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## Chronic Pain and Opioid Abuse: Factors Associated With Health-Related Quality of Life

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## Abstract

**Background and Objectives:** While research on the separate relationships between healthrelated quality of life (HRQOL) and chronic pain, and HRQOL and opioid abuse has been sparse, even less work has investigated the factors associated with HRQOL in individuals who have both chronic pain and meet criteria for opioid use disorder. The data presented in this analysis should allow a better understanding the factors important to quality of life among this dual-diagnosed population.

**Methods:** Individuals with dual diagnoses of chronic pain and opioid use disorder were recruited for clinical research studies at Columbia University Medical Center. Participants (*n*=47) completed inventories to assess pain (Brief Pain Inventory), opioid (ab)use, and depression (Beck Depression Inventory). Variable from these and other inventories, along with demographic factors (age, race, sex, pain severity, depressive symptoms, duration of opioid use, route of opioid use, amount of opioid use) were entered into a regression analysis in order to identify the strongest predictors of SF-36 Health Survey score.

**Results:** In the bivariate analysis we found that demographic and drug use variables were rarely associated with HRQOL. Typically, ratings of pain severity and pain interference were the best

Ethical Approval

Informed Consent

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Declaration of Interest

Over the past 3 years, Sandra D. Comer received compensation (in the form of partial salary support) from investigator-initiated studies supported by Reckitt–Benckiser Pharmaceuticals, Schering–Plough Corporation, Johnson & Johnson Pharmaceutical Research & Development, Endo Pharmaceuticals, and MediciNova. In addition, SDC has also served as a consultant to the following companies: Grunenthal USA, Guidepoint Global, Mallinckrodt, Neuromed, Orexo, Pfizer, and Salix. Jonathan S. Vogelman, Jermaine D. Jones, Mudassir Mumtaz, and Rachel R. Luba report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

The New York State Psychiatric Institute's Institutional Review Board approved all study procedures. This study was conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

predictors. In the multivariate analysis, we found that across the several HRQOL dimensions greater Brief Pain Inventory (BPI) ratings of pain "interference" and Beck Depression Inventory (BDI) scores were consistently associated with lower HRQOL.

**Conclusions and Scientific Significance:** These data suggest that insufficient pain management and depression are significant variables contributing to lower quality of life among individuals with chronic pain and opioid use disorder. (Am J Addict 2017;26:815–821)

## INTRODUCTION

Chronic pain and opioid abuse are two highly prevalent public health concerns in the United States. It is estimated that 100 million Americans suffer from chronic pain and approximately 35% of individuals under prolonged opioid analgesic care to treat pain will suffer from opioid abuse at some point in their lifetime.<sup>1,2</sup> Moreover, research has shown that both opioid misuse and chronic pain are associated with decreased health-related quality of life [HRQOL;<sup>3–5</sup>]. HRQOL is a multidimensional concept that goes beyond direct measures of health, focusing on the impact of health on various domains of quality of life such as: physical, mental, emotional, and social functioning.<sup>6–8</sup> It has been increasingly recognized as one of the most important outcome measurements for individuals with chronic illnesses because it can be used to identify specific patient problems and inform nuanced intervention strategies.<sup>9</sup> Although HRQOL is just one type of quality of life," "quality of life," and "HRQOL" interchangeably throughout this paper, unless otherwise noted.

When compared to the general population, opioid abusers reportedly have lower HRQOL scores.<sup>4,10,11</sup> When examining factors that may affect quality of life among opioid abusers, the literature has found the absence of a causal influence of opioid abuse upon HRQOL<sup>4,12–14</sup> instead, it suggests that low quality of life scores among opioid abusers are mostly modulated by a combination of psychological and social factors associated with long term substance abuse (eg, medical complications, lack of adequate housing, poor financial standing, and social isolation<sup>5</sup>).

Like opioid abusers, individuals with chronic pain have been found to score lower on HRQOL measures than normative samples.<sup>3,15</sup> Findings indicate that while severity of pain does have some effect on HRQOL, pain severity alone does not entirely explain the relationship between chronic pain and HRQOL; rather, complex relationships among multiple factors (ie, depression, coping strategies, perceived social support) lead to lower HRQOL in people who suffer from chronic pain.<sup>16–18</sup>

While research on the relationship between HRQOL and chronic pain, and HRQOL and opioid abuse has been sparse, even less research has been conducted to investigate how HRQOL among individuals with co-morbid chronic pain and opioid abuse. The combination of these two disorders may lead to unique psychological factors that alter HRQOL. The present study is one of the first investigations to assess the psychological and individual variables that predict HRQOL among individuals with chronic pain conditions who also abuse prescription or illicit opioids. Moreover, as this study employs a population of individuals who are not actively engaged in treatment for their substance use disorders, it

may be assessing a uniquely vulnerable sample. The data presented in this analysis should allow for a better understanding of the factors most influential to the quality of life among this comorbid population.

## METHODS

#### **Data Collection**

This investigation utilized a convenience sample of individuals recruited for a clinical research study at the New York State Psychiatric Institute (NYSPI)/Columbia University Medical Center between 2012 and 2014. The parent study sought to investigate the abuse liability of various oral opioids among non-treatment-seeking, opioid-dependent volunteers with and without chronic pain conditions (persistent for at least 3 months). Potential participants were recruited through various print media and online advisements placed throughout the New York City metropolitan area. Participants were required to meet the DSM-IV criteria for opioid abuse and be physiologically dependent on opioids. Participants were excluded from the study if they had a severe Axis I psychiatric diagnosis (eg, acute suicidality, psychosis, or risk of violent behavior), or a primary diagnosis of neuropathic, or malignant pain. Participants were evaluated for these criteria using: clinical assessments of pain conducted by study nurses, assessments of drug (ab)use with a research psychologist, and a physical and mental examination with a study physician.

Both heroin and prescription opioid users were recruited for this study. Participants with valid prescriptions for opioid analgesics were assessed for abusive patterns of use (eg, unsanctioned dose escalations, intravenous or intranasal use, buying opioid medication off the street, etc.) during the clinical interview with a research psychologist. To compare opioid use across the various types of opioids, opioid use was converted into a daily morphine equivalence to use as a point of reference between the heroin and prescription opioid users. In order to estimate milligram (mg) quantities of heroin use, we used recent information from the U.S. Drug Enforcement Administration (DEA) reporting that heroin in New York City cost an average of \$.99 per mg pure.<sup>19</sup> As our participants report an average heroin price of  $\approx$ \$10 per bag (the unit of street purchase), we roughly estimated that a bag consists of  $\approx$ 10mg of pure heroin.

A number of self-report questionnaires were also administered and utilized as data for the current analysis. The Beck Depression Inventory (BDI) was used to assess the presence and severity of depressive symptoms among participants. The BDI is a 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression.<sup>20</sup> The Brief Pain Inventory (BPI) was used to evaluate pain severity and interference with life.<sup>21</sup> The BPI contains three questions regarding pain severity during the past 24 hours, and a fourth item measuring pain at present. Interference with life is measured by seven questions on the impact of pain on aspects of daily life: general activity, mood, walking ability, work, social activity, sleep, and life enjoyment. All eleven items are rated on a 0–10 scale, and two composite scores, the Pain Severity Index and the Pain Interference Index, are calculated by taking the mean of the four severity items and seven interference items separately.

The SF-36 Health Survey was used to assess HRQOL. The SF-36 questionnaire is a selfadministered, 36-item questionnaire that measures health-related functions in eight domains: physical functioning, role limitations due to physical problems, bodily pain, vitality, general health, social functioning, role limitations due to emotional problems, and emotional wellbeing.<sup>22</sup> Each subscale was calculated by taking the average of the patient's responses to the questions contained in the subscale and then standardizing it so that each had a final range of 0 (lowest level of functioning) to 100 (highest level of functioning).<sup>23</sup> The SF-36 can also be examined as summaries of physical QOL (Physical Component Summary; PCS) and emotional QOL (Mental Component summary; MCS) by calculating the mean average of all of the physically and emotionally relevant items, respectively.

#### **Statistical Analysis**

Continuous and categorical variables were summarized descriptively. These variables were entered into a linear regression to identify factors associated with the eight dimensions of SF-36, along with PCS and MCS summary scores. Categorical independent variables with two levels (eg, sex, users type: heroin vs. Rx Opioids) were coded as a binary variable and directly entered into the regression model. Level of education was coded in number of years (Years of Grades 1 thru 12 completed, in addition to # of years of post-secondary education completed). To avoid situations where strongly confounded variables could hide important predictors of HRQOL, a liberal *p*-value of <.20 was defined in a bivariate analysis to select eligible factors for the multivariate models and then, a stepwise backward selection procedure was used, based on a p<.05 to identify the best multivariate model.

## RESULTS

#### Sample Characteristics

Complete data sets were obtained from 47 participants. The mean age of participants was 49 years and 21% (*n*=10) of participants were female. Average daily equivalent morphine dose was 183.91mg per day, and the average duration of opioid use was 13.46 years. A detailed list of sample characteristics can be found in Table 1.

#### Correlates of Health-Related Quality of Life

Table 2 shows the factors that were correlated (p<0.20) with each of the HRQOL dimensions in the bivariate analyses. Table 3 shows the multivariate models that predict HRQOL, with BPI pain interference and BDI score as most predictive across the eight domains of the SF-36. Higher BPI pain interference was associated with a lower score on the physical functioning and vitality sub-scales, and a higher BDI score was associated with a lower score on the emotional well-being sub-scale. Additionally, a higher BPI pain severity score was associated with a lower score on the pain sub-scale, and higher BPI pain interference and higher BDI scores were both associated with a lower score on the role limitations due to physical health, social functioning role limitations due to emotional problems, and general health sub-scales. Concerning the Physical Component Summary, only BPI pain interference was associated with a lower score, while BDI was significantly negatively associated with Mental Component Summary score, while a positive association was found with morphine dose.

## CONCLUSIONS

This analysis sought to investigate HRQOL among an opioid-abusing population with chronic pain, in order to identify factors that affect it. Like other studies, our analysis confirmed the disease burden of these two conditions, as reflected by lower QOL in comparison to healthy populations and on par larger studies among other opioid-use disorder populations.<sup>15,24</sup> According to our multiple regression models, BPI Pain Interference ratings, and BDI ratings were the best predictors of SF-36 scores, among the variables considered. Although average BDI scores were low (<13 of a 63 total score), BDI ratings was associated with scores on the emotional well-being sub scale. The relationship we found between BDI scores and HRQOL supports previous research suggesting that both opioid abusers and individuals with chronic pain who suffer from depression have lower quality of life than people with these conditions who are not depressed.<sup>15,25</sup> Depression is a serious problem in both of these populations; studies have shown that 15.8–56% of opioid users have a diagnosis of major depression  $^{26-29}$  and that as much as 87% of people with chronic pain also suffer from depression.<sup>30</sup> Furthermore, studies have shown that psychiatric comorbidity in general can lower quality of life in physical, psychological, and social domains.<sup>31,32</sup> An interesting etiological explanation of the comorbidity between chronic pain and depression was proposed by Garland et al.<sup>33</sup> In their neuropsychopharmacological model of the comorbidity of pain, opioid abuse, and depression, the presence of chronic pain and its subsequent treatment with long-term opioid therapy, leads to hypervigilance for pain, increased salience for opioid drug cues, and dysregulation of stress and reward circuitry. This relationship is mediated by opioid-induced effects on dopaminergic activity, which promotes recurrent self-medication with opioids, resulting in a positively reinforced connection among pain, depression, and opioid abuse.

BDI along with BPI Pain Interference together was associated with scores on four of the SF-36 sub-scales: social functioning, role limitations due to physical health, role limitations due to emotional problems, and general health. BPI Pain Interference was also associated with two additional subscale scores: physical functioning and vitality. It is not surprising that BPI Pain Interference significantly was associated with scores on six of the eight SF-36 sub-scales because both measures assess similar constructs. The more noteworthy finding is that BPI Pain Severity was only associated with scores on one SF-36 sub-scale: pain. This disparity suggests that the severity of chronic pain alone has little impact of quality of life, and the more important factor is the degree to which pain interferes with the individual's ability to fulfill their day-to-day responsibilities. Other investigations also support this hypothesis regarding how chronic pain exacts its detrimental effects of HRQOL.<sup>3,16,34</sup>

Curiously, no drug abuse measures were found to be significant in our final multivariate models. Previous findings suggest that drug abuse itself may not directly affect HRQOL. Instead, drug abuse appears to mediate the relationship between the two through other psychosocial factors such as inability to maintain employment.<sup>31,35,36</sup> Although this study did not have a comparator sample of non-abusers, the lack of significance of factors commonly used as indicators of addiction severity (eg, route of abuse (oral vs. parenteral), and type of opioid abused (Rx vs. heroin) can be used as cautious support of this hypothesis.

In other studies, educational level has been shown to affect the impact of pain on quality of life,<sup>8</sup> yet in our investigation this factor only approached significance as a predictor of two SF-36 sub-scales. Differences between the current study and the previous literature may be due to the relatively small sample size of the current analysis. Using a smaller, convenience sample may have left us underpowered to observe the influence of education level, along with other demographic factors such as sex and race/ ethnicity. A larger sample size would have also enabled us to distinguish primarily prescription opioid users from primarily heroin users in our analysis, which may have been informative considering that research has shown meaningful differences between these two groups in patterns of drug use, psychiatric comorbidities, and social stability.<sup>37–39</sup> A power analysis was conducted to determine the achieved power, using the mean number of predictors in the multivariate models and the mean  $R^2$ . This analysis confirmed that the current analysis was slightly underpowered (>80%).

An additional limitation of the current study is also our use of only one assessment of HRQOL (SF-36).SF-36quantifiesquality of life in terms of physical, social, and mental wellbeing, while other measures, such as Global Quality of Life assesses the individual's satisfaction with life and covers life domains such as physical and material well-being, personal development, relationships with others, participation in social, community, and civic activities, and recreation.<sup>40</sup> Future studies should employ multiple scales as dependent variables, in order to validate the relationship between the predictors and quality of life.<sup>41</sup>

In summary, our findings suggest that depressive symptoms and pain interference could be the most viable predictors of quality of life among opioid abusers with chronic pain. Future research should focus on identifying specific psychosocial variables that explain the relationship between depression, pain interference, and quality of life in this population, and also explore potential group differences between individuals who primarily abuse illicit as opposed to prescription opioids. Additionally, medications development should begin to explore novel interventions that treat depression and pain simultaneously, given the possible neurological relationship among these disorders, a pharmacotherapy of this type could be more effective than current medications. Continued investigation of this topic will hopefully lead to a clearer understanding of the mechanisms that marginalize individuals with these two conditions, which will in turn inform more effective interventions.

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## Table 1.

## Sample characteristics

	Participants (%), median (IQR), or mean (SD)
Hepatitis Cþ	16 (34)
Age (years)	49 (25–66)
Sex Male	37 (79)
Female	10 (21)
Ethnic/racial category	
African American	15 (32)
Caucasian	9 (19)
Hispanic	16 (34)
Other/not reported	7 (15)
Years of education	12.3 (2.0)
Preferred route of opioid administration	
Heroin	
Intranasal	14 (30)
Intravenous	8 (17)
Prescription opioids	
Oral	25 (53)
Daily equivalent morphine dose $(mg)^a$	183.9 (162.9)
Years of opioid use	13.4 (12.7)
BDI score	12.1 (9.5)
BPI ratings	
BPI pain severity rating	6.1 (2.0)
BPI pain interference rating	5.0 (2.5)
SF-36 scales	
Physical functioning	55.5 (33.5)
Role limitations due to physical functioning	51.6 (46.4)
Role limitations due to emotional problems	66.3 (41.7)
Vitality	52.8 (21.4)
Emotional well-being	68.5 (19.2)
Social functioning	67.5 (29.9)
Pain	41.3 (24.8)
General health	65.4 (23.2)

<sup>a</sup>Based on reported use over the past month.

 $b_{\mbox{\scriptsize Based}}$  on most preferred method of administration.

#### Table 2.

Bivariate analyses of factors associated with SF-36 health-related quality of life scales

	Bivar <u>analy</u>			Bivariate analysis	
	β	<i>p</i> -value		ß	<i>p</i> -value
Physical functioning	-		Emotional well-being		
Hepatitis C status	.24	<.20	BDI score	61	<.001
BDI score	35	<.05	BPI pain severity rating	27	<.10
BPI pain severity	62	<.001	BPI pain interference rating	40	<.01
BPI pain interference	70	<.001	Daily equivalent morphine dose	24	<.20
Years of	.27	<.10			
Role limitations due to physical health			Social functioning		
BDI score	55	<.001	BPI pain severity rating	34	<.05
BPI pain severity rating	33	<.05	BPI pain interference rating	57	<.001
BPI pain interference rating	61	<.001	Daily equivalent morphine dose	.31	<.05
Daily equivalent morphine dose	.20	<.20	Educational level	.26	<.10
			BDI score	51	<.001
Role limitations due to emotional problems			Pain		
BDI score	56	<.001	BPI pain severity rating	66	<.001
BPI pain severity rating	36	<.05	BPI pain interference rating	65	<.001
BPI pain interference rating	56	<.001	Years of use	.24	<.20
Daily equivalent morphine dose	.32	<.05			
Educational level	.27	<.10			
Vitality			General health		
BDI score	48	<.01	BDI score	60	<.001
BPI pain severity rating	40	<.01	BPI pain severity rating	23	<.20
BPI pain interference rating	57	<.001	BPI pain interference rating	42	<.01
Daily equivalent morphine dose	.21	<.20	Daily equivalent morphine dose	.30	<.05
Educational level	20	<.20	Educational level	.29	<.10
Physical component summary			Mental component summary		
Age	.26	<.10	Age	24	<.20
Sex	.36	<.05	Sex	.28	<.10
BDI score	41	<.01	BDI score	38	<.01
BPI pain severity rating	57	<.01	BPI pain severity rating	29	<.10
BPI pain interference rating	60	<.001	BPI pain interference rating	32	<.05
Daily equivalent morphine dose	.33	<.05	Daily equivalent morphine dose	.31	<.05
Years of use	.32	<.05			

Bivariate analyses are based on linear regression models (n=47).

#### Table 3.

Multivariate analyses of factors associated with SF-36 health-related quality of life scales

	Multivariate analysis			Multivariate analysis	
	<b>β</b> (95%CI)	<i>p</i> -value		<b>β</b> (95%CI)	<i>p</i> -value
Physical functioning			Emotional well-being		
BPI pain interference	-9.09 (-12.05 to -6.13)	<.001	BDI score	-1.02 (-1.46 to -0.49)	<.001
			BPI pain interference	-1.77 (-3.73 to -0.20)	.076
Role limitations due to physical health			Social functioning		
BDI score	-1.71 (-2.87 to -0.55)	.005	BPI pain interference	-5.51 (-8.43 to -2.59)	<.001
BPI pain interference	-9.00 (-13.32 to -4.70)	<.001			
Role limitations due to emotional problems			Pain		
BDI score	-1.41 (-2.52 to -0.28)	.014	BPI pain interference	-2.80 (-6.20 to 0.55)	.100
BPI pain interference	-7.47 (-11.36 to -3.58)	<.001	BPI pain severity	-5.50 (-9.72 to 1.28)	.012
Educational level	7.82 (-0.52 to 16.17)	.066			
Vitality			General health		
BDI score	-0.50 (-0.11 to 0.08)	.091	BPI pain interference	-2.35 (-4.68 to -0.02)	.048
BPI pain interference	-4.11 (-0.62 to -2.07)	<.001	BDI score	-1.24 (-1.87 to -0.61	<.001
Physical component summary			Mental component summary	0.31 (0.00 to .009)	.029
BPI pain interference	-5.93 (-8.41 to -3.46)	<.001	Daily equivalent morphine dose	0.31 (0.00 to .009)	.029
			BDI score	-0.35 (-1.75 to -0.20)	.015

Multivariate analyses are based on linear regression models (n=47).