THE AMERICAN JOURNAL ON ADDICTIONS

The American Journal on Addictions, 19: 409–415, 2010

ISSN: 1055-0496 print / 1521-0391 online
DOI: 10.1111/j.1521-0391.2010.00065.x

The Timing of Onset of Pain and Substance Use Disorders

Mark A. Ilgen, PhD,[1,2] Brian Perron, PhD,[1,3] Ewa K. Czyz, MA,[2] Ryan J. McCammon, BA,[2] Jodie Trafton, PhD[4,5]

[1]VA Serious Mental Illness Treatment Research and Evaluation Center, Ann Arbor, Michigan
[2]University of Michigan Department of Psychiatry, Ann Arbor, Michigan
[3]University of Michigan School of Social Work, Ann Arbor, Michigan
[4]Department of Veterans Affairs Palo Alto Health Care System, Palo Alto, California
[5]Stanford University School of Medicine, Palo Alto, California

Using data from the National Comorbidity Survey—Replication, this study examined the timing of onset of self-report comorbid chronic nonarthritis pain and substance use disorders (SUDs) and characteristics associated with different onset patterns. Most individuals (58.2%; N = 351/632) report that the SUD preceded the onset of pain. Relative to those with SUDs prior to the onset of chronic pain, those experiencing pain first were less likely to have a drug use disorder, more likely to have head pain, to be younger at the onset of the first condition, and to have a shorter duration between condition onsets. (Am J Addict 2010;19:409–415)

INTRODUCTION

Chronic pain and substance use disorders (SUDs) are often long-standing conditions associated with significant loss of productivity and quality of life.[1–4] Also, these conditions frequently co-occur. For example, population surveys in the United States (U.S.) have generally found an elevated rate of SUDs in those with chronic pain compared to those without.[5–7] The rates of co-occurrence in clinical samples of patients seeking treatment for either a SUD or pain are usually much higher than those found in the general population.[8–12] Specifically, data from clinical samples indicate that up to 52% of patients in SUD treatment report chronic pain and up to 19% of patients seeking treatment for pain report a current SUD.[10,11]

Several possible reasons exist for the frequent co-occurrence of pain and SUDs, and a number of hypotheses for this high rate of co-occurrence have been proposed. Perhaps the best know explanation is that drugs or alcohol are used to "self-medicate" or manage the physiological aspects of pain.[11,13] Others (eg, Gatchel, 1991 in Dersh et al.[14]) have proposed that the association between chronic pain and multiple forms of psychopathology may be explained by a diathesis-stress model in which preexisting characteristics (in this case, an underlying predisposition for SUDs) become activated by the stress created by a chronic pain condition. A third potential explanation for the association between chronic pain and SUDs is that the risky lifestyle associated with prolonged substance use increases the likelihood of injury, which, over time, leads to the development of chronic pain conditions.[15,16] In all of these proposed models, one of the disorders causes or triggers the development of the other disorder, thus implying an obvious temporal patterning to the development of the two disorders.

One way to evaluate the plausibility of these hypotheses is to examine the temporal ordering of the onset of both disorders. In the case of the self-medication hypothesis and the diathesis-stress model in which pain increases the odds of SUDs, one would expect that the pain condition would predate the onset of the SUD. Alternatively, if chronic pain were caused by injury during a period of problematic substance use, then one would expect that the pattern of onset would reflect this as well. A small number of studies in clinical samples have examined the temporal ordering of pain and SUDs. These indicate the vast majority of patients with co-occurring pain and SUDs (from 77% to 94%) report that the date of onset for the SUD preceded the onset of the chronic pain condition.[10,17] However, Brown et al.[17] found that, although in their sample of primary care patients the overall rates of lifetime and current SUDs were no greater in those with chronic back pain compared to those without, chronic pain patients were at an increased risk for the onset of a new SUD during the first 5 years

Received March 19, 2009; revised May 27, 2009; accepted October 28, 2009.

The views expressed in this report are those of the authors and do not necessarily represent those of the VA. Address correspondence to Dr. Ilgen, 4250 Plymouth Road, Ann Arbor, MI 48109-5763. E-mail: marki@umich.edu.

following the onset of chronic pain compared with other 5-year periods in their lives.

Better data are needed to examine the pattern of onset of pain and SUDs in nonclinical samples. Previous studies describing the temporal order of the onset of these two conditions have been based entirely on patients treated for back pain.[10,17] Moreover, the number of patients with both conditions in these studies was small and the extent to which these findings generalize to untreated samples is unknown. More broadly, the characteristics of those with differing patterns of onset have not been well studied. It is possible that individual characteristics will distinguish between patients with differing patterns of onset.

Thus, the present study was undertaken to examine the co-occurrence of nonarthritis pain and SUDs in a nationally representative sample of U.S. households. First, we examined the extent of lifetime association between back pain, head pain, or other nonarthritis pain and SUDs and the prevalence of the co-occurrence of SUDs and pain. Then, within the subset of individuals with both pain and SUDs, we described the patterns of onset of these two conditions (ie, the onset of the SUD preceded the pain condition, the onset of the SUD and pain condition occurred during the same year, and the onset of the pain condition preceded the SUD). Finally, in those with pain and SUDs, we examined which demographic factors, psychiatric disorders and pain conditions are differentially associated with one pattern of onset or another. These analyses are undertaken in order to describe some of the heterogeneity among the population with both conditions.

METHODS

Sample

The present study was based on the publicly accessible data from the National Comorbidity Survey Replication (NCS-R). These data are available at http://www.icpsr.umich.edu/CPES/. Using a multistage clustered area probability sample of the English-speaking U.S. household population, the NCS-R was carried out between February 2001 and April 2003.[18] As described in detail by Kessler et al.,[19] this study had two parts. Part I assessed for lifetime and 12-month DSM-IV mental disorders (n = 9,282). The second part, which included the measures of pain, was administered to 5,692 of the original respondents. The present analyses were conducted on those who participated in Part II. The public access version of the NCS-R dataset provides sampling weights that adjust for differential probabilities of selection, over-sampling of Part I respondents with a mental disorder and unit nonresponse, while also post-stratifying the sample to the 2000 Census on sociodemographic and geographic variables, allowing the Part II sample to remain representative of the English-speaking U.S. household population.[18] The NCS-R did not have an upper age limit. In the present analyses, 11 cases with comorbid pain and SUDs were excluded because the temporal ordering of the conditions could not be established.

Measures

The *World Health Organization Composite International Diagnostic Interview* (CIDI) version 3.0[20] was used to obtain DSM-IV diagnoses and the date of onset for each disorder.

Substance Use Disorders

Based on responses to the CIDI, the initial interview yielded lifetime diagnoses of alcohol abuse, alcohol dependence, drug abuse, and drug dependence. For the present study, these were combined into a single dichotomous (categorical) measure indicating the presence or absence of "any lifetime SUD."

Pain

The present study focused on nonarthritic pain. Nonarthritic pain was measured using three self-report items that assessed for lifetime experiences of "chronic back or neck problems," "frequent or severe headaches," and "any other chronic pain condition." "Any other chronic pain condition" referred specifically to pain not attributable to arthritis, back or neck pain, or headaches. Each item was dichotomously scored (yes/no). For the current study, a lifetime nonarthritic pain measure was created by combining these items into a single dichotomous (categorical) indicator. Specifically, subjects who endorsed any of the three pain items were classified as having a lifetime history of nonarthritic pain.

Pattern of Onset

The pattern of onset, or temporal ordering, of pain and SUDs was determined by comparing the year of onset for pain and SUDs. Three patterns of onset were possible: (1) pain preceding SUD, (2) SUD preceding pain, and (3) pain and SUD with same-year onset. Also, for all individuals with both a pain and SUD diagnosis, we coded several variables related to onset of conditions including: age of onset of the SUD (or the first SUD for those with multiple SUDs), age of onset of the pain condition age (or the first pain condition for those with more than one pain condition), age of onset of first condition, age of comorbid SUD and pain onset, and length of time in years between the onset of the SUD and pain conditions.

Other Psychiatric Conditions

Lifetime diagnoses of mood disorders and anxiety disorders from the CIDI were also examined using the DSM-IV criteria. Respondents were coded as having a lifetime *anxiety disorder* if they met criteria for generalized anxiety disorder, adult separation anxiety disorder, social

phobia, specific phobia, panic disorder, agoraphobia, or posttraumatic stress disorder; all those who met criteria for bipolar disorder, major depressive disorder, or dysthymia were coded as having a *mood disorder*. Each of these indicators (lifetime mood disorder and lifetime anxiety disorder) was coded dichotomously, indicating the presence or absence of the disorder.

Demographic Variables

This study examined age, gender, race, educational attainment, marital status, and poverty level income.

Analyses

The present study begins by describing the lifetime association between SUDs and pain. The remaining analyses focus on the subset of individuals who report both SUDs and pain in their lifetime. First, we describe the frequency of differing patterns of onset of the two conditions (ie, pain preceding SUD, same-year onset, SUD preceding pain). Next, in bivariate analyses, we examine how patient demographic and diagnostic factors relate to pattern of onset. Finally, in a multiple logistic regression analysis, we examine the patient characteristics associated with the likelihood of pain preceding SUDs versus SUDs preceding pain. Odds ratios from this model are presented as measures of association. This model includes all demographic (except age), psychiatric and specific pain conditions, which were significant in the bivariate analyses. The multinomial multiple logistic regression model only included age of first onset and years between onset of the two conditions. Also, it is important to note that this study was undertaken to aid in hypothesis generation and no correction was made for conducting multiple comparisons.

In the present study, all analyses were carried out using the NCS-R sampling weights and sample design variables in SAS 9.2 procedures that use a Taylor series linearization to estimate standard errors corrected for the complex sample design.

RESULTS

Lifetime pain and SUDs co-occur at rates that are greater than chance (OR = 1.5; 95% CI: 1.3, 1.8). In those with SUDs, 52.8% (95% CI: 49.2, 56.4) reported pain; 17.6% (95% CI: 15.9, 19.3) of those with pain reported a lifetime SUD. In the general population, the rates of any lifetime chronic pain and any lifetime SUD were 43.9% (95% CI 41.9, 45.9) and 14.6% (95% CI: 13.5, 15.8), respectively. Additionally, in those with both pain and SUDs, 6.4% reported same-year onset of SUD and pain, 35.4% reported that their pain preceded their SUD, and 58.2% reported that their SUD preceded their pain.

The remaining analyses focus on those individuals with pain and SUDs and examine differences between those with same-year onset of pain and SUDs, pain preceding SUDs, and SUDs preceding pain (see Table 1). In bivariate analyses, gender was differentially associated with membership in these three groups; specifically, a higher proportion of those with pain preceding SUDs were women relative to those with SUDs preceding pain. Compared to those with pain preceding SUD, those with same-year onset and those with SUDs preceding pain were more likely to have a drug use disorder. Those with pain preceding SUDs and those with same-year onset were more likely to have head pain than those with SUD preceding pain. No differences were found between groups with differing patterns of onset of pain and SUDs on measures of race, education, rates of anxiety disorders, mood disorders, alcohol use disorders, back pain or "other" pain conditions.

In terms of age, those with same-year onset and those with pain preceding SUDs were, on average, younger than those with SUDs then pain. Those with simultaneous onset reported a younger age of SUD onset than those whose pain preceded SUDs; those with pain then SUDs were older at age of onset of the SUD than those with SUDs then pain. The age of chronic pain onset was youngest for the pain then SUD group followed by those with simultaneous onset and SUD then pain. In terms of age of onset of either condition, those with pain then SUD had the earliest age of onset, followed by those with simultaneous onset and SUDs then pain. All three groups differed from one another in terms of age of comorbid onset with the youngest group being those with simultaneous onset, the next oldest group being pain preceding SUDs and the oldest group being the SUD preceding pain group. Finally, the length of time between onsets of conditions was greater for those who first experienced a SUD compared to those who first experienced pain.

A logistic regression analysis was used to examine the relative impact of patient demographic and diagnostic factors on the likelihood of onset of pain then SUD relative to SUD then pain. This analysis included all variables that were significantly associated with different patterns of onset in the bivariate analyses with the exception of the age-related variables. For the logistic regression analysis we used two age-related variables: (1) age of onset of the first condition and (2) length of time in years between onset of conditions. This decision was made because the endpoint of interest (co-diagnosis) is an event, which has already occurred in all participants by the time of the survey. Additionally, the two variables that were included allowed for a determination of whether younger age of onset of either condition was of importance and whether the length of time between onsets of conditions differed meaningfully between groups. Finally, the multivariable analyses excluded those with simultaneous age of onset. This was done because the time between onsets of conditions would be zero for all participants in this group and, thus, would not meaningfully add to our analyses.

The results of the final logistic regression analysis are presented in Table 2. Relative to those with SUDs followed

TABLE 1. Unadjusted associations between demographic and diagnostic factors and different patterns of onset of pain and substance use disorders

		A Simultaneous onset (n = 38)			B Pain then Substance Use (n = 243)			C Substance Use then Pain (n = 351)			Model tests: Overall		A versus B		A versus C		B versus C	
Categorical measures		n	%	95% CI	n	%	95% CI	N	%	95% CI	χ^2	p	χ^2	p	χ^2	p	χ^2	p
Gender	Female	16	33.5	(15.7–51.4)	119	46.4	(39.4–53.4)	139	33.7	(29.7–37.8)	12.7	.002	1.8	.186	.0	.982	11.9	.001
	Male	22	66.5	(48.6–84.3)	124	53.6	(46.6–60.6)	212	66.3	(62.2–70.3)								
Race	Non-white	10	19.5	(7.5–31.6)	59	22.6	(16.3–29.0)	91	28.4	(19.8–37.0)	3.9	.140						
	White	28	80.5	(68.4–92.5)	184	77.4	(71.0–83.7)	260	71.6	(63.0–80.2)								
Education	0–12	18	53.4	(33.4–73.5)	129	56.9	(48.9–64.9)	191	57.5	(50.0–65.0)	.1	.937						
	13+	20	46.6	(26.5–66.6)	114	43.1	(35.1–51.1)	160	42.5	(35.0–50.0)								
Lifetime anxiety disorder	No	15	46.1	(25.4–66.7)	74	35.4	(27.4–43.5)	126	39.5	(30.4–48.5)	1.1	.568						
	Yes	23	53.9	(33.3–74.6)	169	64.6	(56.5–72.6)	225	60.5	(51.5–69.6)								
Lifetime mood disorder	No	19	58.6	(42.4–74.8)	111	50.1	(43.0–57.3)	200	59.5	(53.0–65.9)	4.6	.099						
	Yes	19	41.4	(25.2–57.6)	132	49.9	(42.7–57.0)	151	40.5	(34.1–47.0)								
Lifetime alcohol disorder	No	4	8.0	(.0–16.4)	21	8.2	(4.6–11.8)	36	10.1	(5.9–14.2)	.5	.792						
	Yes	34	92.0	(83.6–100.0)	222	91.8	(88.2–95.4)	315	89.9	(85.8–94.1)								
Lifetime drug disorder	No	12	29.2	(13.2–45.2)	118	51.9	(44.1–59.7)	139	41.8	(35.9–47.6)	11.8	.003	5.6	.018	1.7	.190	7.4	.007
	Yes	26	70.8	(54.8–86.8)	125	48.1	(40.3–55.9)	212	58.2	(52.4–64.1)								
Back pain	No	11	26.8	(9.0–44.6)	64	26.6	(20.1–33.1)	94	24.7	(20.6–28.8)	.2	.904						
	Yes	27	73.2	(55.4–91.0)	179	73.4	(66.9–79.9)	257	75.3	(71.2–79.4)								
Head pain	No	13	39.8	(24.4–55.2)	72	30.3	(22.3–38.3)	210	59.9	(53.4–66.5)	36.3	.000	1.0	.320	4.2	.040	34.8	.000
	Yes	25	60.2	(44.8–75.6)	171	69.7	(61.7–77.7)	141	40.1	(33.5–46.6)								
Other pain	No	27	72.0	(55.5–88.4)	178	72.3	(64.6–80.1)	249	72.5	(67.9–77.1)	.0	.997						
	Yes	11	28.0	(11.6–44.5)	65	27.7	(19.9–35.4)	102	27.5	(22.9–32.1)								
Continuous measures		n	Years	95% CI	N	Years	95% CI	n	Years	95% CI	Overall F	Overall p	A versus B t	A versus B p	A versus C t	A versus C p	B versus C t	B versus C p
Age		38	35.9	(29.4–42.4)	243	40.3	(38.0–42.5)	351	43.1	(41.6–44.7)	7.0	.002	1.2	.246	2.3	.028	2.2	.032
Comorbid pain and SUD age of onset		38	18.2	(16.7–19.8)	243	23.4	(22.2–24.7)	351	31.0	(29.8–32.2)	109.4	.000	5.0	.000	14.5	.000	8.1	.000
SUD age of onset		38	18.2	(16.7–19.8)	243	23.4	(22.2–24.7)	351	19.7	(19.1–20.4)	15.7	.000	5.0	.000	1.8	.074	5.0	.000
Chronic pain age of onset pain or SUD age of first onset		38	18.2	(16.7–19.8)	243	15.1	(14.0–16.3)	351	31.0	(29.8–32.2)	176.8	.000	3.1	.003	14.4	.000	17.0	.000
		38	18.2	(16.7–19.8)	243	15.1	(14.0–16.3)	351	19.7	(19.1–20.4)	23.8	.000	3.1	.003	1.8	.074	6.8	.000
Years between onsets		38	.0	(.0–.0)	243	8.3	(7.2–9.3)	351	11.3	(10.3–12.2)	21.8	.000	—	—	—	—	4.7	.000

TABLE 2. Multinomial multiple logistic regression predicting pain prior to substance use disorder onset versus substance use disorder prior to pain onset

	Pain then Substance Use	
Predictor	OR	95% CI
Female	1.35	(.92–1.96)
Drug disorder	.29***	(.20–.43)
Head pain	2.45***	(1.54–3.91)
Age of first onset	.87***	(.83–.91)
Years between onsets	.94***	(.92–.96)
	$n = 594$	

The reference group for this model is Substance Use then Pain.
This model excludes the Simultaneous Onset cases from the analysis.
*$p < .05$; **$p < .01$; ***$p < .001$.

by pain, those with pain preceding SUDs were less likely to have a drug use disorder and more likely to have head pain. Additionally, those with pain then a SUD had a younger age of onset of the first condition and a shorter time between onset of conditions than those with a SUD then pain.

DISCUSSION

In a national representative sample of U.S. adults, the presence of lifetime pain is significantly associated with a lifetime diagnosis of a SUD. In those with both lifetime pain and lifetime SUDs, the majority reported that the SUD started prior to the pain. Additionally, relative to individuals who reported onset of the SUD prior to the onset of pain, those for whom the pain disorder preceded the SUD had a younger age of onset of the first condition, shorter time between onset of conditions, were less likely to have a drug use disorder, and more likely to have head pain.

These findings highlight the high degree of heterogeneity in the pattern of onset of pain and SUDs. In the majority of cases, SUDs preceded pain, although it is important to note that in a substantial proportion of individuals, pain did precede the development of a SUD. Thus, as proposed in the self-medication hypothesis,[11,13] some individuals could have developed a SUD as a consequence of their attempts to manage their pain. It is unlikely that a single explanation for the reasons for comorbidity will apply to all individuals, and it would be more fruitful for the field to focus on identifying those who may be at particularly high risk for different patterns of onset.

The present findings indicate that certain characteristics can distinguish between those who report different patterns of onset. Those with SUDs prior to pain report, on average, an older age of onset of either condition, a longer interval between onset of conditions, and a lower likelihood of head pain. It is possible that injuries following SUDs are more likely to involve back pain or "other" pain than headaches and that these forms of pain take time to develop. On the other hand, SUDs may develop more rapidly and at a younger age after the onset of chronic head pain.

Interestingly, the pattern of onset of the two conditions does not seem to be associated with co-occurring mood or anxiety disorders. One might expect if a general diathesis-stress model accounted for the onset of a SUD following pain (eg, Gatchel, 1991 in Dersh et al.[14]), that these individuals would also be at an elevated risk for other common conditions that often follow stress. In these data, this does not appear to be the case.

We note, however, that lack of a consistent temporal pattern of SUD and chronic pain development is also consistent with an alternative hypothesis suggesting that these two disorders share underlying risk factors (eg, a tendency to overrespond to opportunities for immediate positive and negative reinforcement), but which do not drive the development of the other disorder. Were this true, the pattern of onset of these disorders would reflect the patterns of development of the individual disorders. Initiation of substance use most typically occurs in adolescence, with greater than 50% of the U.S. population reporting being drunk from alcohol by 12th grade and having experimented with illicit drugs by college age.[21] Moreover, earlier initiation of use has been associated with greater likelihood of developing a dependence disorder.[22] Musculoskeletal disorders may develop at any time, but increase in prevalence occurs in older populations.[23] Thus all individuals, irrespective of substance use, are at increased risk for pain over time. Migraines are most frequently first experienced during childhood or adolescence, with over 80% of those with migraines experiencing their first migraine before age 30.[24] Given these patterns of onset, one would expect that the majority of patients with musculoskeletal pain would have developed a SUD before their chronic musculoskeletal pain started (eg, a typical patient would initiate substance use in adolescence and develop back pain at age 50). In contrast, one would expect that patients with migraine and a SUD would have a more mixed order of onset, as both disorders commonly begin around adolescence. These expectations are consistent with the observed associations between age of first onset of comorbid condition, time between conditions and head pain versus other pain in our sample.

The present study has several limitations that should be noted. All analyses were cross-sectional and the determination of ordering of SUDs and pain was based on retrospective report. These estimates are likely to be influenced by patient expectancies and recall bias. Also, the present data only allowed for the determination of the year of onset of each condition. Improved precision of timing of onset measures of both conditions would decrease the size of the "same-year onset" group and decrease the error in measurement of the two primary groups of interest: pain preceding SUDs and SUDs preceding pain.

Additionally, the measures of pain were based on a series of single items. The validity of these items and their

relationship to established pain conditions is unknown. These are clearly crude measures of pain and they do not capture the full spectrum of possible pain conditions. Also, the publicly available data in the NCS-R do not allow for more finely grained analyses of the type of drug use disorder for either drug abuse or drug dependence diagnoses. The use of the aggregate measures of many of the variables of interest (eg, drug use disorders) may combine heterogeneous elements and fail to detect other factors that could meaningfully differentiate between those with differing patterns of onset of pain and SUDs. Furthermore, even if these data were available, it is unlikely that this study would have been able to examine difference based on different substances given the low base rate of these disorders in the general population.[25] In addition, due to the structure of the questions used to render a diagnosis of alcohol dependence or drug dependence in the NCS-R, this dataset slightly underestimates the true prevalence of these disorders.[26,27] The NCS-R is designed to be representative of the English-speaking U.S. household population but the findings may not apply to individuals who are hospitalized. It is also important to note that the primary analyses were limited to those who had time to develop both pain and SUDs. Some individuals who had one condition may have gone on to ultimately develop the other but had not done so, or had died, prior to completion of the survey.

Despite these limitations, this is the first study of which we are aware to examine the pattern of co-occurrence of SUDs and pain in the general U.S. population. These findings indicate that pain and SUDs co-occur at rates that are higher than chance and different patterns of onset are common. Given these findings, and those that have been reported previously based on results from clinical samples, it is unlikely that a single explanation, such as the "self-medication hypothesis," will fully account for the relationship between SUDs and chronic pain in all individuals. Instead, it is important to examine how different characteristics may influence the likelihood of onset of one condition following the other. Future longitudinal research is needed to accomplish this goal.

Future research should also be careful to distinguish mechanisms that explain the development of this comorbidity from mechanisms in which the two disorders interact to modify the severity or course of the disorders. For example, even if a person developed a SUD stemming from a period of experimentation in adolescence and then developed chronic pain after a back injury at age 40, stress from the pain could exacerbate the SUD or the pain itself could become a cue, which triggers substance use. Thus, the stress-diathesis and self-medication models may be relevant to understanding maintenance of the disorders over time even if they do not explain how the disorders developed in the first place. Although understanding developmental mechanisms is important for developing prevention programs, understanding ongoing interactions between chronic pain and substance use is apt to be more relevant for development of treatment interventions.

This work was supported by grant MRP 05-137 from the Department of Veterans Affairs Health Services Research and Development Service, Washington, DC (Dr. Ilgen).

We would like to thank the members of the NCS-R research group for allowing other researchers to access their data. A complete list of other NCS-R publications and the measures used in the NCS-R is available at http://www.hcp.med.harvard.edu/ncs. This manuscript has not been reviewed or endorsed by the NCS-R research group and does not necessarily represent the opinions of its members who are not responsible for the content.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1. Becker N, Bondegaard Thomsen A, Olsen AK, et al. Pain epidemiology and health related quality of life in chronic non-malignant pain patients referred to a Danish multidisciplinary pain center. *Pain*. 1997;73:393–400.
2. Kerr S, Fairbrother G, Crawford M, et al. Patient characteristics and quality of life among a sample of Australian chronic pain clinic attendees. *Intern Med J*. 2004;34:403–409.
3. Smith KW, Larson MJ. Quality of life assessments by adult substance abusers receiving publicly funded treatment in Massachusetts. *Am J Drug Alcohol Abuse*. 2003;29:323–335.
4. Welsh JA, Buchsbaum DG, Kaplan CB. Quality of life of alcoholics and non-alcoholics: Does excessive drinking make a difference in the urban setting? *Qual Life Res*. 1993;2:335–340.
5. Demyttenaere K, Bruffaerts R, Lee S, et al. Mental disorders among persons with chronic back or neck pain: Results from the world mental health surveys. *Pain*. 2007;129:332–342.
6. Saunders K, Merikangas K, Low NCP, et al. Impact of comorbidity on headache-related disability. *Neurology*. 2008;70:538–547.
7. Von Korff M, Crane P, Lane M, et al. Chronic spinal pain and physical-mental comorbidity in the United States: Results from the national comorbidity survey replication. *Pain*. 2005;113:331–339.
8. Dersh J, Gatchel RJ, Mayer T, et al. Prevalence of psychiatric disorders in patients with chronic disabling occupational spinal disorders. *Spine*. 2006;31:1156–1162.
9. Kinney RK, Gatchel RJ, Polatin PB, et al. Prevalence of psychopathology in acute and chronic low back pain patients. *J Occup Rehabil*. 1993;2:95–103.
10. Polatin PB, Kinney RK, Gatchel RJ, et al. Psychiatric illness and chronic low-back pain. The mind and the spine—which goes first? *Spine*. 1993;18:66–71.
11. Rosenblum A, Joseph H, Fong C, et al. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. *JAMA*. 2003;289:2370–2378.
12. Trafton JA, Oliva EM, Horst DA, et al. Treatment needs associated with pain in substance use disorder patients: Implications for concurrent treatment. *Drug Alcohol Depend*. 2004;73:23–31.

13. Karasz A, Zallman L, Berg K, et al. The experience of chronic severe pain in patients undergoing methadone maintenance treatment. *J Pain Symptom Manage*. 2004;28:517.
14. Dersh J, Polatin PB, Gatchel RJ. Chronic pain and psychopathology: Research findings and theoretical considerations. *Psychosom Med*. 2002;64:773–786.
15. Compton P, Darakjian J, Miotto K. Screening for addiction in patients with chronic pain and "problematic" substance use: Evaluation of a pilot assessment tool. *J Pain Symptom Manage*. 1998;16:355–363.
16. Gatchel RJ, Dersh J. Psychological disorders and chronic pain: Are there cause-and-effect relationships? In: Turk DC, Gatchel RJ, eds. *Psychological Approaches to Pain Management: A Practitioner's Handbook*, 2nd edn. New York: Guilford Press; 2002:30–51.
17. Brown RL, Patterson JJ, Rounds LA, et al. Substance abuse among patients with chronic back pain. *J Fam Pract*. 1996;43:152–161.
18. Kessler RC, Merikangas KR. The National Comorbidity Survey Replication (NCS-R): Background and aims. *Int J Methods Psychiatr Res*. 2004;13:60–68.
19. Kessler RC, Berglund P, Chiu WT, et al. The US National Comorbidity Survey Replication (NCS-R): Design and field procedures. *Int J Methods Psychiatric Res*. 2004;13:69–92.
20. Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res*. 2004;13:93–121.
21. Johnston LD, O'Malley PM, Bachman JG, et al. *Monitoring the future national survey results on drug use, 1975-2007: Volume II, college students and adults ages 19–45 (NIH Publication No. 08-6418B)*. Bethesda, MD: National Institute on Drug Abuse; 2008.
22. Substance Abuse and Mental Health Services Administration. *Results from the 2006 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-32, DHHS Publication No. SMA 07-4293)*. Rockville, MD; 2007.
23. Lawrence RC, Helmick CG, Arnett FC, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum*. 1998;41:778–799.
24. Lipton RB, Bigal ME. Migraine: Epidemiology, impact, and risk factors for progression. *Headache*. 2005;45(Suppl. 1):S3–S13.
25. Stinson FS, Grant BF, Dawson DA, et al. Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug Alcohol Depend*. 2005;80:105–116.
26. Grant BF, Compton WM, Crowley TJ, et al. Errors in assessing DSM-IV substance use disorders. *Arch Gen Psychiatry*. 2007;64:379–380; author reply 381–372.
27. Kessler RC, Merikangas KR. Drug use disorders in the National Comorbidity Survey: Have we come a long way?—Reply. *Arch Gen Psychiatry*. 2007;64:381–382.