Published in final edited form as:

Am J Drug Alcohol Abuse. 2019 ; 45(5): 470–478. doi:10.1080/00952990.2019.1569670.

Anxiety Sensitivity and Opioid Misuse among Opioid-using Adults with Chronic Pain

Andrew H. Rogers, M.A.¹, Brooke Y. Kauffmann, M.A.¹, Jafar Bakhshaie, M.D.¹, R. Kathryn McHugh, Ph.D.², Joseph W. Ditre, Ph.D.³, Michael J. Zvolensky, Ph.D.^{1,4,5}

¹Department of Psychology, University of Houston

²Department of Psychiatry, McLean Hospital

³Department of Psychology, Syracuse University

⁴Department of Behavioral Science, The University of Texas MD Anderson Cancer Center

⁵HEALTH Institute, University of Houston

Abstract

Background: The opioid epidemic is a significant public health crisis, and this problem is particularly prevalent among individuals with chronic pain. Accordingly, there is an urgent need for interventions to mitigate the risk for opioid misuse and opioid use disorder among people with pain. Given that mental health problems, specifically anxiety, are common among people who misuse opioids, it is important to examine factors that link mental health problems with opioid misuse to ultimately inform the development of novel interventions. Anxiety sensitivity, a transdiagnostic vulnerability factor, may be one important mechanism in elevated opioid misuse among persons with chronic pain.

Method: Therefore, the current cross-sectional study examined anxiety sensitivity (and construct sub facets) as a predictor of opioid misuse among adults with chronic pain.

Results: Results indicated that anxiety sensitivity was associated with multiple aspects of opioid misuse, and the magnitude of effects ranged from medium to large. Results were observed over and above the variance accounted for by age, sex, income, education, perceived health, and pain severity.

Conclusion: These findings suggest that future research should continue to explore the explanatory relevance of anxiety sensitivity in opioid misuse among individuals with chronic pain.

Keywords

Opioid misuse; Anxiety Sensitivity; Chronic Pain; Transdiagnostic; Comorbidity

The opioid epidemic poses a significant public health crisis, with increasing rates of opioid-involved overdose observed every year [1,2]. Research suggests that the majority of individuals who misuse opioids initiated use with a prescription, but then proceeded to use

in a manner that deviated from what was prescribed, or turned to other opioid forms, such as heroin [3,4]. Opioids are often prescribed for the treatment and management of chronic pain, and pain is associated with both the initiation of opioid misuse and the development of opioid use disorder [5,6], implicating chronic pain as one of the leading risk factors for opioid misuse [7]. Although effective treatments are available for opioid use disorder, there is significant need for improvement. For instance, first line pharmacological treatments (e.g. methadone, buprenorphine) are associated with reduction in opioid use; however, approximately 50% of people who received these treatments either dropout of treatment early or relapse [8,9]. Furthermore, there is a clear need for better interventions across the spectrum of opioid misuse, such as interventions to prevent the transition from opioid use to opioid misuse and the transition from opioid misuse to opioid use disorder. Yet, little work has examined specific psychological vulnerabilities that may confer heightened risk for opioid misuse, which in turn, could ultimately inform the development of more efficacious psychosocial treatments via an experimental therapeutic framework [10].

Due to the fact that mood and anxiety disorders are elevated among people misusing opioids [11], studies have begun to investigate transdiagnostic affective vulnerability factors that may link mood and anxiety disorders to opioid misuse [12]. Anxiety sensitivity, defined as the fear of anxiety-related physical sensations [13], represents one transdiagnostic risk factor that may be differentially associated with opioid misuse. The vast majority of research suggests that anxiety sensitivity consists of three facets reflecting physical concerns, cognitive concerns, and social [14]. Across studies, the three first-order facets measure fears of adverse physical outcomes (Physical Concerns), fears of cognitive dyscontrol (Cognitive Concerns), and fears of the public display of anxiety symptoms [14, Social Concerns, 15]. Importantly, anxiety sensitivity is distinct from trait anxiety [16] and neuroticism [17].

Limited research has examined the relationship between anxiety sensitivity and opioid misuse among individuals with chronic pain. Of the available work, one study found treatment-seeking individuals who primarily used heroin (compared to those who reported polysubstance use) evinced the highest levels of anxiety sensitivity [18]. In this same study, Physical and Social dimensions of anxiety sensitivity were associated with elevated heroin use [18]. In a single case study, a brief intervention targeting anxiety sensitivity reduction among adults seeking treatment for heroin use was successful in lowering anxiety sensitivity as well as heroin craving [19]. Other work has found that anxiety sensitivity is associated with sedative misuse among adults with opioid use disorder [20,21], and that anxiety sensitivity is prospectively predictive of treatment dropout among adults using heroin and/or crack [22]. Although promising, research on anxiety sensitivity has thus far focused on treatment-seeking adults with opioid use disorder and has largely neglected adults with chronic pain despite the linkages between pain experience and opioid use [23,24] and the well-established link between anxiety sensitivity and pain-related functioning [e.g., 25,26].

The fear-avoidance model of chronic pain [27,28] may provide a theoretical framework to understand why AS may be associated with opioid misuse among individuals with chronic pain. This model posits that, following an experience of pain, interpreting such pain as catastrophic (e.g., “I am losing control”) may lead to fear of pain and avoidance of pain-related stimuli, ultimately being associated with increased pain. In the context of the current

examination, individuals higher in AS may be more likely to catastrophically interpret physical and mental sensations. Consequently, such high AS persons may be more apt to try to reduce experiential distress by using opioids as an avoidance-based coping strategy.

Overall, empirical knowledge pertaining to the potential role of anxiety sensitivity among people with chronic pain and opioid use is highly limited. Moreover, no direct tests have been conducted using measures that assess clinically-relevant and multidimensional aspects of opioid use, such as current opioid misuse, severity of opioid dependence, and the number of opioids used in the past month to get high, among a chronic pain population. Thus, it is unclear to what extent anxiety sensitivity uniquely predicts aspects of opioid misuse among those with chronic pain. Thus, the present study was designed to evaluate anxiety sensitivity in relation to current opioid misuse, severity of opioid dependence, and the number of opioids used in the past month to get high. It was hypothesized that higher global levels of anxiety sensitivity would be associated with greater current opioid misuse, severity of opioid dependence, and the number of opioids used in the past month to get high.

METHOD

Participants

Participants were 429 adults (73.9% female, $M_{age} = 38.32$ years, $SD = 11.07$) reporting current chronic pain and opioid use. Participants were recruited via an online survey. Participant eligibility criteria included: (1) being between the ages of 18–64, (2) reported chronic pain (defined as persistent, chronic pain lasting for at least 3 months in duration), (3) having current moderate to severe pain over the previous four weeks, and (4) current use of opioid pain medication. Exclusion criteria included being a non-English speaker (to ensure comprehension of the study questions), and inability to give informed, voluntary, written consent to participate.

The majority of the sample was White/Caucasian (77.9%), with 8.4% identifying as Black/African American, 13.3% Hispanic/Latino, 3.3% Native American/Alaska Native, 1% Asian/Pacific Islander, and 2.8% multiracial. Level of education of the current sample was as followed: 2.3% reported less than a high school education, 3.5% did not complete high school, 30.3% reported attaining a high school diploma (or equivalent), and 22.4% percent reported “some college,” and of the remaining 41.5% indicated completing an associate degree or higher (see Table 1).

Measures

Demographics Questionnaire.—Participants provided data regarding sex, race/ethnicity, age, annual income, and educational level. Demographic information was used to characterize the sample. Age, sex, income level, and education were included as covariates.

Patient Health Questionnaire-4.—The Patient Health Questionnaire-4 (PHQ-4) is a 4-item self-report measure based, in part, upon the PHQ-2 for depression and the GAD-2 for anxiety [29–31]. Items are rated on a 5-point Likert scale ranging from 0 (*not at all*) to 4 (*nearly every day*), with values greater than 5 indicative of moderate to severe depression and/or anxiety [32]. The PHQ-4 has a composite score and two subscales (anxiety and

depression) and has been validated individually and as a composite questionnaire [32]. The PHQ-4 total score was included as a covariate (Cronbach's $\alpha = .91$).

Graded Chronic Pain Scale.—The Graded Chronic Pain Scale (GCPS) is an 8-item measure of self-reported pain severity and pain disability [33]. Pain severity items are rated on 10-point scale from 0 (No pain) to 10 (Pain as bad as could be) while pain disability items are rated on a 10-point scale from 0 (No interference) to 10 (Unable to carry on activities). Higher scores reflect greater pain severity and disability. The GCPS pain severity ($\alpha = .84$) scale was used as a covariate.

Anxiety Sensitivity Index-3.—The Anxiety Sensitivity Index-3 [ASI-3; 34], derived, in part, from the 16-item ASI [13], is an 18-item self-report measure of the sensitivity to and fear of the potential negative consequences of anxiety-related symptoms and sensations [e.g., 34]. Respondents are asked to indicate on a 5-point Likert-type scale ranging from 0 (*very little*) to 4 (*very much*) the degree to which they are concerned about these possible negative consequences. The ASI-3 yields a total score (Cronbach's $\alpha = .97$) as well as three subscales: Physical ("It scares me when my heart beats rapidly"; Cronbach's $\alpha = .93$), Cognitive ("When I cannot keep my mind on a task, I worry that I might be going crazy"; Cronbach's $\alpha = .95$), and Social ("It is important for me not to appear nervous"; Cronbach's $\alpha = .92$) concerns. The ASI-3 has sound psychometric properties, including excellent internal consistency and predictive validity [34].

Current Opioid Misuse Measure.—The Current Opioid Misuse Measure (COMM) is a 17-items questionnaire used to identify people on opioid therapy who are exhibiting behaviors of opioid misuse [35]. Each item is rated on a 5-point scale from 0 (*never*) to 4 (*very often*). A composite score can be created by summing the scores of each item. Test-retest reliability has been established and construct validity demonstrated with positive correlations with urine toxicology results among individuals with chronic pain [35,36]. The COMM total score was used as a criterion variable ($\alpha = .97$).

Severity of Dependence Scale.—Severity of Dependence Scale (SDS) is a 5-item measure of severity of dependence to substances that has been validated for opioid use [37]. The responses are rated on a 4-point scale from 0 (*Never*) to 3 (*Always*) and items are summed to create a total score [38]. The SDS total score was used as a criterion variable (Cronbach's $\alpha = .87$).

Self-Reported Opioid Analgesic Abuse.—Opioid misuse was measured via a self-reported questionnaire assessing past-month misuse of 14 different opioid analgesics [39]. Respondents were asked to indicate whether they used any of the following opioid analgesics in the past month to get high. Response options were yes (1) or no (0) with a total composite score created with higher scores indicating a greater number of opioids used over the past month to get high. The measure has shown strong psychometric properties in samples of opioid misusers, some of whom had concurrent pain [39].

Procedure

Participants were recruited nationally through Qualtrics, an online survey management system. Adults with a Qualtrics Panels account that endorsed moderate to severe chronic pain and current use of opioid pain medication were sent a survey advertisement. Respondents were screened for eligibility and directed to the online anonymous survey. Five hundred and forty-one participants provided informed consent prior to completing the 30-minute survey, and 429 completed the survey. Data quality was screened and verified by Qualtrics staff. Participants could opt to receive their compensation in varying forms (e.g., cash-based incentives [i.e., gift cards], rewards miles, rewards points, etc.) the level of compensation remained consistent across respondents and was equated to 20% to 35% of \$12 (the total cost per complete survey). The study protocol was approved by the Institutional Review Board at the University of Houston.

Analytic Strategy

Analyses were conducted using SPSS version 24. Sample descriptive statistics and zero-order correlations among study variables were analyzed. Second, to evaluate the incremental predictive power of ASI-3, two separate 2-step hierarchical regressions were conducted for the continuous criterion variables (COMM, SDS). Following the primary analyses, additional exploratory analyses were conducted to evaluate specific sub-facets of anxiety sensitivity (i.e., Physical, Cognitive, and Social Concerns) on criterion variables. For all primary analyses, step 1 included covariates (age, sex, income, education, PHQ-4, and pain severity), and step 2 included ASI-3 total score. Model fit for each of the steps was evaluated with the F statistic and increase in variance accounted for (change in R^2) and squared semi-partial correlations (sr^2) were used as measures of effect size for each of the individual predictors.

Investigation of the structure of the composite score of the number of opioids used to get high in the past month showed many people denied any use of opioids to get high, and examining the mean and variance of this outcome revealed overdispersion (variance larger than the mean); thus, we used a negative binomial regression [40]. Model fit was determined using χ^2 criteria and an omnibus test of the tested model compared to the intercepts only model.

RESULTS

Descriptive Statistics

Correlations revealed ASI-3 total score to be positively associated with each of the criterion variables (COMM, SDS, and number of opioids used to get high in the past month) and age, gender, education, pain severity, and PHQ-4 (see Table 2).

Hierarchical Regression Analyses

For COMM total score, step 1 of the model including covariates only was statistically significant ($R^2 = .48$, $F(6, 422) = 65.71$, $p < .001$). Examining the individual predictors indicated that age, gender, PHQ-4, and pain severity were significant predictors of COMM total score. In step 2, where ASI-3 total score was added, the model was significant (R^2

$= .56, F(7, 421) = 75.04, p < .001$) and accounted for a significant increase in R^2 ($R^2 = .07, F(1, 421) = 68.25, p < .001$); ASI-3 total score was a significant predictor of COMM total score (see Table 3).

In predicting SDS total score, step 1 of the model including covariates was significant ($R^2 = .31, F(6, 422) = 31.78, p < .001$). Examining the individual predictors indicated that age, gender, PHQ-4, and pain severity were significant predictors of SDS total score. In step 2, where ASI-3 total score was added, the model was significant ($R^2 = .36, F(7, 421) = 34.46, p < .001$) and accounted for a significant increase in R^2 ($R^2 = .05, F(1, 421) = 35.14, p < .001$), and ASI-3 total score was a significant predictor of SDS total score (see Table 3).

For number of opioids used to get high in the past month, the model fit the data well ($\chi^2(421) = 928.83, \text{value/df} > .001$; omnibus test $< .001$). Examining individual predictors revealed that age, gender, PHQ-4 total score, pain severity, and ASI-3 total score was significantly associated with the outcome variable (see Table 3).

Exploratory Analyses

We then conducted exploratory post hoc tests focused on the anxiety sensitivity lower-order dimensions. For all secondary analyses, step 1 included covariates (age, sex, income, education, PHQ-4, and pain severity), and step 2 included ASI-3 subscales.

For COMM total score, the model with the addition of ASI-3 subscales was significant ($R^2 = .56, F(9, 419) = 59.16, p < .001$) and accounted for a significant increase in R^2 ($R^2 = .08, F(3, 419) = 24.30, p < .001$). Specifically, ASI-3 physical and ASI-3 cognitive concerns were significant predictors of COMM total score (see Table 4).

For SDS total score, exploratory analyses with the addition of ASI-3 subscales was significant ($R^2 = .37, F(9, 419) = 26.91, p < .001$) and accounted for a significant increase in R^2 ($R^2 = .06, F(3, 419) = 12.15, p < .001$). Examining the specific sub-facets indicated that ASI-3 cognitive concerns was the only significant predictor of SDS total score (see Table 4).

In predicting number of opioids used in the past month to get high, analyses examining the individual subscales of ASI-3 revealed that physical, social, and cognitive concerns were all significantly associated with the number of opioids used to get high in the past month (see Table 4).

DISCUSSION

The current study examined the relationship between anxiety sensitivity and opioid misuse among adults with chronic pain who use opioids. Results revealed that, after accounting for covariates, anxiety sensitivity global score was significantly associated with current opioid misuse, severity of opioid dependence, and number of opioids used to get high in the past month. The magnitude of the effect sizes for each of these three models can be characterized as medium to large [41]. These results are largely consistent with past work suggesting that anxiety sensitivity is related to heroin use among treatment-seeking adults [18,19], and extends the findings to adults with chronic pain who use opioids. Importantly, the results from the current investigation suggest that anxiety sensitivity may serve as a putative risk

factor for the expression of more severe opioid misuse among individuals with chronic pain. Additionally, results from the current study are in line with past research suggesting that anxiety-related constructs may, in fact, be more strongly related to opioid use and misuse than pain complaints among individuals with chronic pain [42]. These data are broadly consistent with anxiety sensitivity-informed models of substance use that emphasize the role of expectancies for personal threat as a fundamental construct in negative reinforcement processes related to drug use [43]. Future research should seek to further examine mechanisms that may underlie these associations, such as coping-specific use and drug craving [44].

Exploratory analyses of the sub dimensions of anxiety sensitivity revealed differential associations with each of the opioid misuse criterion variables. Specifically, physical and cognitive concerns were associated with current opioid misuse, whereas cognitive concerns were associated with severity of dependence, and physical, cognitive, and social concerns were each associated with the number of opioids used to get high in the past month. Importantly, the observed effects were evident after considering the shared variance of each of the subscales. Although these data suggest some explanatory specificity, it is noteworthy that at the bivariate level, the magnitude of relations between each of the subscales and outcomes is similar. Thus, these data collectively may suggest that the anxiety sensitivity global factor may be the more parsimonious explanation for elevated opioid misuse. Future longitudinal research can help further parse out the unique contributions of each sub-dimension, and how they may differentially relate to opioid misuse trajectories (e.g., risk for transition from opioid prescription to misuse), or whether a global factor is the best explanatory model.

This finding further contributes to the literature linking anxiety to opioid misuse [12,45] and highlights the potential clinical utility assessing and treating anxiety in this population. For instance, it may be particularly important, prior to prescribing opioids for chronic pain, for practitioners to assess levels of anxiety sensitivity to gauge level of opioid misuse risk. Further, there may be clinical utility in reducing anxiety sensitivity in those who use opioids to mitigate risk of misuse. This approach may be important to reduce catastrophic interpretations of painful experiences that ultimately lead to avoidance-oriented coping behavior (using opioids). Extending upon current work showing efficacy for using Cognitive-Behavioral Therapy and mindfulness techniques to reduce anxiety in the context of chronic pain [46,47], several treatments exist that specifically target anxiety sensitivity may be useful. Some work has shown efficacy for an anxiety sensitivity reduction program among people who use heroin [19], and it is possible this may provide similar benefits for adults with chronic pain who use opioids. Additionally, a number of brief, single session anxiety sensitivity interventions have proven effective for reducing anxiety sensitivity generally [48,49], and have extended to targeting specific sub-dimensions of anxiety sensitivity [50]. Future research should extend these existing interventions to opioid misusing adults with chronic pain.

The current study has several limitations. First, the data were cross-sectional, prohibiting causal and temporal claims to be made. Future longitudinal modeling of the relationships between anxiety sensitivity and opioid misuse among adults with chronic pain would

provide additional evidence as to the direction of observed effects. Additionally, while the current study uses a national sample, it is primarily comprised of Caucasian participants, and thus the results may not be generalizable to different racial and ethnic groups experiencing chronic pain. Third, the current study was comprised exclusively of self-report measures, suggesting that the observed results may be due to shared method variance. Future research should seek to collect a combination of objective and subjective measures to support the validity of these findings. Fourth, examining the item content of the COMM suggests that this measure primarily captures aberrant drug use behaviors, and not overall opioid misuse. Therefore, future research should develop a more balanced, comprehensive measure of opioid misuse and test the relationship with AS, and confirm the current findings with other indices of opioid misuse [e.g., 51]. Further, the Self-Reported Opioid Analgesic Abuse questionnaire was merely a checkbox questionnaire where participants indicated how many of the listed opioids they used in the past month. It is important to recognize that some individuals may use more than 1 type of opioid infrequently (2 types, 4 times a month), compared to someone who uses 1 type of opioid daily, and this may not, ultimately be the most robust measure of opioid misuse. However, coupled with the other measures in the study, we believe this provides an important proxy for opioid misuse that should be explored in future research.

Overall, the current study provides initial empirical evidence that anxiety sensitivity is associated with increased opioid misuse among adults with chronic pain who use opioids. These results may provide potentially useful information about a transdiagnostic construct that may be important to better understanding the complexities of opioid misuse.

References

- [1]. Center for Disease Control and Prevention. Provisional counts of drug overdose deaths, as of 8/6/2017. 2017.
- [2]. Rudd RA, Seth P, David F, Scholl L. Increases in Drug and Opioid-Involved Overdose Deaths - United States, 2010–2015. *MMWR Morb Mortal Wkly Rep* 2016;65:1445–52. doi:10.15585/mmwr.mm65051e1. [PubMed: 28033313]
- [3]. Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years. *JAMA Psychiatry* 2014;71:821–6. doi:10.1001/jamapsychiatry.2014.366. [PubMed: 24871348]
- [4]. Nelson LS, Juurlink DN, Perrone J. Addressing the Opioid Epidemic. *JAMA* 2015;314:1453–4. doi:10.1001/jama.2015.12397. [PubMed: 26461995]
- [5]. Blanco C, Wall MM, Okuda M, Wang S, Iza M, Olfson M. Pain as a Predictor of Opioid Use Disorder in a Nationally Representative Sample. *Am J Psychiatry* 2016;173:1189–95. doi:10.1176/appi.ajp.2016.15091179. [PubMed: 27444794]
- [6]. Novak SP, Glasheen C, Roland CL. Prescription pain reliever misuse and levels of pain impairment: 3-year course in a nationally representative outpatient sample of US adults. *Subst Abuse Rehabil* 2016;7:87–98. doi:10.2147/SAR.S102251. [PubMed: 27418863]
- [7]. Dowell D, Haegerich T, Chou R. CDC Guidelines for Prescribing Opioids for Chronic Pain - United States, 2016 2016;1:1–49. doi:10.15585/mmwr.rr6501e1.
- [8]. Lee JD, Nunes EV, Novo P, Bachrach K, Bailey GL, Bhatt S, et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. *The Lancet* 2018;391:309–18. doi:10.1016/S0140-6736(17)32812-X.
- [9]. Weiss RD, Potter JS, Fiellin DA, Byrne M, Connery HS, Dickinson W, et al. Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid

- dependence: a 2-phase randomized controlled trial. *Arch Gen Psychiatry* 2011;68:1238–46. doi:10.1001/archgenpsychiatry.2011.121. [PubMed: 22065255]
- [10]. Lewandowski KE, Ongur D, Keshavan MS. Development of novel behavioral interventions in an experimental therapeutics world: Challenges, and directions for the future. *Schizophr Res* 2018;192:6–8. doi:10.1016/j.schres.2017.06.010. [PubMed: 28629888]
- [11]. Martins SS, Fenton MC, Keyes KM, Blanco C, Zhu H, Storr CL. Mood and anxiety disorders and their association with non-medical prescription opioid use and prescription opioid-use disorder: longitudinal evidence from the National Epidemiologic Study on Alcohol and Related Conditions. *Psychol Med* 2012;42:1261–72. doi:10.1017/S0033291711002145. [PubMed: 21999943]
- [12]. McHugh RK, Weiss RD, Cornelius M, Martel MO, Jamison RN, Edwards RR. Distress Intolerance and Prescription Opioid Misuse Among Patients With Chronic Pain. *J Pain* 2016;17:806–14. doi:10.1016/j.jpain.2016.03.004. [PubMed: 27058161]
- [13]. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Behav Res Ther* 1986;24:1–8. [PubMed: 3947307]
- [14]. Zinbarg RE, Mohlman J, Hong NN. Dimensions of anxiety sensitivity. *Anxiety Sensit Theory Res Treat Fear Anxiety* 1999.
- [15]. Stewart SH, Taylor S, Baker JM. Gender differences in dimensions of anxiety sensitivity. *J Anxiety Disord* 1997;11:179–200. [PubMed: 9168341]
- [16]. Rapee RM, Medoro L. Fear of physical sensations and trait anxiety as mediators of the response to hyperventilation in nonclinical subjects. *J Abnorm Psychol* 1994;103:693–9. [PubMed: 7822570]
- [17]. Zvolensky MJ, Kotov R, Antipova AV, Schmidt NB. Cross cultural evaluation of smokers risk for panic and anxiety pathology: a test in a Russian epidemiological sample. *Behav Res Ther* 2003;41:1199–215. [PubMed: 12971940]
- [18]. Lejuez CW, Paulson A, Daughters SB, Bornovalova MA, Zvolensky MJ. The association between heroin use and anxiety sensitivity among inner-city individuals in residential drug use treatment. *Behav Res Ther* 2006;44:667–77. doi:10.1016/j.brat.2005.04.006. [PubMed: 16002042]
- [19]. Tull MT, Schulzinger D, Schmidt NB, Zvolensky MJ, Lejuez CW. Development and initial examination of a brief intervention for heightened anxiety sensitivity among heroin users. *Behav Modif* 2007;31:220–42. doi:10.1177/0145445506297020. [PubMed: 17307936]
- [20]. Hearon BA, Calkins AW, Halperin DM, McHugh RK, Murray HW, Otto MW. Anxiety sensitivity and illicit sedative use among opiate-dependent women and men. *Am J Drug Alcohol Abuse* 2011;37:43–7. doi:10.3109/00952990.2010.535581. [PubMed: 21090958]
- [21]. McHugh RK, Votaw VR, Bogunovic O, Karakula SL, Griffin ML, Weiss RD. Anxiety sensitivity and nonmedical benzodiazepine use among adults with opioid use disorder. *Addict Behav* 2017;65:283–8. doi:10.1016/j.addbeh.2016.08.020. [PubMed: 27575980]
- [22]. Lejuez CW, Zvolensky MJ, Daughters SB, Bornovalova MA, Paulson A, Tull MT, et al. Anxiety sensitivity: A unique predictor of dropout among inner-city heroin and crack/cocaine users in residential substance use treatment. *Behav Res Ther* 2008;46:811–8. doi:10.1016/j.brat.2008.03.010. [PubMed: 18466878]
- [23]. Parsells Kelly J, Cook SF, Kaufman DW, Anderson T, Rosenberg L, Mitchell AA. Prevalence and characteristics of opioid use in the US adult population. *PAIN* 2008;138:507–13. doi:10.1016/j.pain.2008.01.027. [PubMed: 18342447]
- [24]. Volkow ND, McLellan AT. Opioid Abuse in Chronic Pain — Misconceptions and Mitigation Strategies. *N Engl J Med* 2016;374:1253–63. doi:10.1056/NEJMr1507771. [PubMed: 27028915]
- [25]. Asmundson GJG, Taylor S. Role of anxiety sensitivity in pain-related fear and avoidance. *J Behav Med* 1996;19:577–86. doi:10.1007/BF01904905. [PubMed: 8970916]
- [26]. Norton PJ, Asmundson GJG. Anxiety sensitivity, fear, and avoidance behavior in headache pain. *Pain* 2004;111:218–23. doi:10.1016/j.pain.2004.06.018. [PubMed: 15327826]

- [27]. Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain* 2000;85:317–32. doi:10.1016/S0304-3959(99)00242-0. [PubMed: 10781906]
- [28]. Lethem J, Slade PD, Troup JD, Bentley G. Outline of a Fear-Avoidance Model of exaggerated pain perception--I. *Behav Res Ther* 1983;21:401–8. [PubMed: 6626110]
- [29]. Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003;41:1284–92. doi:10.1097/01.MLR.0000093487.78664.3C. [PubMed: 14583691]
- [30]. Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med* 2007;146:317–25. [PubMed: 17339617]
- [31]. Löwe B, Kroenke K, Gräfe K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). *J Psychosom Res* 2005;58:163–71. doi:10.1016/j.jpsychores.2004.09.006. [PubMed: 15820844]
- [32]. Löwe B, Wahl I, Rose M, Spitzer C, Glaesmer H, Wingenfeld K, et al. A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord* 2010;122:86–95. doi:10.1016/j.jad.2009.06.019. [PubMed: 19616305]
- [33]. Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. *Pain* 1992;50:133–49. [PubMed: 1408309]
- [34]. Taylor S, Zvolensky MJ, Cox BJ, Deacon B, Heimberg RG, Ledley DR, et al. Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. *Psychol Assess* 2007;19:176–88. doi:10.1037/1040-3590.19.2.176. [PubMed: 17563199]
- [35]. Butler SF, Budman SH, Fernandez KC, Houle B, Benoit C, Katz N, et al. Development and Validation of the Current Opioid Misuse Measure. *Pain* 2007;130:144–56. doi:10.1016/j.pain.2007.01.014. [PubMed: 17493754]
- [36]. Wasan AD, Butler SF, Budman SH, Benoit C, Fernandez K, Jamison RN. Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. *Clin J Pain* 2007;23:307–15. doi:10.1097/AJP.0b013e3180330dc5. [PubMed: 17449991]
- [37]. Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W, et al. The Severity of Dependence Scale (SDS): Psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction* 1995;90:607–14. doi:10.1111/j.1360-0443.1995.tb02199.x. [PubMed: 7795497]
- [38]. Iraurgi Castillo I, González Saiz F, Lozano Rojas O, Landabaso Vázquez MA, Jiménez Lerma JM. Estimation of cutoff for the Severity of Dependence Scale (SDS) for opiate dependence by ROC analysis. *Actas Esp Psiquiatr* 2010;38:270–7. [PubMed: 21117001]
- [39]. Smith M, Rosenblum A, Parrino M, Fong C, Colucci S. Validity of self-reported misuse of prescription opioid analgesics. *Subst Use Misuse* 2010;45:1509–24. doi:10.3109/10826081003682107. [PubMed: 20590372]
- [40]. Hilbe JM. *Negative Binomial Regression*. Cambridge University Press; 2011.
- [41]. Ferguson CJ. *An Effect Size Primer : A Guide for Clinicians and Researchers*. *Prof Psychol Res Pract* 2009;40:532–8.
- [42]. Martel MO, Finan PH, McHugh RK, Issa M, Edwards RR, Jamison RN, et al. Day-to-day pain symptoms are only weakly associated with opioid craving among patients with chronic pain prescribed opioid therapy. *Drug Alcohol Depend* 2016;162:130–6. doi:10.1016/j.drugalcdep.2016.02.047. [PubMed: 27021805]
- [43]. Leventhal AM, Zvolensky MJ. Anxiety, Depression, and Cigarette Smoking: A Transdiagnostic Vulnerability Framework to Understanding Emotion-Smoking Comorbidity. *Psychol Bull* 2015;141:176–212. doi:10.1037/bul0000003. [PubMed: 25365764]
- [44]. Martel MO, Jamison RN, Wasan AD, Edwards RR. The association between catastrophizing and craving in patients with chronic pain prescribed opioid therapy: A preliminary analysis. *Pain Med* 2014;15:1757–64. doi:10.1111/pme.12416. [PubMed: 24612286]

- [45]. Martel MO, Wasan AD, Jamison RN, Edwards RR. Catastrophic thinking and increased risk for prescription opioid misuse in patients with chronic pain. *Drug Alcohol Depend* 2013;132:335–41. doi:10.1016/j.drugalcdep.2013.02.034. [PubMed: 23618767]
- [46]. Garland EL, Manusov EG, Froeliger B, Kelly A, Williams JM, Howard MO. Mindfulness-oriented recovery enhancement for chronic pain and prescription opioid misuse: results from an early-stage randomized controlled trial. *J Consult Clin Psychol* 2014;82:448–59. doi:10.1037/a0035798. [PubMed: 24491075]
- [47]. Asmundson GJG, Katz J. Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. *Depress Anxiety* 2009;26:888–901. doi:10.1002/da.20600. [PubMed: 19691031]
- [48]. Keough ME, Schmidt NB. Refinement of a brief anxiety sensitivity reduction intervention. *J Consult Clin Psychol* 2012;80:766–72. doi:10.1037/a0027961. [PubMed: 22468909]
- [49]. Schmidt NB, Eggleston AM, Woolaway-Bickel K, Fitzpatrick KK, Vasey MW, Richey JA. Anxiety Sensitivity Amelioration Training (ASAT): A longitudinal primary prevention program targeting cognitive vulnerability. *J Anxiety Disord* 2007;21:302–19. doi:10.1016/j.janxdis.2006.06.002. [PubMed: 16889931]
- [50]. Schmidt NB, Capron DW, Raines AM, Allan NP. Randomized clinical trial evaluating the efficacy of a brief intervention targeting anxiety sensitivity cognitive concerns. *J Consult Clin Psychol* 2014;82:1023–33. doi:10.1037/a0036651. [PubMed: 24821096]
- [51]. Jamison RN, Sheehan KA, Scanlan E, Matthews M, Ross EL. Beliefs and attitudes about opioid prescribing and chronic pain management: survey of primary care providers. *J Opioid Manag* 2014;10:375–82. doi:10.5055/jom.2014.0234. [PubMed: 25531955]

Table 1.**Demographics**

Gender	N	%
Female	317	73.9
Male	111	25.9
Race/Ethnicity	N	%
White/Caucasian	334	77.9
Black/African American	36	8.4
Hispanic/Latino	57	13.3
Native American/Alaska Native	14	3.3
Asian/Pacific Islander	4	1
Multiracial	12	2.8
Level of Education	N	%
Less than High School Education	10	2.3
Some High School Education	15	3.5
High School Diploma	130	30.3
Some College	96	22.4
Associate Degree	68	15.9
Bachelor's Degree	70	16.3
Master's Degree	26	6.1
Professional or Doctoral Degree	14	3.3
Income Level	N	%
\$0-\$4,999	22	5.1
\$5,000-\$9,999	27	6.3
\$10,000-\$14,999	32	7.5
\$15,000-\$24,999	46	10.7
\$25,000-\$34,999	61	14.2
\$35,999-\$49,999	75	17.5
\$50,000-\$74,999	88	20.5
> \$75,000	70	16.3
Did not Disclose	8	1.9

Table 2.

Bivariate correlations

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age	-												
2. Gender	-.027	-											
3. Income	-.040	.058	-										
4. Education	-.040	.060	.409**	-									
5. Pain Severity	.156**	-.077	-.029	-.045	-								
6. PHQ-4	-.176**	.144**	-.006	.139**	.138**	-							
7. ASI3-Total	-.242**	.096*	.048	.096*	.178**	.673**	-						
8. ASI3-Physical	-.151**	.088	.039	.074	.175**	.603**	.946**	-					
9. ASI3-Cognitive	-.297**	.140**	.042	.102*	.147**	.679**	.952**	.852**	-				
10. ASI3-Social	-.241**	.046	.054	.098*	.184**	.633**	.947**	.840**	.853**	-			
11. COMM	-.277**	.250**	.083	.145**	.165**	.633**	.659**	.609**	.668**	.597**	-		
12. SDS	-.186**	.204**	.063	.126**	.193**	.502**	.536**	.495**	.540**	.490**	.708**	-	
13. Opioid Misuse	-.200**	.166**	.070	.088	.146**	.403**	.453**	.433**	.468**	.387**	.641**	.631**	-

Note. N = 429;

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

Table 3.**Hierarchical Regression Results**

Current Opioid Misuse Measure (COMM)							
Model		b	SE	β	t	p-value	sr²
1	Age	−0.30	0.06	−0.19	−5.23	<.001	.03
	Gender	6.72	1.34	0.18	5.03	<.001	.03
	Income	0.49	0.32	0.06	1.55	.121	.00
	Education	0.28	0.43	0.03	0.65	.515	.00
	PHQ-4	2.46	0.17	0.56	14.91	<0.001	.27
	Pain Severity	0.41	0.11	0.13	3.54	<0.001	.02
2	Age	−0.22	0.05	−0.14	−4.09	<.001	.02
	Gender	6.50	1.24	0.17	5.24	<.001	.03
	Income	0.35	0.30	0.04	1.19	.236	.00
	Education	0.34	0.40	0.03	0.85	.398	.00
	PHQ-4	1.42	0.20	0.32	7.15	<.001	.05
	Pain Severity	0.27	0.12	0.09	2.55	.011	.01
	ASI-3 Total	0.30	0.04	0.37	8.26	<.001	.07
Severity of Dependence Scale (SDS)							
Model		b	SE	β	t	p-value	sr²
1	Age	−0.05	0.01	−0.10	−2.30	.022	.01
	Gender	1.24	0.35	0.13	3.18	.002	.02
	Income	0.05	0.08	0.04	0.79	.431	.00
	Education	0.10	0.11	0.03	0.67	.501	.00
	PHQ-4	0.42	0.04	0.46	10.80	<.001	.20
	Pain Severity	0.12	0.03	0.17	4.07	<.001	.03
2	Age	−0.03	0.01	−0.09	−2.12	.034	.01
	Gender	1.20	0.33	0.15	3.66	<.001	.02
	Income	0.03	0.08	0.02	0.34	.734	.00
	Education	0.11	0.11	0.05	1.05	.293	.00
	PHQ-4	0.22	0.05	0.23	4.24	<.001	.03
	Pain Severity	0.09	0.03	0.14	3.31	.001	.02
	ASI-3 Total	0.06	0.01	0.32	5.93	<.001	.05
Opioid Misuse							
Model		b	SE	CI (l)	CI (u)	χ^2	p-value
1	Age	−0.04	0.01	−0.05	−0.03	31.08	<.001
	Gender	0.40	0.14	0.12	0.68	7.76	.005
	Income	0.04	0.03	−0.03	0.10	1.11	.292
	Education	−0.03	0.04	−0.12	0.05	0.54	.464
	PHQ-4	0.08	0.02	0.04	0.12	13.14	<.001
	Pain Severity	0.05	0.01	0.02	0.07	14.25	<.001
	ASI-3 Total	0.02	0.00	0.02	0.03	34.13	<.001

Models represent 2-step hierarchical regressions, with step 1 including covariates (age, gender, income, education, PHQ-4, pain severity), and step 2 included all covariates plus ASI-3 total score. b = unstandardized beta coefficient, SE = standard error, β = standardized beta coefficient, t = t statistic, $CI(l)$ = lower 95% confidence interval, $CI(u)$ = upper 95% confidence interval, sr^2 = squared semi-partial correlation.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 4.

Post-Hoc Hierarchical Regression Results

		Current Opioid Misuse Measure (COMM)					
Model		b	SE	β	t	p-value	sr ²
1	Age	−0.30	0.06	−0.19	−5.23	<.001	.03
	Gender	6.72	1.34	0.18	5.03	<.001	.03
	Income	0.49	0.32	0.06	1.55	.121	.00
	Education	0.28	0.43	0.03	0.65	.515	.00
	PHQ-4	2.46	0.17	0.56	14.91	<.001	.27
	Pain Severity	0.41	0.11	0.13	3.54	<.001	.02
2	Age	−0.22	0.06	−0.14	−3.93	<.001	.02
	Gender	6.12	1.25	0.16	4.88	<.001	.03
	Income	0.37	0.30	0.04	1.24	.215	.00
	Education	0.35	0.40	0.03	0.87	.383	.00
	PHQ-4	1.40	0.20	0.32	6.99	<.001	.05
	Pain Severity	0.28	0.11	0.09	2.64	.009	.01
	ASI-3 Physical	0.41	0.16	0.18	2.52	.012	.01
	ASI-3 Cognitive	0.51	0.18	0.23	2.92	.004	.01
	ASI-3 Social	−0.02	0.16	−0.01	−0.10	.919	.00
		Severity of Dependence Scale (SDS)					
Model		b	SE	β	t	p-value	sr ²
1	Age	−0.05	0.01	−0.10	−2.30	.022	.01
	Gender	1.24	0.35	0.13	3.18	.002	.02
	Income	0.05	0.08	0.04	0.79	.431	.00
	Education	0.10	0.11	0.03	0.67	.501	.00
	PHQ-4	0.42	0.04	0.46	10.80	<.001	.20
	Pain Severity	0.12	0.03	0.17	4.07	<.001	.03
2	Age	−0.03	0.02	−0.08	−1.96	.050	.01
	Gender	1.14	0.33	0.14	3.42	.001	.02
	Income	0.03	0.08	0.02	0.37	.711	.00
	Education	0.11	0.11	0.05	1.06	.292	.00
	PHQ-4	0.22	0.05	0.22	4.09	<.001	.03
	Pain Severity	0.10	0.03	0.14	3.35	.001	.02
	ASI-3 Physical	0.06	0.04	0.12	1.44	.150	.00
	ASI-3 Cognitive	0.10	0.05	0.20	2.10	.037	.01
	ASI-3 Social	0.01	0.04	0.03	0.30	.763	.00
		Opioid Misuse					
Model		b	SE	CI (l)	CI (u)	χ^2	p-value
1	Age	−0.04	0.01	−0.05	−0.03	31.60	<.001
	Gender	0.27	0.15	−0.01	0.56	3.47	.063
	Income	0.04	0.03	−0.02	0.11	1.61	.204
	Education	−0.03	0.04	−0.11	0.06	0.34	.561

PHQ-4	0.07	0.02	0.03	0.12	10.23	.001
Pain Severity	0.05	0.01	0.03	0.08	15.20	<.001
ASI-3 Physical	0.08	0.02	0.03	0.12	11.49	.001
ASI-3 Cognitive	0.09	0.02	0.05	0.14	15.31	<.001
ASI-3 Social	-0.10	0.02	-0.14	-0.05	15.55	<.001

Models represent 2-step hierarchical regressions, with step 1 including covariates (age, gender, income, education, PHQ-4, pain severity), and step 2 included all covariates plus ASI-3 subscales (Physical, Cognitive, Social). b = unstandardized beta coefficient, SE = standard error, β = standardized beta coefficient, t = t statistic, $CI(l)$ = lower 95% confidence interval, $CI(u)$ = upper 95% confidence interval, sr^2 = squared semi-partial correlation.