Title: Pain Severity Ratings Among Patients with Comorbid Chronic Pain and PTSD: A Retrospective Cohort Study

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ABSTRACT

Background: Posttraumatic stress disorder (PTSD) is a psychiatric disorder that may occur after experiencing or witnessing a traumatic event. PTSD is characterized by physiological symptoms such as sleep disturbances and hyperarousal. One understudied symptom in PTSD patients is chronic pain (CP). Acute pain can lead to CP when it persists beyond adaptation. The interconnection between stress and pain has been well-established in fields of neuroscience and psychology, though we still do not fully understand the nature of this clinical relationship.

Methods: In the current retrospective cohort study, we use a sample of patients with PTSD and CP through a database of numerous healthcare organizations called TriNetX. We compare the reported pain severity rating between three groups: those with PTSD and no CP, those with CP and no PTSD, and those with comorbid PTSD and CP. The summary data was compared using a one-way analysis of variance with the Welch statistic.

Results: The average reported pain severity was significantly different between all three groups ($F(2, 21288)=279.80$, $p < .001$). The patients with comorbid PTSD and CP reported the highest average pain severity, followed by patients with only CP and then patients with only PTSD.

Conclusion: Our results demonstrate a need to further investigate the complex relationship between PTSD and CP. The higher average pain severity in patients with both disorders suggest that integrated pain management and mental health interventions must be prioritized in this population.

Key Words: Chronic pain; post-traumatic stress disorder; anxiety disorder; trauma, psychological; pain severity; retrospective cohort study; pain management; mental health comorbidities.

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience often due to tissue damage. Often, pain is an adaptive experience to let the body know of this damage. However, pain can turn into chronic pain when it persists beyond adaptation. Chronic pain is frequently comorbid with other medical and psychiatric problems.

Posttraumatic stress disorder (PTSD) is a psychiatric disorder that may occur after experiencing or witnessing a traumatic event. Symptoms of PTSD include panic attacks, avoidance of triggers of the event, sleep disturbances, hyperarousal, and irritability. PTSD is often comorbid with other psychiatric disorders, mainly depression and substance use disorders, as reviewed by Morasco et al. (2013).[1]

A number of studies have documented the comorbidity and mutual maintenance between chronic pain and PTSD.[2-4] In several cohorts of veterans, those diagnosed with PTSD had higher pain severity, pain interference, and pain catastrophizing than those without PTSD.[5, 6] In a meta-analysis of studies from 1995 to 2016, PTSD prevalence was about 20% among patients with widespread chronic pain.[7] This appears to be a bidirectional relationship, where severity of initial pain of injury predicts development of PTSD, and the onset of PTSD is equally as predictive of development of chronic pain.[8] Further, there is a well-established correlation between pain symptom severity and PTSD-like symptoms.[9, 10] Though the frequency of the comorbidity is well-established, there are still questions about the nature of the relationship between the two disorders and whether the relationship is temporal.

There is also research demonstrating that having comorbid PTSD and chronic pain exacerbates symptoms of both disorders. In a systematic review of studies using traumatized refugees, those with chronic pain had more severe PTSD symptoms than those without chronic pain.[11] A similar result was found in a population of patients seeking chronic pain treatment in Sweden.[12] In 28.7% of the patients that met criteria for PTSD, patients exhibited higher severity of pain, fear of pain from movement, anxiety, and depression. These results and others, such as those reported by Reed et al. (2024), show that patients with comorbid PTSD and chronic pain are more likely to have additional psychiatric disorders and are more likely to commit suicide than those with PTSD or chronic pain alone.[13] Further, those with comorbid PTSD and chronic pain are more likely to heavily use opioids and benzodiazepines, which may escalate to dependence.[14, 15]

This comorbidity is unsurprising given the overlap of neural pathways for pain and traumatic memories.[2] Fearful and negative memories, including fear and memory of pain, have been long associated with the limbic system.[16] A number of neurological indicators have been observed in both PTSD and chronic pain, including significant elevations in neuropeptide Y, allopregnanolone, and pregnanolone. Other systems

that appear to play roles in both disorders include GABAergic neuroactive steroids, opioids and endocannabinoids, immune factors, and several second messengers.

Despite evidence of this comorbidity, there is a lack of research on comorbid PTSD and chronic pain patients across these populations. In the current study, we seek to compare the severity of pain reported by patients with PTSD, chronic pain (CP), and comorbid PTSD and CP in a retrospective cohort of patients from the TriNetX database. Establishing a relationship in the pain severity of these populations will better allow providers to manage and treat these conditions together.

METHODS

We gathered a retrospective cohort of patients across multiple healthcare organizations who were reported to be diagnosed with chronic pain only, PTSD only, and comorbid PTSD and chronic pain, respectively. The retrospective cohort was obtained through the TriNetX database. TriNetX is a research network providing researchers access to extensive deidentified patient information extracted from the electronic health records (EHRs) of over 250 million patients worldwide. Our study focused on a network of 61 HCOs, encompassing over 105 million patients exclusively from the United States.

We included patients between the ages of 18 and 90 years and records reported from 2000 to 2024. We identified our three cohorts using inclusion and exclusion criteria from the International Classification of Diseases, 10th Revision (ICD-10) codes, which were reported in the TriNetX database. Patients in the PTSD group were required to have ICD-10-CM F43.1 Post-traumatic stress disorder (PTSD) and were excluded if they met criteria for any of the following ICD-10-CM chronic pain diagnoses: R52 Pain, unspecified; F45.41 Pain disorder exclusively related to psychological factors; G89.2 Chronic pain, not elsewhere classified; G89.29 Other chronic pain; G89.4 Chronic pain syndrome. The CP (chronic pain) group met at least one of the five pain criteria and were excluded if they met criteria for PTSD. The PTSD/CP group met at least one of the five pain criteria and they met criteria for PTSD. There were no exclusions for other psychiatric and pain disorders.

Finally, all three cohorts were reduced to those with a self-reported pain severity value. The pain severity rating was on a scale from 1 to 10, with 1 being no pain and 10 being the most severe pain level. The means and standard deviations (SDs) of the reported pain severity was recorded for each of the three cohorts. Using the SPSS Statistics program, we performed a Welch one-way analysis of variance (ANOVA) to compare the means for these three groups. The Welch statistic was used since homogeneity of variance could not be assumed due to the lack of raw data provided by TriNetX. Finally, a post hoc

Tukey Honest Significant Difference (HSD) test was performed to determine pairwise differences between groups. We did not adjust for confounders in this study.

Ethical Considerations: Given the use of de-identified patient records and the absence of any collection, use, or transmission of individually identifiable data in this retrospective cohort study, it was deemed exempt from institutional review board approval and informed consent as per the Health Insurance Portability and Accountability Act (HIPAA). Furthermore, we strictly adhered to the reporting guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) framework throughout all phases of our investigation.

RESULTS

The US collaborative Network TriNetX has 105,703,806 patients across 61 healthcare organizations (HCOs). We were able to identify 5,673 patients in the PTSD/CP group, 6,113 patients in the PTSD group, and 9,505 patients in the CP group (Figure 1, Table 1). The PTSD/CP group had M=5.07 and SD=2.94, the PTSD group had M=3.75 and SD=3.20, and the CP group had M=4.34 and SD=2.97.

A one-way ANOVA was run using the summary data provided by TriNetX. The test was significant between the three groups, Welch's $F(2, 21288)=279.80$, $p<.001$ (Table 2). A Tukey Honest Significant Difference (HSD) test was performed in order to compare each pair of groups. All three pairs of groups (PTSD/CP-PTSD only, PTSD/CP-CP only, PTSD only-CP only) were significantly different with $p<.001$ for each pairing. The eta-squared value of effect size was .026, indicating a small effect. Demographic data was not available for this cohort.

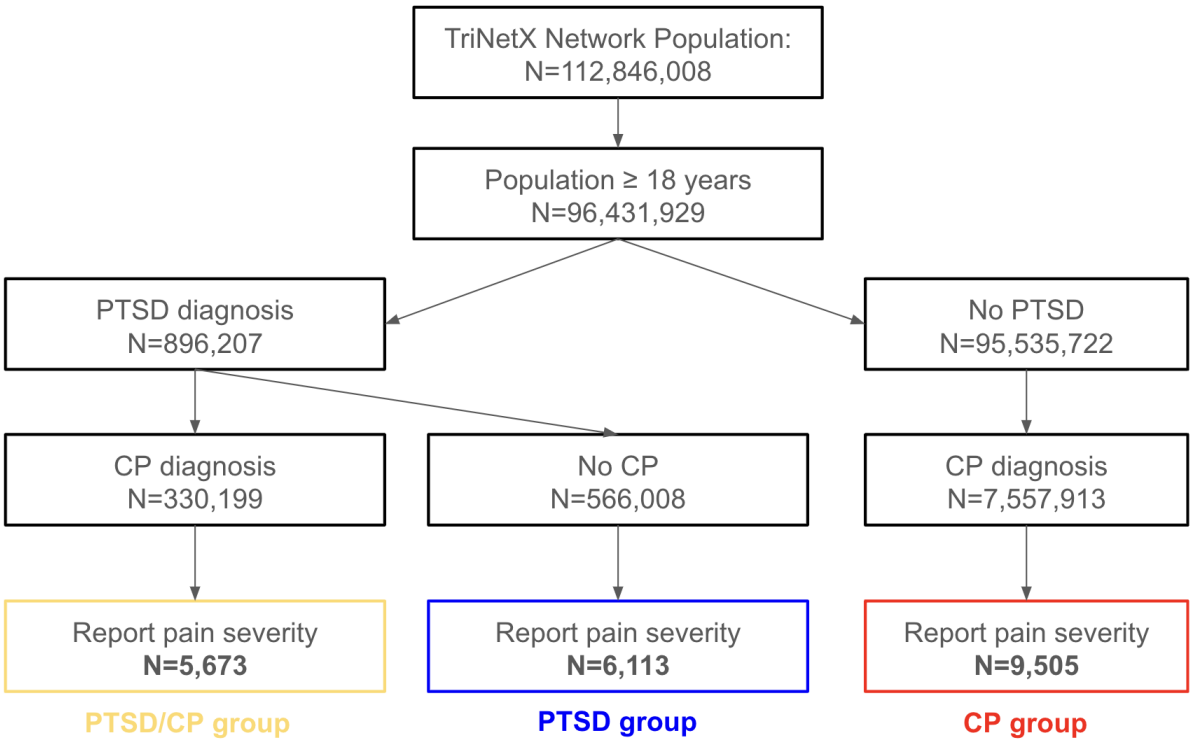

Figure 1. Study flowchart.

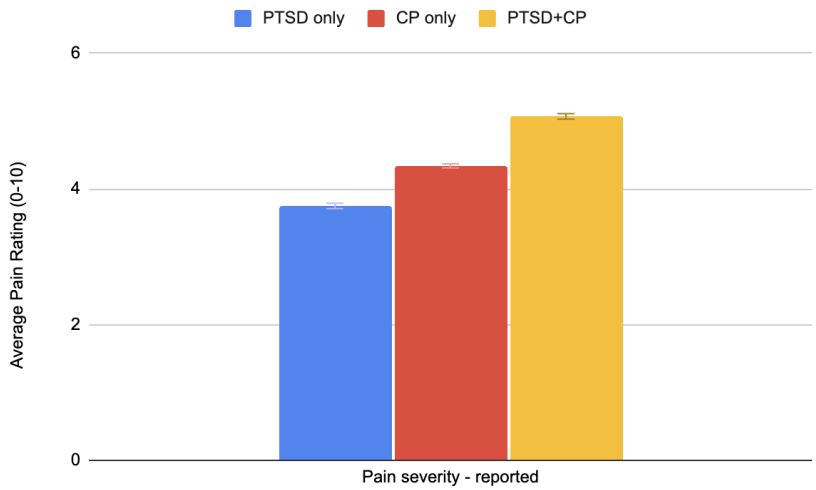

Figure 2. Average pain severity of each group. Pain was on a scale from 1-10 with 1 being no pain and 10 being the most severe pain. Error bars represent standard error (SE) for each group.

Table 1. Descriptive statistics. SD = Standard Deviation; SE = Standard Error.

Group	N	Mean	SD	SE	95% Confidence Interval	
					Lower Bound	Upper Bound
PTSD	6113	3.75	3.20	.04	3.67	3.83
CP	9505	4.34	2.97	.03	4.28	4.40
PTSD+CP	5673	5.07	2.94	.04	4.99	5.15
Total	21291	4.37	3.07	.02	4.32	4.41

Table 2. Welch one-way ANOVA.

	Sum of Squares	df	Mean Square	F	Sig
Between Groups	5137.65	2	2568.83	279.83	<.001
Within Groups	195447.21	21288	9.18		
Total	200584.87	21290			

DISCUSSION

In the current study, the pain severity experienced by those with chronic pain was exacerbated when the patients also had a PTSD diagnosis. Patients with both PTSD and chronic pain reported significantly higher pain severity than those with PTSD alone. This was a small effect size. Expectedly, patients with only PTSD reported the lowest pain severity levels. These results add to the growing body of literature on comorbid PTSD and chronic pain.

There are a number of theories explaining the frequent comorbidity of these disorders. Otis et al.[17] reviewed several of these. One hypothesis, known as the Shared Vulnerability Model, theorizes that patients with a predisposition for anxiety are more vulnerable to developing both chronic pain and PTSD. In this model, a person with high anxiety sensitivity is more likely to become fearful in response to physiological sensations, including pain. Anxiety sensitivity also increased people's fear and avoidance of pain, also known as pain catastrophizing, allowing chronic pain maintenance to persist.[18] The effect of pain catastrophizing on PTSD and chronic pain symptoms is seen in youth as well as adults.[19] Another proposed theory is the Triple Vulnerability Model, which postulates that three factors must be present for the comorbidity to occur: a general biological vulnerability, a general psychological vulnerability, and a more specific psychological vulnerability where one focuses their anxiety on a specific situation. This model is supported by research that demonstrates a lower pain threshold in those with PTSD in comparison to those with other anxiety disorders and a control group.[20, 21]

Further, the current literature also points to a mutual maintenance relationship between these two disorders.[22, 23] Cognition related to pain, meaning the interpretation of and excessive attention to pain, is associated with higher levels of distress and avoidance, which may exacerbate or precipitate PTSD symptoms. The shared aspect of fear-based avoidance in both PTSD and chronic pain seems to underpin this mutual maintenance model. Our findings support the theory of mutual maintenance as pain was exacerbated in patients with comorbid PTSD. Similar to the mutual maintenance model is the shared vulnerability model of PTSD-chronic pain comorbidity, as previously described.[18, 24, 25] These models are the basis of current evidence-based therapies for these disorders. These treatments primarily involve cognitive behavioral therapy (CBT) and interdisciplinary pain programs (IPPs).[25] By targeting anxiety as a common thread between the two disorders, CBT may be an effective way to reduce occurrence of both PTSD and chronic pain.[26] Since our current analysis did not look at temporality between PTSD and chronic pain, the possibility of shared vulnerability in this cohort is unclear. Prospective studies are needed to illustrate the causality between these two disorders.

Interestingly, studies have shown that previous trauma does not have to be physical or pain-related to see this association with chronic pain. Kascakova et al.[27] found that childhood emotional abuse and

emotional neglect, in addition to physical neglect, were associated with higher odds of chronic pain and anxiety conditions later in life. Results such as these point to the significant role of emotional trauma, rather than physical trauma, in the relationship between PTSD and chronic pain.

For the same reasons it is associated with PTSD, chronic pain is frequently comorbid with several other psychiatric disorders. As described in the aforementioned models, anxiety disorders play a large role in the relationship between chronic pain and PTSD.[9, 10] Similarly, depression has been demonstrated to be associated with PTSD and pain severity.[8] Depression is often comorbid with PTSD and has been found to be a mediator of PTSD and higher pain severity and interference.[1]

One systematic review found different rates of PTSD among patients with different types of chronic pain.[28] For example, the prevalence of both PTSD and chronic pain were highest in the veteran population. This result may be because veterans are more likely to experience traumatic events and physical injuries resulting in pain and does not necessarily illustrate the association between the two disorders. Since the majority of PTSD literature focuses on veterans, this point indicates that PTSD research on non-veterans should be further explored. Another aspect of this relationship that must be further explored is that of patients with complex PTSD (CPTSD), usually driven by childhood trauma and/or recurrent traumatic events.[29] Some studies have shown that patients with CPTSD have even higher rates of chronic pain than those with PTSD. This result may be due to the more severe avoidance and anxiety symptoms observed in those with CPTSD. Further research of this population is needed to explore the association with different presentations and sources of PTSD. Future investigations are also needed to assess integrated treatment of these disorders and screen for this comorbidity.

Limitations: There are several limitations to our analysis. First, we were only able to run our analysis using the summary data provided by TriNetX, as the raw data on pain severity ratings was not provided. Due to the lack of raw data, we were unable to run the homogeneity of variances test needed to ensure the ANOVA assumptions were not violated, and needed to rely on the Welch statistic which does not share this assumption. This is important given the large difference in sample sizes for each of our groups and may affect the validity of our results. Because a limited number of HCOs provided pain severity ratings, the TriNetX platform was also unable to provide demographic information for our three study groups. This information could have been valuable to understanding the characteristics of our patient population and for comparison to other study populations with PTSD and chronic pain and limits the generalizability of these results. Further, we were not able to verify the validity of the ICD-10 codes reported by TriNetX, leading to potential misclassification. We also cannot necessarily attribute the significant increase in pain severity of the PTSD+CP group to the presence of PTSD. As previously noted, patients with PTSD are likely to have other comorbid disorders such as depression which may serve as a mediator to exacerbate the chronic pain severity.

Conclusion

The relationship between PTSD and chronic pain is complex, and still requires examination. In this current study we illustrated the effect of comorbid PTSD and chronic pain on reported pain severity using a retrospective cohort of patients from around the United States between 2000 and 2024. That this comorbidity had significantly higher ratings of pain severity compared the patients with only PTSD or chronic pain indicates a need to focus on this population for pain management and psychiatric care. Our findings emphasize the needed for integrative approaches to treatment of these comorbid conditions to best improve patient outcomes.

REFERENCES

1.Morasco BJ, Lovejoy TI, Lu M, Turk DC, Lewis L, Dobscha SK. The relationship between PTSD and chronic pain: Mediating role of coping strategies and depression. PAIN. 2013;154(4).
2.Kind S, Otis JD. The Interaction Between Chronic Pain and PTSD. Current Pain and Headache Reports. 2019;23(12):91.
3.Siqveland J, Hussain A, Lindstrøm JC, Ruud T, Hauff E. Prevalence of Posttraumatic Stress Disorder in Persons with Chronic Pain: A Meta-analysis. Frontiers in Psychiatry. 2017;8.
4.Sharp TJ. The prevalence of post-traumatic stress disorder in chronic pain patients. Current Pain and Headache Reports. 2004;8(2):111-5.
5.Benedict TM, Keenan PG, Nitz AJ, Moeller-Bertram T. Post-Traumatic Stress Disorder Symptoms Contribute to Worse Pain and Health Outcomes in Veterans With PTSD Compared to Those Without: A Systematic Review With Meta-Analysis. Military Medicine. 2020;185(9-10):e1481-e91.
6.Bair MJ, Outcalt SD, Ang D, Wu J, Yu Z. Pain and Psychological Outcomes Among Iraq and Afghanistan Veterans with Chronic Pain and PTSD: ESCAPE Trial Longitudinal Results. Pain Medicine. 2020;21(7):1369-76.
7.Siqveland J, Ruud T, Hauff E. Post-traumatic stress disorder moderates the relationship between trauma exposure and chronic pain. European Journal of Psychotraumatology. 2017;8(1):1375337.
8.Brennstuhl M-J, Tarquinio C, Montel S. Chronic Pain and PTSD: Evolving Views on Their Comorbidity. Perspectives in Psychiatric Care. 2015;51(4):295-304.
9.Gasperi M, Afari N, Goldberg J, Suri P, Panizzon MS. Pain and Trauma: The Role of Criterion A Trauma and Stressful Life Events in the Pain and PTSD Relationship. J Pain. 2021;22(11):1506-17.
10.Asmundson GJG, Katz J. Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. Depression and Anxiety. 2009;26(10):888-901.
11.Rometsch-Ogioun El Sount C, Windthorst P, Denkinger J, Ziser K, Nikendei C, Kindermann D, et al. Chronic pain in refugees with posttraumatic stress disorder (PTSD): A systematic review on patients' characteristics and specific interventions. J Psychosom Res. 2019;118:83-97.
12.Åkerblom S, Perrin S, Rivano Fischer M, McCracken LM. 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. 2017;24(2):249-59.
13.Reed DE, Fischer IC, Williams RM, Na PJ, Pietrzak RH. Co-occurring Chronic Pain and PTSD Among US Military Veterans: Prevalence, Correlates, and Functioning. Journal of General Internal Medicine. 2024;39(11):2009-16.
14.Sullivan M. Dangerously numb: opioids, benzodiazepines, chronic pain, and posttraumatic stress disorder. PAIN. 2018;159(3).
15.Phifer J, Skelton K, Weiss T, Schwartz AC, Wingo A, Gillespie CF, et al. Pain symptomatology and pain medication use in civilian PTSD. PAIN®. 2011;152(10):2233-40.
16.Scioli-Salter ER, Forman DE, Otis JD, Gregor K, Valovski I, Rasmusson AM. The Shared Neuroanatomy and Neurobiology of Comorbid Chronic Pain and PTSD: Therapeutic Implications. The Clinical Journal of Pain. 2015;31(4).
17.Otis JD, Keane TM, Kerns RD. An examination of the relationship between chronic pain and post-traumatic stress disorder. J Rehabil Res Dev. 2003;40(5):397-405.
18.Gilliam WP, Craner JR, Schumann ME, Gascho K. The Mediating Effect of Pain Catastrophizing on PTSD Symptoms and Pain Outcome. The Clinical Journal of Pain. 2019;35(7).
19.Janssen J, Abou-Assaly E, Rasic N, Noel M, Miller JV. Trauma and pain sensitization in youth with chronic pain. PAIN Reports. 2022;7(2).
20.Defrin R, Ginzburg K, Solomon Z, Polad E, Bloch M, Govezensky M, et al. Quantitative testing of pain perception in subjects with PTSD – Implications for the mechanism of the coexistence between PTSD and chronic pain. PAIN. 2008;138(2).
21.Gasperi M, Panizzon M, Goldberg J, Buchwald D, Afari N. Posttraumatic Stress Disorder and Chronic Pain Conditions in Men: A Twin Study. Psychosomatic Medicine. 2021;83(2).
22.Sharp TJ, Harvey AG. Chronic pain and posttraumatic stress disorder: mutual maintenance? Clinical Psychology Review. 2001;21(6):857-77.

23.Jenewein J, Wittmann L, Moergeli H, Creutzig J, Schnyder U. Mutual influence of posttraumatic stress disorder symptoms and chronic pain among injured accident survivors: A longitudinal study. Journal of Traumatic Stress. 2009;22(6):540-8.
24.Asmundson GJ, Coons MJ, Taylor S, Katz J. PTSD and the experience of pain: research and clinical implications of shared vulnerability and mutual maintenance models. Can J Psychiatry. 2002;47(10):930-7.
25.Bosco MA, Gallinati JL, Clark ME. Conceptualizing and Treating Comorbid Chronic Pain and PTSD. Pain Research and Treatment. 2013;2013(1):174728.
26.Asmundson GJG, Hadjistavropolous HD. Addressing Shared Vulnerability for Comorbid PTSD and Chronic Pain: A Cognitive-Behavioral Perspective. Cognitive and Behavioral Practice. 2006;13(1):8-16.
27.Kascakova N, Furstova J, Hasto J, Madarasova Geckova A, Tavel P. The Unholy Trinity: Childhood Trauma, Adulthood Anxiety, and Long-Term Pain. International Journal of Environmental Research and Public Health [Internet]. 2020; 17(2).
28.Fishbain DA, Pulikal A, Lewis JE, Gao J. 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. 2017;18(4):711-35.
29.Karimov-Zwienenberg M, Symphor W, Peraud W, Décamps G. Childhood trauma, PTSD/CPTSD and chronic pain: A systematic review. PLOS ONE. 2024;19(8):e0309332.