

# OPIOIDS & SUBSTANCE USE DISORDERS SECTION

## Original Research Article

# Low Risk of Producing an Opioid Use Disorder in Primary Care by Prescribing Opioids to Prescreened Patients with Chronic Noncancer Pain

Martin D. Cheatle, PhD,\* Rollin M. Gallagher, MD,<sup>†,‡</sup> and Charles P. O'Brien, MD, PhD\*

\*Center for Studies of Addiction, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; <sup>†</sup>Michael J. Crescenz VA Medical Center, Philadelphia, Pennsylvania; <sup>‡</sup>Departments of Psychiatry and Anesthesiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

*Correspondence to:* Martin D. Cheatle, PhD, Center for Studies of Addiction, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, 3535 Market Street, 5th Floor, Room 541, Philadelphia, PA 19104, USA. Tel: 215-746-7365; E-mail: cheatle@mail.med.upenn.edu.

*Funding sources:* The authors (MDC, COB) would like to acknowledge support from Grants P60-DA05186 and 1R01DA032776-01 from the National Institute on Drug Abuse, National Institutes of Health, in the writing of this manuscript. The funder had no role in the design, conduct, analysis, or interpretation of the data.

*Conflicts of interest:* None of the authors has any conflicts of interest related to the content of this manuscript.

## Abstract

**Objective.** To examine the risk of developing aberrant behaviors that might lead to a substance use disorder (addiction) when prescribing opioids for the relief of chronic noncancer pain in primary care settings.

**Design.** Longitudinal, prospective, descriptive design with repeated measures.

**Setting.** Private community-based internal medicine and family medicine clinics.

**Subjects.** Patients with chronic musculoskeletal pain.

**Methods.** Standardized measures of patient status (pain, functional impairment, psychiatric disorders, family history) and treatments provided, urine drug monitoring, and medical chart audits (presence of aberrant drug-related behaviors) were obtained in a cohort of 180 patients at the time of initiating opioids for chronic noncancer pain and at three, six, and 12 months thereafter.

**Results.** Over the 12-month follow-up period, subjects demonstrated stable, mild to moderate levels of depression (PHQ-9 scores ranging from 9.43 to 10.92), mild anxiety (BAI scores ranging from 11.80 to 14.67), minimal aberrant drug-related behaviors as assessed by chart reviews, and a low percentage of illicit drug use as revealed by results of urine drug monitoring. Less than 5% of our study population revealed any evidence of substance use disorder.

**Conclusions.** This prospective study suggests that patients without a recent or prior history of substance use disorder who were prescribed primarily short-acting opioids in low doses for chronic noncancer pain have a low risk for developing a substance use disorder. This finding supports the importance of prescreening patients being considered for opioid therapy and that prescription of opioids for noncancer pain may carry a lower risk of abuse in selected populations such as in private, community-based practices.

**Key Words.** Chronic Pain; Opioids; Primary Care; Substance Use Disorders

## **Introduction**

Approximately 30% of the American population is affected by chronic pain, and this number continues to grow rapidly [1,2]. At the individual level, chronic pain can cause emotional and physical suffering and lead to disability. The impact of chronic pain on society is also noteworthy. The annual cost of chronic pain in the United States has been estimated at between \$565 and \$635 billion dollars [2]. A related concern is the increasing prevalence of opioid misuse, abuse, addiction, and opioid-related overdose fatalities. For example, 4.9 million individuals age 12 years or older were current nonmedical users of pain relievers in 2012 [3], and in 2011 there were 488,004 emergency department visits related to nonmedical use of opioids [4] and 186,986 admissions to treatment facilities for opioid dependence [5]. Of the 38,329 pharmaceutical-related deaths in 2010 in the United States, 16,651 of these deaths were related to opioids alone or in combination with other drugs, most commonly benzodiazepines [6]. In spite of these concerns, due to a number of factors including the limited availability of effective treatment alternatives, opioids continue to be used for controlling pain and improving function for a number of patients with chronic noncancer pain (CNCP).

Many patients with CNCP present with one or more medical and psychiatric comorbidities. Ideally these patients should be evaluated and managed in an interdisciplinary pain clinic. In practice, the majority of pain care is delivered by primary care physicians [7] who typically do not have the training or resources or time to effectively evaluate, treat, and monitor these complex cases [8], especially when opioids are prescribed.

When treating pain in a patient without a life-shortening cancer diagnosis, the prescriber must weigh the need to relieve pain against the risk of producing a substance use disorder (SUD). Many clinicians believe that the risk of abuse is so great that opioids can never be justified except in the presence of cancer. Most studies on this question have been cross-sectional or retrospective in design. The goal of the present study, therefore, was to prospectively evaluate the risk of developing abuse in patients with CNCP who did not already have known risk factors such as aberrant drug-related behaviors (ADRBs), behaviors associated with SUDs, or prior history of a SUD.

Numerous studies have identified high prevalence rates of SUD in chronic pain patients [9–15]. Many of these studies have been conducted in specialty pain medicine settings, not in primary care. Two reports on the use of opioids for chronic pain in primary care indicated that ADRB and substance misuse and abuse occur frequently in this setting as well. However, both papers described patient samples that were referred to specialty programs from primary care because of problems with or concerns about opioid use. Ives et al. [11] reported substance misuse based on urine drug monitoring (UDM) in 32% of 196 primary care patients who were

referred over a 12-month period to a multispecialty pain clinic. Wiedemer et al. [16] described a longitudinal, observational study of 335 primary care patients being treated with opioids for chronic pain who were referred to a structured opioid renewal program because of ADRB or apparent addiction risk. Absent in both studies and in the literature are prospective studies of the prevalence of substance misuse and abuse in samples of primary care patients who do not have a prior history of ADRB or other risk factors for abuse or addiction.

The objective of this study was to assess the extent of pain, substance use, ADRB, substance use disorders, co-occurring psychiatric disorders, and functional problems presented by a cohort of patients prescreened for SUD initiating opioid therapy for CNCP provided by community-based primary care physicians.

## **Methods**

### *Research Design*

This study was a longitudinal, prospective, descriptive design with repeated measures employing standardized measures of patient status and treatments provided at time of commencing a new course of opioid therapy for CNCP in a primary care setting (baseline) and at three, six, and 12 months thereafter. Institutional review boards at the University of Pennsylvania and the Reading Medical Center approved this research.

### *Participants and Setting*

Physicians and subjects were recruited from the internal medicine and family medicine practices of the Reading Hospital Medical Center located in West Reading, Pennsylvania. Characteristics of physicians were obtained from a survey of their demographics and their past education in pain management. Inclusion criteria were 1) complaining of CNCP (at least three months) as determined by the physician and subject self-report; 2) initiation of a new course of opioid analgesic medication within three months of enrollment; 3) age 18 to 75 years; and 4) speaking, understanding, and writing either English or Spanish. Exclusion criteria were 1) the use of opioid pain medications longer than three months as determined by physician report and confirmed by subject self-report; 2) inpatient hospitalization for a psychiatric or substance use disorder in the last three months; 3) current use of illicit drugs exclusive of marijuana within three months of enrollment as determined by self-report; 4) subjects testing positive for illegal drugs on the urine drug screen (with the exception of THC) at the initial visit; 5) alcohol abuse within the last three months; 6) current symptoms of mania or psychosis; and 7) active suicidal ideation to include a plan or attempt in the prior three months. THC was allowed due to the frequency of use in this patient population, and we wanted to employ a lower threshold for inclusion in the study to truly investigate what actually transpires in the real-world setting of primary care. As

Pennsylvania did not have a prescription drug monitoring program in place at the time this study was conducted, we had to rely on medical record review to confirm eligibility.

*Patient Recruitment and Data Collection*

Subjects were recruited by the participating physicians and their staff and by recruitment fliers placed in the examination rooms and waiting rooms and mailed to all patients in the selected practices. Interested subjects, after providing verbal consent, were contacted by the research nurse, who explained the purpose of the study, assessed eligibility, and arranged for an initial appointment. During this appointment, after signing of the informed consent form, a urine specimen for drug testing was obtained and a time was scheduled for completion of baseline assessments. In addition, the patients' records were reviewed to corroborate eligibility. The baseline, three-, six-, and 12-month follow-up assessments were conducted via telephone interview by a trained research technician and entered into an encrypted data base at the University of Pennsylvania. Urine specimens for urine drug testing were also collected at three, six, and 12 months. These were not random. Chart reviews of each subject's medical records and pharmacy records were conducted by the research nurse and a trained research technician that included the time period from six months prior to baseline through 12 months after baseline.

*Outcome Measures*

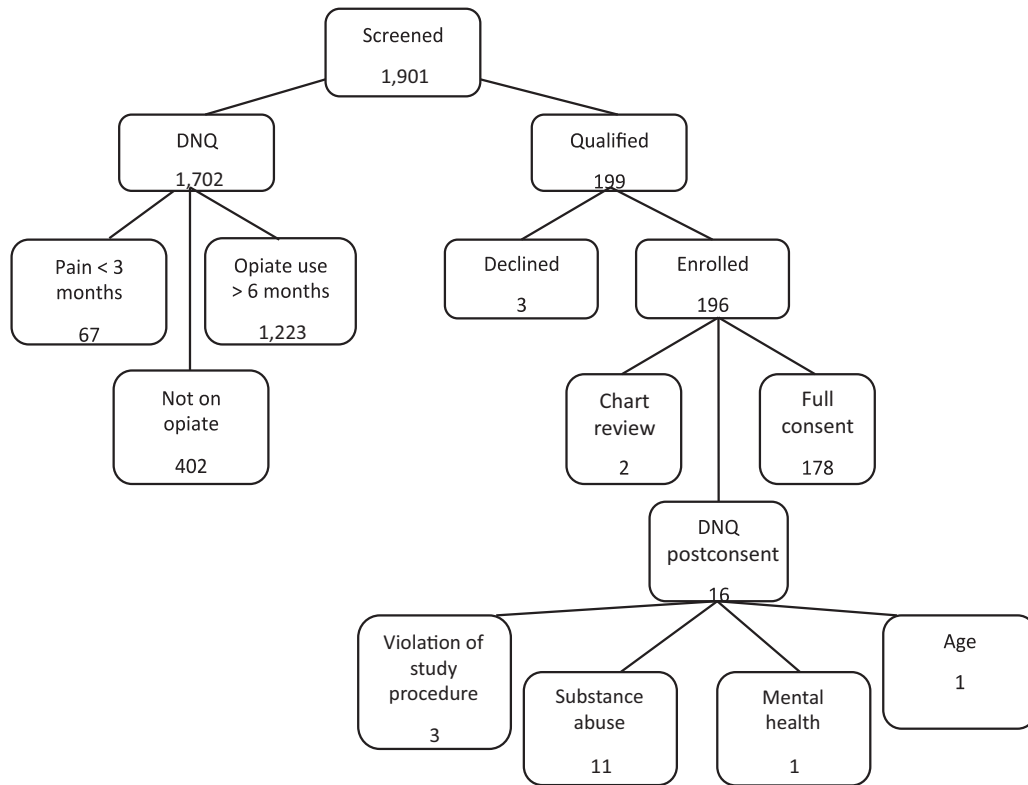
The assessment battery included instruments designed to identify pain-related functional impairment, physical illness, psychiatric diagnosis, and level of current and lifetime substance abuse.

1. Demographics. Demographic characteristics including: age, gender, race, socioeconomic status, education level, and ethnicity were assessed at baseline interview.
2. MINI International Neuropsychiatric Interview (MINI). The MINI was used to establish the diagnoses for mania, panic disorder, PTSD, GAD, psychotic symptoms, and drug and alcohol dependence (current and lifetime) based on DSM-IV criteria [17].
3. DSM checklist for abuse or dependence. Based on the MINI interview, a checklist of the DSM-IV items for substance abuse and dependence was administered at each assessment. This checklist was used to define substance use over the course of the study.
4. PHQ-9. The PHQ-9 is a brief nine-item checklist of DSM depression symptoms that is a reliable method for making a criteria-based diagnosis of depression and measuring severity of symptoms [18].

**Table 1** Demographics (N = 180)

Marital status	%
Married/partnered	52
Never married	18
Divorced	17
Widowed	7
Separated	7
Level of education	
Grade 6 or less	2
Grade 7–12	11
Graduated HS or equivalent	32
Part college	21
Graduated 2-y college	10
Graduated 4-y college	11
Part grad school	3
Complete grad school	11
Household population	
Live alone	16
Live with 1 person	28.7
Live with > 1 person	55.3
Ethnicity	
Hispanic	11.2
White	81
Black	6.7
Other	1.1
Sex	
Male	33
Female	67
Employment info	
Employed	65.4
Unemployed	34
Age	47.8 y

5. Beck Anxiety Inventory (BAI). The BAI is a 21-item scale that measures the severity of anxiety in adults and adolescents [19]. The BAI consists of 21 descriptive statements of anxiety symptoms that are rated on a four-point scale consisting of not at all, mildly, moderately, and severely.
6. Urine drug screen. Standard urine drug screens were collected at each visit and assayed using Gas Chromatography/Mass Spectrometry for the standard six drugs of abuse: nonprescribed opioids, cocaine, amphetamine, marijuana, barbiturates, and benzodiazepines.
7. Aberrant drug-related behaviors. Aberrant behaviors were assessed primarily from extensive chart reviews on each patient. Nine aberrant behaviors were targeted based on previous research in this area and from published work from our laboratory (see Table 1).
8. Pain Catastrophizing Scale (PCS). The PCS is a well-validated and reliable 13-item measure of



**Figure 1** Recruitment. DNQ =

catastrophizing as a coping style in chronic pain patients [23]. Catastrophizing has been associated with poor adjustment and heightened distress.

9. Brief Pain Inventory. The BPI includes two dimensions: pain intensity and pain interference [24]. The pain interference scale measures interference in seven areas: general activity, mood, walking ability, work, sleep, enjoyment of life, and relationships.
10. Duke Social Support. This is a 14-item, self-administered, multidimensional, functional social support questionnaire [25]. The Social Support Index will be used as a moderating variable in predicting development of ADRBs or substance use disorder.
11. Chart review. The chart review records pain diagnosis, treatment plan, recognition of substance abuse and aberrant behaviors noted by the physician, medications prescribed and dosage, and prescription of nonpharmacologic treatments.

**Statistical Analysis**

Summary statistics were used, including percentage of population, means, and standard deviations. Repeated analyses of variance were employed for continuous variables assessed at baseline, three, six, and 12 months.

For all tests, an alpha level of 0.05 ( $p < 0.05$ ) was considered a significant difference. Simple *t* tests were used in comparing patients who completed all assessments and those who did not.

**Results**

**Recruitment**

One thousand nine hundred and one patients volunteered for participation in our study; 1,702 of these volunteers did not qualify after screening, with 1,233 patients being disqualified as they had been taking opioids longer than three months (average duration of opioid use 2.4 years), 67 having pain less than three months, and 402 were not on opioid analgesics. Of the 199 patients who qualified, after further screening three declined and 196 patients were enrolled. Sixteen patients were disqualified postconsent, with 11 being disqualified as they were positive for illicit drugs on baseline urine drug screens, three for violation of study procedure, one for mental health reasons identified on baseline screening, and one exceeding age limitations (see Figure 1).

**Retention Rates**

Retention rates for performing chart reviews to assess ADRBs and prescribing behaviors were 167 (93%),

**Table 2** Depression, anxiety, history of substance use disorders, ADRB, and pain coping

Variable	Month	N	Mean	SD
PHQ-9	0	180	10.92	6.99
	3	149	9.97	6.56
	6	137	9.75	6.38
	12	101	9.43	6.41
ADRB (sum 0–9)	0	180	0.80	0.98
	3	167	0.37	0.70
	6	164	0.23	0.57
	12	152	0.31	0.67
Beck Anxiety Inventory	0	180	14.14	13.81
	3	149	14.67	13.53
	6	137	12.80	12.24
	12	101	11.80	12.83
PCS (1–13)	0	—	—	—
	3	—	—	—
	6	137	19.75	13.78
	12	101	15.63	15.26
Lifetime history of alcohol use disorder (0–7)	0	180	0.33	1.04
	3	—	—	—
	6	—	—	—
	12	—	—	—
Lifetime history of drug use (0–7)	0	180	0.16	0.61
	3	—	—	—
	6	—	—	—
	12	—	—	—

164 (91%), and 152 (84%) at three, six, and 12 months, respectively. Charts not available for review were due to patients leaving the practice. Retention rates for completing follow-up phone interviews were 149 (83%), 137 (76%), and 101 (56%) at three, six, and 12 months, respectively. In comparing patients who completed all assessments with those who did not, there were no statistically significant differences on demographics other than the percentage of patients receiving disability benefits was lower in patients who completed all assessments as compared with those who did not complete all assessments (22.4% vs 42.4%,  $p = 0.025$ ) and completers were statistically older than noncompleters (mean age in years = 52.23,  $SD = 13.52$  vs 44.33,  $SD = 11.73$ ,  $p < 0.001$ ). On baseline clinical characteristics, completers tended to have lower average pain scores than noncompleters (mean 0–10 pain intensity score = 5.76,  $SD = 1.80$  vs 6.36,  $SD = 1.65$ ,  $p = 0.021$ ) and were less depressed based on PHQ-9 scores (9.31,  $SD = 6.59$  vs 12.22,  $SD = 6.84$ ,  $p = 0.004$ ).

**Demographics**

Demographics of the enrolled patients are outlined in Table 1. US Census Bureau data for Berks County, Pennsylvania, where the majority of subjects were recruited during the recruitment period of 2008 to 2012,

**Table 3** Average morphine equivalent daily dose and average pain rating

	Months	No. of subjects	Dose	SD
Daily morphine equiv. dose	0	—	—	—
	3	167	18.69	26.7
	6	164	23.94	37.12
	12	152	13.88	28.3
Average pain rating (0–10)	0	180	6.02	2.07
	3	149	5.37	2.08
	6	137	4.93	2.22
	12	101	5.13	2.15

were also examined. The average age of our sample was 47.8 years, with the median age of Berks County residents being 39.4 years. Sixty-seven percent of the study population was female, as compared with 51% in Berks County. A majority had completed high school or higher education (87%), which was comparable with educational attainment of Berks county residents (84%). In the study population, 65.4% were employed full time as compared with 91% of Berks county residents between age 16 and 75 years, which included retired persons who had been employed full time.

**Psychiatric Disorders, Coping, Social Support, and Substance Abuse History**

At baseline, three months, six months, and 12 months, depression as measured by the PHQ-9 revealed that enrolled patients were mildly to moderately depressed (10.92, 9.97, 9.75, 9.43). Likewise results of the Beck Anxiety Inventory at baseline, three, six, and 12 months indicated that these patients experienced mild anxiety (14.14, 14.67, 12.80, 11.80). For both anxiety and depression, there were no statistically significant differences between times measured. Baseline measures of history of lifetime alcohol use disorder and drug use disorder of the enrolled patients revealed that the mean number of DSM-IV criteria was 0.33 (0–7) for alcohol and 0.16 (0–7) for drugs. Subjects tended to cope relatively well with pain as measured by the Pain Catastrophizing Scale at six and 12 months (19.75, 15.63) (see Table 2). The MINI revealed that patients in this sample had low levels of personality disorders and other significant psychiatric conditions (bipolar disorder, etc.). Results from the Duke Social Support Index indicated that patients in this cohort self-reported unimpaired subjective social support (mean = 19.10,  $SD = 4.76$ ), indicating an adequate support system.

**Aberrant Behaviors/Urine Drug Monitoring**

Aberrant behaviors were assessed primarily from extensive chart reviews on each patient. Nine aberrant behaviors were targeted based on previous research in this

**Table 4** Discontinuation of opioids

6 mo (N = 164)		12 mo (N = 152)	
% taking opioids	% not taking opioids	% taking opioids	% not taking opioids
87 (144)	13 (20)	72 (109)	28 (43)
Reasons for discontinuation:			
1. intoxication = 1			
2. fear of addiction = 5			
3. pain improved/resolved = 19			
4. no relief from opioids = 7			
5. adverse effects = 10			
6. no insurance = 1			
Self or MD discontinued opioids:			
1. self-initiated = 41			
2. MD initiated = 2			

area, preliminary data from our laboratory, and expert consensus opinion (see Table 6). Validated measures of ADRB were not utilized as these assessment tools were unavailable or newly published when this study was developed and funded (2006–2007). In addition, these assessment tools rely on patient self-report, which can be highly biased, not on actual observed behaviors, which a chart review can reveal over time. Also, this was an observational cohort study of subjects recruited from primary care physician (PCP) sites, and use of these tools was not part of standard practice. The majority of patients did not engage in aberrant behaviors (0–9) at three, six, and 12 months (the mean number of ADRBs per patient was 0.37, 0.23, and 0.31, respectively) (see Table 2). Urine drug screens for the major types of illicit drugs or absence of prescribed opioids or for opioids that were not prescribed were evaluated. At baseline, 8.4% of patients tested positive for cannabis. At three months, 4.7% tested positive for cannabis and 1.6% for cocaine, and prescribed opioids were absent in 26%. At six months, 4.3% tested positive for cannabis, 1.7% for cocaine, and prescribed opioids were absent in 20.9%. At 12 months, 9.7% tested positive for cannabis, 0% for cocaine, and prescribed opioids were not detected in 16.1%.

**Opioid Dosing/Use and Pain**

In patients who completed all assessments, their pain generally improved from baseline to 12 months after initiating opioids, but these differences were not statistically significant (6.02, 5.37, 4.93, 5.13). At three months, the average morphine equivalent daily dosage (MEDD) was 18.69 milligrams MEDD (SD = 26.7), at six months it was 23.94 MEDD milligrams (SD = 37.1), and at 12 months it was 13.88 milligrams MEDD (SD = 28.3) (Table 4). Extended-release opioids were only prescribed in 9% of the cases. At 12 months, 43 (28%) of the patients enrolled had discontinued the use of opioids. The patients self-discontinued opioids for a

**Table 5** Characteristics of prescribing clinicians

Specialty	%
Family medicine	61 (71)
Internal medicine	39 (46)
Pain management education	
Yes	15 (18)
No	80 (94)
Unknown	5 (5)
Ethnicity	
Hispanic	2 (2)
White	75 (89)
Black	2 (2)
Asian	9 (11)
Unknown	12 (14)
Sex	
Male	71 (83)
Female	29 (34)
Age	48.68 y

number of reasons, including feeling intoxicated, pain improvement, no relief from opioids, adverse effects, and having no insurance (Table 4).

**Physician Characteristics and Behaviors**

Table 5 outlines the demographics of the physician cohort. One hundred seventeen PCPs participated in this study and prescribed the first prescription for opioids. The majority of the PCPs were from family medicine (61%), were white (75%), and were male (71%). The majority of these PCPs had no additional education/training in pain management (80%). Only 7% of treating physicians collected urine drug screens (not including the urine screens conducted for research), 9% utilized opioid treatment agreements, and none employed screening and monitoring tools.

**Discussion**

The literature based on limited, retrospective, or cross-sectional studies in specialty clinics [9–16] suggests that CNCP patients receiving continuous opioid therapy (COT) display frequent ADRBs and have a high rate of illicit drug use. However, Fishbain’s meta-analysis [14] suggests that if cohorts are prescreened for risk, opioid abuse and misuse rates are relatively low. Boscarino and colleagues’ recent cross-sectional studies of a population of patients in a large health system utilizing direct telephone diagnostic interviews based on DSM-IV [26] and DSM-5 [27] of randomly selected patients exposed to long-term opioid therapy generally support Fishbain’s findings [28]. They identified factors such as younger age, psychiatric conditions (depression, generalized anxiety, illicit drug use, a history of substance abuse treatment, suicidal thoughts), sleep and pain conditions, fair/poor health status, and higher opioid dose that are

**Table 6** Aberrant drug-related behaviors

---

Positive urine drug screen or self-reported illicit drug use
Self-reported prescription drug misuse [20]
Obtaining narcotics from more than 1 physician [21]
Complaints of pain in more than 1 body system, other than original complaint on subsequent visits [20]
More than 1 ER visit for pain per study period
More than 1 unscheduled primary care clinic visit for pain per follow-up visit [22]
More than 2 calls to the primary care clinic for pain/pain meds per month [20–22]
Reporting of lost or stolen prescriptions [21]
Reports of obtaining medications from other sources [21,22]

---

associated with the 13.2% of COT patients with moderate-severe opioid use disorder based on DSM-5 criteria. This is the subgroup that is most likely at risk for addiction. Our study, through chart review and telephone screening and using validated clinical instruments, attempted to eliminate subjects with psychiatric/substance abuse risks. We note that the average doses of our study subjects were relatively low, a morphine equivalent daily dose of three to five doses of 5 mg oxycodone or hydrocodone. Our results suggest that patients initiating short-acting opioids in a primary care population with mild psychiatric symptoms and no substantial past history of a SUD display minimal ADRBs, that illicit drug use is fairly low, that doses generally did not escalate, and that a number of patients stopped opioids. These findings were similar to an earlier influential paper that evaluated 38 patients with CNCP on long-term opioid therapy. They discovered that there was a lower likelihood of patients engaging in ADRBs when they were prescribed lower doses and had no history of a SUD [29]. The prescribed opioid being absent occurred at a rate of 26%, 20.9%, and 16.1% at three, six, and 12 months, respectively. However, 91% of the subjects were prescribed short-acting opioid preparations, and, depending on the timing of the last dose and when the urine specimen was obtained, the opioid metabolite may not have been detected. This interpretation is consistent with the relatively low average daily doses (three to five pills) of short-acting opioids prescribed to the sample, such that a substantial subset may have used pills episodically, not regularly. Alternatively, this could be suggestive of diversion. These findings in general are consistent with the prevailing literature showing that the most predictive risk factor for developing an opioid use disorder is having a past history of substance abuse [30] and risk for abuse is higher in patients with significant co-occurring psychiatric disorders and higher opioid doses [14,26,27,31].

A substantial number of patients (28%) self-discontinued opioids at 12 months, which is consistent with the 2010 Cochrane review on efficacy of long-term opioids [32], and there was no direct evidence of diversion.

Current opioid guidelines strongly recommend the use of screening tools, urine drug monitoring, and treatment

agreements [33–35]. In our physician study population, there was a low rate of use of these risk assessment/mitigation tools. In spite of the recognition of the dangers of opioid misuse and diversion, these results underscore the lack of training in appropriate pain management and risk assessment and mitigation strategies in PCPs. It also speaks to the failure of “best practices” being adopted by PCPs although over 50% of pain care is delivered by these clinicians [7].

Our finding that the rates of detected abuse/misuse are very low when opioids are used in patient samples with lower risk even without monitoring, as we did by studying this sample, has implications for clinical practice. Pain management specialty and primary care clinical practice experience over several decades has suggested that several subpopulations of patients with chronic pain exist with respect to the effective use of opioid analgesia. One subgroup of patients appears to do well without developing SUD when prescribed opioids in low doses to recover from acute pain or flares of chronic pain. In these patients, the use of short-acting opioids with close monitoring along with other indicated treatments could help restore function and quality of life in conjunction with other adjunctive medications and nonpharmacologic interventions (physical, psychological, and integrative therapies, for example). Our selected sample of patients with musculoskeletal pain, even without monitoring or other specific pain treatments, did not develop symptoms and behaviors suggestive of progression to SUD as a result of their exposure to opioid analgesics over a 12-month period. Other subgroups, such as those with known risk factors (moderate to severe psychiatric disorders and history of SUD) who were excluded from our study population, predictably have difficulty and demonstrate misuse, abuse, and SUD symptoms and signs. The tendency to lump all patients together as at similar risk for trials of opioids, and planning care accordingly, does not seem to be a prudent or an effective strategy to address the public health problem of chronic pain. The result is an over-concern about iatrogenic addiction, and it deprives patients of a trial of opioid analgesia, which might reduce the risks of function-limiting pain and inability to work. Instead, health systems must address the needs of large subpopulations of patients with chronic pain conditions

who may benefit from selective, integrated treatments, including opioid analgesia for selected patients, based on their clinical profiles including their pain conditions, strengths, comorbidities, and risks.

**Limitations**

The majority of primary care physicians in this study were quite cautious in prescribing high doses of opioids (>90 mg morphine equivalent daily dose). There is literature that suggests that high dosing may lead to increased risk of abuse and misuse [31,36]. Perhaps the low rate of ADRBs may be related to opioid dosing.

Patients could have received opioids from other sources. However, this was a relatively closed community with only two hospitals in the catchment area, the majority of patients are cared for by PCPs at the study site (Reading Health System), and, based on chart reviews, there was no indication of doctor shopping or frequent emergency department visits and a substantial number of patients voluntarily discontinued opioids due to adverse effects or lack of efficacy. As noted previously, Pennsylvania did not have a drug monitoring program at the time this study was conducted, so we cannot be absolutely certain that a subgroup of patients did not attempt to receive opioids from outside the study site. Also, at 12 months we had only a 56% retention rate of completing follow-up interviews and urine drug screening, such that potentially high-risk patients could have selectively dropped out. However, our retention rate was 76% at six months and we were able to capture ADRB via chart review in 91% and 84% of the cases at six and 12 months, respectively. It is unlikely that patients would have converted to abusing their opioids or using illegal drugs after six months, and the ABRB data revealed no evidence of misuse or abuse.

We relied on extensive medical record chart reviews to assess for ADRB. While there are a number of “validated” risk assessment tools, these tools have many limitations including lack of content validity—having items not directly assessing inappropriate use, many are based on small sample sizes and have limited psychometrics [37]. It was the belief of the authors that, based on expert consensus opinion and the literature [20–22], assessing ADRBs from detailed longitudinal review of the patient medical records and urine drug screens [38] would be less prone to subject bias than the cross-sectional use of a self-report brief risk assessment tool.

Inherent in studies of this type, there is potential for selection bias and the effect of being monitored both in the subjects and the prescribing physicians. Regarding subject selection bias, the institutional review board–approved recruitment materials (advertisements, fliers) were appropriately vague regarding the aim of the study. During the consenting process, the full aims of the study were reviewed and only three subjects declined out of 199 who volunteered and were eligible. The effect of monitoring on subject and physician

behavior is difficult to ascertain. Although physicians volunteered to participate in this study, their involvement was nominal, consisting of allowing the research staff to display recruitment fliers in their waiting room referring patients to the study and permission to send out recruitment material to all of their patients regardless of their diagnosis or medication use. The research team had minimal contact with the participating physicians, and it is doubtful the physicians knew which of their patients were actually enrolled in the study. Subjects, although cognizant that they were being monitored, were followed over 12 months and most likely individuals susceptible to abusing their opioids or developing an opioid use disorder would have displayed ADRBs.

**Conclusion**

A great deal of scholarly activity has been devoted to identifying risk factors for prescription opioid abuse in an effort to select appropriate patients for whom opioids may be efficacious in improving pain and function vs patients who may be vulnerable to misusing or abusing opioids. Most studies in this area are retrospective or cross-sectional and include patients in specialty pain clinics. In this prospective, longitudinal cohort study, we followed patients initiating opioids in community-based primary care practices and collected extensive data on both patient and physician characteristics. The results of this study suggest that the rate (risk) of substance abuse (less than 5%) or ADRBs in well-selected patients (minimal psychopathology, no preexisting history of SUD, good social support, adequate pain coping skills) is low. These findings can serve as a basis to develop additional screening tools and early interventions to mitigate risk of opioid misuse or abuse while maximizing the potential benefit of opioids when used for low-risk patients. Secondary results on physician characteristics agree with previous studies indicating that PCPs often lack the skills/knowledge to effectively assess and monitor patients receiving long-term opioids.

**References**

- 1 Tsang AM, Von Korff S, Lee J, et al. Common chronic pain conditions in developed and developing countries: Gender and age differences and comorbidity with depression-anxiety disorders. *J Pain* 2008;9(10):883–91.
- 2 Institute of Medicine. *Relieving Pain in America: a Blueprint for Transforming Prevention, Care, Education, and Research*. Washington, DC: The National Academies Press; 2011.
- 3 Substance Abuse and Mental Health Services Administration. *Results from the 2012 National Survey on Drug Use and Health: Summary of national findings*. NSDUH Series H-46, HHS



- Publication No. (SMA) 13-4795. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013.
- 4 Substance Abuse and Mental Health Services Administration. Drug Abuse Warning Network, 2011: National estimates of drug-related emergency department visits. HHS Publication No. (SMA) 13-4760, DAWN Series D-39. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013.
  - 5 Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Treatment Episode Data Set (TEDS): 2001–2011. National admissions to substance abuse treatment services. BHSIS Series S-65, HHS Publication No. (SMA) 13-4772. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013.
  - 6 Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. *JAMA* 2013; 309:657–9.
  - 7 Breuer B, Cruciani R, Portenoy RK. Pain management by primary care physicians, pain physicians, chiropractors, and acupuncturists: A national survey. *South Med J* 2010;103(8):738–47.
  - 8 Upshur CC, Luckmann RS, Savageau JA. Primary care provider concerns about management of chronic pain in community clinic populations. *J Gen Intern Med* 2006;21(6):652–5.
  - 9 Reid MC, Engles-Horton LL, Weber MB, et al. Use of opioid medications for chronic noncancer pain syndromes in primary care. *J Gen Intern Med* 2002;17(3):173–9.
  - 10 Katz N, Sherburne S, Beach M, et al. Behavioral monitoring and urine toxicology testing in patients receiving long-term opioid therapy. *Anesth Analg* 2003;97(4):1097–102.
  - 11 Ives TJ, Chelminski PR, Hammett-Stabler CA, et al. Predictors of opioid misuse in patients with chronic pain: A Prospective Cohort Study. *BMC Health Serv Res* 2006;6:46.
  - 12 Martell BA, O'Connor PG, Kerns RD, et al. Systematic review: Opioid treatment for chronic back pain: Prevalence, efficacy, and association with addiction. *Ann Intern Med* 2007;146(2): 116–27.
  - 13 Fleming MF, Balousek SL, Klessig CL, Mundt MP, Brown DD. Substance use disorders in a primary care sample receiving daily opioid therapy. *J Pain* 2007;8(7):573–82.
  - 14 Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med* 2008;9(4): 444–59.
  - 15 Manchikanti L, Pampati V, Damron KS, et al. Controlled substance abuse and illicit drug use in chronic pain patients: An evaluation of multiple variables. *Pain Physician* 2001;4(4):358–65.
  - 16 Wiedemer NL, Harden PS, Arndt IO, Gallagher RM. The opioid renewal clinic: A primary care, managed approach to opioid therapy in chronic pain patients at risk for substance abuse. *Pain Med* 2007;8(7):573–84.
  - 17 Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998; 59(suppl 20):22–33.
  - 18 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *Gen Intern Med* 2001;16(9):606–13.
  - 19 Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. *J Consult Clin Psychol* 1988;56(6):893–7.
  - 20 Cheatle MD, O'Brien CP, Mathai K, et al. Aberrant behaviors in a primary care-based cohort of patients with chronic pain identified as misusing prescription opioids. *J Opioid Manag* 2013;9(5): 315–24.
  - 21 Chabal C, Erjavec MK, Jacobson L, Mariano A, Chaney E. Prescription opiate abuse in chronic pain patients: Clinical criteria, incidence, and predictors. *Clin J Pain* 1997;13(2):150–5.
  - 22 Dunbar SA, Katz N. Chronic opioid therapy for non-malignant pain in patients with a history of substance abuse: Report of 20 cases. *J Pain Symptom Manage* 1996;11:163–71.
  - 23 Sullivan MJ, Thorn B, Haythornthwaite JA, et al. Theoretical perspectives on the relation between catastrophizing and pain. *Clin J Pain* 2001;17(1):52–64.
  - 24 Cleeland CS, Ryan KM. Pain assessment: Global use of the Brief Pain Inventory. *Annals Acad Med* 1994;23:129–38.

- 25 Broadhead WE, Gehlbach SH, de Gruy FV, Kaplan BH. "The Duke-UNC Functional Social Support Questionnaire. Measurement of social support in family medicine patients." *Med Care* 1988;26(7):709–23.
- 26 Boscarino JA, Rukstalis M, Hoffman SN, et al. Risk factors for drug dependence among out-patients on opioid therapy in a large US health-care system. *Addiction* 2010;105(10):1776–82.
- 27 Boscarino JA, Hoffman SN, Han JJ. Opioid-use disorder among patients on long-term opioid therapy: Impact of final DSM-5 diagnostic criteria on prevalence and correlates. *Subst Abuse Rehabil* 2015;6:83–91.
- 28 Von Korff M. Commentary on Boscarino et al: Understanding the spectrum of opioid abuse, misuse and harms among chronic opioid therapy patients. *Addiction* 2010;105(10):1783–4.
- 29 Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: Report of 38 cases. *Pain* 1986;25(2):171–86.
- 30 Turk DC, Swanson KS, Gatchel RJ. Predicting opioid misuse by chronic pain patients: A systematic review and literature synthesis. *Clin J Pain* 2008;24(6):497–508.
- 31 Edlund MJ, Austen MA, Sullivan MD, et al. Patterns of opioid use for chronic noncancer pain in the Veterans Health Administration from 2009 to 2011. *Pain* 2014;155(11):2337–43.
- 32 Noble M, Treadwell JR, Tregear SJ, et al. Long-term opioid management for chronic noncancer pain. *Cochrane Database Syst Rev* 2010;(1):CD006605.
- 33 Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain* 2009;10(2):113–30.
- 34 National Opioid Use Guideline Group. Canadian guideline for safe and effective use of opioids for chronic non-cancer pain. Hamilton, ON: McMaster University; 2010. Available at: [http://nationalpaincentre.mcmaster.ca/opioid/cgop\\_a00\\_executive\\_summary.html](http://nationalpaincentre.mcmaster.ca/opioid/cgop_a00_executive_summary.html) (accessed December 2016).
- 35 Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep* 2016;65(1):1–49.
- 36 Edlund MJ, Martin BC, Russo JE, et al. The role of opioid prescription in incident opioid abuse and dependence among individuals with chronic noncancer pain: The role of opioid prescription. *Clin J Pain* 2014;30(7):557–64.
- 37 Smith SM, Paillard F, McKeown A, et al. Instruments to identify prescription medication misuse, abuse, and related events in clinical trials: An ACTION Systematic Review. *J. Pain* 2015;16: 389–411.
- 38 Michna E, Jamison RN, Pham LD, et al. Urine toxicology screening among chronic pain patients on opioid therapy: Frequency and predictability of abnormal findings. *Clin J Pain* 2007;23(2):173–9.