis. *Cognitive Behaviour Therapy*, 1–30. Advance online publication. https://doi.org/10.1080/16506073.2021.1942541

Åkerblom, S., Perrin, S., Rivano Fischer, M., & McCracken, L. M. (2017). The impact of PTSD on functioning in patients seeking treatment for chronic pain and validation of the Posttraumatic Diagnostic Scale. *International Journal of Behavioral Medicine*, *24*(2), 249–259. Doi: 10.1007/s12529-017-9641-8

Ashbaugh, A. R., Houle-Johnson, S., Herbert, C., El-Hage, W., & Brunet, A. (2016). Psychometric validation of the English and French versions of the Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5). *PloS One*, *11*(10), e0161645. doi:10.1371/journal.pone.0161645

Back, S. E., Killeen, T. K., Teer, A. P., Hartwell, E. E., Federline, A., Beylotte, F., & Cox, E. (2014). Substance use disorders and PTSD: An exploratory study of treatment preferences among military veterans. *Addictive Behaviors*, *39*, 369–373. doi: 10.1016/j.addbeh .2013.09.017

Bilevicius, E., Sommer, J. L., Asmundson, G. J. G., & El-Gabalawy, R. (2018). Posttraumatic stress disorder and chronic pain are associated with opioid use disorder: Results from a 2012-2013 American nationally representative survey. *Drug and Alcohol Dependence*, *188*, 119-125. doi:10.1016/j.drugalcdep.2018.04.005

Boffa, J. W., Short, N. A., Gibby, B. A., Stentz, L. A., & Schmidt, N. B. (2018). Distress tolerance as a mechanism of PTSD symptom change: Evidence for mediation in a treatment-seeking sample. *Psychiatry Research*, 267, 400-408. doi:10.1016/j.psychres.2018.03.085

Bovin, M. J., Marx, B. P., Weathers, F. W., Gallagher, M. W., Rodriguez, P., Schnurr, P. P., & Keane, T. M. (2016). Psychometric properties of the PTSD Checklist for the Diagnostic and Statistical Manual of Mental Disorders–Fifth Edition (PCL-5) in veterans. *Psychological Assessment*, *28*(11), 1379–1391. doi:10.1037/pas0000254

Buckheit, K. A., De Vita, M., & Maisto, S. A. (2020). A multimethod investigation of distress tolerance and problematic alcohol use. *Experimental and Clinical Psychopharmacology*, *28*(2), 137–142. doi:10.1037/pha0000307

Busse, J. W., Wang, L., Kamaleldin, M., Craigie, S., Riva, J. J., Montoya, L., Mulla, S. M., Lopes, L. C., Vogel, N., Chen, E., Kirmayr, K., De Oliveira, K., Olivieri, L., Kaushal, A., Chaparro, L. E., Oyberman, I., Agarwal, A., Couban, R., Tsoi, L., Lam, T., Guyatt, G. H. (2018). Opioids for chronic noncancer pain: A systematic review and meta-analysis. *JAMA*, *320*(23), 2448–2460. doi:10.1001/jama.2018.18472

Butler, S., Budman, S., Fernandez, K., Houle, B., Benoit, C., Katz, N., & Jamison, R. (2007). Development and validation of the Current Opioid Misuse Measure. *Pain*, *130*(1-2), 144–156. doi:10.1016/j.pain.2007.01.014

Califf, R. M., Woodcock, J., & Ostroff, S. (2016). A Proactive Response to Prescription Opioid Abuse. *The New England Journal of Medicine*, *374*(15), 1480–1485. doi:10.1056/NEJMsr1601307

Dahlby, L., & Kerr, T. (2020). PTSD and opioid use: implications for intervention and policy. *Substance Abuse Treatment, Prevention, and Policy*, *15*(1), 22. doi:10.1186/s13011-020-00264-8

De Sola, H., Dueñas, M., Salazar, A., Ortega-Jiménez, P., & Failde, I. (2020). Prevalence of therapeutic use of opioids in chronic non-cancer pain patients and associated factors: A systematic review and meta-analysis. *Frontiers in Pharmacology*, *11*, 564412. doi:10.3389/fphar.2020.564412

Ditre, J. W., Zale, E. L., & LaRowe, L. R. (2019). A reciprocal model of pain and substance use: Transdiagnostic considerations, clinical implications, and future directions. *Annual Review of Clinical Psychology*, *15*, 503–528. doi:10.1146/annurev-clinpsy-050718-095440

Fekadu, W., Mekonen, T., Belete, H., Belete, A., & Yohannes, K. (2019). Incidence of Post-Traumatic Stress Disorder After Road Traffic Accident. *Frontiers in Psychiatry*, *10*, 519. doi:10.3389/fpsyt.2019.00519

Fishbain, D. A., Pulikal, A., Lewis, J. E., & Gao, J. (2017). Chronic Pain Types Differ in Their Reported Prevalence of Post -Traumatic Stress Disorder (PTSD) and There Is Consistent Evidence That Chronic Pain Is Associated with PTSD: An Evidence-Based Structured Systematic Review. *Pain Medicine*, *18*(4), 711–735. https://doi.org/10.1093/pm/pnw065

Garland, E. L., Froeliger, B., & Howard, M. O. (2015). Neurophysiological evidence for remediation of reward processing deficits in chronic pain and opioid misuse following treatment with Mindfulness-Oriented Recovery Enhancement: Exploratory ERP findings from a pilot RCT. *Journal of Behavioral Medicine*, *38*(2), 327–336. doi:/10.1007/s10865-014-9607-0

Gasperi, M., Panizzon, M., Goldberg, J., Buchwald, D., & Afari, N. (2021). Posttraumatic Stress Disorder and Chronic Pain Conditions in Men: A Twin Study. *Psychosomatic Medicine*, *83*(2), 109–117. doi: 10.1097/PSY.0000000000000899

Gellatly, R., & Beck, A. T. (2016). Catastrophic thinking: A transdiagnostic process across psychiatric disorders. *Cognitive Therapy and Research*, *40*(4), 441–452. doi:10.1007/s10608-016-9763-3

Gilliam, W. P., Craner, J. R., Schumann, M. E., & Gascho, K. (2019). The mediating effect of pain catastrophizing on PTSD symptoms and pain outcome. *The Clinical Journal of Pain*, *35*(7), 583-588. doi: 10.1097/AJP.0000000000000713

Han, B., Compton, W. M., Blanco, C., Crane, E., Lee, J., & Jones, C. M. (2017). Prescription opioid use, misuse, and use disorders in U.S. adults: 2015 National Survey on Drug Use and Health. *Annals of Internal Medicine*, *167*(5), 293–301. doi:10.7326/M17-0865

Jensen, M.P., & Karoly, P. (2011). Self-Report scales and procedures for assessing pain in adults. In D.C. Turk & R. Melzack (Eds.), *Handbook of pain assessment* (3rd edition; pp. 19-44). Guilford Press.

Jensen, M., Keefe, F., Lefebvre, J., Romano, J., & Turner, J. (2003). One-and two-item measures of pain beliefs and coping strategies. *Pain*, *104*(3), 453–459. doi:0.1016/S0304-3959(03)00076-9

Ketchen, B., Eilender, P., & Fareed, A. (2016). Comorbid post-traumatic stress Disorder, pain, and opiate addiction. In C.R. Martin, V. R. Preedy, & V.P Patel. (Eds.), *Comprehensive Guide to Post-Traumatic Stress Disorders* (pp. 643-668). Springer. doi:10.1007/978-3-319-08359-9_28

LaRowe, L. R., Powers, J. M., Garey, L., Rogers, A. H., Zvolensky, M. J., & Ditre, J. W. (2020). Pain-related anxiety, sex, and co-use of alcohol and prescription opioids among adults with chronic low back pain. *Drug and Alcohol Dependence*, *214*, 108171. doi:10.1016/j.drugalcdep.2020.108171

Lazaridou, A., Franceschelli, O., Boliteanu, A., Cornelius, M., Edwards, R. R., & Jamison, R. N. (2017).Influence of catastrophizing on pain intensity, disability, side effects, and opioid misuse among pain patients in primary care. *Journal of Applied Biobehavioral Research*, *22*(1), e12081. doi:10.1111/jabr.12081

Leyro, T. M., Zvolensky, M. J., & Bernstein, A. (2010). Distress tolerance and psychopathological symptoms and disorders: a review of the empirical literature among adults. *Psychological Bulletin*, *136*(4), 576-600. doi: 10.1037/a0019712.

Linton, S. J. (2013). A transdiagnostic approach to pain and emotion. *Journal of Applied Biobehavioral Research*, *18*(2), 82-103. doi:10.1111/jabr.12007

López-Martínez, A. E., Reyes-Pérez, A., Serrano-Ibáñez, E. R., Esteve, R., & Ramírez-Maestre, C. (2019). Chronic pain, posttraumatic stress disorder, and opioid intake: A systematic review. *World Journal of Clinical Cases*, *7*(24), 4254–4269. doi:10.12998/wjcc.v7.i24.4254

López-Martínez, A. E., Serrano-Ibáñez, E. R., Ruiz-Párraga, G. T., Gómez-Pérez, L., Ramírez-Maestre, C., & Esteve, R. (2018). Physical Health Consequences of Interpersonal Trauma: A Systematic Review of the Role of Psychological Variables. *Trauma, Violence & Abuse*, *19*(3), 305–322. doi:10.1177/1524838016659488

Martel, M. O., Dolman, A. J., Edwards, R. R., Jamison, R. N., & Wasan, A. D. (2014). The association between negative affect and prescription opioid misuse in patients with chronic pain: The mediating role of opioid craving. *The Journal of Pain*, *15*(1), 90–100. doi:10.1016/j.jpain.2013.09.014

Martínez-Calderón, J., Flores-Cortes, M., Morales-Asencio, J. M., & Luque-Suarez, A. (2021). Pain catastrophizing, opioid misuse, opioid use, and opioid dose in people with chronic musculoskeletal pain: A systematic review. *The Journal of Pain*, S1526-5900(21)00017-1. Advance online publication. doi:10.1016/j.jpain.2021.02.002

McHugh, R. K., Nguyen, M. D., Fitzmaurice, G. M., & Dillon, D. G. (2020). Behavioral strategies to reduce stress reactivity in opioid use disorder: Study design. *Health Psychology*, *39*(9), 806–814. doi:10.1037/hea0000862

McHugh, R. K., Weiss, R. D., Cornelius, M., Martel, M. O., Jamison, R. N., & Edwards, R. R. (2016). Distress intolerance and prescription opioid misuse among patients with chronic pain. *The Journal of Pain*, *17*(7), 806–814. doi:10.1016/j.jpain.2016.03.004

Miglin, R., Bounoua, N., Spielberg, J. M., & Sadeh, N. (2020). A transdiagnostic examination of affective motivations for drug use. *Addictive Behaviors Reports*, *12*, 100279. doi:10.1016/j.abrep.2020.100279

Pedler, A., & Sterling, M. (2013). Patients with chronic whiplash can be subgrouped on the basis of symptoms of sensory hypersensitivity and posttraumatic stress. *Pain*, *154*(9), 1640–1648. doi:10.1016/j.pain.2013.05.005

Pegram, S. E., Lumley, M. A., Jasinski, M. J., & Burns, J. W. (2017). Psychological trauma exposure and pain-related outcomes among people with chronic low back pain: Moderated mediation by thought suppression and social constraints. *Annals of Behavioral Medicine*, *51*(2), 316–320. doi:10.1007/s12160-016-9838-0

Pozzato, I., Craig, A., Gopinath, B., Kifley, A., Tran, Y., Jagnoor, J., & Cameron, I. D. (2020). Outcomes after traffic injury: mental health comorbidity and relationship with pain interference. *BMC Psychiatry*, *20*(1), 189. https://doi.org/10.1186/s12888-020-02601-4

Ravn, S., Hartvigsen, J., Hansen, M., Sterling, M., & Andersen, T. (2018). Do post-traumatic pain and post-traumatic stress symptomatology mutually maintain each other? A systematic review of cross-lagged studies. *PAIN*, *159* (11), 2159-2169. doi: 10.1097/j.pain.0000000000001331.

Riquino, M. R., Priddy, S. E., Howard, M. O., & Garland, E. L. (2018). Emotion dysregulation as a transdiagnostic mechanism of opioid misuse and suicidality among chronic pain patients. *Borderline Personality Disorder and Emotion Dysregulation*, *5*, 11. doi:10.1186/s40479-018-0088-6

Rogers, A. H., Bakhshaie, J., Mayorga, N. A., Ditre, J. W., & Zvolensky, M. J. (2018). Distress tolerance and pain experience among young adults. *Psychology, Health & Medicine*, *23*(10), 1231–1238. doi:/10.1080/13548506.2018.1454598

Sauer-Zavala, S., Boswell, J. F., Gallagher, M. W., Bentley, K. H., Ametaj, A., & Barlow, D. H. (2012). The role of negative affectivity and negative reactivity to emotions in predicting outcomes in the unified protocol for the transdiagnostic treatment of emotional disorders. *Behaviour Research and Therapy*, *50*(9), 551–557. doi:10.1016/j.brat.2012.05.005

Scioli-Salter, E. R., Forman, D. E., Otis, J. D., Gregor, K., Valovski, I., & Rasmusson, A. M. (2015). The shared neuroanatomy and neurobiology of comorbid chronic pain and PTSD: therapeutic implications. *The Clinical Journal of Pain*, *31*(4), 363–374. doi: 10.1097/AJP.0000000000000115

Simons, J. S., & Gaher, R. M. (2005). The Distress Tolerance Scale: Development and validation of a self-report measure. *Motivation and Emotion*, *29*(2), 83–102. doi:10.1007/s11031-005-7955-3

Siqveland, J., Hussain, A., Lindstrøm, J. C., Ruud, T., & Hauff, E. (2017). Prevalence of Posttraumatic Stress Disorder in Persons with Chronic Pain: A Meta-analysis. *Frontiers in Psychiatry*, *8*, 164. doi:10.3389/fpsyt.2017.00164

Sterniczuk, R., & Whelan, J. (2016). Cannabis use among Canadian armed forces veterans. *Journal of Military, Veteran and Family Health*, *2*(2), 43–52. doi:10.3138/jmvfh.3836

Vowles, K. E., McEntee, M. L., Julnes, P. S., Frohe, T., Ney, J. P., & van der Goes, D. N. (2015). Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *Pain*, *156*(4), 569–576. doi:10.1097/01.j.pain.0000460357.01998.f1

Vujanovic, A. A., & Zegel, M. (2020). Distress tolerance and posttraumatic stress. In M. T. Tull & N. A. Kimbrel (Eds.), *Emotion in posttraumatic stress disorder* (pp. 343-376). Guilford Press. doi: 10.1016/B978-0-12-816022-0.00012-0

Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (2013a). The Life Events Checklist for DSM-5 (LEC-5) – Standard. [Measurement instrument]. Available from https://www.ptsd.va.gov/

Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P., y Schnurr, P. P. (2013b). The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD. Available from https://www.ptsd.va.gov/

Weiss, N. H., Schick, M. R., Contractor, A. A., & Dixon-Gordon, K. L. (2019). Posttraumatic stress disorder and substance use: Identifying the underlying role of difficulties regulating positive emotions. *Addictive Behaviors*, *96*, 119–126. doi:10.1016/j.addbeh.2019.04.029

Wesley, G., Craner, J.R., Schumann, M.E., & Gascho, K. (2019). The mediating effect of pain catastrophizing on PTSD symptoms and pain outcome. *The Clinical Journal of Pain*, *35*(7), 583-588. doi: 10.1097/AJP.0000000000000713

Zegel, M., Rogers, A. H., Vujanovic, A. A., & Zvolensky, M. J. (2021). Alcohol use problems and opioid misuse and dependence among adults with chronic pain: The role of distress tolerance. *Psychology of Addictive Behaviors*, *35*(1), 42–51. doi:10.1037/adb0000587

Table 1

Demographic and Clinical Characteristics of the Three Groups of Participants

Variables	No-to-mild PTSD symptoms (n = 45)		Moderate PTSD symptoms (n = 61)		Severe PTSD symptoms (n = 62)				
	M (SD)	*N (%)*	*M (SD)*	*N (%)*	*M (SD)*	*N (%)*	χ^2	*F*	*p*
Age	60.98 (11.83)		58.50 (10.16)		60.20 (9.66)			0.79	.45
Sex							4.62		.10
Man		14 (31)		19 (31)		10 (16)			
Woman		31 (69)		42(69)		52 (84)			
Pain diagnosis							69.29		.08
Arthrosis		7 (15)		4 (7)		5 (8)			
Fibromyalgia		7 (16)		25(41)		32 (53)			
Rheumatoid arthritis		5 (11)		4 (7)		2 (4)			
Spinal pain		20 (42)		19 (31)		12 (18)			
Others		6 (16)		9 (14)		11 (17)			
Prescribed opioid									
Buprenorphine		0		0		1 (2)	1.72		.42
Fentanyl		7 (15)		4 (7)		8 (13)	1.43		.49
Morphine		0		1 (2)		2 (3)	0.34		.84
Oxycodone		10 (22)		12 (20)		10 (16)	0.14		.93
Tapentadol		7 (16)		10 (17)		3 (5)	4.69		.10

Tramadol	23 (51)	36 (59)	45 (73)	8.94		.06
Length of pain, y	16.23 (14.68)	15.50 (12.37)	18.81 (12.05)		0.22	.80

Table 2

ANOVA Results. Mean Differences in Pain Intensity, Opioid Misuse, Distress Intolerance, and Catastrophizing in Each Group (N = 168).

Variables	Group	Mean (SD)	*F* (1,167)	*p*	η^2_p	Cohen's *d*	Post-hoc comparisons
	1	7.04 (1.36)					1-2 [ab]
Pain intensity	2	7.23 (1.38)	4.12	.018	.048	.72	1-3 *
	3	7.73 (1.22)					2-3 [b]
	1	12.02 (6.63)					1-2 [b]
Opioid misuse	2	12.98 (6.26)	17.96	< .001	.179	.99	1-3 ***
	3	19.68 (8.95)					2-3***
	1	43.69 (18.45)					1-2 [b]
Distress intolerance	2	48.12 (12.22)	10.44	< .001	.112	.99	1-3***
	3	55.73 (14.63)					2-3**
	1	5.69 (1.96)					1-2 [b]
Pain catastrophizing	2	6.07 (1.73)	6.91	<.01	.077	.92	1-3 **
	3	6.90 (1.62)					2-3 *

Note. 1 = no PTSD symptoms group, 2 = moderate PTSD symptoms group, 3 = severe PTSD symptoms group.

[a] Bonferroni correction, [b] Not significant. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 3

Pearson's Bivariate Correlations in Patients with PTSD Symptoms (N = 123)

Variables	1	2	3	4	5
1 PTSD symptoms	-	.21*	.44***	.35***	.27**
2 Pain intensity		-	.16	.02	.08
3 Opioid misuse			-	.38***	.42***
4 Distress intolerance				-	.32***
5 Pain catastrophizing					-

* $p < .05$. ** $p < .01$. *** $p < .001$.

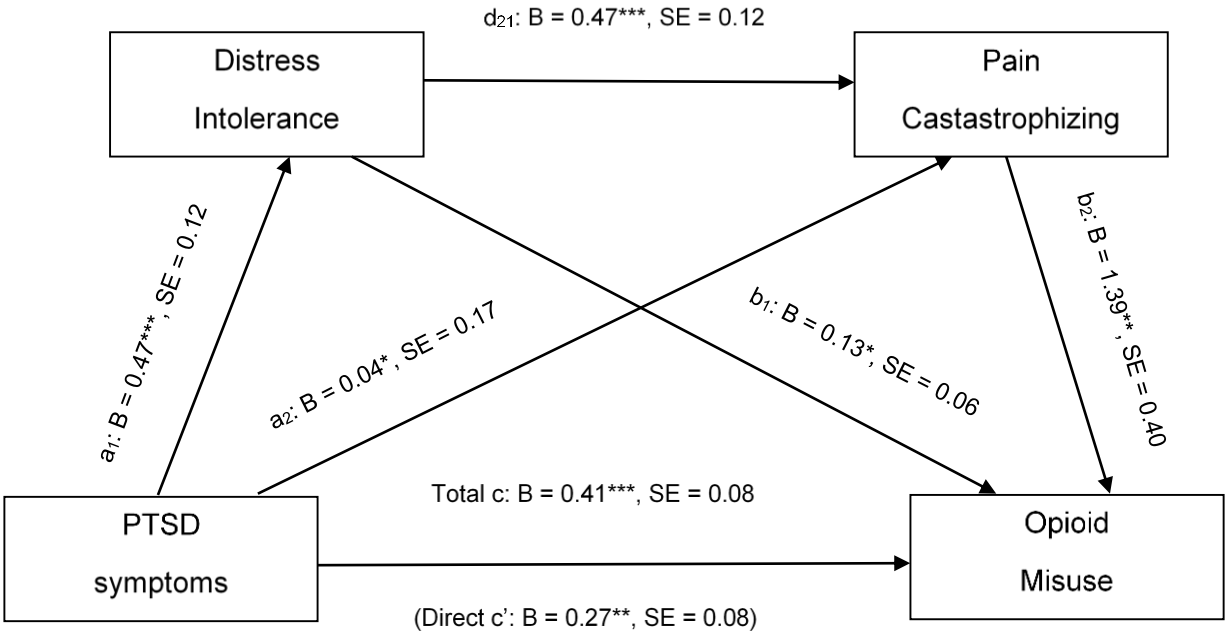

Figure 1. Study mediation model depicting relationships between all model components. Values represent unstandardized path coefficients and their standard errors. * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 4

Results from serial mediation analysis (N = 123)

Path	Direct effects	B	β	95% CI	SE	*t*	*R*	R^2
a_1	PTSD symptoms on distress intolerance	.48***	.36	.25-.71	.12	4.12	.35	.12***
a_2	PTSD symptoms on pain catastrophizing	.04*	.20	.01-.07	.02			
d_{21}	Distress intolerance on pain catastrophizing	.04**	.25	.01-.06	.01	2.79	.38	.14***
b_1	Distress intolerance on opioid misuse	.13*	.19	.01-.24	.06	2.23		
b_2	Catastrophizing on opioid misuse	1.39**	.29	.60-2.19	.40	3.49		
c'	PTSD symptoms on opioid misuse (direct)	.27**	.30	.12-.42	.08	3.55	.57	.32***
	Total effects							
c	PTSD symptoms -> opioid misuse (total)	.41***	.44	.26-.56	.08	5.36	.44	.19***
	Indirect effects							
a_1*b_1	PTSD symptoms -> distress intolerance -> opioid misuse	.06	.07	.01-.14	.03			
a_2*b_2	PTSD symptoms -> pain catastrophizing -> opioid misuse	.05	.06	.01-.10	.02			
$a_1*d_{21}*b_2$	PTSD symptoms -> distress intolerance -> pain catastrophizing -> opioid misuse	.02	.03	.00-.06	.01			
	Total indirect effects	.14	.15	.07-.22	.04			

Note. B = regression coefficients, β = standardized regression coefficients, SE = standard error. * $p < .05$ ** $p < .01$ *** $p < .001$.