Pain Medicine, 2023, **24**, 941–948
https://doi.org/10.1093/pm/pnad043
Advance access publication 4 April 2023
Original Research Article

Suicidal thoughts and behaviors in patients with chronic pain, with and without co-occurring opioid use disorder

Martin D. Cheatle, PhD[1,*], Nicholas A. Giordano, PhD, RN[2], Kristy Themelis, PhD[3], Nicole K. Y. Tang, DPhil[3]

[1]Department of Psychiatry and Anesthesiology and Critical Care, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19106, United States
[2]Nell Hodgson Woodruff School of Nursing, Emory University, Atlanta, GA 30322, United States
[3]Department of Psychology, University of Warwick, CV4 7AL Coventry, United Kingdom

**Corresponding author:* Martin D. Cheatle, PhD, Department of Psychiatry and Anesthesiology and Critical Care, Perelman School of Medicine, University of Pennsylvania, 3535 Market Street, Suite 500, Room 541, Philadelphia, PA, USA. Email: cheatle@pennmedicine.upenn.edu

Abstract

Background: Individuals with chronic pain and a co-occurring substance use disorder present higher risk of suicide, but the individual and joint impacts of chronic pain and substance use disorders on suicide risk are not well defined. The objective of this study was to exam the factors associated with suicidal thoughts and behaviors in a cohort of patients with chronic non-cancer pain (CNCP), with or without concomitant opioid use disorder (OUD).

Design: Cross sectional cohort design

Setting: Primary care clinics, pain clinics, and substance abuse treatment facilities in Pennsylvania, Washington, and Utah

Subjects: In total, 609 adults with CNCP treated with long-term opioid therapy (>/= 6 months) who either developed an OUD (cases, n = 175) or displayed no evidence of OUD (controls, n = 434).

Methods: The predicted outcome was elevated suicidal behavior in patients with CNCP as indicated by a Suicide Behavior Questionnaire-Revised (SBQ-R) score of 8 or above. The presence of CNCP and OUD were key predictors. Covariates included demographics, pain severity, psychiatric history, pain coping, social support, depression, pain catastrophizing and mental defeat.

Results: Participants with CNCP and co-occurring OUD had an increased odds ratio of 3.44 in reporting elevated suicide scores as compared to participants with chronic pain only. Multivariable modeling revealed that mental defeat, pain catastrophizing, depression, and having chronic pain, and co-occurring OUD significantly increased the odds of elevated suicide scores.

Conclusions: Patients with CNCP and co-morbid OUD are associated with a 3-fold increase in risk of suicide.

Keywords: chronic pain; suicide risk; opioid use disorders

Introduction

Death by suicide has become a global epidemic. The World Health Organization published, "Suicide Worldwide 2019," which highlighted the magnitude of this problem: more than 700,000 people die due to suicide every year; every 40 seconds someone in the world dies of suicide; for every suicide there are many more people who attempt suicide; 77% of suicides occur in low and middle-income countries; experiencing conflict, disaster, violence, abuse or loss and a sense of isolation are strongly associated with suicidal ideation; and suicide rates are also high amongst vulnerable groups who experience discrimination.[1] In 2019, suicide was the 10th leading cause of death in the United States among all ages.[2]

Certain patient populations are at higher risk for suicide and suicidal behaviour including patients that suffer from chronic pain and individuals with substance use disorders (SUD). Extant literature reveals that the prevalence of suicidal ideation in patients with chronic pain ranges from 18%–50%.[3–6] A systematic review by Tang and Crane[6] discovered that the risk of death by suicide was doubled in patients with chronic non-cancer pain (CNCP) as compared to non-pain controls. Data from a national household survey of 8,841 individuals in Australia found that the odds of a lifetime and past 12-month suicidality were two to three times greater in individuals with chronic pain as compared to patients with no history of chronic pain and 65% of people who engaged in suicidal behaviour in the previous 12 months had a history of chronic pain.[7] A more recent national study by Campbell and colleagues[3] evaluated 2590 closed cases of intentional deaths in Australia in 2014. CNCP was identified in 14.6% of the cases. Decedents with CNCP were more likely to be older, have more mental and physical health problems, and were more likely to die from an overdose of drugs.

Another population vulnerable to suicide are patients with SUDs. Approximately 40% of patients seeking treatment for SUDs report a history of suicidal attempts.[8–10] Individuals with an alcohol use disorder are almost 10 times more likely to die by suicide and those who inject drugs are approximately 14 times more likely to die by suicide, as compared to the general population.[11] Persons with SUD have multiple

Received: 12 January 2023. **Revised:** 7 March 2023. **Accepted:** 25 March 2023

risk factors for suicidal ideation/suicidal behavior including experiencing co-morbid depression and enduring a myriad of severe stressors such as loss of relationships, jobs, financial problems, and other health conditions related to their SUD. Notably, persons with chronic pain have similar stressors putting them at risk for suicidal ideation/suicidal behavior[12] and approximately 10% of patients with chronic pain exposed to prescription opioids develop an OUD, which is not inconsequential.[13,14] Thus, patients with co-occurring pain and OUD may be at high risk for attempting and/or ending their lives by suicide, but there is scant literature on the prevalence and unique risk factors for this patient population.

The objective of this cross-sectional study was to evaluate risk of suicide and identify factors associated with elevated suicide scores in a cohort of patients with CNCP on prescription opioid therapy with no evidence of OUD and identify independent factors associated with the effect of concomitant OUD.

Methods

Participant eligibility and recruitment

This study presents a secondary analysis of data collected for a larger parent study assessing phenotypic and genotypic characteristics of patients with CNCP who developed an OUD.[15] In this study, cases (n = 175) were patients with CNCP who met DSM-IV[16] criteria for OUD following the initiation of long-term opioid therapy (LTOT) defined as being prescribed opioid analgesia for =/> 6 months. Control participants (n = 434) were patients with CNCP on LTOT who had no evidence of OUD or meeting established criteria for OUD. Controls were recruited from primary care and pain clinics in Pennsylvania (University of Pennsylvania), Washington (University of Washington), and Utah (Lifetree Pain Center). Cases were recruited from SUD treatment facilities associated with all three recruitment sites. Participants entered the study between November 2012 and September 2018. The University of Pennsylvania, the University of Washington and the Lifetree Institutional Review Boards approved and monitored the protocol. Participants provided written consent before beginning the study and were reimbursed for participation.

Inclusion/exclusion criteria

Inclusion criteria included adult patients (age 18 or older) who were White and of European descent; have CNCP of musculoskeletal or neuropathic origin for at least 6 months; without a history of SUD (other than nicotine) before initiating LTOT and either developed an OUD (cases) or did not (controls). The genotypic aims of the parent study excluded the inclusion of patients of non-White races and ethnicities. Exclusion criteria included individuals with severe psychiatric conditions preventing the provision of informed consent or questionnaire completion. Pain disorders due to cancer, gynecologic, abdominal, visceral, dental, trigeminal neuralgia, post-stroke syndrome, migraine-related pain; or neuropathic pains due to metabolic disease were excluded due to the more diverse etiologies of these pain conditions.[17]

Eligibility determination

To establish eligibility including OUD and non-OUD status in patients with CNCP we utilized the Electronic Medical Record (EMR) (controls) and corroboration of clinical staff (nurses, counselors, physicians) from the cases recruitment sites. For controls, the EMR was systematically reviewed by a trained research technician for each subject from 6 months before the date of study consent. Criteria for eligibility and having no evidence of having an OUD included: The patient was on LTOT (≥ 6 months); all urine drug screens (UDS) obtained as part of standard care were appropriate (presence of prescribed opioid metabolite and absence of non-prescribed opioids or illicit drugs); the patient had no record (both in-office notes and diagnostic codes) of current or past SUD (excluding nicotine); and no evidence of aberrant drug-related behaviors (ADRB) which was assessed utilizing an expert developed checklist.[18] To ensure that control participants did not develop an OUD each control subject was monitored by the trained research technician by reviewing EMR records each month for 12 months after completing the baseline assessments.

Eligibility for the OUD (cases group) included: patients with CNCP with no previous history of SUD (except nicotine) as defined by DSM-IV[16] criteria before commencing LTOT; at the time of enrolment meeting DSM-IV criteria for "opioid dependence" (OUD in current DSM-5 terminology) determined by completing the Mini-International Neuropsychiatric Interview (MINI)[19] and DSM-IV checklist obtained during the initial eligibility interview; and actively receiving treatment or had been in formal treatment for an OUD. Following patient consent, research staff conferred with a contact person at each substance use treatment recruitment site, who corroborated that each enrolled case subject was receiving treatment for a prescription OUD and based on records of the facility's initial assessment had no previous history of any SUD (excluding nicotine) before beginning LTOT.

All baseline assessments were conducted over the phone during a single interview for cases and controls. As noted above, controls were re-evaluated at 6 and 12 months following the baseline assessments to confirm that controls did not develop an OUD during the follow-up period.

Measures

Measures were limited to those available in the parent study and variables were selected for analysis based on the known risk factors for suicide in both the general population and the population of patients with CNCP.

Demographics: Demographic characteristics included: age, gender, socio-economic status, and education level.

MINI International Neuropsychiatric Interview (MINI): The MINI based on DSM-IV criteria are used to establish psychiatric diagnoses including major depression-lifetime; and drug and alcohol dependence (current and lifetime) relevant to this study.[19]

Brief Pain Inventory (BPI): The BPI includes 2 dimensions: pain intensity and pain interference. Average pain intensity experienced over the past 24 hours was utilized in this study.[20]

Coping Strategies Questionnaire (CSQ): The CSQ is a validated measure of coping with pain. The CSQ consists of six cognitive and one behavioral pain-coping scales. For this study, only the catastrophizing subscale was used in the analysis as it is the one subscale that has been found to be a significant risk factor for suicide in the CNCP population.[5]

The catastrophizing subscale score ranges from 0 to 36. Normative data from a sample of patients in an inpatient pain

center revealed a mean score of 17.1 and a standard deviation of 8.78.[21]

DSM checklist for abuse or dependence: Based on the MINI interview, a checklist of the DSM items for substance abuse and dependence was administered at each assessment. This checklist was used to define OUD throughout the study.

Duke Social Support Index (DSSI): A 14-item, self-administered, multidimensional, functional social support questionnaire. Construct, concurrent, and discriminant validity have been demonstrated for the two subscales (confidant support–5 items and affective support–3 items).[22]

Pain Self Perception Scale (PSPS): The PSPS assesses the sense of mental defeat associated with the experience of pain. It is comprised of 24 items that describe negative thoughts and feelings people may have about themselves due to pain. Total score ranges from 0 to 96, with higher scores indicating higher levels of mental defeat. The PSPS demonstrated excellent internal consistency (Cronbach $\alpha = 0.98$) and test-retest reliability ($r = 0.92$) when used with patients with chronic pain.[23]

Patient Health Questionnaire-4 (PHQ-4): The PHQ-4[24] is an ultra-brief four-question screening tool for depression and anxiety. It is both a valid and reliable measure of psychological distress in the general population.[24]

Suicide Behavior Questionnaire-Revised (SBQ-R): The SBQ-R is a validated four-item assessment tool that taps into different dimensions of suicidality including lifetime suicidal ideation and/or attempts; frequency of suicidal ideation over the past 12 months; the threat of suicide attempt and self-reported likelihood of suicidal behavior in the future. The SBQ-R has been validated across several clinical and non-clinical populations and the receiver operating characteristic (ROC) analyses revealed that the most predictive cutoff scores on the SBQ-R were 7 for non-suicidal samples, and 8 for clinical samples.[25]

Statistical analysis

In a sample of persons with CNCP the independent variable for this study was the presence of co-occurring chronic pain and OUD at baseline. The dependent variable, risk of suicide was operationalized as SBQ-R score, dichotomized with a cut-off score of ≥ 8 to differentiate the higher risk for suicide in clinical samples.[25] Bivariate tests evaluated associations between covariate sample characteristics and SBQ-R score (0–7 vs ≥ 8). Effects sizes were computed for all differences and magnitude interpreted based on established criteria.[26]

Logistic regression models were constructed to examine the association between the independent variable and covariate demographic and clinical characteristics and an SBQ-R score of ≥ 8. A multivariable logistic regression model was constructed by adding only factors that were observed to have a significant association in the simple logistic regression models. Variance inflation factor (VIF) was computed to assess for potential multicollinearity. Model fit was assessed using the Akaike information criterion (AIC)[27] and the Hosmer–Lemeshow goodness of fit test. All analyses were conducted in R 3.6.1.[28] The final sample size ($n = 609$) achieved sufficient power (97%) to detect an adjusted odds ratio (AOR) of 2.3 between those with and without OUD and an SBQ-R score ≥ 8, at an alpha level of 0.05.[29] A ROC curve was constructed to examine differences in covariates to accurately classify patients presenting with an SBQ-R score of ≥ 8.[30]

Results

Of the 609 patients, 18% reported a score of 8 or greater on the SBQ-R. Those in this group reported SBQ-R scores that were over 6 points higher than patients with SBQ-R scores less than 8, on average (95% confidence interval [CI]: 5.9–6.9). Compared to patients with lower suicide scores, individuals with an SBQ-R score of ≥ 8 were slightly younger and made up a larger proportion of the sample that were not married, not working, and financially could not make ends meet (Table 1). Further, more than half (51.8%) of the 110 patients reporting an SBQ-R of ≥ 8 had co-occurring OUD ($P < .001$).

Patients with SBQ-R scores of ≥ 8 reported significantly higher mean mental defeat scores and pain catastrophizing scores than patients reporting SBQ-R < 8. Specifically, mental defeat scores were an average of 29 points higher in the highly symptomatic group compared to the other study patients (95% CI: 23.9–58.8; $P < .001$). Similarly, catastrophizing scores were over 7 points higher among patients reporting an SBQ-R of ≥ 8, with a mean of 20.9, compared to those reporting scores < 8, who reported a mean of 13.3 ($P < .001$). Patients with SBQ-R scores ≥ 8 also reported having significantly less social support based on the DSSI domains.

In the univariate logistic regression models, several factors were protective against higher SBQ-R scores while other factors were found to increase the odds of higher SBQ-R scores (Table 2). Older age, being married, working, making enough money "to get along" or "to be comfortable," and more social support were all found to be associated with a lower odds ratio of reporting an SBQ-R score of ≥ 8 ($P < .01$). Alternatively, both elevated mental defeat and pain catastrophizing scores were associated with an increased odds ratio (OR) for reporting higher SBQ-R scores ($P < .001$). As hypothesized, participants with co-occurring CNCP and OUD were found to have significantly increased odds (OR = 3.44) for reporting SBQ-R scores ≥ 8 (95% CI: 2.26–5.33). With respect to the effects of psychiatric symptoms on risk of suicide, each additional point on the PHQ-4 was associated with an increased OR of reporting an SBQ-R score of ≥ 8 (OR: 1.30; 95% CI: 1.22–1.39; $P < .001$). Similarly, patients with a depression diagnosis were observed to have a higher OR of increased SBQ-R scores (OR: 4.52; 95% CI: 2.50–8.14; $P < .001$).

Multivariable modeling indicated that mental defeat, pain catastrophizing, lifetime major depression, and OUD together significantly increased the odds of reporting higher suicidality scores on the SBQ-R (Table 3). Each 1-point increase on the mental defeat scale was associated with a 2% increase in the adjusted odds ratio (AOR) of having an SBQ-R score of 8 or greater (95% CI: 1.01–1.04; $P < .001$). For example, a 10-point increase in mental defeat score (score range: 0–96) corresponds to a 20% increase in the AOR of high suicide risk. A 1-point increase in pain catastrophizing scores (score range: 0–36) was observed to increase the AOR of suicide risk by 6% (95% CI: 1.02–1.11; $P < .001$). In the multivariable model, the association between an SBQ-R score of ≥ 8 and OUD was reduced to an AOR of 2.40 but remained statistically significant (95% CI: 1.36–4.29; $P = .003$). Patients presenting with a diagnosis of lifetime major depression had twice as high an AOR of reporting an SBQ-R score of ≥ 8 than those without a diagnosis (AOR = 2.04; 95% CI: 1.01–4.12; $P = .047$). PHQ-4 scores were not statistically significantly associated with SBQ-R scores in the final adjusted

Table 1. Sample characteristics based on SBQ-R score cutoff of ≥8 (N = 609)

		No/Lower Risk (0–7 SBQ-R) N = 499	Higher Risk (≥8 SBQ-R) N = 110	*P*	Effect Size
Sex, n (%)	Male	199 (39.9)	41 (37.3)	.690	0.02
	Female	300 (60.1)	69 (62.7)		
Age, mean (SD)		39.3 (11.7)	34.5 (10.9)	<.001	0.42
Education, n (%)	High school or less	170 (34.1)	44 (40.0)	.285	0.05
	Secondary education	329 (65.9)	66 (60.0)		
Marital status, n (%)	Not married or never married	218 (43.7)	67 (60.9)	.002	0.13
	Married	281 (56.3)	43 (39.1)		
Living situation, n (%)	Live alone	85 (17.0)	15 (13.6)	.466	0.04
	Live with others	414 (83.0)	95 (86.4)		
Working, n (%)	No	359 (71.9)	92 (83.6)	.016	0.11
	Yes	140 (28.1)	18 (16.4)		
Financial situation, n (%)	Cannot make ends meet	114 (22.8)	46 (41.8)	<.001	0.17
	Just enough to get along/comfortable	385 (77.2)	64 (58.2)		
Chronic pain and opioid use	Chronic pain	381 (76.4)	53 (48.2)	<.001	0.24
	Chronic pain + Opioid Use	118 (23.6)	57 (51.8)		
SBQ-R, mean (SD)		3.9 (1.3)	10.3 (2.4)	<.001	4.11
PSPS, mean (SD)		29.1 (26.3)	58.8 (28.4)	<.001	1.11
Catastrophizing, mean (SD)		13.3 (7.7)	20.9 (7.8)	<.001	0.99
Social interaction scale, mean (SD)		5.2 (2.4)	4.5 (2.4)	.008	0.28
Subjective social support, mean (SD)		17.8 (3.3)	15.5 (3.6)	<.001	0.71
Instrumental social support, mean (SD)		8.3 (2.9)	7.6 (3.4)	.018	0.25
PHQ 4, mean (SD)		4.8 (3.6)	8.2 (3.2)	<.001	0.98
Depression, n (%)		29 (5.8)	24 (21.8)	<.001	0.22
Average pain		5.6 (1.8)	5.6 (2.0)	.988	0.001

Categorical variables' effect size computed using Cramer V, continuous variables' effect size computed using Cohen's *d*. PSPS = Pain Self Perception Scale; SBQ-R = Suicide Behavior Questionnaire-Revised.

Table 2. Single variable logistic regression score of estimating odds ratio of SBQ-R score of ≥8 or greater (N = 609)

	Odds Ratio	95% Confidence Interval		*P*
Age	0.97	0.94	0.98	<.001
Male	0.89	0.58	1.37	NS
College education	0.97	0.51	1.89	NS
Married	0.49	0.34	0.75	.001
Live with others	1.31	0.73	2.43	NS
Working	0.46	0.17	0.99	.02
Just enough to get along/comfortable	0.81	0.27	0.64	<.001
PSPS	1.03	1.02	1.05	<.001
Catastrophizing	1.14	1.02	1.17	<.001
Social interaction	0.89	0.81	0.96	.007
Subjective social support	0.90	0.83	0.98	<.001
Instrumental social support	0.92	0.86	0.98	.012
Chronic pain and opioid use	**3.44**	**2.26**	**5.33**	**<.001**
PHQ-4	1.30	1.22	1.39	<.001
Depression diagnosis	4.52	2.50	8.14	<.001
Average pain	1.14	1.02	1.28	.023

PSPS = Pain Self Perception Scale.

model. While not statistically significant, the inclusion of age, marital status, work status, financial situation, and social support subscale items did improve overall model fit (Hosmer-Lemeshow Goodness of Fit $\chi^2 = 5.27$, *P* values = .73). All variance inflation factor (VIF) values in the final model were acceptable (eg, <2.00), suggesting that multicollinearity among the independent variables is not an issue.

Given the statistically significant findings of mental defeat and pain catastrophizing in the multivariable model, a ROC curve was constructed to examine the performance of the two scales in independently classifying SBQ-R scores ≥8. Subsequent ROC analyses indicated that the mental defeat measure performed comparably to pain catastrophizing for classifying patients presenting with SBQ-R scores of ≥8. A mental defeat cutoff score of 40 provided a sensitivity value of 0.69 and a specificity value of 0.70. As presented in Table 4, this cut-off score demonstrated an acceptable ability to predict participant classification as SBQ-R scores ≥8. As seen in Figure 1, the area under the curve (AUC) was 0.77 (95% CI: 0.72, 0.82) and statistically significant ($P < .001$). A pain catastrophizing cutoff score of 16 provided a sensitivity value of .78 and a specificity value of 0.68. As presented in Table 5, this cutoff score demonstrated an acceptable ability to predict participant classification as at high risk for suicide. As seen in Figure 2, the AUC was 0.75 (95% CI: 0.71, 0.81) and statistically significant ($P < .001$). However, the difference between

Table 3. Multivariable model estimating odds ratio of SBQ-R score of ≥8 or greater with variables from significant single variable regression output (N = 609)

	Adjusted Odds Ratio	95% Confidence Interval		*P*	VIF
PSPS	**1.02**	**1.01**	**1.03**	**<.001**	**1.55**
Catastrophizing	**1.06**	**1.01**	**1.10**	**.013**	**1.64**
Social interaction	0.99	0.89	1.11	.905	1.20
Subjective social support	0.99	0.91	1.08	.974	1.65
Instrumental social support	1.00	0.91	1.09	.881	1.33
Have enough money to get by/Comfortable	1.17	0.67	2.05	.577	1.29
Working	0.76	0.39	1.42	.400	1.11
Married	0.78	0.46	1.35	.378	1.28
Age	0.99	0.97	1.02	.793	1.45
Case and controls					
Chronic pain (reference)	-	-	-	-	-
Chronic pain and opioid use	**2.40**	**1.36**	**4.29**	**.003**	**1.46**
PHQ-4	1.05	0.95	1.16	.298	1.88
Depression	**2.04**	**1.01**	**4.12**	**.047**	**1.16**
Average Pain	0.96	0.84	1.10	.593	1.24

AIC 466.1; Hosmer-Lemeshow Goodness of Fit $\chi^2 = 5.27$, *P* values = .73. PSPS = Pain Self Perception Scale; SBQ-R = Suicide Behavior Questionnaire-Revised.

Table 4. ROC curve cut-offs—PSPS

PSPS Score	Sensitivity	Specificity	True Positive	False Positive	True Negative	False Negative
90	13%	99%	19	6	459	125
80	22%	95%	31	22	443	113
70	38%	91%	55	43	422	89
60	48%	84%	69	74	391	75
50	58%	75%	84	116	349	60
45	65%	73%	93	127	338	51
40*	**69%**	**70%**	**100**	**140**	**325**	**44**
35	72%	64%	103	167	298	41
30	74%	60%	106	187	278	38

PSPS = Pain Self Perception Scale; ROC = receiver operating characteristic.

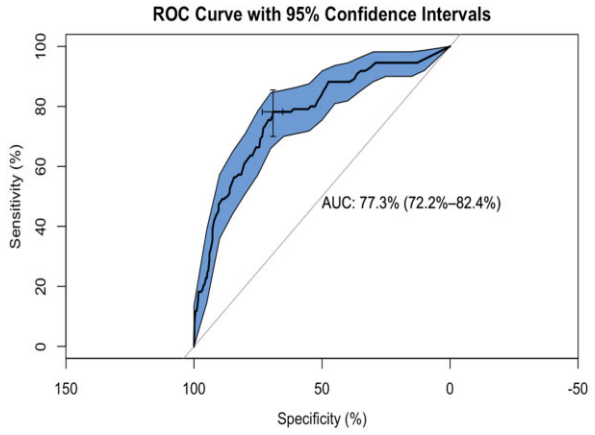

Figure 1. ROC curve and AUC—PSPS. AUC = area under the curve; PSPS = Pain Self Perception Scale; ROC = receiver operating characteristic.

the AUC between the two curves was not statistically significantly different (*P* = .582). This indicates that a mental defeat score of 40 and a pain catastrophizing score of 16 are comparable in estimating an SBQ-R score of ≥8.

Conclusions

Suicidality is a highly sensitive topic and not a focus of routine clinical assessment in patients with CNCP. Using validated measures, we assessed 609 patients with CNCP, with and without OUD, and found that 18% of these patients scored above the clinical cutoff for risk of suicide and that having an OUD increased the odds of meeting the cutoff by >3-fold. This was significant even after considering other sociodemographic and health variables and is in line with previous studies showing that SUD presents an independent risk factor for predisposing individuals to attempt suicide.[11] Identifying individuals with SUD, and specifically OUD, and elevated suicide scores in a chronic pain population is an important finding that substantiates the growing concern around fatal prescription opioid overdose in patients with chronic pain.[12,31] With the increased risk for suicide and easy access to means (prescription of opioids), a concern is that intentional self-harm by overdose has been overlooked in this population.[12,31]

When examining patient demographics, those with elevated suicide scores in this sample tended to be younger, not married, not working, and with financial challenges. Conversely, older age, being married, working, financially secure, and higher levels of social support were all found to correlate with lower suicide risk scores. Unlike other reports,[32] our results showed that sex did not influence the odds of suicide in this cohort of patients with CNCP. In both sexes, substance abuse was associated with elevated suicide scores, The number of male patients in our sample was small relative to female patients, which may have limited the stability of our estimates,[33] however, the findings are consistent with recent studies examining the association between sociodemographic

Table 5. ROC curve cut-offs—CSQ pain catastrophizing

Pain Catastrophizing Score	Sensitivity	Specificity	True Positive	False Positive	True Negative	False Negative
28	17%	96%	19	18	481	91
24	45%	89%	50	55	444	60
20	60%	76%	66	122	377	44
16[a]	**78%**	**63%**	**86**	**187**	**312**	**24**
12	89%	44%	98	281	218	12
8	95%	26%	104	370	129	6
4	97%	12%	107	437	62	3

CSQ = Coping Strategies Questionnaire; ROC = receiver operating characteristic.
[a] Optimal cutoff score for sensitivity and specificity.

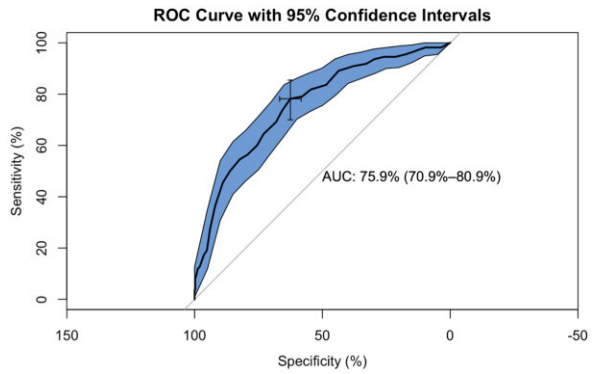

Figure 2. ROC curve cutoffs and AUC—CSQ pain catastrophizing. AUC = area under the curve; CSQ = Coping Strategies Questionnaire; ROC = receiver operating characteristic.

characteristics in various types of chronic pain conditions showing no consistent association between gender and suicidality.[34]

Several psychosocial variables investigated in the current study map on to major theories of suicidal thoughts and behaviors including the Interpersonal Theory of Suicide.[35] The Interpersonal Theory of Suicide provides a conceptual framework for understanding the prevalence and correlates of suicidality and proposes the combination of thwarted belongingness (an unmet need for connectedness) and perceived burdensomeness (a sense of burden to others) precede suicidal ideation. In line with this theory, our study shows that both subjective and instrumental social support, as well as social interaction, are protective factors associated with suicidal behavior.

Pain intensity was not a significant factor associated with elevated suicide scores in this sample when other psychosocial factors were accounted for. This is in line with some,[4,36] but not all of the extant cross-sectional studies.[37–39] Although pain intensity was not significant in our study, it has been proposed as part of the motivational-volitional model of suicidal behavior,[40] that increased physical pain may lead to acquired capability for suicide through habituation to pain, fear, and death in the general population. More recent theories, rooted in the "ideation-to-action" framework, propose that acquired capability in combination with other factors, such as access to means, increases the likelihood that suicidal ideation transitions to suicidal behavior.[40,41] This notion is particularly relevant in patients with a long pain duration who have access to prescription opioids for pain management and individuals with OUD that use illicit opioids especially opioids with fentanyl, which accounts for the majority of drug overdose deaths recorded in the United States;[42] having easy access to lethal means is an important risk factor for suicide.[40] It should be pointed out, however, that patients with CNCP on LTOT often present with a reduced pain threshold compared to the general population (eg, Suokas et al.)[43], thus inconsistent with the tenets of the motivational-volitional model of suicide. Experimental studies have specifically shown decreased tolerance to both heat and cold pain in patients with CNCP receiving opioid therapy compared to healthy individuals.[43,44] Future empirical research is warranted to further test pain tolerance in individuals with chronic pain with and without OUD and how this relates to suicidal behavior.

Our findings highlight the importance of careful monitoring of the benefits and risks of opioid prescriptions and their association with suicidal behavior in this patient group, especially patients with CNCP and history of an OUD. Although widely used, clinical scales that directly assess suicide risk are prone to a high number of false-positive and tend to overcategorize low-risk patients as being at high-risk bringing into question their clinical utility.[45] Instead, it has been suggested that the use of indirect measures through multiple self-report clinical scales and socio-demographics may have a stronger predictive value for suicide attempts.[46] Our findings provide support for the use of several self-report clinical scales, such as the CSQ-CAT and PSPS as significant predictors of elevated suicide risk scores The benefit of using these psychological measures is that in addition to having predictive value, they provide a specific target for intervention. Future validation of the clinical utility of using these measures with patients with CNCP with and without SUD in different clinical settings would be informative.

Following the diagnosis of OUD, a diagnosis of depression was the next strongest factor associated with elevated suicide risk scores in our cohort. This is consistent with studies showing the role of depression in augmenting the risk of suicide in patients living with chronic pain.[6] Examining the characteristics of the higher and lower symptom severity groups based on SBQ-R scores, a diagnosis of depression was significantly more prevalent in the high-symptom group. Indeed, a diagnosis of depression was associated with an almost five-fold increase in the odds of reporting SBQ-R scores $\geq$8, this was reduced to an AOR of 2.04 when considering other factors in our multivariable model which highlights the multifactorial nature of suicide.

In line with previous research, pain catastrophizing was a significant factor associated with elevated suicide scores in our study.[5] Although controversies exist around the definition and effectiveness of interventions aimed at reducing pain-related catastrophizing,[47] catastrophizing screening still has value in predicting risk of suicidal behavior. Our findings

further support the value of screening for catastrophizing in determining the odds of elevated suicide scores.

Patients with CNCP tend to report significantly higher levels of mental defeat compared to other groups including non-treatment-seeking individuals with similar chronic or acute pain.[23] From the perspective of the Schematic Appraisals Model of Suicide the likelihood of suicidality increases when stressful events are appraised as defeating.[48] However, the concept of defeat in this context has not been fully defined. Our findings are consistent with the prevailing literature on the role of mental defeat in suicide demonstrating the value of assessing defeat (described as "a sense of a loss of autonomy, agency, and human integrity"[49] in patients living with chronic pain and its predictive capacity for identifying suicide risk. Improving an individual's self-appraisal through cognitive reframing and developing resilience to mental defeat using adaptative coping strategies may therefore be an important treatment target in the prevention of suicidality.[48] Consistent with previous research, mental defeat and pain catastrophizing each made a significant independent contribution to the multivariable model predicting risk of suicide. The fact that both are significant contributors with acceptable VIF values suggests there are no apparent issues of multicollinearity between the two constructs. This is a theoretically important observation as provides support for the notion that they represent overlapping but distinct concepts.[49]

Our study had some methodological limitations that require consideration. One of the major limitations is its cross-sectional design thereby precluding claims of causality. Prospective longitudinal studies are needed to ascertain the temporal relationships between the factors highlighted. Another limitation is that suicidal behavior was assessed using the SBQ-R which was developed for research contexts and is not a recommended tool to assess the risk of future suicide attempts in clinical populations.[50] Unexamined due to the nature of the secondary data analysis was the role of a history of suicidal ideation and a family history of suicide, both of which are known risk factors[35] as well as other variables that have been demonstrated to be associated with risk of suicide in patients with CNCP such as burdensomeness.[51] Furthermore, the genotypic objectives of the parent study precluded the inclusion of patients of non-White races and ethnicities which importantly limits the generalizability. Another important limitation to this study is lack of consideration on smoking status in both cases and controls. There is a robust literature on the association between smoking and substance use disorders (eg, Fishbain et al.[52]) and future studies evaluating risk factors for suicide in patients with CNCP and SUD should include smoking status as a substance of abuse. Finally, the split in the high-and-low suicide risk group based on SBQ-R scores resulted in unequal group sizes. However, the study sample was sufficiently powered for using logistic regression modeling, which can be used to detect far rarer events occurring with much smaller odds than those observed in this study.[53]

In contrast, the strengths of the current study are the presence of OUD validated through formal treatment for OUD, the use of a rigorous identification procedure, having an adequately powered analysis to investigate the psychosocial factors associated with suicide in patients with CNCP and concomitant OUD using measurements that were theoretically driven, and identifying a clinically useful cutoff for identifying individuals with elevated suicide scores using ROC analysis.

In conclusion, these findings have potentially important theoretical and clinical implications for suicide prevention and intervention in patients with CNCP and co-morbid OUD. It shows that, consistent with previous reports, several psychosocial factors, such as mental defeat, pain catastrophizing, and depression were associated with elevated risk of suicide scores in individuals with CNCP and co-morbid OUD in this patient population. The identified abovementioned factors hold a clinically meaningful predictive value in that they are possible targets of preventative interventions and management to mitigate the escalation of the risk of suicide.

Funding

This work was supported by the National Institutes of Health [NIH/NIDA R01 DA032776-05] (Cheatle). NKYT and KT were supported by the Medical Research Council [grant number MR/S026185/1].

Conflicts of interest: There are no conflicts of interest to report.

References

1. Suicide worldwide in 2019: global health estimates. Geneva: World Health Organization; 2021. Accessed July 23, 2021. Licence: CC BY-NC-SA 3.0 IGO.
2. Kochanek KD, Xu J, Arias E. NCHS Data Brief No. 395, December 2020: Mortality in the United States 2019. 2020;(395): 1-8. Accessed December 30, 2022. https://www.cdc.gov/nchs/products/index.htm
3. Campbell G, Darke S, Degenhardt L, et.al. Prevalence and characteristics associated with chronic noncancer pain in suicide decedents: a national study. Suicide Life-Threat Behav. 2020;50 (4):778–791.
4. Cheatle MD, Wasser T, Foster C, Olugbodi A, Bryan J. Prevalence of suicidal ideation in patients with chronic non-cancer pain referred to a behaviorally based pain program. Pain Physician. 2014;3;17(3;5):E359–E367.
5. Edwards RR, Smith MT, Kudel I, Haythornthwaite J. Pain-related catastrophizing as a risk factor for suicidal ideation in chronic pain. Pain. 2006;126(1-3):272-279.
6. Tang NK, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. Psychol Med. 2006;36(5):575–586.
7. Campbell G, Darke S, Bruno R, Degenhardt L. The prevalence and correlates of chronic pain and suicidality in a nationally representative sample. Aust N Z J Psychiatry. 2015;49(9):803–811.
8. Roy A. Characteristics of cocaine dependent patients who attempt suicide. Arch Suicide Res. 2009;13(1):46–51.
9. Roy A. Risk factors for attempting suicide in heroin addicts. Suicide Life Threat Behav. 2010;40(4):416–420.
10. Roy A, Janal MN. Risk factors for suicide attempts among alcohol dependent patients. Arch Suicide Res. 2007;11(2):211–217.
11. Wilcox HC, Conner KR, Caine ED. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. Drug Alcohol Depend. 2004;76(Suppl):S11–S19.
12. Cheatle MD. Depression, chronic pain, and suicide by overdose: on the edge. Pain Med. 2011;12(Suppl 2):S43–S48.
13. Vowles KE, McEntee ML, Julnes PS, Frohe T, Ney JP, van der Goes DN. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. Pain. 2015;156 (4):569–576.

14. Volkow ND, McLellan AT. Opioid Abuse in Chronic Pain–Misconceptions and Mitigation Strategies. N Engl J Med. 2016; 374(13):1253–1263.
15. Cheatle M, O'Brien C, Berrentini W, Turk D. 2018. Clinical and genetic characteristics of opioid addiction in chronic pain. NIH/NIDA R01 DA032776-05.
16. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Text Revision (DSM-IV-TR). 4th ed. Washington, DC: American Psychiatric Association; 2000. https://doi.org/10.1176/appi.books.9780890423349
17. Fillingim RB, Dworkin RH, Turk DC. The ACTTION-APS Pain Taxonomy initiative: response to Henriques et al. J Pain. 2014;15 (11):1201–1202.
18. Cheatle MD, O'Brien CP, Mathai K, Hansen M, Grasso M, Yi P. Aberrant behaviors in a primary care-based cohort of patients with chronic pain identified as misusing prescription opioids. J Opioid Manag. 2013;9(5):315–324.
19. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998; 59(Suppl 20):22–33.
20. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singap. 1994;23(2):129–138.
21. Lawson K, Reesor KA, Keefe FJ, Turner JA. Dimensions of pain-related cognitive coping: cross-validation of the factor structure of the Coping Strategy Questionnaire. Pain. 1990;43(2):195–204.
22. Broadhead WE, Gehlbach SH, de Gruy FV, Kaplan BH. The duke-UNC Functional Social Support Questionnaire. Measurement of social support in family medicine patients. Med Care. 1988;26 (7):709–723.
23. Tang NK, Salkovskis, NK, Hanna M. Mental defeat in chronic pain: initial exploration of the concept. Clin J Pain. 2007;23 (3):222–232.
24. Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. Psychosomatics. 2009;50(6):613–621.
25. Osman A, Bagge CL, Gutierrez PM, Konick LC, Kopper BA, Barrios FX. The Suicidal Behaviors Questionnaire-Revised (SBQ-R): validation with clinical and nonclinical samples. Assessment. 2001;8(4):443–454.
26. Sawilowsky SS. New effect size rules of thumb. J Mod App Stat Meth. 2009;8(2):597–599.
27. Bozdogan H. Model selection and Akaike's Information Criterion (AIC): the general theory and its analytical extensions. Psychometrika 1987;52:345–370.
28. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2020. Accessed September 23, 2019. http://www.r-project.org
29. NCSS LLC. PASS: Power Analysis and Sample Size Software. Kaysville, UT, USA. 2020. Accessed September 23, 2019. http://ncss.com/software/pass
30. Robin X, Turck N, Hainard A, et al. pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinformatics. 2011;12(1):77.
31. Oquendo MA, Volkow ND. Suicide: a silent contributor to opioid-overdose deaths. N Engl J Med. 2018;378(17):1567–1569.
32. Freeman A, Mergl R, Kohls E, et. al., C. A cross-national study on gender differences in suicide intent. BMC Psychiatry. 2017;17 (1):234.
33. Pate A, Emsley R, Sperrin M, Martin GP, van Staa T. Impact of sample size on the stability of risk scores from clinical prediction models: a case study in cardiovascular disease. Diagn Progn Res. 2020;4(1):14.
34. Racine M, Moulin DE, Nielson WR, et.el. The reciprocal associations between catastrophizing and pain outcomes in patients being treated for neuropathic pain: a cross-lagged panel analysis study. Pain. 2016;157(9):1946–1953.
35. Joiner TE. Why People Die by Suicide. Cambridge, MA: Harvard University Press; 2005.
36. Smith MT, Edwards RR, Robinson RC, Dworkin RH. Suicidal ideation, plans, and attempts in chronic pain patients: factors associated with increased risk. Pain. 2004;111(1):201–208.
37. Hinkley BS, Jaremko ME. Effects of pain duration on psychosocial adjustment in orthopedic patients: the importance of early diagnosis and treatment of pain. J Pain Symptom Manage. 1994;9 (3):175–185.
38. Tang NK, Beckwith P, Ashworth P. Mental defeat is associated with suicide intent in patients with chronic pain. Clin J Pain. 2016; 32(5):411–419.
39. Smith MT, Perlis ML, Haythornthwaite JA. Suicidal ideation in outpatients with chronic musculoskeletal pain: an exploratory study of the role of sleep onset insomnia and pain intensity. Clin J Pain. 2004;20(2):111–118.
40. O'Connor RC, Kirtley OJ. The integrated motivational-volitional model of suicidal behaviour. Phil Trans R Soc B. 2018;373 (1754):20170268.
41. Klonsky ED, Pachkowski MC, Shahnaz A, May AM. The three-step theory of suicide: description, evidence, and some useful points of clarification. Prev Med. 2021;152(Pt 1):106549.
42. United Nations. World Drug Report 2021. United Nations Publication (Sales No. E.21.XI.8). https://doi.org/10.21428/cb6ab371.e39c4e60.
43. Suokas AK, Walsh DA, McWilliams DF, et al. Quantitative sensory testing in painful osteoarthritis: a systematic review and meta-analysis. Osteoarthritis Cartilage. 2012;20(10):1075–1085.
44. Zhang Y, Ahmed S, Vo T, et al. Increased pain sensitivity in chronic pain subjects on opioid therapy: a cross-sectional study using quantitative sensory testing. Pain Med. 2015;16(5):911–922.
45. McMillan D, Gilbody S, Beresford E, Neilly L. Can we predict suicide and non-fatal self-harm with the Beck Hopelessness Scale? A meta-analysis. Psychol Med. 2007;37(6):769–778.
46. Oh J, Yun K, Hwang JH, Chae JH. Classification of suicide attempts through a machine learning algorithm based on multiple systemic psychiatric scales. Front Psychiatry. 2017;8:192.
47. Petrini L, Arendt-Nielsen L. Understanding pain catastrophizing: putting pieces together. Front Psychol. 2020;11:603420.
48. Johnson J, Gooding PA, Wood AM, Tarrier N. Resilience as positive coping appraisals: testing the schematic appraisals model of suicide (SAMS). Behav Res Ther. 2010;48(3):179–186.
49. Tang NKY, Goodchild CE, Hester J, Salkovskis PM. Mental defeat is linked to interference, distress and disability in chronic pain. Pain. 2010;149(3):547–554.
50. Cassidy SA, Bradley L, Cogger-Ward H, Rodgers J. Development and validation of the suicidal behaviours questionnaire - autism spectrum conditions in a community sample of autistic, possibly autistic and non-autistic adults. Mol Autism. 2021;12(1):46.
51. Fishbain DA, Bruns D, Bruns A, et al. The perception of being a burden in acute and chronic pain patients is associated with affirmation of different types of suicidality. Pain Med. 2016;17 (3):530–538.
52. Fishbain DA, Cole B, Lewis JE, Gao J. Is smoking associated with alcohol-drug dependence in patients with pain and chronic pain patients? An evidence-based structured review. Pain Med. 2012;13 (9):1212–1226.
53. King G, Langche Zeng GHE, Alt J, et al. Logistic Regression in Rare Events Data. 2021. https://doi.org/10.1093/oxfordjournals.pan.a004868