



ELSEVIER

## Substance Use Disorders in a Primary Care Sample Receiving Daily Opioid Therapy

Michael F. Fleming,\* Stacey L. Balousek,\* Cynthia L. Klessig,\* Marlon P. Mundt,\* and David D. Brown†

\*Department of Family Medicine, University of Wisconsin, Madison, Wisconsin.

†University of British Columbia, Vancouver, British Columbia, Canada.

**Abstract:** The primary goal of this paper was to present a comprehensive picture of substance use disorders in a sample of patients receiving opioid therapy from their primary care physician. A second goal was to determine the relation of positive urine screens and aberrant drug behaviors to opioid use disorders. The study recruited 801 adults receiving daily opioid therapy from the primary care practices of 235 family physicians and internists in 6 health care systems in Wisconsin. The 6 most common pain diagnoses were degenerative arthritis, low back pain, migraine headaches, neuropathy, and fibromyalgia. The point prevalence of current (DSM-IV criteria in the past 30 days) substance abuse and/or dependence was 9.7% (n = 78) and 3.8% (30) for an opioid use disorder. A logistic regression model found that current substance use disorders were associated with age between 18 and 30 (OR = 6.17; 1.99 to 19.12), severity of lifetime psychiatric disorders (OR = 6.17; 1.99 to 19.12), a positive toxicology test for cocaine (OR = 5.92; 2.60 to 13.50) or marijuana (OR = 3.52; 1.85 to 6.73), and 4 aberrant drug behaviors (OR = 11.48; 6.13 to 21.48). The final model for opioid use disorders was limited to aberrant behaviors (OR = 48.27; 13.63 to 171.04) as the other variables dropped out of the model.

**Perspective:** This study found that the frequency of opioid use disorders was 4 times higher in patients receiving opioid therapy compared with general population samples (3.8% vs 0.9%). The study also provides quantitative data linking aberrant drug behaviors to opioid use disorders.

© 2007 by the American Pain Society

**Key words:** Substance abuse, substance dependence.

Chronic pain affects more than 50 million adults in the United States.<sup>4</sup> A survey by the World Health Organization found that 22% of 26,000 primary care patients surveyed in 5 continents reported severe persistent pain in the previous 12 months.<sup>10</sup> Many of these patients are severely incapacitated and experience pain on a daily basis. Chronic pain can have profound effects on a patient's mental and physical health as well as family and social relationships and is commonly associated with depression, sleep disorders, and deterioration in physical functioning.<sup>2,3</sup> One of the primary treat-

ment modalities for these chronic pain conditions is long-term opioid therapy.<sup>13,15</sup> However, with the widespread reported abuse and diversion of OxyContin (Purdue Pharma L.P., Stamford, CT) and other opioids, there is increasing concern of opioid use disorders.<sup>27</sup>

Despite this concern, there is limited epidemiologic information on the rate of "substance use disorders" and "opioid use disorders" in persons who receive long-term opioid therapy from their primary care physician. One of the most widely cited studies to report the frequency of "opioid use disorders" is the Boston Collaborative Drug Surveillance Program, which reported 4 cases of opioid dependence among 11,882 hospitalized adults who had received at least 1 dose of opioids but had no history of a substance use disorder.<sup>20</sup> Another study frequently reported in the literature is a nationwide survey of 10,000 burn patients that found no new cases of substance abuse after opioids were prescribed.<sup>18</sup> A survey of 2,369 patients being treated at a headache clinic found 3 cases of opioid use disorders.<sup>8</sup> Studies of pain patients with a

Received July 6, 2006; Revised February 20, 2007; Accepted February 27, 2007.

This study was supported by NIDA grant R01 DA013686. There were no pharmaceutical resources used in this study. None of the authors received consultation fees or have investments in pharmaceutical companies.

Address reprint requests to Dr. Michael Fleming, Department of Family Medicine, University of Wisconsin, Madison, 777 S. Mills Street, Madison, WI 53715. E-mail: [m Fleming@fammed.wisc.edu](mailto:m Fleming@fammed.wisc.edu)  
1526-5900/\$32.00

© 2007 by the American Pain Society

doi:10.1016/j.jpain.2007.02.432

history of a substance use disorder suggest opioid use disorder rates of 9% to 27%.<sup>9,22</sup> Recent studies in primary care suggest opioid use disorders rates that vary from 2.8% to 32%.<sup>5,7</sup>

Identifying patients who are addicted to prescription opioids is a complicated issue. The current DSM-IV criteria for "opioid dependence" require that patients meet a minimum of 3 of 7 criteria. However, the 7 primary DSM-IV criteria include tolerance and physical withdrawal, which are normal physiologic effects of chronic opioid therapy. In addition, studies use different time frames such as lifetime history DSM IV criteria, 12-month DSM Criteria, or 30-day criteria.<sup>3</sup> In addition, clinicians often assume that patients with a positive toxicology test for cocaine or other illicit drugs, or patients who demonstrate aberrant behaviors such as early refills and lost prescriptions, have an opioid use disorder. Much of the contradictory evidence on the frequency of "opioid use disorders" is related to the use of different dependence criteria, varying terminology and time frames, and varying interpretation of clinical behaviors.

For this report, "substance use disorders" refers to patients who meet DSM-IV criteria for abuse or dependence. Opioid use disorders is defined by using 30-day DSM-IV criteria for opioid abuse or dependence. We elected to use 30-day criteria based on the Substance Dependence Severity Scale (SDSS). This instrument was developed by the New York Psychiatric Institute and provides a conservative estimate of opioid abuse or dependence.<sup>14</sup> Terms such as "prescription drug abuse" or "substance misuse" are not used in this report, as there are no standard diagnostic criteria for these terms. "Aberrant drug behaviors" include a variety of patient behaviors, including repeated requests for early refills, lost medication, using opioids for non-pain-related reasons, and so forth.<sup>17</sup>

The primary goal of this report was to present a comprehensive picture of substance use disorders in a sample of patients receiving opioid therapy from their primary care physician. A second goal was to determine the relation of positive urine screens and aberrant drug behaviors to opioid use disorders. The study is the largest primary care study to date that reports the frequency of substance use disorders, opioid use disorders, and related behaviors in a primary care sample.

## Methods

### Design

A study was conducted to assess the frequency of opioid use and substance use disorders in a sample of primary care patients receiving opioids for chronic pain. All subjects participated in a single 2-hour interview. Chronic pain was defined as pain that persisted every day for at least 3 months. Subjects were recruited from the practices of 235 primary care physicians practicing in eight counties located throughout the state of Wisconsin. The mean number of patients in each physician's practice receiving opioid therapy was 4.6. These physicians were members of 6 health care systems including

the University of Wisconsin Medical Foundation, Dean Health System, Group Health Cooperative, Medical College of Wisconsin, Aurora Health Care, and Mercy Health Care. Interviews were conducted in primary care clinics and research offices from March 2003 through November 2005.

The study was approved by the Human Subjects Committees of the University of Wisconsin, Aurora Medical Foundation, Medical College of Wisconsin, Dean Care Medical Foundation, Meriter Hospital, and Mercy Health Care. Written informed consent was obtained at the time of the interview.

### Sample

Inclusion criteria included a) age between 18 and 81 years; b) a diagnosis of chronic noncancer pain; and c) current treatment with long-term opioid therapy by a primary care physician. Of the 1,009 patients with chronic pain who met the initial screening criteria and participated in the face-to-face interview, 801 were taking opioids daily over the last 3 months, 115 were taking opioids less than daily, and 93 had not taken opioids in the previous 3 months. A medical record review noted that more than 96% (778) of the sample was being prescribed chronic opioid therapy for the previous 12 months. There were no statistically significant differences on the primary variables of interest between the 801 patients receiving daily opioids and the 208 not receiving daily opioids. Primary variables of interest included age, sex, socioeconomic status, pain location, pain severity, duration of pain, mental health diagnosis, and rates of substance use disorders. We elected to focus this study on daily opioid users ( $n = 801$ ) because this is the group of greatest concern to primary care physicians.

### Research Instruments

Instruments administered include the Addiction Severity Index (ASI),<sup>12</sup> the SDSS,<sup>14</sup> a 15-question chronic pain inventory, a prescription medication survey, and the 12 Aberrant Behavior Items.<sup>16</sup>

Each subject was asked to provide a urine specimen at the end of the interview that was tested for opioids, methadone, propoxyphene, benzodiazepines, cocaine metabolites, amphetamines, PCP, barbiturates, and cannabinoids. Toxicology testing was performed by General Medical Laboratories, using immunoassay technology. Subjects were told about the toxicology screen at the time of the interview when they completed the informed consent materials. Medical record reviews were conducted for the previous 12 months to gather information on treatment of chronic pain syndromes, current medications, current medical problems (including comorbidity diagnoses), health care utilization, and laboratory data.

The primary instrument used to assess the frequency of current drug use disorders was the SDSS, developed at the New York Psychiatric Institute.<sup>14</sup> The SDSS is a semi-structured, clinician-administered interview that assesses

the frequency, quantity, and pattern of use for alcohol, marijuana, cocaine, opioids, heroin, methadone, sedatives, and amphetamines as well as substance abuse and dependence in the previous 30 days. The SDSS uses DSM-IV and ICD-10 criteria to give a diagnosis of current alcohol or drug abuse and/or dependence. The structure of the scale allows separation of mild physical dependence (normal physiologic effects seen when patients receive therapeutic doses of narcotics) from patients with true addiction. The SDSS takes 30 to 60 minutes to complete, depending on the number of drugs used in the previous 30 days. This instrument was chosen to minimize misclassification of subjects who are taking therapeutic doses of opioids. Since the SDSS interview schedule focuses on symptoms of alcohol and drug dependence in the past 30 days, as opposed to past year or lifetime symptoms, the SDSS provides a conservative estimate of addiction.

The ASI assesses 7 areas including medical problems, employment, alcohol use, drug use, legal issues, family problems, and mental health diagnoses. Two of the ASI subscales, a lifetime history of substance abuse and psychiatric disorders, were used to test the substance use disorder risk models. We chose the ASI instrument for a number of reasons. First, it is widely used in Alcohol and Other Drug Abuse treatment and criminal justice programs and allows for comparison to other samples. Second, it provides a wealth of information in 7 domains (legal, family, psychiatric, employment, alcohol, drugs) that could prove useful to pain medicine physicians as part of a comprehensive care plan. Third, it has strong psychometric properties in persons with alcohol and drug disorders and provides a summative score of lifetime addiction severity. Fourth, the subscale scores such as the ASI Psychiatric severity score provides a summative score that can be used in logistic models to determine patient characteristics associated with opioid addiction. We were more interested in an overall psychiatric severity score rather than a specific psychiatric diagnosis.

A list of 12 aberrant drug behaviors was selected, based on the work of Passik and Kirsh<sup>16</sup> and Compton et al.<sup>6</sup> We chose not to include questions that are self-incriminating such as forgery, diversion, or sharing of medication with others, due to concerns of under reporting. The Principal Investigators (PI) chose these questions after consultation with a number of experts in the field. The 12 questions address the following areas of aberrant drug behavior: 1) purposely oversedating oneself, 2) frequency of drug intoxication, 3) involvement in motor vehicle accidents, 4) requesting early renewals, 5) self-directed changes in dosing, 6) lost or stolen prescriptions, 7) obtaining opioids from more than one doctor, 8) non-pain-related use of medication, 9) using alcohol for pain, 10) success in obtaining additional medication, 11) missed doctor appointment, and 12) hoarding of medication. Each question was asked as a lifetime experience and had 5 possible responses, including never, once, twice, 3 times, or 4 or more times.

## Research Procedures

Physicians used a number of strategies to identify patients being treated with opioids for chronic pain. These strategies included obtaining patient lists from billing records, using ICD-9 codes for chronic pain diagnoses, pharmacy records, patient opioid logs maintained by individual physicians, and electronic medical record searches. At the time of the study, electronic medical records or physician order entry had not been implemented in the practices involved in the study. The goal of the recruitment efforts was to enroll 100% of the chronic pain patients receiving opioid prescriptions in each of the 235 physician practices, so as to minimize selection bias. The second step was to mail potential subjects a letter of invitation from their primary care physicians. Patients who did not return an "opt-out" postcard were contacted by a study researcher by telephone and invited to participate in a face-to-face interview. Written informed consent was obtained at the time of the interview.

Response rates were variable across physicians and clinics. The overall response rate across all the clinics was 78% (1,009/1,252). Two hundred forty-three patients identified by their physicians as meeting the inclusion criteria for the study declined to participate in the study. Due to human subject constraints, we were not allowed to collect any information on the nonresponders. The primary reasons given to the research staff for nonparticipation were lack of time, day care issues, confidentiality concerns related to their chronic pain treatment, and transportation barriers. The study provided taxi and bus vouchers as needed for interested subjects. We elected not to conduct interviews in patient homes. Research subjects were paid \$50 for their time commitment.

## Research Procedures

Before initiation of the interview, each subject received a written and verbal explanation of the study protocol, its risks, and potential benefits from the interviewer. The consent form outlined methods used to ensure patient confidentiality and included statements that patients could withdraw from the study at any time and that names would be destroyed after the study was completed. The Health Insurance Portability and Accountability Act authorization form explained which patient health information would be obtained during the study. After resolution of any questions, subjects who understood the study were asked to sign a consent form. Each subject received a copy of the consent form to take home. The interview began with the Medication Checklist, copying the information from each subject's medication bottles for more accurate recording of current medications. The subject and interviewer went through all medications, dosages, and the last time administered. They then completed the Pain Inventory. The SDSS and ASI were then administered by interview. Afterward, subjects completed questionnaires on their own with the interviewer accessible to address any questions or prob-

**Table 1. Predictors of Substance Use Disorders**

VARIABLE	ADJUSTED ODDS RATIO (95% CI)	P VALUE
Age		
18–30	6.17 (1.99–19.12)	.002
31–50	2.12 (1.04–4.33)	.038
51+	1.00 – Reference category	
Sex		
Male	1.04 (0.55–1.94)	.912
Race		
Caucasian	1.00 – Reference category	
African-American	0.83 (0.41–1.67)	.594
Other race	3.21 (0.32–32.46)	.323
Education		
Less than high school	1.05 (0.46–2.42)	.907
High school	1.00 – Reference category	
Some college	1.09 (0.53–2.24)	.815
College degree	0.85 (0.34–2.09)	.722
Monthly income, per \$1000	1.08 (0.94–1.23)	.276
Lifetime history of alcohol or drug treatment (ASI)	1.05 (0.54–2.05)	.878
ASI psychiatric composite score $\geq$ 0.50	2.88 (1.50–5.53)	.001
Pain severity	0.94 (0.80–1.09)	.402
Positive tox screen for cocaine	5.92 (2.60–13.50)	< .001
Positive tox screen for marijuana	3.52 (1.85–6.73)	< .001
Aberrant drug behaviors	11.48 (6.13–21.48)	< .001

The dependent variable compared subjects 9.7% ( $n = 79$ ) who met DSM-IV criteria for substance abuse or dependence vs those who did not ( $n = 706$ ).

lems. A urine drug sample was obtained at the end of the interview before receiving \$50 for their time and participation in the study. The entire process usually took 2 hours.

The lead interviewer/trainer was certified by the developers of the ASI and the SDSS to administer those instruments and provide training to the study researchers. Researcher training began with a 6-hour, in-house session covering study protocols and details of each instrument and ending with role-plays of the interview. In the field, each interview trainee first observed several actual interviews conducted by the trainer and subsequently was observed by the trainer for his/her initial real-life interviews.

### Analysis

Data were entered manually into an Access database (Microsoft Corp, Redmond, WA). All data entry were carefully monitored for accuracy and reviewed by the data manager; SAS software was used to conduct the analysis. The SDSS was scored with the use of a software program provided by developers of the scale at the New York Psychiatric Institute. This program identified subjects who met DSM-IV criteria for abuse and/or dependence in the previous 30 days.<sup>14</sup> The ASI was scored with the use of a weighted formula for each of the 7 domains.<sup>12</sup> The study used morphine sulfate (MS) equiva-

lent doses for analysis and comparison. MS equivalents were calculated as follows: a) oxycodone and hydrocodone 1:1 with MS, b) 10 mg methadone = 30 mg MS; c) 25  $\mu$ g fentanyl = 50 mg MS; d) 2 mg hydromorphone = 10 mg MS; e) 65 mg propoxyphene = 3 mg MS; and f) 50 mg oral meperidine = 20 mg MS. Pain severity scales ranged from 1 to 10, with 10 being the worst possible pain. The lifetime aberrant drug behavior questionnaire included 12 questions, with each item being scored for 0 to 4, with 0 being no reported behavior and 4 coinciding with 4 or more times. Potential scores ranged from 0 to 48.

Descriptive statistics were used to describe the characteristics of the sample, the frequency of various pain diagnoses, and urine toxicology tests. *t* Tests were used to compare continuous measures and  $\chi^2$  tests for dichotomous measures. Logistic regression models were used to assess factors associated with substance use disorders (Table 1) or opioid use disorders (Table 2). Exploratory models included a number of variables based on a priori hypotheses from the literature and the clinical experience of the PI. These variables included sociodemographic variables, pain severity, geographic location of the clinics, mental health problems, psychiatric severity based on the ASI, pain location, opioid dosages, urine toxicology screen, lifetime history of substance use disorder, and aberrant drug behaviors.

We chose to use 4 of the 12 aberrant behaviors selected

**Table 2. Predictors of Opioid Use Disorder**

VARIABLE	ADJUSTED ODDS RATIO (95% CI)	P VALUE
Age		
18–30	2.57 (0.37–17.96)	.340
31–50	2.44 (0.83–7.16)	.105
51+	1.00 – Reference category	
Sex		
Male	0.70 (0.27–1.83)	.465
Race		
Caucasian	1.30 (0.45–3.74)	.632
Other race	1.00 – Reference category	
Education		
Less than high school	3.60 (0.95–13.64)	.060
High school	1.00 – Reference category	
Some college	2.26 (0.75–6.81)	.146
College degree	2.05 (0.60–6.94)	.249
Monthly income, per \$1000	1.06 (0.84–1.33)	.637
Lifetime history of alcohol or drug treatment (ASI)	0.92 (0.34–2.48)	.865
ASI psychiatric composite score $\geq$ 0.50	1.66 (0.64–4.26)	.294
Pain severity	1.02 (0.81–1.29)	.861
Positive tox screen for cocaine	1.65 (0.42–6.42)	.470
Positive tox screen for marijuana	1.40 (0.50–3.90)	.516
Aberrant drug behaviors	48.27 (13.63–171.04)	< .001

The dependent variable compared subjects 3.8% ( $n = 30$ ) who met DSM-IV criteria for opioid abuse or dependence versus those who did not ( $n = 771$ ).

for the study for inclusion in logistic regression models. These four questions included a) purposely oversedating oneself, b) using opioids for nonpain reasons, c) increasing opioid dose without authorization, and d) felt intoxicated. These 4 behaviors were chosen on the basis of an analysis reported in another study focused on aberrant behaviors (Fleming, Brown, and Passik, in review, *Pain*). For the model, we used the total scores for the 4 behaviors (0 to 16). The final models are presented in Tables 1 and 2. Odds ratios and confidence intervals were used to assess the statistical significance of these factors.

## Results

Table 3 shows the sociodemographic characteristics of the primary care sample. The mean age was 48.6, with

**Table 3. Characteristics of the Primary Care Chronic Pain Sample**

	WOMEN (N = 541)		MEN (N = 260)		TOTAL (N = 801)	
	%	N	%	N	%	N
Age	48.5		48.8		48.6	
Range	18–81		20–73		18–81	
Race						
White or Caucasian	75.9	411	74.9	195	75.6	606
Black or African-American	22.8	123	23.9	62	23.1	185
Native American	0.7	4	0.0	0	0.5	4
Hispanic	0.6	3	1.2	3	0.7	6
Education						
Less than high school	15.2	82	16.9	44	15.7	126
High school	38.1	206	45.0	117	40.3	323
Some college	27.0	146	21.9	57	25.3	203
College degree	19.8	107	16.2	42	18.6	149
Employment						
Full time	25.6	138	34.6	90	28.5	228
Part time	13.5	73	6.9	18	11.4	91
Student	0.7	4	1.5	4	1.0	8
Disability	48.7	263	45.4	118	47.6	381
Unemployed, looking for work	11.5	62	11.5	30	11.5	92
Marital Status						
Married	36.7	199	53.5	139	42.1	338
Widowed	7.0	38	1.9	5	5.4	43
Separated or divorced	36.3	196	25.0	65	32.6	261
Never married	20.0	108	19.6	51	19.9	159
Chronic Nociceptive pain	89.5	484	83.8	223	88.4	707
Chronic Neuropathic pain	10.5	57	16.2	37	11.6	94
Smoking status (yes in past 30 days)	42.9	232	53.9	140	46.4	372
Monthly employment income (mean)	\$491		\$966		\$645	
Total monthly income (mean)	\$1,241		\$1,869		\$1,445	

32% (n = 260) of the sample being male and 75.6% (n = 606) Caucasian. This is a highly educated sample, with 44% (n = 352) having attended college. Forty-eight percent (n = 381) were receiving disability income. Less than one third (28.5%) were working full time. The mean total monthly income was \$1,445, with the majority of the income derived from nonemployment resources such as Social Security Disability. Nearly half of the sample (46.4%) reported current tobacco use. The majority (88%) reported nociceptive pain syndromes.

Table 4 reports the medications prescribed for chronic pain control. The mean daily dose of morphine equivalent dosage was 92 mg per day. The most common opioids used were short- and long-acting oxycodone preparations (58.9%). The highest daily dose of oxycodone medication was 640 mg per day. One hundred seventy-eight patients (20%) were receiving prescription OxyContin (Purdue Pharma L.P.). Hydrocodone was the second most frequently used opioid. Methadone was prescribed for pain for 59 patients (7.5%), with a range of 10 to 340 mg per day. Demerol (Sanofi Aventis, Bridgewater, NJ) and hydromorphone were used by 0.8% (n = 6) and 1.3% (n = 10) of the sample.

Table 5 which is based primarily on information from the medical record, reports the most frequent 27 pain diagnoses. Nearly half of the sample had a diagnosis of degenerative arthritis (24.3%) or chronic low back pain (not otherwise specified, NOS) (21.4%). The third most common diagnosis was migraine headache (8.1%). Other common diagnoses include neuropathy (NOS) (5.5%), trauma and other injuries (3.9%), and fibromyalgia (3.9%), with fibromyalgia nearly 4 times higher in women than men (5.2% vs 1.1%). NOS was used for 6 conditions in which pain location was the recorded diagnosis. These conditions include chronic low back pain (NOS), neuropathy (NOS), chronic abdominal disorder (NOS), headaches (NOS), shoulder disorders (NOS), and knee pain (NOS). The primary pain diagnosis was not clear in nearly 10% of cases. For these subjects, the PI reviewed information obtained from the research subject, the medical record, clinic pain logs, and other data available to select 1 primary diagnosis. The average duration of chronic pain in the sample was 16 years.

Table 6 reports the frequency of DSM-IV substance abuse and/or dependence. The table includes self-reported use for alcohol, cocaine, marijuana, heroin, amphetamines, sedatives, methadone, and opioids as well as the frequency of DSM-IV substance abuse and/dependence. Subjects needed to meet DSM-IV criteria in the previous 30 days.

The majority of patients who reported alcohol and drug use did not meet DSM-IV criteria for abuse or dependence. Alcohol use was reported by 35.7% (n = 286) of the sample, marijuana by 13.2% (n = 106) subjects, and cocaine by 3.2% (n = 26). All 15 subjects who reported amphetamine use (1.9%, n = 15) were taking prescription amphetamines for a mental health disorder. Forty percent of subjects reported sedative use, primarily prescription benzodiazepines, with less than

**Table 4. Opioid Analgesics Prescribed by the Subjects' Primary Care Physicians**

PRESCRIPTION	N <sup>†</sup> (PATIENTS)	PERCENT	RANGE (MG)	MEAN (MG)	SD (MG)
Oxycodone (5, 10, 20, 40, 80 mg doses)	261	32.6	2.5–640	91.6	104.2
Oxycodone (5, 7.5, 10 mg with acetaminophen or aspirin)	211	26.3	2.5–60	23.9	15.9
Hydrocodone (5, 7.5, 10 mg with acetaminophen)	210	26.2	0.5–100	22.8	16.8
*Morphine (10, 15, 20, 30, 60, 100 mg)	138	17.2	1–800	125.0	153.1
Codeine (30 mg with acetaminophen)	68	8.6	15–480	138.5	114.9
Fentanyl (25, 50, 75, 100 µg)	66	8.3	2.5–400	70.8	71.2
Methadone (5, 10, 40 mg)	59	7.5	10–340	86.5	70.0
Hydromorphone (2, 4, 8 mg)	10	1.3	2–144	25.2	42.2
Demerol (50 mg)	6	0.8	25–100	58.3	25.8

\*Morphine medication includes a) morphine IR, b) morphine SR, c) MS Contin, d) MS ERT, e) MS liquid, f) Morphine suppositories, and g) Kadian.

†Total prescriptions equal 1029; 202 (24%) patients were taking more than one opioid analgesic.

1% meeting 30-day DSM-IV criteria for sedative abuse or dependence.

The highest rate of dependence was for opioids (3.1%,  $n = 25$ ) and alcohol (2.1%,  $n = 17$ ). The overall rate of substance dependence (alcohol and/or drug dependence) was 5.6% ( $n = 45$ ), with some individuals meeting dependence criteria for more than 1 substance. Alcohol

and/or drug abuse was present in 4.1% ( $n = 33$ ) of the sample. Taken together, these groups account for a total substance use disorder rate of 9.7% ( $n = 78$ ). This is a conservative estimate, as subjects needed to meet DSM-IV criteria in the last 30 days.

Table 7 reports the results of toxicology screens. Toxicology results were successfully obtained in 771 subjects.

**Table 5. Percent of Patients with Pain Diagnosis (Total  $n = 801$ )**

PRIMARY DIAGNOSIS	WOMEN ( $N = 541$ )		MEN ( $N = 260$ )		TOTAL ( $N = 801$ )	
	%	N	%	N	%	N
Arthritis	24.6	133	23.8	62	24.3	195
Chronic low back pain NOS	18.1	98**	28.1	73**	21.4	171
Migraine	9.6	52*	5.0	13*	8.1	65
Neuropathy NOS	5.4	29	5.8	15	5.5	44
Trauma and other injuries	3.3	18	5.0	13	3.9	31
Fibromyalgia	5.2	28†	1.1	3†	3.9	31
Rheumatoid arthritis	3.3	18	2.3	6	3.0	24
Diabetic neuropathy	2.4	13	4.2	11	3.0	24
Cervical spine disease	2.2	12	4.2	11	2.9	23
Lupus	3.9	21†	0.0	0†	2.6	21
Myofascial syndrome	2.8	15	1.5	4	2.4	19
Chronic pancreatitis	1.8	10	2.7	7	2.1	17
Chronic abdominal disorder NOS	1.7	9	2.3	6	1.9	15
Spinal stenosis	2.2	12	0.8	2	1.7	14
Shoulder disorder NOS	1.7	9	0.8	2	1.4	11
Headaches NOS	1.3	7	0.8	2	1.1	9
Lumbar disc disease and nerve compression	0.6	3	1.9	5	1.0	8
Reflex sympathetic dystrophy	1.3	7	0.4	1	1.0	8
Herniated lumbar disc	0.9	5	0.4	1	0.7	6
Sickle cell	0.6	3	1.2	3	0.7	6
Avascular necrosis of hip	0.6	3	0.8	2	0.6	5
Knee disorder NOS	0.9	5	0.0	0	0.6	5
Restless leg syndrome	0.7	4	0.4	1	0.6	5
Scoliosis	0.4	2	0.8	2	0.5	4
Temporomandibular joint disorder	0.7	4	0.0	0	0.5	4
Carpal tunnel syndrome	0.2	1	0.8	2	0.4	3
Other	3.7	20	5.0	13	4.1	33

Whereas some patients (28%,  $n = 176$ ) had more than 1 pain diagnosis or anatomic location for their chronic pain, each subject was assigned a single primary diagnosis by the Principal Investigator. Data sources used to make a pain diagnosis included patient report and medical records.

As noted in the text, 6 diagnoses were classified as NOS. NOS (not otherwise specified) is an ICD-9 term used when a precise diagnosis cannot be determined.

\* $P < .05$ .

† $P < .01$ .

**Table 6. Frequency of Substance Use Disorders in the Primary Care Sample by Diagnostic Interview**

	WOMEN (N = 541) % (N)	MEN (N = 260) % (N)	TOTAL (N = 801) % (N)
Alcohol use: Any in past 30 days	33.6 (182)	40.0 (104)	35.7 (286)
Alcohol dependence, DSM-IV	2.0 (11)	2.3 (6)	2.1 (17)
Alcohol abuse, DSM-IV	1.5 (8)	2.3 (6)	1.8 (14)
Cocaine use: Any in past 30 days	3.3 (18)	3.1 (8)	3.2 (26)
Cocaine dependence, DSM-IV	0.7 (4)	1.1 (3)	0.9 (7)
Cocaine abuse, DSM-IV	0.7 (4)	0.4 (1)	0.6 (5)
Marijuana use: Any in past 30 days	10.7 (58)	18.5 (48)	13.2 (106)
Marijuana dependence, DSM-IV	0.9 (5)	0.8 (2)	0.9 (7)
Marijuana abuse, DSM-IV	1.8 (10)	3.5 (9)	2.4 (19)
Heroin use: Any in past 30 days	0.0 (0)	1.1 (3)	0.4 (3)
Heroin dependence, DSM-IV	0.0 (0)	0.4 (1)	0.1 (1)
Heroin abuse, DSM-IV	0.0 (0)	0.4 (1)	0.1 (1)
Amphetamine use: Any in past 30 days	2.0 (11)	1.5 (4)	1.9 (15)
Amphetamine dependence, DSM-IV	0.0 (0)	0.0 (0)	0.0 (0)
Amphetamine abuse, DSM-IV	0.0 (0)	0.0 (0)	0.0 (0)
Sedative use: Any in past 30 days	43.1 (233)	33.5 (87)	39.9 (320)
Sedative dependence, DSM-IV	0.4 (2)	0.4 (1)	0.4 (3)
Sedative abuse, DSM-IV	0.6 (3)	0.4 (1)	0.5 (4)
Methadone use: Any in past 30 days	6.1 (33)	8.8 (23)	7.0 (56)
Methadone dependence, DSM-IV	0.0 (0)	0.0 (0)	0.0 (0)
Methadone abuse, DSM-IV	0.2 (1)	0.0 (0)	0.1 (1)
Opioid use: Any in past 30 days	100.0 (541)	100.0 (260)	100.0 (801)
Opioid dependence, DSM-IV	3.5 (19)	2.3 (6)	3.1 (25)
Opioid abuse, DSM-IV	0.4 (2)	1.1 (3)	0.6 (5)
Dependence: Any substance	6.1 (33)	4.6 (12)	5.6 (45)
Abuse: Any substance	3.0 (16)	6.5 (17)	4.1 (33)
Abuse or dependence: Any substance	9.1 (49)	11.1 (29)	9.7 (78)

Eleven subjects did not participate in toxicology testing because of time restraints or a medical problem that made donation of a urine specimen difficult. There were laboratory process issues with 19 of the specimens. Twenty-four percent of the sample (n = 185) tested positive for cannabinoids, cocaine, and other illicit drugs. When comparing self-reported drug use data with urine toxicology data, the urine drug screening identified 50 additional cases of marijuana use (156 by urine toxicology test vs 106 by self-report) and 34 additional cases of cocaine use (60 by tox screen vs 26 by self-report).

Table 8 compares the frequency of 12 lifetime aberrant drug behaviors endorsed by subjects who met criteria for opioid addiction or substance use disorder status. The first group met criteria for opioid abuse/dependence (n = 30), the second met criteria for any substance use disorder (n = 79), and the third group (n = 706) did not meet criteria. The table reports the percentage of subjects in each group who reported the behavior 1 or more times. In the Opioid Abuse/Dependence group (group 1), behaviors 1, 2, 4, 5, and 9 had the highest frequency. As illustrated at the bottom of the table, groups 1 and 2 had both a higher mean score (16.3 and 13.2 vs 4.9) and mean number of items endorsed (5.8 and 5.2 vs 2.3) compared with the non-substance use disorder group.

Table 1 reports a logistic regression model that reports the final model developed to assess factors associated with current substance use disorders. The model found that predictors of current DSM-IV substance use disorders included age between 18 and 30 years (OR = 6.17; 1.99 to 19.12), age between 31 and 50 years (OR = 2.12; 1.04 to 4.33), a lifetime history of psychiatric disorders (OR = 6.17; 1.99 to 19.12), positive toxicology test for cocaine (OR = 5.92; 2.60 to 13.50) or marijuana (OR = 3.52; 1.85 to 6.73), and aberrant drug behavior (OR = 11.48; 6.13 to 21.48). A lifetime history of substance abuse was not statistically associated with current substance use disorders.

Table 2 focuses on subjects who met criteria for opioid use disorder (n = 30). The dependent variable for the model is based on 30-day DSM-IV symptoms of opioid abuse or dependence. The independent variables were the same as those used to model substance use disorder variables in Table 1. All of the variables significant in Table 1 dropped out of the model except for aberrant drug behaviors (OR = 48.27; 13.63 to 171.04). These 4 aberrant drug behaviors included purposely oversedating oneself, using opioids for nonpain reasons, increasing dose without authorization, and having felt intoxicated when using opioids.

## Discussion

The primary finding of this study is that the frequency of opioid use disorders is four times higher than reported in general population samples (3.8% vs 0.9%). Although

**Table 7. Urine Toxicology Results for Three Illicit Drugs**

	WOMEN (N = 521)		MEN (N = 250)		TOTAL (N = 771)	
	%	(N)	%	(N)	%	(N)
Cannabinoids	18.4	(96)	24.0	(60)	20.2	(156)
Cocaine	7.7	(40)	8.8	(22)	8.0	(62)
Phencyclidine	0.2	(1)	0.0	(0)	0.1	(1)
Any illicit substance	22.5	(117)	27.2	(68)	24.0	(185)

n = 771 subjects; no lab data obtained on 30 subjects.

**Table 8. Percentage of Subjects That Reported Engaging in Specific Aberrant Behaviors One or More Times by Abuse/Dependence Pattern**

	GROUP 1 (N = 30) OPIOID ABUSE/Dep		GROUP 2 (N = 79) ANY SUBSTANCE ABUSE/DEP		GROUP 3 (N = 706) NO ABUSE/DEP	
	%	N	%	N	%	N
Item 1: Purposely oversedated oneself	76.7	23	62.0	49	19.1	137
Item 2: Felt intoxicated from pain medication	80.0	24	63.3	50	29.2	210
Item 3: Motor vehicle or other accident	10.0	3	11.4	9	7.2	52
Item 4: Requested early refills	76.7	23	69.6	55	42.0	302
Item 5: Increased dose on own	86.7	26	73.4	58	33.2	230
Item 6: Lost or had medication stolen	40.0	12	46.8	37	27.7	199
Item 7: Tried to obtain opioid from more than one MD	30.0	9	19.0	15	5.1	37
Item 8: Successfully obtained extra opioids from other doctors	30.0	9	17.7	14	5.3	38
Item 9: Used opioids for purpose other than pain	63.3	19	45.6	36	12.4	89
Item 10: Drank alcohol to relieve pain	30.0	9	49.4	39	16.0	115
Item 11: Missed clinic appointment	36.7	11	36.7	29	24.3	175
Item 12: Hoarded pain medication	20.0	6	20.3	16	10.2	73
	<i>MEAN</i>	<i>(SD)</i>	<i>MEAN</i>	<i>(SD)</i>	<i>MEAN</i>	<i>(SD)</i>
Summative score on 12 items by group (range of scores, 0–48)*	16.3	(6.2)	13.2	(7.1)	4.9	(5.3)
Number of items reported at least once by group (0–12)†	5.8	(2.1)	5.2	(2.3)	2.3	(2.1)

\*Each item had 5 possible responses, including 0 times, 1 time, 2 times, 3 times, 4 or more.

†Each of the 12 items was scored between 0 and 4. The highest possible score for the 12 items was 48.

the frequency is low, about 1 case for every 25 patients on opioid therapy, it is of concern. Since this is a cross-sectional study focused on patients already taking opioids, we were unable to determine the relation between current opioid therapy and the development of opioid use disorders. It is possible that patients were opioid-dependent before they started opioid therapy. However, the study does provide the best point estimate of opioid use disorders in a primary care pain sample.

Other important findings include a 24% rate of positive toxicology tests for illicit drugs, significant underreporting of drug use, and a strong association between illicit drug use and substance use disorders (Table 1). Eighty-four of 185 (46%) patients with positive toxicology testing denied illicit drug use during the research interview, even when they were guaranteed anonymity. This finding confirms clinical observations that patients with chronic pain often mislead physicians about illicit drug use.

The 4.1% frequency of alcohol abuse and dependence found in our sample is lower than a 2005 national study that reported a frequency of 7.7%.<sup>24</sup> This finding is not surprising, as physicians are reluctant to use opioids in patients who have alcohol problems because of concerns of overdose, associated illicit drug use, noncompliance, and so forth. The sample in our study does not include all patients with chronic pain disorders, only those receiving daily opioids.

Another important finding is the association of 4 aberrant behaviors with substance abuse and opioid addiction. Table 1 reports an odds ratio of 11.48 (6.13 to 21.48) and Table 2 an odds ratio of 48.27 (13.63 to 171.04) for

aberrant drug behaviors. These 4 behaviors included sedating oneself, using opioids for nonpain reasons, increasing dose without authorization, and having felt intoxicated when using opioids. Although the model in Table 1 found that age, psychiatric problems, illicit drug use, and aberrant behaviors were associated with substance use disorders, these variables dropped out of Table 2 because of extremely strong relations between these behaviors and opioid use disorders.

There is increasing evidence concerning the frequency of aberrant drug behaviors and their potential relation to opioid use disorders. These behaviors were first described by Portenoy<sup>19</sup> to describe a set of behaviors such as early refills, lost prescriptions, and unauthorized increases in medication. Although many physicians consider these behaviors indicative of substance abuse disorders, there can be other explanations for these behaviors. These behaviors could also occur because of inadequate pain treatment due to underdosing of opioids, which Waisman and Haddox<sup>25</sup> called pseudoaddiction. Other potential causes of aberrant drug behaviors outlined by Passik and Kirsch<sup>16</sup> include untreated psychiatric syndromes, organic mental syndromes, chemical coping, situational stressors, and criminal intent.

In a recent meta analysis, Martell et al<sup>11</sup> reported the frequency of aberrant medication taking behaviors in 5 studies ranged from 5% to 24%. Reid et al<sup>21</sup> reported that co-occurring medical disorders, higher lifetime rates of substance use disorders, and younger age were associated with, and increased the frequency of, 3 aberrant behaviors: Lost or stolen medication, documented use of

multiple physicians, and request for 2 or more early refills. Webster and Webster<sup>26</sup> assessed the association of 21 aberrant drug behaviors and found that patients with a family or personal history of substance abuse were more likely to exhibit aberrant behaviors. The primary limitation of the current evidence on aberrant drug behaviors are small sample sizes, absence of DSM-IV substance use disorders, diagnostic assessments in the samples, and lack of regression modeling to adjust for other causes of aberrant behaviors besides substance problems. The limited empiric data found in the literature support the need for naturalistic cohort studies to assess the relation of aberrant behavior and other cofactors to substance use disorders in patients receiving long-term opioid therapy.

Strengths of the study include a large sample size, high rates of patient participation, and a diverse sample of primary care physician clinics located in 8 counties throughout the state of Wisconsin. The clinic sites include rural, suburban, and urban settings. The population was highly educated, with nearly half the sample having attended college. The study used state-of-the-art assessment instruments and collected a variety of measures, including urine toxicology screens and aberrant drug behaviors. The research staff completed extensive training and had prior experience assessing patients for addiction and mental health issues. Research staff and their interviews were monitored throughout the study. An additional strength of the study is the inclusion of tobacco, alcohol, illicit drugs, and prescription drug use disorders. Prior studies have primarily focused on opioid abuse and dependence.

Weaknesses of the study include the absence of prospective data, lack of information before patients being placed on opioids, and lack of corroborative reports by family members and close friends. Minimization of drug use and drug problems by patients is a major concern in all studies that try to estimate rates of addiction, especially for illegal drugs.<sup>1</sup> The issue of selection bias is another concern. We used a variety of methods to identify patients who were receiving opioids for chronic pain, in-

cluding computer searches of billing records, chart reviews, pain logs, and prospective enrollment, as patients came in for monthly refills. Although the response rate was 78%, it is possible that the nonrespondents had higher rates of substance use disorders. With the new HIPAA regulations, researchers are not allowed to collect medical record data on persons who are not willing to participate.

Estimating the frequency of opioid use disorders is a complex issue that is difficult to assess during a single interview. Symptoms of opioid use disorders vary over time. Prospective long-term cohort studies are needed to estimate rates of addiction in a chronic pain sample on opioids and the relation of opioid therapy to the development of opioid use disorders. The addiction and pain medicine fields need to develop DSM-IV–like criteria for patients taking opioids for chronic pain. The consensus statement developed by the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine provides an excellent framework on which to develop standard criteria.<sup>2</sup> These criteria probably need to include aberrant drug behaviors but exclude normal pharmacologic properties of opioids such as tolerance and physical dependence. Once these criteria are accepted, we can develop and standardize the diagnosis of opioid addiction in persons reporting chronic pain. Although this will not be easy, there is sufficient scientific evidence to develop criteria and diagnostic instruments.

Are opioids worth the risk? Patients living with severe chronic pain have limited therapeutic options. Many will respond to other therapies such as exercise, nonopioid medication, nutrition and nutritional supplements, nerve blocks, prolotherapy, local treatment with massage, spinal manipulations, and heat. However, there is a large group of patients who require daily opioids. Considering the potential benefit to improving the lives of patients with chronic pain, a 3.8% rate of opioid addiction is a small risk compared with the alternative of continuous pain and suffering. The data presented in this paper support the use of opioids for the treatment of chronic pain by primary care physicians.

## References

1. Ackini I, Tartar R, Kirisci H: Concordance between verbal report and urine screen of recent marijuana use in adolescents. *Addict Behav* 25:613-619, 2001
2. American Pain Society: Definitions related to the use of opioids for the treatment of pain: A consensus document from the American Academy of Pain Medicine, the American Pain Society and the American Society of Addiction Medicine, 2001
3. Ballantyne J, Mao J: Opioid therapy for chronic pain. *N Engl J Med* 349:1943-1953, 2003
4. Brookoff D: Chronic pain: A new disease? *Hosp Pract (Minneapolis)* 35:45-52, 2000
5. Chelminski P, Ives T, Felix K, Prakken S, Miller T, Perhac J, Malone R, Bryant M, DeWalt DA, Pignone M: A primary care, multi-disciplinary disease management program for opioid-treated patients with chronic non-cancer pain and a high burden of psychiatric comorbidity. *BMC Health Serv Res* 5:3, 2005
6. 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 Sympt Manage* 16:355-363, 1998
7. Cowan D, Wilson-Barnett J, Griffiths P, Allan L: A survey of chronic non-cancer pain patients prescribed opioid analgesics. *Pain Med* 4:340-351, 2003
8. Diamond S, Freitag F, Solomon G, Millstein E: Migraine headache: Working for the best outcome. *Postgrad Med* 81L174-L176, 1987
9. Fishbain D, Rosomoff H, Rosomoff R: Drug abuse, depen-

dence, and addiction in chronic pain patients. *Clin J Pain* 8:77-85, 1992

10. Gureje O, Von Korff M, Simon G, Gater R: Persistent pain and well being: A world Health Organization Study in Primary Care. *JAMA* 280:147-151, 1998

11. Martell B, O'Connor P, Kerns R, Becker W, Morales K: Systematic review: Opioid treatment for chronic back pain: Prevalence, efficacy and association with addiction. *Ann Intern Med* 146:116-127, 2007

12. McLellan AT, Kushner H, Metzger D, Peters R, Smith I, Grissom G, Pettinati H, Argeriou M: The fifth edition of the Addiction Severity Index. *J Substance Abuse Treat* 9:199-213, 1992

13. McQuay H: Opioids in pain management. *Lancet* 353: 2229-2232, 1999

14. Miele G, Carpenter K, Smith Cockerham M, Dietz Trautman K, Blaine J, Hasin D: Concurrent and predictive validity of the Substance Dependence Severity Scale (SDSS). *Drug Alcohol Depend* 59:77-88, 2000

15. Novak S, Nemeth W, Lawson K: Trends in medical use and abuse of sustained-release opioid analgesics: A revisit. *Pain Med* 5:59-65, 2004

16. Passik S, Kirsh K: Assessing aberrant drug taking behaviors in the patient with chronic pain. *Curr Pain Headache Rep* 8:289-294, 2004

17. Passik S, Kirsh K, Whitcomb L, Dickerson P, Theobald DE: Pain clinicians' rankings of aberrant drug-taking behaviors. *J Pain Palliat Care Pharmacother* 16:39-49, 2002

18. Perry S, Heidrich G: Management of pain during debridement: A survey of US burn units. *Pain* 13:267-280, 1982

19. Portenoy R: Chronic opioid therapy in non malignant pain. *J Pain Symptom Manage* 5(Supplement):S46-S62, 1990

20. Porter J, Jick H: Addiction rate in patients treated with narcotics. *N Engl J Med* 302:123, 1980

21. Reid M, Engles-Horton L, Weber M, Kerns R, Rogers E: Use of opioid medications for chronic non cancer pain syndrome in primary care. *J Gen Intern Med* 17:173-179, 2002

22. Savage S: Long-term opioid therapy: Assessment of consequences and risks. *J Pain Symptom Manage* 11:274-286, 1996

23. Stewart W, Ricci J, Chee E, Morganstein D, Lipton R: Lost productive time and cost due to common pain conditions in the US workforce. *JAMA* 290:2443-2454, 2003

24. Substance Abuse and Mental health Services Administration (SAMHSA) Office of Applied Studies: Results from the 2005 National Survey on Drug Use and Health: National Findings. <http://www.oas.samhsa.gov/nsduh.htm>. Pages 71-75.

25. Waisman D, Haddox J: Opioid pseudo addiction: An iatrogenic syndrome. *J Pain Symptom Manage* 19:274-286, 2000

26. Webster L, Webster R: Predicting aberrant behaviors in opioid treated patients: Preliminary validation of the opioid risk tool. *Pain Med* 6:432-438, 2005

27. Wilson P: Opioid use and diversion: report on recent hearing by FDA and DEA: ASA statement to FDA committee. *ASA Newsletter* 66:9-10, 2002