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Biopsychosocial Factors Associated with Pain in Veterans with the Hepatitis C Virus

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Abstract

Background—Little research has examined etiological factors associated with pain in patients with the hepatitis C virus (HCV). The purpose of this study was to evaluate the relationship between biopsychosocial factors and pain among patients with HCV.

Methods—Patients with HCV and pain (n=119) completed self-report measures of pain, mental health functioning, pain-specific psychosocial variables (pain catastrophizing, self-efficacy for managing pain, social support), prescription opioid use, and demographic characteristics.

Results—In multivariate models, biopsychosocial factors accounted for 37% of the variance in pain severity and 56% of the variance in pain interference. In adjusted models, factors associated with pain severity include pain catastrophizing and social support, whereas variables associated with pain interference were age, pain intensity, prescription opioid use, and chronic pain self-efficacy (all *p*-values<0.05).

Conclusions—The results provide empirical support for incorporating the biopsychosocial model in evaluating and treating chronic pain in patients with HCV.

Keywords

Chronic pain; Biopsychosocial model; Hepatitis C

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Introduction

Chronic pain is a debilitating illness that impacts over one-third of U.S. adults (Institute of Medicine, 2011). Chronic pain is associated with high medical and psychiatric comorbidity (Demyttenaere et al., 2007), decreased quality of life (Breivik et al., 2006), and increased medical utilization (Blyth et al., 2004). The best available data suggest biopsychosocial factors are associated with the etiology of chronic pain, as well as the transition from acute to chronic pain (Gatchel et al., 2007). The biopsychosocial model posits that chronic pain is not solely a function of physical pathology (somatogenic) or primarily attributable to psychosocial factors (psychogenic); but rather the model suggests that a set of psychosocial and environmental factors along with biological perturbations all contribute to the experience, maintenance, and exacerbation of pain. Further, the biopsychosocial model suggests that the successful treatment of patients with chronic pain will depend on addressing the contributions of each of these sets of variables (Flor & Turk, 2011).

The hepatitis C virus (HCV) is the most common blood-borne infection and affects nearly 2% of the general United States population (Alter et al., 1999; Armstrong et al., 2006). It is a leading cause of liver disease, cirrhosis, hepatocellular carcinoma, and liver transplantation (Lauer & Walker, 2001), and is associated with very high medical and psychiatric comorbidity (Butt et al., 2007; Louie et al., 2012).

Recent data suggest that patients with HCV also have disproportionately high rates of pain-related diagnoses (Silberbogen et al., 2007; Whitehead et al., 2008). HCV is associated with peripheral neuropathy, arthritis, and fibromyalgia (Cacoub et al., 1999; Goulding et al., 2001; Mohammad et al., 2012). In samples of patients treated in hepatology clinics, 50–70% had co-occurring musculoskeletal pain (Rivera et al., 1997; Barkhuizen et al., 1999). Relative to patients with HIV alone, those who are co-infected with HCV had higher rates of pain disorders and were more likely to experience pain that interfered with daily living (Tsui et al., 2012). Additionally, patients with HCV and chronic pain utilize more medical services than patients with HCV alone, including overall hospital services, primary care visits, as well as pain specialty services (Lovejoy et al., 2012).

Research has begun to examine the link between pain and HCV. Immune mechanisms have been hypothesized to play a role in the development of chronic pain among patients with HCV (Cacoub et al., 1999; Thompson & Barkhuizen, 2003); however, the results are inconsistent and a recent empirical study did not confirm this association (Tsui et al., 2012). A preliminary cross-sectional study indicated biopsychosocial factors, particularly depressive symptoms, were associated with pain intensity and pain-related function; these results remained significant after controlling for the effects of demographic and disease-related variables (Morasco et al., 2010). This prior study, however, was limited by a small sample size and restricted assessment of pain-specific psychosocial variables. Other potential etiological factors for pain among patients with HCV include the presence of comorbid psychiatric and substance use disorders, which co-occur at high rates among samples of patients with HCV (Fireman et al., 2005; Golden et al., 2005), and are associated with chronic pain (Demyttenaere et al., 2007; Tunks et al., 2008; Barry et al., 2012). For example, a prior study found that patients with HCV and comorbid substance use disorder

had significantly higher rates of pain-related diagnoses than patients without a substance use disorder (Whitehead et al., 2008). No prior studies to our knowledge have examined a set of biopsychosocial factors, including pain-specific psychosocial factors, associated with pain in patients with HCV.

Treatment for pain most often occurs in primary care and some common medications used for pain may not be compatible with patients who have HCV. For example, non-steroidal anti-inflammatory drugs (NSAIDs) may need to be limited or avoided among patients with HCV who have severe liver disease (Larson et al., 2005) and opioid medications may not be optimal in patients with HCV, as this population has high rates of comorbid substance use disorders, and may be at increased risk of prescription opioid misuse (Morasco et al., 2011). Current antiviral medications that are designed to treat HCV (boceprevir and telaprevir) may lead to adverse medication interactions for pain in patients undergoing treatment for HCV. Additionally, patients with HCV are often chronically ill, have multiple comorbidities, and may be receiving multiple medications, which can interfere with the use of pain medications. By developing a better understanding of the factors that contribute to pain in patients with HCV, clinicians may be able to individualize more optimal pain interventions for this complex patient population.

The primary aim of this study was to evaluate the extent to which biopsychosocial factors are associated with pain intensity and pain interference in patients with HCV. We hypothesized that pain-specific psychosocial variables (self-efficacy, catastrophizing, social support, and coping) demonstrated to be important in studies with other chronic pain diagnoses (e.g., Anderson et al, 2005; Clint et al., 2008; Lopez-Martinez et al., 2008; Jensen et al., 2011) would be associated with pain intensity and pain interference, above and beyond the effects of demographic, disease-related, and general psychosocial variables.

Methods

Participants

Participants were recruited from a single VA Medical Center in the Pacific Northwest. Recruitment methods included posted advertisements in the Medical Center, letters sent to HCV patients who had pending appointments in primary care, announcements made in mental health classes, and referral of patients being treated in the Hepatology Clinic. Each participant gave informed consent to participate, completed a clinical interview and self-report questionnaires, and received a \$30 store gift card as compensation. Study evaluations were completed between March 2009 and August 2011. This study was approved by the Institutional Review Board of the VA Medical Center where the study was conducted.

Inclusion criteria for this study were a diagnosis of HCV, defined as a positive HCV antibody result confirmed with detectable HCV RNA level on polymerase chain reaction test, age 18 years or older, and English speaking. Participants were excluded if they were HCV antibody-positive and HCV RNA-negative (believed to have spontaneously cleared the virus), age older than 70 years, current untreated psychotic-spectrum disorder or bipolar disorder, any pending litigation or disability compensation for pain, history of advanced liver disease, or current or past treatment with antiviral therapy or chemotherapy. Patients

with advanced liver disease and those who had received antiviral therapy or chemotherapy were excluded because these conditions are associated with acute or emerging medical illnesses, which could confound our assessment of pain. Advanced liver disease was defined as having a current or past diagnosis of hepatocellular carcinoma, Stage 4 liver disease on biopsy, decompensated cirrhosis, prior liver transplantation, or aspartate aminotransferase to platelet ratio index (APRI) > 1.5 (the APRI is an estimate of liver disease severity and is described in greater detail below). In addition to the overall study's inclusion/exclusion criteria, to be included in these analyses, participants must have reported current pain of at least moderate to severe intensity (scores > 2 on the pain severity scale of the Multidimensional Pain Inventory [MPI]; Kerns et al., 1985).

A total of 289 participants with HCV were screened, of which 188 (65.1%) met full eligibility criteria. Individuals with HCV were excluded for current or past treatment with antiviral therapy or chemotherapy ($n=38$, 13.1% of all participants screened), currently seeking disability compensation for a pain-related condition ($n=28$, 9.7% of all participants screened), history of advanced liver disease ($n=19$, 6.6% of all participants screened), or another reason ($n=16$, 5.5% of all participants screened). An additional 19 individuals declined to participate after screening. We excluded an additional 50 participants due to report of no or mild pain (i.e., scores of 0–2 on the pain severity scale of the MPI). Our analytic sample was comprised of $n=119$ participants with HCV and moderate to severe pain; this represents 63.3% of those interested and screened as eligible for the study.

Measures

Demographic characteristics were collected by self-report. These included age, gender, race, marital status, and yearly income.

Pain severity and pain interference were assessed with the MPI (Kerns et al., 1985). The MPI is a frequently used and well-validated measure. It includes 52 self-report items that make up 12 scales. For this analysis, we focused on the pain severity and pain interference subscales. Internal consistency in this sample was 0.67 for pain severity and 0.84 for pain interference. Scale scores on the MPI ranged from 0 to 6, with higher scores reflecting more severe pain or interference.

Current depressive symptoms were assessed with the Beck Depression Inventory – 2 (BDI-II; Beck et al., 1996). The BDI-II contains 21 self-report items assessing symptoms of depression. Scores on the BDI-II are summed and higher scores reflect more severe symptoms of depression. The BDI-II provides cutoff scores for symptom severity, scores 17 are commonly used to indicate clinically significant depressive symptoms of moderate to severe intensity (Beck et al., 1996). Internal consistency of the BDI-II in this sample was 0.93.

Pain-related catastrophizing was assessed with the Pain Catastrophizing Scale (PCS; Sullivan et al., 1995). The PCS includes 13 self-report items that assess exaggerated negative orientation toward pain. Responses are summed and higher scores reflect heightened distress responses to pain. Internal consistency of the PCS in this sample was 0.94.

Self-efficacy for managing pain was assessed with the Chronic Pain Self-Efficacy Scale (CPSS; Anderson et al., 1995). This is a 22-item self-report questionnaire. CPSS total scores are obtained by adding responses to each item, with higher scores reflecting greater self-efficacy for managing pain. Internal consistency of the CPSS in this sample was 0.94.

The Chronic Pain Coping Inventory (CPCI; Jensen et al., 1995) is a 64-item self-report measure used to assess the ways in which participants cope with chronic pain. Responses to the CPCI can be categorized into 8 subscales. For this analysis, we examined only responses to the Seeking Social Support subscale of the CPCI. This includes 8 items. The scale is scored by averaging the items, with higher scores indicating greater use of this coping strategy. Internal consistency of the Seeking Social Support scale in this sample was 0.84.

The Structured Clinical Interview for DSM-IV (SCID; First et al., 2002) was used to assess current and past substance use disorders (SUDs). SCID interviews were conducted by masters-level research clinicians or students enrolled in graduate-level clinical psychology or social work programs. All interviewers received extensive training by a licensed psychologist. Regular supervision of SCID interviews was conducted to reduce likelihood of coder drift.

The Timeline Followback (TLFB) was used to assess self-reported use of prescription opioids in the 30 days prior to the study assessment. TLFB is a reliable and valid method that uses calendar prompts to track the frequency of substance or medication use (Sobell & Sobell, 1992).

All self-report measures have been used in prior studies, including samples of chronic pain patients, and have demonstrated good to excellent reliability and validity. The measures were selected for inclusion in the current study because of their strong psychometric properties, frequent use in the pain literature, and they measure constructs of the biopsychosocial model of chronic pain (DeGood & Cook, 2011).

HCV status and liver disease variables were collected through comprehensive review of medical record data. In addition to determining study inclusion, the APRI was also used as a measure of liver disease severity, which is an estimate that reliably predicts fibrosis and cirrhosis using routine laboratory data (Wai et al., 2003; Lackner et al., 2005). Higher APRI scores indicate more advanced liver disease. Quantitative polymerase chain reaction tests were used as an indicator of viral load, which reflects the amount of virus present in the blood.

Pain diagnostic and current antidepressant medication data were obtained from the medical record using the Veterans Integrated Service Network-20 (VISN-20) Data Warehouse. The VISN-20 Data Warehouse contains extracts of data from the clinical records of regional VA facilities and national VA databases. Pain diagnoses were obtained using ICD-9-CM codes listed in medical encounter data for the five years prior to the study assessment.

Data Analysis

Descriptive statistics characterized the demographic variables, diagnosis of current SUD, HCV genotype, HCV viral load, and pain diagnoses. Bivariate correlations evaluated the

relationship between dependent variables (pain severity and pain interference), biological variables (age, liver disease severity), general psychosocial variables (depressive symptoms assessed by the BDI-II, diagnosis of current SUD, marital status), and pain-specific psychosocial variables (pain catastrophizing, self-efficacy for managing pain, and social support).

We conducted two, 4-level hierarchical multiple regression analyses to evaluate the extent to which general and pain-specific psychosocial variables were associated with pain severity and pain interference, respectively, after accounting for covariates and biological variables. In Step 1, we controlled for reported prescription opioid use in the past 30 days and current antidepressant medication prescription. Pain severity was included as a third covariate in the model that evaluated factors associated with pain interference. Step 2 included biological variables age, race, and liver disease severity. We did not include gender as a biological variable in this step due to the disproportionate number of male participants (92%) in this sample. Step 3 included general psychosocial variables depression severity, diagnosis of current SUD, and marital status. Step 4 included the set of pain-specific psychosocial variables, namely, pain catastrophizing, chronic pain self-efficacy, and seeking social support. Prior studies examining biopsychosocial correlates of pain severity and pain interference have similarly first controlled for covariates then evaluated biological and psychosocial correlates in subsequent and distinct model steps (Osborne et al., 2007; Clint et al., 2008). We were also interested in the extent to which pain-specific psychosocial variables were associated with perceived pain severity and interference above and beyond general psychosocial variables and thus entered these variables into the model as a fourth step.

Multiple regression model diagnostics were evaluated, and assumptions of linearity, normally distributed residuals, and homoscedasticity were met (Cohen et al., 2003). In both multivariate models, a single multivariate outlier, due to younger age of the participant (34 years old relative to the mean age of 57 years for the sample), was identified using Mahalanobis distance. We deleted this outlier and performed multivariate analyses in the reduced sample. Results were unchanged, and we thus report findings from the full sample. All statistical analyses were conducted using SPSS v18. Inferential analyses employed two-tailed tests of significance and an alpha-level of 0.05.

Results

Participants ($n=119$) on average were 57 years old ($SD=6$ years), 92% were male, and over two-thirds were White, non-Hispanic. Fifty-eight participants (49%) reported depressive symptoms of moderate to severe intensity on the BDI-II, and 64 participants (54%) were currently prescribed antidepressant medication. HCV genotype data were available for 65.5% of participants. Of individuals with genotype data available, 71.8% were HCV genotype 1, 14.1% were genotype 2, 12.8% were genotype 3, and 1.3% were genotype 4. The average liver disease severity score on the APRI for the sample was 0.5 ($SD=0.3$). The median HCV viral load was 1,630,000.

The most common pain-related diagnoses among participants were neck or joint pain (75%), low back pain, (63%), and arthritis (61%). Fifty percent ($n=59$) of participants had two or three pain diagnoses in their medical record and 22% ($n=27$) had four or more pain diagnoses. One-half of the sample (59 of 119 participants) self-reported past-month use of prescription opioid medications. Sample characteristics are further detailed in Table 1. Table 2 provides zero-order correlations for multivariate model variables.

Biopsychosocial Model of Pain Severity

The covariates opioid use and antidepressant prescription were cumulatively associated with pain severity, $F=4.61$, $p=0.011$. Participants who reported using prescription opioids in the past 30 days reported more severe pain, while antidepressant prescription status was not independently associated with pain severity. After controlling for covariates, biological variables (age, race, and liver disease severity) were not collectively associated with pain severity, $F\ change=1.35$, $p=0.263$. General psychosocial variables (depression severity, substance use disorder status, marital status) accounted for 6% of the variance in pain severity in the presence of covariates and biological variables, $F\ change=2.72$, $p=0.048$. Depression severity, but not substance use or marital status, was significantly related to pain severity. Pain-specific psychosocial variables (pain catastrophizing, chronic pain self-efficacy, and chronic pain coping social support) collectively accounted for an additional 20% of the variance in pain severity after accounting for all other model variables, $F\ change=11.07$, $p<0.001$. In particular, increased pain catastrophizing and use of social support to cope with chronic pain were associated with higher pain severity. See Table 3 for model statistics, as well as partial correlations and variance inflation factors.

Biopsychosocial Model of Pain Interference

In a multivariate model, the covariates opioid use, antidepressant prescription, and pain severity cumulatively accounted for 45% of the variance in pain interference ($F=31.57$, $p<0.001$). Opioid use and pain severity, but not antidepressant prescription, were each independently associated with pain interference. After controlling for covariates, biological variables (age, race, liver disease severity) were not associated with pain interference ($F\ change=1.32$, $p=0.272$). General psychosocial variables (depression severity, substance use disorder status, marital status) jointly accounted for 3% of the variance in pain interference in the presence of covariates and biological variables ($F\ change=2.49$, $p=0.064$). Depression severity, but not substance use or marital status, was significantly related to pain interference. Pain-specific psychosocial variables (pain catastrophizing, chronic pain self-efficacy, and chronic pain coping social support) collectively accounted for an additional 5% of the variance in pain interference after accounting for all other model variables ($F\ change=3.87$, $p=0.011$). Decreased chronic pain self-efficacy was significantly related to greater pain interference. No other pain-specific psychosocial variables were significantly related to pain interference. See Table 4 for model statistics.

Discussion

Results from this study extend findings from a preliminary study examining biopsychosocial factors associated with pain in patients with HCV (Morasco et al., 2010). We found that

general and pain-specific psychosocial factors were most strongly associated with pain severity and pain interference in patients with HCV. When evaluating pain severity, general psychosocial factors were significant predictors above and beyond opioid and antidepressant prescription status and biological variables. Pain-specific factors, including pain catastrophizing and using social support to cope with chronic pain, were additionally found to be associated with pain severity. The final model accounted for 37% of the variance in pain severity scores. When evaluating pain interference, general psychosocial variables, namely depressive symptom severity, were significant above and beyond the effects of prescription opioid and antidepressant status, pain severity scores, and biological variables. Pain-specific factors were additionally associated and the final model accounted for 56% of the variance in pain interference scores. These findings are consistent with other research highlighting the association between psychosocial factors, above and beyond the effects of disease markers or structural variables, and pain severity and interference (Caragee et al., 2005; Jarvik et al., 2005).

Prior research examining biopsychosocial factors associated with pain in patients with HCV has revealed mixed findings regarding the relationship between disease markers and pain-related variables. HCV genotype (Mohammad et al., 2012) and liver disease severity (Morasco et al., 2010) have been associated with pain-related outcomes in prior research. In the current study, liver disease severity was not independently associated with pain severity or pain interference, after controlling for the effects of covariates. Several methodological factors may contribute for the apparently discrepant findings. Mohammad and colleague's (2012) sample included only patients with fibromyalgia and 59% were female, in contrast to the present study where the participants were predominantly male with a wide array of pain-related diagnoses. Moreover, the Mohammad et al. study found that HCV genotype was associated with pain-related outcomes. Unfortunately, we were unable to examine the potential role of HCV genotype as we had insufficient data to include this variable in the analyses. Our own prior research (Morasco et al., 2010) was a small pilot study (n=49) that included limited assessment of pain-specific psychosocial variables. Consequently the results we observed in the initial pilot study may not have been stable. In contrast, in the present study, we had sufficient statistical power, planned hypotheses, and comprehensive assessment of relevant pain-specific psychosocial variables. Future research should investigate the contributions of these differences to clarify and confirm the results. Other hypothesized biological mechanisms for the relationship between pain and HCV have, thus far, not been predictive of pain outcomes. For example, pro-inflammatory cytokines have been associated with pain in general (Wieseler-Frank et al., 2005) and hypothesized to play a role in developing pain in patients with HCV. However, a recent study did not identify a significant relationship between cytokines and pain in patients with HCV (Tsui et al., 2012). Additional research is needed to understand the role of biological and disease-related variables, and their contribution to pain-related outcomes, among patients with HCV.

Findings from this study have implications for pain assessment in patients with HCV. A thorough evaluation of chronic pain among patients with HCV may include assessment of general psychosocial factors (severity of depression, current alcohol and substance use) and pain-specific psychosocial factors (pain catastrophizing, self-efficacy for managing pain, chronic pain coping social support). Consistent with research in other clinical settings, study

findings indicate that pain-specific psychosocial factors were most strongly associated with pain-related outcomes (Turk & Okifuji, 2002; Keefe et al., 2004; Jensen et al., 2011), above and beyond biological variables, yet these factors may be seldom evaluated in clinical settings. In a busy primary care practice, conducting comprehensive assessments for general and pain-specific psychosocial factors may be difficult (Dansie & Turk, 2013). To assess these concepts, potential pain-specific measures that could be used include those utilized in this study (i.e., Pain Catastrophizing Scale, Chronic Pain Self-Efficacy Scale, the Seeking Social Support subscale of the Chronic Pain Coping Inventory). Collectively, 43 items comprise these three pain-specific measures, and patients could complete these measures in less than 10 minutes. Additionally, clinicians may incorporate open-ended questions into their clinical practice that assess these constructs (e.g., to what extent do you feel that you can take an active role in managing your pain, what can you do to better manage your pain), though the extent to which a single question comprehensively assesses a construct like pain catastrophizing or self-efficacy remains untested.

Study results also have implications for the treatment of chronic pain in patients with HCV. The use of interventions that specifically address and modify pain-related cognitions and seek to optimize self-efficacy for managing pain is critical. Cognitive-behavior therapy is an evidence-based psychological treatment that may help to improve pain intensity, pain-related function, and quality of life among patients with chronic pain (Dixon et al., 2007; Turk et al., 2011). This treatment addresses catastrophic thoughts and can help build self-efficacy for pain management. Given the high rates of current and past substance use disorders among patients with HCV, pain interventions that incorporate relapse prevention may be particularly useful. Although preliminary studies have integrated pain treatments with relapse prevention (Currie et al., 2003; Ilgen et al., 2011), cognitive-behavior therapy has not been tested in patients with HCV, which is a population that may be more difficult to treat, due to the high medical, psychiatric, and substance use disorder comorbidities. Other psychosocial interventions, such as Acceptance and Commitment Therapy or Mindfulness Based Stress Reduction, could be considered in this population. However, the extent to which these particular approaches directly address the pain-specific psychosocial correlates of pain identified as being significant in this study (i.e., pain catastrophizing, self-efficacy for managing pain) is unclear.

In this study, increased use of social support was associated with pain severity, but not pain interference. This is consistent with prior research indicating that satisfaction with social support is significantly associated with pain intensity, but not functional disability (Lopez-Martinez et al., 2008). Social support is generally a protective factor for pain. Participants in the current study who experienced the highest pain severity may have also sought the most social support for their pain and/or social support networks may have reinforced pain behaviors. Further research into the ways that members of one's family and social network can best support patients with chronic pain is needed (Cano & Williams, 2010). Future research may also include assessment of attachment style, which has been associated with pain-related outcomes (Forsythe et al., 2012) and with depressive symptoms among patients with HCV (Sockalingam et al., 2013).

There are important limitations to consider when reviewing the results from this study. We excluded HCV genotype and viral load from multivariate models because these data were not available for all participants. We relied on the APRI as a measure of liver disease severity, which can reliably detect HCV-related fibrosis, but has limited sensitivity and specificity for values greater than 0.5 (Shaheen et al., 2007). Although we controlled for opioid use and antidepressant prescriptions in multivariate models, we did not distinguish between classes of antidepressant medications. Moreover, we did not control for patients' use of other non-opioid analgesics or non-pharmacologic treatments for depression. Data are based on a cross-sectional design, which restricts understanding of causal relationships. Finally, study participants were predominately male and recruited from a single VA medical center. Results may not be generalizable to women or other patient populations.

There are also important strengths of this study, including a clinical sample of patients with diverse pain-related diagnoses, use of frequently administered and well-validated measures, and statistical control for confounding variables. Study results indicate that general and pain-specific psychosocial factors are important in understanding pain severity and interference in patients with HCV. These findings have significant implications for clinical practice. Patients with HCV should be screened for pain and the impact of pain on function. Treatment for chronic pain in patients with HCV should not be limited to a purely biomedical approach and may include interventions that address relevant components of pain. Multi-modal pain interventions that focus on improvements in functioning may offer opportunities to address the pain-specific psychosocial variables that most significantly contribute to chronic pain in this patient population.

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Table 1

Demographic characteristics and clinical variables of a sample of U.S. veteran participants with HCV and pain, n=119

Variable	
Age	56.6 ± 5.6
Male Gender	91.6% (109)
White Race	68.1% (81)
Greater than 12 Years of Education	74.8% (89)
Less than \$15,000 Annual Income	65.5% (78)
Marital Status, n = 118	
Single, Never Married	22.0% (26)
Married	22.0% (26)
Divorced/Separated	49.2% (58)
Widowed	6.8% (8)
Current Substance Use Disorder	19.3% (23)
Type of Chronic Pain Diagnosis	
Neck or Joint Pain	74.8% (89)
Low Back Pain	63.0% (75)
Rheumatism/Arthritis	60.5% (72)
Migraine Headache	22.7% (27)
Neuropathy	8.4% (10)
Fibromyalgia	8.4% (10)
Pain Severity	3.8 ± 0.9
Pain Interference	4.1 ± 1.3
Depression Severity	18.0 ± 11.6
Pain Catastrophizing	25.2 ± 12.4
Chronic Pain Self-Efficacy	12.8 ± 3.9
Chronic Pain Coping – Social Support	2.2 ± 1.7

Note: Column values indicate % (n) for categorical variables or Mean ± Standard Deviation for continuous variables.

Table 2

Bivariate intercorrelations of multiple regression model variables.

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Pain Severity	1.00												
2. Pain Interference	0.65**	1.00											
3. Opioid Use	0.28**	0.38**	1.00										
4. Antidepressant Prescription	0.12	0.17	0.18	1.00									
5. Age	-0.03	0.11	0.03	0.08	1.00								
6. Race	-0.08	-0.01	-0.01	0.09	0.00	1.00							
7. Liver Disease Severity	-0.16	-0.12	-0.08	-0.09	0.04	0.00	1.00						
8. Depression Severity	0.27**	0.32**	0.13	0.22*	-0.22*	0.01	0.03	1.00					
9. Current SUD	0.04	0.03	0.03	0.20*	-0.16	-0.03	0.09	0.16	1.00				
10. Currently Married	-0.07	0.05	0.04	0.00	0.26**	0.14	-0.03	-0.04	-0.21*	1.00			
11. Pain Catastrophizing	0.51**	0.51**	0.19*	0.18*	-0.08	0.04	-0.20*	0.53**	0.19*	-0.03	1.00		
12. Chronic Pain Self-Efficacy	-0.41**	-0.52**	-0.35**	-0.11	0.00	0.11	0.13	-0.28**	-0.04	-0.10	-0.47**	1.00	
13. Chronic Pain Coping – Social Support	0.27**	0.09	0.14	-0.02	0.06	-0.23*	-0.19*	-0.05	-0.06	0.06	0.07	-0.10	1.00

Note: SUD=substance use disorder.

* $p < 0.05$,** $p < 0.01$.

Table 3

Hierarchical multiple regression analysis examining biopsychosocial predictors of pain severity.

Variable	R ²	R ²	F	β	p-value	Partial Correlation	Variance Inflation Factor
Step 1. Covariates	0.08	0.08	4.67		0.011		
Opioid Use				0.20		0.13	1.18
Antidepressant Prescription				0.17		0.01	1.16
Step 2. Biological	0.11	0.03	1.35		0.263		
Age				0.00		0.03	1.19
Race				-0.08		-0.05	1.12
Liver Disease Severity				-0.06		-0.03	1.14
Step 3. General Psychosocial	0.17	0.06	2.72		0.048		
Depression				0.00		0.03	1.57
Current Substance Use Disorder				-0.13		-0.07	1.16
Currently Married				-0.22		-0.12	1.16
Step 4. Pain-Specific Psychosocial	0.37	0.20	11.07		< 0.001		
Pain Catastrophizing				0.03**		0.34	1.79
Chronic Pain Self-Efficacy				-0.04		-0.17	1.47
Chronic Pain Coping Social – Support				0.11*		0.24	1.13

Note: Values in columns with heading labels β , p-value, partial correlation, and variance inflation factor are for the final model that includes all predictors.

* $p < 0.05$,

** $p < 0.01$.

Table 4
Hierarchical multiple regression analysis examining biopsychosocial predictors of pain interference.

Variable	R ²	R ²	F	β	p-value	Partial Correlation	Variance Inflation Factor
Step 1. Covariates	0.45	0.45	31.57		<0.001		
Opioid Use				0.39*		0.21	1.20
Antidepressant Prescription				0.00		0.00	1.17
Pain Severity				0.64**		0.48	1.58
Step 2. Biological	0.47	0.02	1.32		0.272		
Age				0.04*		0.22	1.19
Race				0.05		0.02	1.12
Liver Disease Severity				-0.03		-0.01	1.14
Step 3. General Psychosocial	0.51	0.04	2.49		0.064		
Depression				0.01		0.12	1.57
Current Substance Use Disorder				-0.05		-0.02	1.16
Currently Married				0.07		0.03	1.17
Step 4. Pain-Specific Psychosocial	0.56	0.05	3.87		0.011		
Pain Catastrophizing				0.01		0.12	2.02
Chronic Pain Self-Efficacy				-0.06*		-0.23	1.51
Chronic Pain Coping Social – Support				-0.06		-0.11	1.20

Note: Values in columns with heading labels β , p-value, partial correlation, and variance inflation factor are for the final model that includes all predictors.

* $p < 0.05$.

** $p < 0.01$.