Pain Medicine Advance Access published September 20, 2016

Pain Medicine 2016; 0: 1–11
doi: 10.1093/pm/pnw228

Original Research Article

Opioid Overdose History, Risk Behaviors, and Knowledge in Patients Taking Prescribed Opioids for Chronic Pain

Kelly E. Dunn, PhD,* Frederick S. Barrett, PhD,* Michael Fingerhood, MD† and George E. Bigelow, PhD*

*Departments of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine Baltimore, MD, USA; †Department of Internal Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA 21224

Correspondence to: Kelly Dunn, PhD, 5510 Nathan Shock Drive, Baltimore MD 21224, USA. Tel: 410-550-2254; Fax: 410-550-0030; E-mail: kdunn9@jhmi.edu.

Funding sources: This study was supported by NIDA R21DA035327 (Dunn), R01DA035246 (Dunn), and T32DA007209 (Bigelow).

Conflicts of interests: The authors have no relevant conflicts of interest to disclose.

Abstract

Objective. More than 100 million adults in the United States experience chronic pain, and prescription opioids are the third most widely prescribed class of medications. Current opioid overdose prevention efforts almost exclusively target illicit opioid users, and little is known about the experience of overdose among patients being treated for chronic pain (CP) with a prescription opioid.

Methods. Patients experiencing CP for three or more months and receiving a prescription opioid for pain management (N = 502) completed a self-report survey that asked questions about opioid overdose history, past 30-day risk factors, and knowledge of opioid overdose, overdose risk, and naloxone.

Results. Approximately one in five CP participants reported experiencing a lifetime overdose. CP participants reported engaging in several behaviors associated with overdose risk and were unlikely to have been trained to administer naloxone. Fewer than 50% of participants answered any knowledge item correctly. The likelihood of having experienced an overdose increased as the scores on the SOAPP-R and DSM-5 opioid use disorder checklist increased, and a SOAPP-R score of 7 or higher or meeting DSM-5 mild opioid use disorder criteria were significantly associated with reporting a lifetime overdose (85% and 84% of participants who experienced an overdose, respectively).

Conclusions. Opioid overdose occurs at a high rate among CP participants, and this group is relatively uninformed about risk factors for overdose. Established SOAPP-R and DSM thresholds provide an opportunity to identify participants at elevated risk for having experienced an opioid overdose. These data support development of additional concentrated efforts to prevent overdose among chronic pain patients.

Introduction

There have been focused efforts to increase the detection and treatment of pain in the United States [1,2], and currently more than 100 million adults (30.7% of the population) in the United States are believed to experience chronic pain [3,4]. Prescription opioid analgesics are widely used treatments for chronic pain [5] and are increasingly used for the treatment of chronic noncancer pain [6]; as a result, there have been continuous increases in the rate of opioid prescriptions over the past 10 years. In the United States, prescription opioids were the third most widely prescribed class of medications between 2009 and 2013, and the prescription opioid hydrocodone (Vicodin) was the single most widely prescribed medication [7]. With increased use and availability of these medications, there has been a corresponding increase in the incidence of opioid-related problems. For instance, in 2013 more than 10 million people reportedly abused (e.g., used to get high and/or outside of a prescription) a prescription opioid, 2 million people met

criteria for problematic use, and 772,000 people received treatment for abuse of prescription opioids [8].

Consistent with greater availability and problematic use of prescriptions, the incidence of opioid-related overdose has quadrupled from 2000 to 2014 [9]. Between 2013 and 2014, the rate of overdose related to prescription opioids and heroin has increased by two- and three-fold, respectively. In 2014, opioids were involved with 61% of all overdose deaths, representing more than 28,000 individuals [9]. Though the increase in opioid overdose was initially reported in drug abusers, it is now apparent in all segments of society including children, adolescents, elderly, patients with chronic pain, and women [10–19]. Further, drug poisonings, which are driven by opioids, are now the leading cause of accidental death in persons age 25 to 64 years [20]. In response to this emergent epidemic, interventions were developed to distribute the fast-acting opioid antagonist naloxone (Narcan) to heroin abusers. These efforts have now expanded to target opioid abusers and their families more generally, to increase the ability to reverse overdoses beyond medical personnel to include laypersons. These efforts are leading to measurable decreases in overdose rates in targeted areas [21] and have resulted in increased public health actions to make naloxone more widely available [22].

Due to the nature of this epidemic, and the fact that overdose interventions were developed in response to an acute crisis, the vast majority of overdose intervention programs have targeted illicit drug users. While this is an important public health need, there has been comparatively little attention paid to chronic pain (CP) patients. These individuals also have many risk factors for experiencing an overdose, including that they are maintained on opioid medications for extended periods of time (which increases their exposure rate), often have concurrent medical illnesses (e.g., obstructive sleep apnea, sleep disordered breathing) that may increase their susceptibility for an overdose, may be prescribed high doses of long-acting opioids, may be coprescribed other medications (such as benzodiazepines) that could increase their vulnerability to opioid overdose, and may be instructed to combine short and long-acting opioids to help manage break-through pain [12,23–30]. Though guidelines published by the American Society of Addiction Medicine (ASAM) and American Medical Association (AMA) have begun emphasizing the need to coprescribe naloxone to patients who are receiving extended opioid treatment for chronic pain [31,32], we know of only two programs that have begun actively dispensing naloxone to this population. The first program, Project Lazarus, has reported decreases in overdose rates from 46.6/100,000 to 29.0/100,000 in just one year, demonstrating that this approach is feasible and valuable [33,34]. The second program, the Opioid Overdose Education and Naloxone Distribution (OEND), recently began distributing naloxone to at-risk veterans, and initial outcomes suggest the program is being favorably received [35].

There are few empirical data regarding the experience and understanding of opioid overdose risks among CP patients, and this information is necessary to develop overdose prevention resources for this population. The present study assessed the frequency of overdose, overdose risk behaviors, and overdose knowledge among individuals who self-reported having CP for three months or more and using prescribed opioid medication for pain management. Results indicate surprisingly high rates of overdose and substantial knowledge deficits among CP patients and support the need for more public health efforts targeting CP patients.

Methods

Participants

This study was approved by the Johns Hopkins University Institutional Review Board (IRB) using a waiver of written informed consent. Chronic pain (CP) patients were recruited during March 2015 using crowdsourcing technology through Amazon Mechanical Turk (MTurk), which is an emerging platform for participant recruitment [36]. MTurk allows researchers ("requesters") to post advertisements ("human intelligence tasks" or "HITs") for online studies in which participants ("workers") can elect to participate. This survey was restricted to participants who resided within the United States and had a greater than 80% approval rate from completion of previous HITs through MTurk. Participants were required to complete a brief introductory survey to assess their eligibility for the primary survey, and the population being targeted for recruitment was concealed to prevent individuals from misrepresenting themselves. A total of 3,157 individuals completed the eligibility survey, and 502 (15.9%) met eligibility criteria and were allowed to participate in the primary study. Eligibility criteria were responding "yes" to the first item on the Brief Pain Inventory (BPI) indicating CP for three months or more, reporting currently taking an opioid for pain management, being over age 18 years, and being fluent in English. Participants were compensated approximately $3.00 for survey completion.

Survey Questions

All questions were administered as self-report surveys and completed online through the questionnaire manager Qualtrics.

Demographic, Drug Use, and Overdose History

A brief demographic survey characterized the sample, and a Diagnostic and Statistical Manual (DSM)-5 checklist was used to identify symptoms of opioid use disorder (OUD); illicit opioid use was defined for participants as "heroin or prescription pain pills that were not prescribed to them." Participants were asked questions regarding their history of opioid overdose. To define overdose, the instructions stated, "An overdose occurs when you take

too high a dose of opioids, and it is not always fatal. Please answer these questions even if you are NOT SURE whether you ever overdosed on these medications, but know that you had a bad or scary experience from taking them." Participants then answered questions regarding their history of personally experiencing and/or witnessing an overdose and their knowledge and experience with naloxone. Past 30-day engagement in several behaviors that incur increased risk of overdose were also assessed. These included using opioids by themselves (either via prescription or illicitly, because no one will be available to administer aid if needed) [37–39], combining opioids with alcohol [37,38,40–43], taking the long-acting opioid methadone [44,45], and having a recent decrease in opioid tolerance (e.g., having recently completed an opioid detoxification or being released from jail/prison) [43,46–48]. This study did not differentiate between accidental and intentional overdose.

Opioid and Opioid Overdose Knowledge

Participants completed a nine-item self-report survey to assess their knowledge of opioids, opioid overdose, and naloxone; to discourage random guessing, response options were "True," "False," and "I Don't Know" [49–51]. Questions were derived based on known associations between opioid overdose and risk. Results were coded dichotomously as correct and incorrect for analyses, with "I don't know" being coded as incorrect. Total possible score range was 0–9, and the specific items asked are listed in Table 3.

Brief Pain Inventory (BPI) [52]

The BPI was used to assess study eligibility and to characterize pain severity and functional interference with daily activities. Individual BPI severity and interference ratings were rated on a 0 (no pain at all/does not interfere) to 10 (pain as bad as you can imagine/completely interferes) scale, respectively, and summed into severity (range = 0–40) and interference (range = 0–100) subscale scores [53]. Severity ratings were then categorized as mild (1–4), moderate (5 and 6), and severe (≥7), consistent with recommendations for using the BPI in clinical trials [54].

Screener and Opioid Assessment for Patients with Pain (SOAPP-R) [55]

The SOAPP–R is designed to assess risk of a patient developing problematic opioid use and was administered to evaluate the degree to which SOAPP-R scores would be significantly associated with overdose history. Participants answered items on a scale of 0 (never) to 4 (very often), and a total risk score (range = 0–96) was derived for each participant to be used in analyses. A SOAPP-R total score of 7 or higher has been associated with heightened risk of developing problematic opioid use.

Current Opioid Misuse Measure (COMM) [56]

The COMM is a self-report measure designed to assess aberrant medication-related behaviors among participants who have been maintained chronically on opioids for the treatment of pain. The COMM was administered to evaluate the degree to which COMM results were associated with overdose history. Participants answered items on a scale of 0 (never) to 4 (very often), and a total risk score (range = 0–68) was derived for each participant to be used in analyses. A COMM total score value of 9 or higher has been identified as evidence of medication misuse.

Data Analysis

Demographic, drug use, and overdose characteristics were summarized descriptively. A logistic regression was used to evaluate correlates of a lifetime history of overdose (yes/no) in this sample, and a multiple linear regression was used to evaluate correlates of the number of lifetime overdoses among participants. Both regression models included the following a priori–hypothesized variables as potential correlates: number of endorsed DSM-5 criteria for OUD, BPI Severity category (mild, moderate, severe), BPI Interference subscale score, SOAPP-R total score, COMM total score, and the duration of time in years the patient reported being maintained on a prescription opioid for pain management. Receiver operating characteristic (ROC) curves were then used to determine whether responding on the SOAPP-R and DSM checklist could be used to correctly differentiate CP participants who reported a lifetime history of overdose from those who reported no lifetime history of overdose [57]. To increase generality of findings to clinical treatment settings, thresholds for ROC analyses were defined a priori using values that have been previously established as indicating increased risk for problematic opioid use on each measure. This included the SOAPP-R cut-off for identifying problematic prescription opioid use (≥7) and DSM-5 criteria cut-offs for mild (2–3 symptoms), moderate (4–5 symptoms), and severe (≥6 symptoms) OUD. Missing data were rare (<1%), so no corrections were made. All analyses were conducted using SPSS v. 21, and alpha values were set at 0.05.

Results

Participant Characteristics

Consistent with their self-report of pain, participants reported moderate levels of pain severity (mean = 3.3, SD = 1.7, out of 10) and interference with daily activities (mean = 3.6, SD = 2.2, out of 10) on the BPI. Participants reported regular use of a prescription opioid for pain management for less than one year (57.1% of

Table 1 Demographic and drug use characteristics

	Chronic pain, % (N = 502)
Demographic characteristics	
Male	55.1
Older than age 30 y	32.5
Caucasian	80.3
Never married	38.8
Employed	85.5
Health Insurance	90.6
Substance use (past 30 days)	
Alcohol	53.7
Any illicit drug use	40.8
Cannabis	31.3
Prescription opioids*	22.5
Other psychotherapeutics*,†	21.0
Cocaine	5.4
Methamphetamine	5.0
Hallucinogens	3.9
Heroin	3.5
Lifetime injection drug use	10.4
Opioid-related measures	
SOAPP-R score ≥7	61.9
COMM score ≥9	66.1
DSM-5 mild OUD	20.7
DSM-5 moderate OUD	11.4
DSM-5 severe OUD	22.9

*Values represent illicit use, use outside of a prescription, or nonprescribed use for the purpose of getting high.
†Defined as prescription stimulants or benzodiazepines.
COMM = Current Opioid Misuse Measure; OUD = Opioid Use Disorder; SOAPP-R = Screener and Opioid Assessment for Patients with Pain.

participants), between one and four years (29.9%), and more than five years (13.0%). Twenty-one percent of participants reported using opioids (either a prescription opioid or heroin) in the past 30 days with the intent of getting high, and 55% met criteria for any level of OUD (Table 1).

Overdose History

Overall, 19.3% (N = 97) of the sample reported overdosing from opioids more than once in their lifetime, and 9.3% (N = 9) of those individuals reported experiencing their last overdose in the past 30 days. Among the 19.3% of participants who endorsed experiencing an OD, participants endorsed a total mean of 2.2 (SD = 2.8) lifetime overdoses, with a range of one to more than 21 lifetime ODs. Of these overdoses, participants maintained consciousness in a mean of 1.9 (SD = 3.1) events and lost consciousness in a mean of 1.1 (SD = 1.7) events. The percent of participants who experienced an overdose during their lifetime as a function of DSM-5 OUD category were 16.5% (no OUD), 16.5% (mild OUD), 20.1% (moderate OUD), and 46.4% (severe OUD). A total of 37.8% (N = 190) of participants reported witnessing an overdose; of the overdoses witnessed, a mean of 3.2 (SD = 6.3) people survived and 0.5 (SD = 1.5) people died (Table 2). The percent of participants who witnessed an overdose during their lifetime as a function of DSM-5 OUD category were 35.2% (no OUD), 21.1% (mild OUD), 14.7% (moderate OUD), and 28.9% (severe OUD).

The percent of participants who reported engaging in behaviors considered to increase risk of overdose in the past 30 days is presented in Table 2. The most frequent risk behaviors reported in this sample were using opioids by themselves (53.8%) or combining opioids with alcohol (37.5%). Participants who reported a lifetime history of overdose reported having used prescription opioids (79.4% of participants), alcohol (68.0%), psychotherapeutics (defined as prescription stimulants and/or benzodiazepines, 49.5%), and/or cannabis (38.1%) at the time of the overdose. Only 3% of the participants surveyed reported having a naloxone prescription or being trained to deliver naloxone.

Predictors of Overdose

A logistic regression was used to evaluate correlates of experiencing a lifetime overdose among the CP participants. The model was significant ($\chi^2(4) = 73.3$, $P < 0.001$) and revealed that having a higher SOAPP-R score ($\chi^2(1) = 6.1$, $P = 0.01$, odds ratio [OR] = 1.05, 95% confidence interval [CI] = 1.01–1.04) and endorsing more DSM-5 criteria ($\chi^2(1) = 15.3$, $P < 0.001$, OR = 1.22, 95% CI = 1.10–1.34) were both significantly and independently associated with lifetime history of experiencing an overdose. None of the following was significantly associated with overdose history: the BPI Severity category ($P = 0.78$), the BPI Interference subscale ($P = 0.50$), the COMM score ($P = 0.54$), or the duration of time maintained on a prescription opioid ($P = 0.66$). A significant linear regression ($R^2 = .11$, $P < 0.001$) revealed that the SOAPP-R score (Beta = 0.17, t = 2.03, $P = 0.04$) and number of DSM-5 criteria met (Beta = 0.21, t = 3.50, $P < 0.001$) were also associated with the number of lifetime overdoses; no associations were identified for BPI Severity category ($P = 0.24$), BPI Interference subscale ($P = 0.24$), COMM score ($P = 0.89$), or duration of time maintained on a prescription opioid ($P = 0.53$).

ROC curves were estimated for the total SOAPP-R score and the number of DSM-5 criteria endorsed, as these measures were the only ones to be significantly associated with both lifetime history of an overdose and the number of lifetime overdoses (Table 4). ROC curves calculated for SOAPP-R score and lifetime history of overdose revealed an AUC of 0.74; a SOAPP-R rating of 7.5 had a sensitivity level of .84, indicating that 84% of CP participants with a history of overdose had

Table 2 Overdose history and risk behaviors

	Chronic pain (N = 502)
Past 30-day risk behaviors, %	
Using opioids by themselves	53.8
Combining opioids with alcohol	37.5
Taking methadone	3.8
Completing an opioid detoxification	3.0
Having been released from jail or prison	2.2
Overdose history	
Lifetime opioid OD, %	19.3
Number lifetime ODs*, mean (SD)	2.2 (2.8)
OD maintained consciousness*, mean (SD)	1.9 (3.1)
OD became unconscious*, mean (SD)	1.1 (1.7)
Minimum lifetime ODs*, mean	1
Maximum lifetime ODs*, mean	>21
Last OD within 30 d, %*	9.3
Last OD within 1 y, %*	36.1
Substances used during OD, %	
Prescription opioids	79.4
Alcohol	68.0
Other psychotherapeutics†	49.5
Cannabis	38.1
Heroin	19.6
Cocaine	15.5
Methadone	12.4
Witnessed OD in lifetime, %	37.8
Number times OD survived‡	3.2 (6.3)
Number times OD died‡	0.5 (1.5)
Have prescription for naloxone, %	3.2
Trained to deliver naloxone, %	3.0
Trained to deliver CPR, %	50.0

*Values represent percent of participants with a lifetime history of an OD.
†Defined as prescription stimulants or benzodiazepines.
‡Values represent percent of participants who have witnessed an OD.

SOAPP-R ratings greater than the 7 threshold that has been established as increased risk of developing problematic opioid use. ROC curves calculated with the DSM-5 criteria and lifetime history of overdose revealed an AUC of 0.76. DSM scores of 1.5 had a sensitivity of 0.84, indicating that 84% of CP participants with a history of overdose met two or more DSM criteria, consistent with mild OUD. DSM scores of 3.5 had a sensitivity of 0.68, suggesting that 68% of CP participants with a history of overdose met four or more DSM criteria, consistent with moderate OUD. Finally, DSM scores of 5.5 had a sensitivity of 0.47, suggesting that 47% of CP participants with a history of overdose met six or more DSM criteria, consistent with severe OUD.

Knowledge Outcomes

As shown in Table 3, fewer than 50% of CP participants provided the correct answer on any of the nine knowledge questions asked. Specifically, the percent of participants answering questions correctly ranged from 47.0% ("It is only considered an overdose if the person dies") to 10.2% ("If you are overdosing, you may need more than one dose of Narcan to reverse the overdose").

Discussion

Despite efforts to refine clinical treatment guidelines regarding the treatment of chronic pain with prescription opioids [31,58], these medications remain among the most highly prescribed in the United States. The results of this study indicate that nearly one in five patients who have experienced chronic pain for three months or more and are receiving a prescription opioid for pain management report having experienced at least one nonfatal opioid-related overdose during their lifetime. CP participants in this study who reported engaging in behaviors that could increase their risk of experiencing an overdose were unlikely to have received and/or been trained to administer naloxone and had poor response rates to the overdose knowledge items queried. This combination of elevated risk and poor protective knowledge argues for the need for improved risk management attention in this population.

Several indicators suggest that a subgroup of CP participants may be at heightened risk of experiencing an opioid-related overdose. Nine percent of CP participants reported experiencing an overdose in the past 30 days, 53.8% reported using opioids by themselves in the past 30 days, and 37.5% reported combining opioids with alcohol. These are all known risk factors for experiencing a fatal overdose, and recent evidence has suggested that combining opioids with alcohol or benzodiazepines, which have similar pharmacological profiles, is particularly dangerous and is uniquely contributing to recent increases in overdose deaths [59,60]. These outcomes are especially alarming given that only 19.3% of participants correctly identified combining sedatives and opioids as a risk factor for experiencing an opioid overdose on the knowledge questions (Table 3). Further, 38.7% of CP participants had witnessed an overdose, which has itself been associated with an increased risk for experiencing an overdose in the future [61,62]. Finally, the majority of CP participants reported not having received and/or been trained to administer naloxone, and fewer than 50% of participants answered knowledge questions correctly for each of the items asked. These results likely reflect the fact that national efforts have worked to expand naloxone training and overdose education efforts to recognized illicit drug-using populations, while directing relatively limited attention toward other risk groups such as chronic pain patients.

Table 3 Knowledge of opioid overdose and risk factors

		Chronic pain* (N = 502)
1	It is only considered an overdose if the person dies. (F)	47.0
2	Opioids will not ever make you feel drowsy. (F)	46.4
3	Opioids should always be used to help you fall asleep. (F)	46.2
4	Opioids are only active if they are injected. (F)	43.3
5	Short-acting opioids are used to treat severe or sudden pain. (T)	28.9
6	If you see a person overdose on opioids you should put them in a cold bath. (F)	26.7
7	Extreme drowsiness or slow and shallow breathing with little chest movement is a sign of an overdose. (T)	19.7
8	Combining opioids with other medications, like sedative or anti-anxiety medications, can be dangerous. (T)	19.3
9	If you are overdosing, you may need more than 1 dose of Narcan to reverse the overdose. (T)	10.2

*Values represent percent of participants answering correctly. T = True; F = False.

Though only 21% of the CP sample reported abusing their prescriptions, 55% met criteria for some level of opioid use disorder on a DSM-5 checklist. This rate is consistent with previous assessments of opioid use disorder within patients being treated for chronic pain [63,64]. In this study, both the SOAPP-R, a measure of risk for developing problematic opioid use, and the number of DSM OUD criteria endorsed were significantly associated with lifetime history of and number of lifetime overdoses. Number of DSM OUD criteria have been previously associated with increased likelihood of reporting lifetime history of overdose [65]; however, this study is the first to evaluate the threshold at which overdose risk may increase based upon these risk assessments. Specifically, ROC analysis showed that 85% of participants who met the SOAPP-R threshold that has been established as a risk for developing problematic opioid use (score $\geq$ 7) and that 84% of participants who endorsed two or more DSM OUD criteria, representing mild OUD, reported having experienced an overdose in their lifetime. Increasing the DSM-5 criteria threshold to moderate and severe OUD substantially decreased sensitivity for predicting an overdose event (68% and 47%, respectively) in this sample, suggesting that mild OUD may be the more sensitive threshold for identifying overdose risk. Altogether, these results suggest that the subgroup of CP patients who display problematic opioid use may be at greatest risk for experiencing an overdose. However, among the remaining 54% of participants who did not meet criteria for OUD, 16% and 35% endorsed experiencing and witnessing a lifetime overdose, respectively. As experiencing and witnessing an overdose are both significantly associated with having a future overdose [41,61,62,66–69], this group should still be considered high risk. Overall these data suggest that there is value in educating all CP patients about the risk of opioid-related overdose and that scores on the SOAPP-R and DSM-5 checklist may provide an easy method to quickly assess a patient's likelihood for experiencing an overdose and to potentially implement a brief intervention in clinical settings.

Strengths of this study are its large sample size and its focus on individuals who are currently prescribed opioids. Limitations include that the sample was very homogenous (e.g., young, Caucasian, high education), so it is not clear how these results would generalize to other samples of chronic pain patients. This study did not differentiate accidental from intentional overdose and responses were based on self-report, which prevented objective corroboration of pain, substance use history, details regarding patient prescriptions, or collateral reports from family or other caregivers. Responses were also self-generated and did not include the geographic location of the participants, which is problematic as efforts to educate individuals about opioid overdose risks and to dispense naloxone vary substantially across the United States [70]. In addition, this study did not assess the specific opioid prescribed, and absence of this detail prevents evaluation of the well-established association between dose and duration of drug action with overdose risk [24,71–73]. Further, the application of DSM-5 for the identification of OUD among patients who are physically dependent upon prescribed opioids is problematic [74]. This study also did not collect sufficient information to calculate a score on the Risk Index for Overdose of Serious Opioid-induced Respiratory Depression (RIOSORD). This index yields a numerical risk value for experiencing an opioid-related overdose and may provide a particularly sensitive method for assessing overdose risk that should be assessed in the CP population in future studies [75]. The study combined prescription benzodiazepine and stimulant use as a single variable. That decision was made out of concern that participants would not be able to accurately differentiate those classes of medications, though the combined variable prevents evaluation of the contribution of concurrent benzodiazepine use to results. Finally,

Table 4 Receiver operating characteristic (ROC) curve sensitivity and specificity values

Screener and opioid assessment for patients with pain (SOAPP-R)*			DSM-5 opioid use disorder†		
Outcome value‡	Sensitivity	1–specificity	Outcome value‡	Sensitivity	1–specificity
−1	1.00	1.00	−1	1.00	1.00
0.5	1.00	0.89	0.5	0.93	0.67
1.5	1.00	0.84	1.5	0.84	0.47
2.5	0.96	0.78	2.5	0.77	0.33
3.5	0.93	0.72	3.5	0.68	0.25
4.5	0.90	0.68	4.5	0.58	0.21
5.5	0.87	0.62	5.5	0.47	0.16
6.5	0.85	0.56	6.5	0.35	0.10
7.5	0.84	0.52	7.5	0.25	0.06
8.5	0.81	0.48	8.5	0.17	0.04
9.5	0.78	0.45	9.5	0.12	0.03
10.5	0.75	0.41	10.5	0.05	0.02
11.5	0.70	0.38			
12.5	0.68	0.36			
13.5	0.68	0.32			
14.5	0.68	0.29			
15.5	0.65	0.26			
16.5	0.60	0.23			
17.5	0.58	0.21			
18.5	0.55	0.20			
19.5	0.52	0.19			
20.5	0.49	0.17			
21.5	0.47	0.16			
22.5	0.45	0.15			
23.5	0.41	0.13			
24.5	0.38	0.13			
25.5	0.36	0.12			
26.5	0.33	0.10			
27.5	0.30	0.08			
28.5	0.26	0.07			
29.5	0.22	0.06			
30.5	0.21	0.05			
31.5	0.17	0.04			
32.5	0.13	0.03			
33.5	0.12	0.03			
34.5	0.11	0.02			
35.5	0.10	0.01			
36.5	0.08	0.01			
37.5	0.07	0.01			
38.5	0.07	0.00			
39.5	0.06	0.00			
40.5	0.05	0.00			
41.5	0.03	0.00			
44.5	0.02	0.00			
49.5	0.01	0.00			
53.0	0.00	0.00			

*SOAPP-R total score; range = 0–96; ≥7 associated with increased risk of problematic opioid use.
†DSM-5 criteria for opioid use disorder, range = 0–11, mild = 2–3, moderate = 4–5, severe ≥ 6.
‡Values positive if greater than or equal to outcome.

the rate of overdose in this group (approximately 20%) is significantly higher than a previous study that reported a rate of overdose of less than 1% among data collected from pharmacy records between 1997 and 2005 [16]. The high rate of reported overdose in the current study may be due to increased sensitivity to identifying overdose events (self-report vs pharmacy records), the misinterpretation of opioid adverse events as overdoses among individuals who are not educated about the symptoms of an opioid overdose, or a true increase in the experience of overdose among chronic pain patients. The mechanism underlying this result cannot be determined from the data available here, and these results highlight the need for additional research to more sensitively evaluate opioid overdose among CP patients.

In conclusion, these data demonstrate that nearly one in five individuals with CP report having experienced an opioid-related overdose and that this group is largely uninformed about behaviors that increase their risk of overdose. These results support recent ASAM and AMA recommendations that naloxone be distributed to all CP patients [31,32] and suggest the opioid overdose risk interventions, including provision of naloxone, be targeted toward CP patients who show evidence of problematic opioid use (assessed via the SOAPP-R or DSM OUD criteria). However, as history of a nonfatal overdose and witnessing an overdose are both highly predictive of experiencing a fatal overdose [41,61,62,66–69], these data suggest that CP patients with any overdose experience are at a heightened risk of experiencing a nonfatal overdose and should be targeted with prevention efforts. In addition, future studies should be done to evaluate these associations within a patient population for whom objective verification of pain and opioid prescriptions are available and to assess the relative predictive value of other measures of risk for opioid overdose, including the RIOSORD score. Ultimately, these data argue for further study and improved efforts to prevent overdose among pain patients.

Acknowledgments

The authors are responsible for the study development, conduct, data management, and manuscript preparation.

References

1 Institute of Medicine. Relieving Pain in America: A Blue Print for Transforming Prevention, Care, Education, and Research. Washington, DC: National Academy of Sciences; 2011.

2 Steglitz J, Buscemi J, Ferguson MJ. The future of pain research, education, and treatment: A summary of the IOM report "Relieving pain in America: A blueprint for transforming prevention, care, education, and research." Transl Behav Med 2012;2:6–8.

3 Gaskin DJ, Richard P. The economic costs of pain in the United States. J Pain 2012;13:715–24.

4 Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH. The prevalence of chronic pain in United States adults: Results of an Internet-based survey. J Pain 2010;11:1230–9.

5 Chou R, Fanciullo GJ, Fine PG, et al. Opioids for chronic noncancer pain: Prediction and identification of aberrant drug-related behaviors: A review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. J Pain 2009;10:131–46.

6 Boudreau D, Von Korff M, Rutter CM, et al. Trends in long-term opioid therapy for chronic non-cancer pain. Pharmacoepidemiol Drug Saf 2009; 18: 1166–75.

7 IMS Institute for Healthcare Informatics. 100 IMS Drive, Parsippany NJ, 07054, USA.

8 Substance Abuse and Mental Health Services Administration, Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-48, HHS Publication No. (SMA) 14-4863. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2014.

9 Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths—United States, 2000–2014. MMWR Morb Mortal Wkly Rep 2016;64:1378–82.

10 Hasegawa K, Espinola JA, Brown DF, Camargo CA Jr. Trends in U.S. emergency department visits for opioid overdose, 1993–2010. Pain Med 2014;15: 1765–70.

11 Bailey JE, Campagna E, Dart RC, RADARS System Poison Center Investigators. The underrecognized toll of prescription opioid abuse on young children. Ann Emerg Med 2009;53:419–24.

12 Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. JAMA 2011; 305: 1315–21.

13 Centers for Disease Control and Prevention (CDC). Vital signs: Overdoses of prescription opioid pain relievers and other drugs among women–United States, 1999–2010. MMWR Morb Mortal Wkly Rep 2013;62:537–42.

14 Cobaugh DJ, Krenzelok EP. Adverse drug reactions and therapeutic errors in older adults: A hazard

factor analysis of poison center data. Am J Health Syst Pharm 2006;63:2228–34.

15 Coben JH, Davis SM, Furbee PM, et al. Hospitalizations for poisoning by prescription opioids, sedatives, and tranquilizers. Am J Prev Med 2010;38:517–24.

16 Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: A cohort study. Ann Intern Med 2010;152:85–92.

17 Palmiere C, Staub C, La Harpe R, Mangin P. Parental substance abuse and accidental death in children. J Forensic Sci 2010;55:819–21.

18 Paulozzi LJ, Budnitz DS, Xi Y. Increasing deaths from opioid analgesics in the United States. Pharmacoepidemiol Drug Saf 2006;15:618–27.

19 Rosca P, Haklai Z, Goldberger N, et al. Mortality and causes of death among users of methadone maintenance treatment in Israel, 1999–2008. Drug Alcohol Depend 2012. 125 (1–2), pp 160–163.

20 Centers for Disease Control and Prevention (CDC). 10 Leading causes of death by age group, United States—2011. Natl Vital Stat Syst, Natl Center Health Stat 2012. Available at http://www.cdc.gov/injury/wisqars/leadingcauses.html, last accessed on September 2, 2016.

21 Walley AY, Xuan Z, Hackman HH, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: Interrupted time series analysis. BMJ 2013;346:f174.

22 Hewlett L, Wermeling DP. Survey of naloxone legal status in opioid overdose prevention and treatment. J Opioid Manag 2013;9:369–77.

23 Barry DT, Sofuoglu M, Kerns RD, Wiechers IR, Rosenheck RA. Prevalence and correlates of coprescribing psychotropic medications with long-term opioid use nationally in the Veterans Health Administration. Psychiatry Res 2015;227:324–32.

24 Dasgupta N, Funk MJ, Proescholdbell S, et al. Cohort study of the impact of high-dose opioid analgesics on overdose mortality. Pain Med 2016. 17 (1), pp 85–98.

25 Ernst FR, Mills R, Berner T, House J, Herndon C. Opioid medication practices observed in chronic pain patients presenting for all-causes to emergency departments: Prevalence and impact on health care outcomes. J Manag Care Spec Pharm 2015; 21:925–36.

26 Kobus AM, Smith DH, Morasco BJ, et al. Correlates of higher-dose opioid medication use for low back pain in primary care. J Pain 2012;13:1131–8.

27 Kuehn BM. Methadone overdose deaths rise with increased prescribing for pain. JAMA 2012;308: 749–50.

28 Narayana A, Katz N, Shillington AC, et al. National breakthrough pain study: Prevalence, characteristics, and associations with health outcomes. Pain 2015;156:252–9.

29 Nielsen S, Lintzeris N, Bruno R, et al. Benzodiazepine use among chronic pain patients prescribed opioids: Associations with pain, physical and mental health, and health service utilization. Pain Med 2015;16:356–66.

30 Quinlan J, Carter K. Acute pain management in patients with persistent pain. Curr Opin Support Palliat Care 2012;6:188–93.

31 Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) national practice guideline for the use of medications in the treatment of addiction involving opioid use. J Addict Med 2015;9: 358–67.

32 American Medical Association (AMA). Increasing access to naloxone: Help save lives from opioid overdose. Available at http://www.ama-assn.org/ama/pub/advocacy/topics/preventing-opioid-abuse/increase-naloxone-access.page, last accessed on September 2, 2016.

33 Albert S, Brason FW 2nd, Sanford CK, et al. Project Lazarus: Community-based overdose prevention in rural North Carolina. Pain Med 2011;12(suppl 2) :S77–85.

34 Brason FW 2nd, Roe C, Dasgupta N. Project Lazarus: An innovative community response to prescription drug overdose. N C Med J 2013;74:259–61.

35 Oliva EM, Nevedal A, Lewis ET, et al. Patient perspectives on an opioid overdose education and naloxone distribution program in the US department of veterans affairs. Subst Abus 2016. 37 (1), pp 118–126.

36 Buhrmester M, Kwang T, Gosling SD. Amazon's mechanical turk: A new source of inexpensive, yet high-quality, data? Perspect Psychol Sci 2011;6:3–5.

37 Davidson PJ, McLean RL, Kral AH, et al. Fatal heroin-related overdose in San Francisco, 1997–2000: A case for targeted intervention. J Urban Health 2003;80:261–73.

38 Dietze P, Jolley D, Fry CL, Bammer G, Moore D. When is a little knowledge dangerous? Circumstances of recent heroin overdose and links to knowledge of overdose risk factors. Drug Alcohol Depend 2006;84:223–30.

39 Shah NG, Lathrop SL, Reichard RR, Landen MG. Unintentional drug overdose death trends in New Mexico, USA, 1990–2005: Combinations of heroin, cocaine, prescription opioids and alcohol. Addiction 2008;103:126–36.

40 Coffin PO, Galea S, Ahern J, et al. Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990–98. Addiction 2003;98:739–47.

41 Coffin PO, Tracy M, Bucciarelli A, et al. Identifying injection drug users at risk of nonfatal overdose. Acad Emerg Med 2007;14:616–23.

42 Laberke PJ, Bartsch C. Trends in methadone-related deaths in Zurich. Int J Legal Med 2010;124 :381–5.

43 Seal KH, Kral AH, Gee L, et al. Predictors and prevention of nonfatal overdose among street-recruited injection heroin users in the San Francisco Bay Area, 1998–1999. Am J Public Health 2001;91:1842–6.

44 Bunn TL, Yu L, Spiller HA, Singleton M. Surveillance of methadone-related poisonings in Kentucky using multiple data sources. Pharmacoepidemiol Drug Saf 2010;19:124–31.

45 Webster LR, Cochella S, Dasgupta N, et al. An analysis of the root causes for opioid-related overdose deaths in the United States. Pain Med 2011; 12(suppl 2):S26–35.

46 Kinner SA, Milloy MJ, Wood E, et al. Incidence and risk factors for non-fatal overdose among a cohort of recently incarcerated illicit drug users. Addict Behav 2012;37:691–6.

47 Merrall EL, Kariminia A, Binswanger IA, et al. Meta-analysis of drug-related deaths soon after release from prison. Addiction 2010;105:1545–54.

48 Ravndal E, Amundsen EJ. Mortality among drug users after discharge from inpatient treatment: An 8-year prospective study. Drug Alcohol Depend 2010; 108:65–9.

49 Harris DK, Changas PS. Revision of Palmore's second facts on aging quiz from a true–false to a multiple-choice format. Educ Gerontol 1994; 20:741–54.

50 Pennington HR, Pachana NA, Coyle SL. Use of the facts on aging quiz in New Zealand: Validation of questions, performance of a student sample, and effects of a don't know option. Educ Gerontol 2001;27:409–16.

51 Herrmann ES, Heil SH, Sigmon SC, et al. Characterizing and improving HIV/AIDS knowledge among cocaine-dependent outpatients using modified materials. Drug Alcohol Depend 2013;127:220–5.

52 Cleeland CS, Ryan KM. Pain assessment: Global use of the Brief Pain Inventory. Ann Acad Med Singapore 1994;23:129–38.

53 Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005;113:9–19.

54 Atkinson TM, Mendoza TR, Sit L, et al. The Brief Pain Inventory and its "pain at its worst in the last 24 hours" item: Clinical trial endpoint considerations. Pain Med 2010;11:337–46.

55 Butler SF, Fernandez K, Benoit C, Budman SH, Jamison RN. Validation of the revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R). J Pain 2008;9:360–72.

56 Butler SF, Budman SH, Fernandez KC, et al. Development and validation of the current opioid misuse measure. Pain 2007;130:144–56.

57 Hajian-Tilaki K. Receiver Operating Characteristic (ROC) curve analysis for medical diagnostic test evaluation. Caspian J Intern Med 2013;4:627–35.

58 Nuckols TK, Anderson L, Popescu I, et al. Opioid prescribing: A systematic review and critical appraisal of guidelines for chronic pain. Ann Intern Med 2014;160:38–47.

59 Jones CM, Paulozzi LJ, Mack KA, Centers for Disease Control and Prevention (CDC). Alcohol involvement in opioid pain reliever and benzodiazepine drug abuse-related emergency department visits and drug-related deaths—United States, 2010. MMWR Morb Mortal Wkly Rep 2014;63:881–5.

60 Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert AS. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: Case-cohort study. BMJ 2015; 350:h2698.

61 Bohnert AS, Tracy M, Galea S. Characteristics of drug users who witness many overdoses: Implications for overdose prevention. Drug Alcohol Depend 2012;120:168–73.

62 Man L, Best D, Gossop M, Noble A, Strang J. Risk of overdose: Do those who witness most overdoses also experience most overdoses? J Subst Use 2002;7:136–40.

63 Boscarino JA, Rukstalis MR, Hoffman SN, et al. Prevalence of prescription opioid-use disorder among chronic pain patients: Comparison of the DSM-5 vs. DSM-4 diagnostic criteria. J Addict Dis 2011;30:185–94.

64 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.

65 Darke S, Williamson A, Ross J, Teesson M. Non-fatal heroin overdose, treatment exposure and client characteristics: Findings from the Australian treatment outcome study (ATOS). Drug Alcohol Rev 2005;24:425–32.

66 Britton PC, Wines JD Jr, Conner KR. Non-fatal overdose in the 12 months following treatment for substance use disorders. Drug Alcohol Depend 2010; 107:51–5.

67 Darke S, Williamson A, Ross J, et al. Patterns of nonfatal heroin overdose over a 3-year period: Findings from the Australian treatment outcome study. J Urban Health 2007;84:283–91.

68 Stoove MA, Dietze PM, Jolley D. Overdose deaths following previous non-fatal heroin overdose: Record linkage of ambulance attendance and death registry data. Drug Alcohol Rev 2009;28 :347–52.

69 Wines JD Jr, Saitz R, Horton NJ, Lloyd-Travaglini C, Samet JH. Overdose after detoxification: A prospective study. Drug Alcohol Depend 2007;89:161–9.

70 Paulozzi LJ, Mack KA, Hockenberry JM. Variation among states in prescribing of opioid pain relievers and benzodiazepines–United States, 2012. J Safety Res 2014;51:125–9.

71 Liang Y, Turner BJ. Assessing risk for drug overdose in a national cohort: Role for both daily and total opioid dose? J Pain 2015;16:318–25.

72 Miller M, Barber CW, Leatherman S, et al. Prescription opioid duration of action and the risk of unintentional overdose among patients receiving opioid therapy. JAMA Intern Med 2015;175:608–15.

73 Paulozzi LJ, Kilbourne EM, Shah NG, et al. A history of being prescribed controlled substances and risk of drug overdose death. Pain Med 2012;13:87–95.

74 Heit HA. Addiction, physical dependence, and tolerance: Precise definitions to help clinicians evaluate and treat chronic. J Pain Palliat Care Pharmacother 2003;17:15–29.

75 Zedler B, Xie L, Wang L, et al. Development of a risk index for serious prescription opioid-induced respiratory depression or overdose in veterans' health administration patients. Pain Med 2015;16:1566–79.