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Original Research Article

Risk Factors for Prescription Opioid-Related Death, Utah, 2008–2009

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Authors' Contributions:
Dr. Lanier had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study conception and design: Lanier, Johnson, Rolfs.
Acquisition of data: Lanier, Johnson, Friedrichs, Grey.
Analysis and interpretation of data: Lanier, Johnson, Rolfs, Friedrichs.
Drafting of the manuscript: Lanier, Johnson.
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Additional Contributions:
Kristina Russell, MPH, and Jonathan Anderson, MPH (Utah Department of Health) provided assistance with data collection and writing. Connor McKeown, BA (Utah Department of Health), W. Brandon Callor, BS, and Joshua J. Byrd, BA (Utah Office of the Medical Examiner) provided assistance with data collection. Jacob Crook, BA, (Utah Department of Health) provided assistance with analysis. Betsy L. Cadwell, MSPH (Centers for Disease Control and Prevention) provided assistance with statistical methods. Leonard J. Paulozzi, MD, MPH (Centers for Disease Control and Prevention) provided assistance with manuscript review. None of these individuals received compensation for their contributions.

Abstract

Objective. Utah prescription opioid death rates increased nearly fivefold during 2000–2009. Inadequate understanding of risk factors hinders

prevention. The goal of this study was to determine risk factors for prescription opioid death in Utah.

Design. Case-control study. Cases were 254 Utah decedents with ≥1 prescription opioid causing death during 2008–2009 with nonintentional manner of death (information obtained via next-of-kin interviews). Controls were 1,308 Utah 2008 Behavioral Risk Factor Surveillance System respondents who reported prescription opioid use during the previous year.

Outcome Measures. Exposure prevalence ratios (EPRs) for selected characteristics and confidence intervals (CIs) were calculated.

Results. Decedents were more likely than the comparison group to have used prescription pain medication more than prescribed (52.9% vs 3.2%; EPR, 16.5; 95% CI, 9.3–23.7), obtained prescription pain medication from nonprescription sources (39.6% vs 8.3%; EPR, 4.8; 95% CI, 3.6–6.0), smoked daily (54.5% vs 9.7%; EPR, 5.6; 95% CI, 4.4–6.9), not graduated high school (18.5% vs 6.2%; EPR, 3.0; 95% CI, 2.0–3.9), and been divorced or separated (34.6% vs 9.4%; EPR, 3.7; 95% CI, 3.0–4.4). Decedents were more likely to have had chronic pain than the comparison group (94.2% vs 31.6%; EPR, 3.0; 95% CI, 2.7–3.3).

Conclusions. Use of pain medication outside prescription bounds was a risk factor for death. However, decedents were more likely to have had chronic pain, and the majority of both groups had obtained pain medication by prescription. Other factors (e.g., smoking status) might also play important roles in prescription opioid-related death. Prescribers should screen chronic pain patients for risk factors.

Key Words. Overdose; Analgesics, Opioid; Drug Prescriptions; Prevalence; Risk Factors

Opioid analgesics have long been used to treat acute pain and cancer-associated chronic pain. In the late 1990s, because of increasing concerns regarding undertreatment of pain, scientific publications recommended that physicians consider prescription opioids for treating chronic non-cancer-related pain [1–3]. Subsequently, opioid prescribing began to increase; during 1997–2006, the combined distribution of hydrocodone, oxycodone, morphine, and methadone quadrupled nationally and increased sixfold in Utah [4].

Prescription opioids can provide analgesia but can also have unwanted side effects, including potentially fatal respiratory depression and drug dependence. In 2000, the Utah Office of the Medical Examiner (OME) reported an alarming increase in the number of unintentional deaths caused by prescription opioid pain medication. During 2000–2009, unintentional deaths in Utah from prescription opioids increased approximately fivefold from 56 to 265. Similar trends have been observed nationally [5–7].

Efforts to prevent prescription opioid overdose deaths have been hindered by an inadequate understanding of the risk factors contributing to these deaths. Researchers have suggested that injudicious or careless prescribing practices might be contributing to the increase in deaths [8,9]. Others have proposed that behaviors associated with misuse of prescription opioids, including drug diversion [10,11] or using opioids in a manner other than prescribed [10] are also contributing. Factors shown to be associated with use of pain medication outside prescription bounds among pain patients include low education level, depression, history of substance abuse, benzodiazepine use, higher opioid doses, younger age, and male sex [12–14]. In a study of adults enrolled in an ongoing study of behavior, factors shown to predict use of pain medication outside the bounds of prescription included history of substance abuse, unemployment, and living with a noncustodial parent [15].

Recent analytic studies using prescription data suggested a link between prescription history and risk of opioid overdose death. A case-control study based on New Mexico prescription drug monitoring program data showed that frequent and high-dose opioid prescription was associated with higher risk of death [16]. Similarly, a case-cohort study using Veteran's Health Administration prescription records demonstrated that death risk increased with higher prescription opioid dose, although comorbid conditions were not considered and methadone was excluded from this analysis [17].

Analytical studies are lacking with regard to behavioral and personal characteristics potentially associated with increased risk of death. However, recently published case-series studies of prescription drug decedents have offered some clues. A Utah study of prescription drug deaths noted higher death rates among males than females and among those who are overweight or obese compared with those who are not overweight or obese [18]. West Virginia studies noted that the majority of prescription drug decedents were male and that other commonalities included low education, low socioeconomic status, nonmedical use, drug diversion, past or current substance abuse [19], and mental illness [20]. Researchers in Washington State reported that Medicaid enrollees were at increased risk of dying from prescription opioids [21].

Although descriptive studies are useful for hypothesis generation, conducting analytic studies to assess behavioral and personal characteristics as potential risk factors has remained difficult due to a lack of detailed knowledge about decedents and about a suitable comparison group. To better understand the characteristics of opioid decedents that might represent risk factors for such deaths, the Utah Department of Health (UDOH) ascertained characteristics of opioid decedents by interviewing the next of kin of persons who had died from prescription opioids during

October 2008 to October 2009 [22]. To obtain information about a comparison group, questions regarding prescription opioid use were added to the Utah 2008 Behavioral Risk Factor Surveillance System (BRFSS) survey [23,24]. In this study, we compared the prevalence of characteristics of prescription opioid decedents with that of prescription opioid-using BRFSS respondents to determine risk factors for death from prescription opioids in Utah.

Methods

Decedents

Decedents who had died in Utah during October 26, 2008 to October 25, 2009 were identified from OME records. Manner and causes of death (CODs) were determined on the basis of scene-of-death investigation, autopsy, and toxicology findings. Decedents were included in the study if they were Utah residents aged ≥18 years, had a manner of death characterized by the OME as either unintentional or undetermined, had a prescription opioid listed as a COD, did not have a violent event (e.g., fall or drowning) as a COD, and had a completed next-of-kin interview. Data regarding decedent sex, age, body mass index (BMI), race/ethnicity, education level, county of residence, and marital status were obtained from OME and death certificates.

Because heroin is metabolized to morphine in the body, only decedents for whom the source of morphine listed as a COD was determined to have been prescription morphine were identified as prescription opioid-related deaths. Among decedents where morphine was identified during toxicology testing but where source of the morphine was not stated by OME (N = 69), morphine source was determined by further review of OME records as follows: 1) from prescription morphine (N = 34) if evidence existed of recent prescription morphine use (prescription morphine at scene of death, evidence of current morphine prescription, or report by witness to OME investigator that morphine had recently been used); 2) from heroin (N = 14) if evidence existed of recent heroin use (illicit drug paraphernalia at scene of death, recent needle punctures identified on autopsy, or report by witness to OME investigator that heroin had recently been used); or 3) undetermined (N = 21) if neither or both of 1) and 2) prescription morphine or heroin criteria were met.

Next-of-Kin Interviews

A data collection instrument was designed to solicit information about decedents from their next of kin [22]. Questions included use of prescription pain medication during the year before death, pattern of use (as prescribed or other), and source of medication (by prescription from a health care provider, a nonprescription source, or both); the presence of chronic pain; tobacco (and other substance) use during the 2 months before death; military service; employment during the 2 months before death; health care coverage at the time of death; and number of living companions at the time of death. The instrument was pretested with seven volunteers who had experienced the death of a family member from drug overdose; minor modifications were made on the basis of feedback.

Telephone interviews were conducted with persons who were identified by OME death-scene investigators as next of kin (or best person to contact). Interviewers followed scripts for introducing the questionnaire, leaving telephone messages, and responding to participants' study-related questions. Interviewers referred all participants' case-specific questions to OME. This study received approval from the UDOH's institutional review board and was reviewed by a Human Research Protection Coordinator at the Centers for Disease Control and Prevention.

Epi Info™ Version 3.5.1 (Centers for Disease Control and Prevention, Atlanta, GA, USA) was used for interview data entry and to facilitate creation of the survey database in Microsoft Access® 2007 (Microsoft Corporation, Redmond, WA, USA). Interview data were linked by OME case number to OME records and death certificates.

Utah 2008 BRFSS Survey

BRFSS conducts state-based surveillance for health-related behaviors and risk factors among noninstitutionalized US adults aged ≥18 years. Respondents were selected by random-digit dialing, were uncompensated, and were interviewed by telephone by trained interviewers employed by UDOH. Utah responses are weighted on the basis of age, sex, geographic strata, and probability of selection to reflect the Utah adult population. Detailed information about BRFSS methodology has been published elsewhere [25]. In 2008, UDOH added questions to the BRFSS survey regarding the use of prescription pain medications during the past year, their pattern of use (as prescribed or other) when last prescribed, their source (by prescription from a health care provider, a nonprescription source, or both), names of medications, and the presence of chronic pain [23,24]. Questions pertinent to the study in the core of the BRFSS survey included age, sex, BMI, race/ethnicity, education level, county of residence, marital status, current tobacco use, military service, current employment, health care coverage, and number of living companions [23].

Statistical Analysis

Persons who had died from prescription opioids (decedents) were compared with BRFSS respondents who reported prescription opioid use during the previous year (comparison group). Study characteristics included demographics, behaviors, and prescription pain medication use history. All analyses were completed using SAS® 9.2 (SAS Institute, Inc., Cary, NC, USA). Median ages (weighted median in the comparison group) of the 2 groups were calculated.

Exposure prevalence rates of study characteristics and associated standard errors were calculated. For the comparison group, BRFSS weighting and stratification were

considered when calculating exposure prevalence and standard error. Exposure prevalence estimate reliability was determined by calculating the coefficient of variation (CV), with a CV >0.3 regarded as having questionable reliability. Exposure prevalence ratios [26] (EPRs) were calculated by dividing decedent exposure prevalence by comparison group exposure prevalence. Standard errors and 95% confidence intervals (CIs) for EPRs were calculated. Similar analyses were performed after stratifying for sex and marital status. Age-sex–adjusted and education level-adjusted EPRs were also compared. A subanalysis limited to chronic pain patients, defined as those with reported chronic pain and use of prescription pain medications obtained from a health care provider during the previous year, was also performed. EPRs for each prescription opioid in the study were calculated, both overall and among chronic pain patients only, by dividing the prevalence among decedents of each opioid listed as a COD by the prevalence among the comparison group of reported use of the opioid.

Results

Of 451 drug-related deaths in Utah during the study period, 278 decedents met the study criteria. Next-of-kin interviews were completed for 254 (91.4%) of these 278 decedents. Of the 5,330 Utah 2008 BRFSS respondents, 1,308 (24.5%) indicated that they had used a prescription opioid during the previous year (comparison group).

Having chronic pain was reported for 81.3% of the decedents overall. Among decedents who reportedly had used their own prescription pain medication during the previous year, the prevalence of chronic pain (93.6%) was 3.0 times that of the comparison group (31.6%) (Table 1). Approximately 90% of both populations had obtained prescription pain medication by prescription from a health care provider. Having obtained prescription pain medication from a nonprescription source was 4.3 times more common among decedents (35.8% vs 8.3%). Among those who obtained pain medication by prescription, 52.9% of decedents used pain medication more often or in higher doses than prescribed, whereas only 3.2% of the comparison group used in this manner. Results of the subanalysis limited to chronic pain sufferers were not substantially different from the overall comparison (Table 1).

Median ages of decedents and the comparison group were 41 and 40 years, respectively. Males comprised 53.1% of decedents and 41.4% of the comparison group (Table 1). The majority of both groups were White people. Prevalence rates of living in an urban county and having served in the military did not differ significantly between groups.

Being divorced or separated, and living alone were each more common among decedents (Table 1). Especially among males, decedents were more likely than the comparison group to be divorced and to live alone (Table 2). Living alone was more common among decedents, even when adjusting for marital status (EPR, 2.3; 95% CI, 1.9–2.7).

Not graduating from high school, being unemployed, and lacking health coverage were more common among decedents. Approximately half of the decedents smoked cigarettes daily, which is >5 times more common than among the comparison group. Decedents were more likely than the comparison group to be daily smokers in the subanalysis limited to chronic pain sufferers (56.6% vs 13.7%; EPR, 4.1; 95% CI, 2.7–5.6) (Table 1) and in the overall comparison when adjusting for education level (49.1% vs 9.7%; EPR, 5.0; 95% CI, 4.0–6.1).

Overall, decedents did not differ markedly from the comparison group in BMI category, although decedents were slightly more obese (BMI ≥30) (Table 1). Compared with females in the comparison group, female decedents were more likely to be obese (BMI ≥30) and less likely to be overweight (BMI ≥25 but <30) (Table 2). Female decedents were slightly more likely to be severely obese (BMI ≥35) than females in the comparison group (EPR, 1.3; 95% CI, 1.02–1.7). Similar BMI category differences were not observed for males. Other than previously noted, results of analyses stratified by sex or adjusted for age-sex, education level, and marital status did not differ markedly from those of the overall, unadjusted analysis (data not shown).

Ratios for exposure to specific opioids, both among all study subjects and among chronic pain patients only, are displayed in Table 3. For analyses both among all study subjects and limited to chronic pain patients, oxycodone was the most frequent opioid COD among decedents, and hydrocodone was the most frequently reported opioid among the comparison group. In both analyses, methadone had the highest EPR (chronic pain patients: EPR, 6.7; 95% CI, 2.9–10.5); fentanyl and morphine were also more common among decedents than the comparison group. Compared with the comparison group, tramadol was more common among decedents in the overall analysis but was less common when limited to chronic pain patients only. In both analyses, hydrocodone and codeine were less common among decedents than among the comparison group. Data were unavailable for determining sustained-release drug formulations.

Discussion

A high rate of chronic pain has previously been reported among prescription opioid decedents [20]. In the present study, chronic pain was much more common among decedents than the comparison group, which suggests that overdose prevention efforts might best be focused on those suffering from chronic pain.

Behaviors indicating use outside prescription bounds (obtaining from nonprescription source or using more than prescribed) were more common among decedents than the comparison group, implying increased risk for death associated with these behaviors. However, drug diversion

Table 1 Comparison of characteristics among prescription opioid decedents (2008–2009) and prescription opioid-using 2008 BRFSS respondents, Utah

	All Study Subjects				Chronic Pain Patients*					
	Decedents		Comparison‡		Decedents		Comparison‡		EPR† (95% CI)	
Variables	No.§ (254)	EP (%)	No.§ (1,308)	EP (%)	No.§ (180)	EP (%)	No.§ (457)	EP (%)	All Study Subjects	Chronic Pain Patients*
Prescription-related characteristics										
Chronic pain sufferer¶	191	94.2	1,253	31.6	NA	NA	NA	NA	3.0 (2.7–3.3)	NA
Obtained via prescription	222	91.9	1,308	96.2	NA	NA	NA	NA	0.96 (0.94–0.97)	NA
Obtained via prescription only	222	59.5	1,300	91.7	NA	NA	NA	NA	0.65 (0.63–0.66)	NA
Obtained via nonprescription source	230	39.6	1,300	8.3	180	32.8	454	5.6	4.8 (3.6–6.0)	5.9 (2.9–8.8)
Used more than prescribed**	155	52.9	1,245	3.2	139	53.2	448	4.5	16.5 (9.3–23.7)	11.8 (5.1–18.5)
Male	254	53.1	1,308	41.4	180	47.8	457	38.4	1.3 (1.2–1.4)	1.2 (1.05–1.44)
Age category (years)	254		1,303		180		455			
18–24		7.9		15.2		5.0		12.0	0.5 (0.4–0.7)	0.4 (0.2–0.6)
25–34		26.4		24.4		23.9		13.1	1.1 (0.9–1.2)	1.8 (1.2–2.4)
35–44		23.2		18.5		22.2		17.2	1.3 (1.1–1.4)	1.3 (0.9–1.6)
45–54		29.5		18.5		35.0		22.6	1.6 (1.4–1.8)	1.5 (1.2–1.9)
55–64		11.0		12.5		12.2		17.3	0.9 (0.7–1.0)	0.7 (0.5–0.9)
≥65		2.0		10.9		1.7		17.7	0.18 (0.15–0.21)	0.09 (0.07–0.11)
Race/ethnicity										
White	254	98.0	1,307	92.7	180	98.3	457	92.5	1.06 (1.03–1.08)	1.06 (1.02–1.10)
Hispanic, all races	254	3.9	1,304	6.6	180	3.9	453	6.7	0.6 (0.4–0.8)	0.6 (0.3–0.9)
Marital status/living situation										
Divorced/separated	254	34.6	1,276	9.4	180	35.6	442	13.1	3.7 (3.0–4.4)	2.7 (1.9–3.5)
Lived alone	250	23.2	1,308	6.7	177	23.2	457	9.8	3.5 (2.9–4.0)	2.4 (1.8–2.9)
BMI category	242		1,274		171		443			
<25 (ideal or underweight)		33.1		33.6		31		29.5	1.0 (0.9–1.1)	1.0 (0.8–1.3)
≥25 but <30 (overweight)		28.1		35.6		26.9		36.1	0.8 (0.7–0.9)	0.7 (0.6–0.9)
≥30 (obese)		38.8		30.8		42.1		34.3	1.3 (1.1–1.4)	1.23 (1.02–1.43)
Other characteristics										
Not high school grad/equivalent	254	18.5	1,307	6.2	180	20.6	457	7.7	3.0 (2.0–3.9)	2.7 (1.3–4.1)
Uninsured	243	29.2	1,307	12.5	175	23.4	457	12.6	2.3 (1.8–2.8)	1.9 (1.2–2.5)
Unemployed	250	63.2	1,302	39.0	179	69.3	455	50.9	1.6 (1.5–1.8)	1.4 (1.2–1.5)
Smoked cigarettes daily	244	54.5	1,307	9.7	173	56.6	457	13.7	5.6 (4.4–6.9)	4.1 (2.7–5.6)
Resident of urban county	254	78.0	1,298	76.4	180	78.9	453	73.9	1.02 (0.99–1.06)	1.07 (1.01–1.13)
Previously served in military	254	8.3	1,305	8.8	180	9.4	455	13.2	0.9 (0.7–1.1)	0.7 (0.5–0.9)

Overall and chronic pain-only comparisons were shown.

* Study subjects who reportedly had chronic pain and used pain medication during the previous 12 months obtained from a health care provider.

† Ratio of decedent/comparison group (BRFSS) prevalence rates.

‡ Comparison group (BRFSS) rates are weighted on the basis of age, race/ethnicity, sex, and probability of selection to reflect the Utah population aged ≥18 years.

§ Number of study subjects about whom characteristic information was available. Total population indicated in parentheses. Unless otherwise noted, numbers less than total population are because of respondents not knowing or refusing to answer, or to missing data.

¶ Among those who used prescribed pain medication during the prior year.

** Among those who used prescribed pain medication during the prior year and for whom frequency of use was known.

BMI = body mass index; BRFSS = Behavioral Risk Factor Surveillance System; CI = confidence interval; EP = exposure prevalence; EPR = exposure prevalence ratio; NA = not applicable.

Table 2 Comparison of selected characteristics among prescription opioid decedents (2008–2009) and prescription opioid-using 2008 BRFSS respondents, Utah

	Male				Female					
	Decedents		Comparison*		Decedents		Comparison*		EPR† (95% CI)	
Variables	No.‡ (135)	EP (%)	No.‡ (494)	EP (%)	No.‡ (119)	EP (%)	No.‡ (814)	EP (%)	Male	Female
Prescription-related characteristics										
Chronic pain sufferer§	94	91.5	464	30.4	97	96.9	789	32.5	3.0 (2.5–3.5)	3.0 (2.6–3.4)
Obtained by prescription	112	89.3	494	92.6	110	94.5	814	98.6	0.96 (0.93–1.0)	0.96 (0.95–0.97)
Obtained by prescription only	112	54.5	494	88.6	110	64.5	806	93.9	0.61 (0.59–0.64)	0.69 (0.67–0.70)
Obtained by nonprescription source	118	44.1	494	11.4	112	34.8	806	6.1	3.9 (2.6–5.2)	5.7 (3.6–7.8)
Used more than prescribed¶	76	52.6	461	3.7	79	53.2	784	2.9**	14.3 (6.1–22.4)	18.4 (6.5–30.4)
Age category (years)	135		493		119		810			
18–24		12.6		10.9		2.5		18.2	1.2 (0.7–1.7)	0.14 (0.10–0.18)
25–34		30.4		24.0		21.8		24.8	1.3 (1.0–1.6)	0.9 (0.7–1.0)
35–44		24.4		20.4		21.8		17.1	1.2 (0.9–1.5)	1.3 (1.05–1.5)
45–54		23.0		22.1		37.0		16.1	1.0 (0.8–1.2)	2.3 (1.9–2.7)
55–64		8.1		13.2		14.3		12.1	0.6 (0.5–0.8)	1.2 (0.9–1.4)
≥65		1.5		9.5		2.5		11.9	0.16 (0.12–0.19)	0.21 (0.17–0.26)
Marital status/living situation										
Divorced/separated	135	34.8	482	7.4	119	34.5	794	10.8	4.7 (3.2–6.3)	3.2 (2.5–3.9)
Lived alone	133	21.8	494	4.7	117	24.8	814	8.1	4.7 (3.3–6.1)	3.0 (2.5–3.6)
BMI category	131		493		111		781			
<25 (ideal or underweight)		30.5		24.2		36.0		40.4	1.3 (1.0–1.5)	0.9 (0.8–1.0)
≥25 but <30 (overweight)		35.1		41.2		19.8		31.5	0.9 (0.7–0.97)	0.6 (0.5–0.7)
≥30 (obese)		34.4		34.6		44.1		28.0	1.0 (0.8–1.2)	1.6 (1.3–1.8)

* Comparison group (BRFSS) rates are weighted on the basis of age, race/ethnicity, sex, and probability of selection to reflect the Utah population aged ≥18 years.
† Ratio of decedent/comparison group (BRFSS) prevalence rates.
‡ Number of study subjects about whom characteristic information was available. Total population indicated in parentheses. Unless otherwise noted, numbers less than total population are because of respondents not knowing or refusing to answer, or to missing data.
§ Among those who used prescribed pain medication during the prior year.
¶ Among those who used prescribed pain medication during the prior year and for whom frequency of use was known.
** Rate has a BRFSS prevalence coefficient of variation of 0.3, indicating questionable reliability.
BMI = body mass index; BRFSS = Behavioral Risk Factor Surveillance System; CI = confidence interval; EP = exposure prevalence; EPR = exposure prevalence ratio.

Table 3 Comparison of opioid* causes of death among prescription opioid decedents (2008–2009) and reported opioid use among prescription opioid-using 2008 BRFSS respondents, Utah, by drug name

	Exposure Prevalence (%)					
	All Study Subjects		Chronic Pain Patients†		EPR‡ (95% CI)	
Drug	Decedents (N = 253¶)	Comparison§ (N = 1,308)	Decedents (N = 179¶)	Comparison§ (N = 457)	All Study Subjects	Chronic Pain Patients†
Methadone	28.1	1.8**	24.1	3.6	15.5 (6.3–24.6)	6.7 (2.9–10.5)
Fentanyl	7.1	0.8**	7.9	2.5**	8.6 (2.5–14.8)	3.2 (0.8–5.5)
Morphine	13.4	2.4	13.8	5.1	5.7 (3.5–7.9)	2.7 (1.5–3.9)
Oxycodone	37.9	28.4	34.5	31.7	1.3 (1.2–1.5)	1.1 (0.9–1.3)
Tramadol	12.3	4.9	9.9	12.5	2.5 (1.8–3.1)	0.8 (0.5–1.0)
Propoxyphene	3.2	3.0	3.4	5.2	1.1 (0.7–1.5)	0.7 (0.3–1.0)
Hydrocodone	25.3	69.6	20.7	65.7	0.36 (0.35–0.38)	0.31 (0.29–0.34)
Codeine	3.2	8.2	2.0	8.3	0.4 (0.3–0.5)	0.2 (0.1–0.3)
Meperidine	0.0	1.0**	0.0	2.2**	NA	NA

* Opioids with rates <1% not shown.
† Study subjects who reportedly had chronic pain and used pain medication during the previous 12 months obtained from a health care provider.
‡ Ratio of decedent/comparison group (BRFSS) prevalence rates.
§ Comparison group (BRFSS) rates are weighted on the basis of age, race/ethnicity, sex, and probability of selection to reflect the Utah population aged ≥18 years.
¶ Excludes one decedent with a cause of death of an unspecified prescription opioid; Σn > N because more than one drug might be associated with each person.
** Rate has a BRFSS prevalence coefficient of variation of ≥0.3, indicating questionable reliability.
BRFSS = Behavioral Risk Factor Surveillance System; CI = confidence interval; EPR = exposure prevalence ratio; NA = not applicable.

and misuse cannot explain all of the increase in deaths; reportedly, only 39.6% of decedents obtained pain medications from nonprescription sources and only one-half of the decedents who used their own prescribed pain medication used more than prescribed. Additional evidence suggests that factors other than use outside prescription bounds are contributing to this problem. Although the rate of death related to prescription opioids increased nearly fourfold during 1999–2008, nonmedical use of prescription pain relievers among those aged ≥12 years increased only 60% from 3.0% to 4.8%, according to the Substance Abuse and Mental Health Services Administration (SAMHSA) [27]. Similarly, although decedents were relatively concentrated among persons aged 25–54 years, rates of nonmedical use of prescription opioids are highest for those aged 12–24 years, according to SAMHSA data [28]. Hence, factors other than use outside prescription bounds likely also play key roles in the increasing deaths caused by prescription opioids. Use outside prescription bounds might have been regarded as socially undesirable to next-of-kin and comparison group respondents and might have led to underreporting. Theoretically, because both groups might have been affected, the overall effect of this potential bias might be minimal. However, a relatively large number (N = 27) of next of kin reported not knowing decedents' pattern of pain medication use; these decedents probably were using more than prescribed, which would have increased both the actual decedent prevalence and EPRs of this characteristic.

The higher rates of being divorced or separated, and living alone among decedents likely indicates a lack of social support, which increases the chances that drug misuse might go undetected and lowers the chances of interventions to counter risky use. Moreover, living alone might have precluded anyone from recognizing signs of an overdose and obtaining emergency care for the victim.

Unemployment typically results in lack of health coverage and therefore might be associated with other risk factors (e.g., chronic pain). Persons without health coverage are less likely to obtain needed health care [29], and lack of coverage makes finding treatment more difficult for both those with chronic pain and opioid addiction. Not having health coverage might encourage obtaining and using drugs nonmedically among those who have overdosed. Low education level might be a marker for other risk factors demonstrated in this study (e.g., unemployment and lack of health coverage).

Approximately half of decedents were daily cigarette smokers, which is >5 times the rate of smoking among the comparison group. Smoking rates have been reported to be higher among those with low education level [30,31] and chronic pain [32], both of which were common among decedents. However, in our study, the observed association with smoking was only minimally confounded by education level and remained in the subanalysis limited to chronic pain patients. The association between

smoking and overdose death might also be confounded by other factors (e.g., mental illness [33] and substance abuse [34]).

High rates of obesity have previously been reported among prescription drug decedents [18]. In the present study, sex appeared to modify the observed association with obesity; obesity (BMI ≥30) appeared to be a risk factor for females but not for males. Reasons for the observed sex-BMI differences are unclear but might include differences in pharmacokinetics between sex-BMI categories. Alternatively, social desirability bias might explain the findings; females have been reported to underreport their weight on BRFSS [35], which would have caused an underestimation of the true prevalence of obesity among comparison group females. Prior research has revealed that obesity is associated with chronic pain [36], which was common among decedents.

The finding that methadone appears to be associated with greater risk than other prescription opioids is consistent with findings from previous research [37,38]. Methadone has pharmacological properties that are unique among opioids and should be prescribed and used with caution [39]. Oxycodone was the most frequent COD among decedents and the second most frequently used among the comparison group; the fact that the EPR was approximately 1.0 does not indicate that risk does not necessarily exist but rather that oxycodone is a common COD among prescription opioid decedents and is also commonly used.

Several factors were not able to be assessed in this study because comparable data were not available for the comparison group. These include: history of substance abuse; history of mental illness; potential contributions to death of other substances, such as benzodiazepenes, antidepressants, alcohol, and illicit drugs; and additional details about recent prescription history, such as prescriptions during the previous month and dose amount of most recent opioid prescription. Previous researchers have noted high rates of illicit substance abuse [19], mental illness [20], evidence of recent use of other substances [7,19], and high dose of prescribed opioids among prescription drug decedents [16,17]. Additionally, one recent study showed that pain patients with a history of depression are more apt to be treated with prescription opioids [40]. Future research regarding factors not able to be assessed for association with risk of death related to prescription opioids is recommended. Furthermore, additional research is warranted regarding certain associations observed in this study, including use outside prescription bounds, daily smoking, chronic pain, the interaction between obesity and sex, and risk differences between specific opioids.

This study has other notable limitations. Decedent data were reported by next of kin, whereas comparison group data were self-reported. The periods represented by the data sets overlap only partially. For certain characteristics compared, data were collected differently for each data set. This is true for smoking status; next of kin were asked about decedents' last 2 months of life, and the comparison group was asked about current status. The chance that this difference had a substantial effect is minimal, but asking next of kin about decedents' current status might have resulted in a slightly lower prevalence of daily cigarette smoking, which would have lowered the EPR.

Conclusion

This study used next-of-kin interview, medical examiner, and household survey data to demonstrate behavioral and personal characteristics associated with increased risk of death from prescription opioids. Study findings highlight the complicated nature of the risk for death. Evidence demonstrates that use outside prescription bounds of prescription pain medication increases risk. However, use outside prescription bounds is only part of the story; the majority of persons in this study who died from prescription opioids had chronic pain and obtained pain medication through prescription. Other characteristics (e.g., education level and social support strength) might also play crucial roles. For certain decedents, factors contributing to death probably include a combination of use outside prescription bounds and other characteristics.

Health care providers were reportedly a major source of prescription pain medication for decedents in this study, revealing that prescribers can play a critical role in recognizing factors associated with increased risk of prescription opioid death among chronic pain patients. Although certain patients might also seek prescription opioids from nonprescription sources, only a minority of decedents reportedly obtained prescription pain medication in this manner. Limiting the amount of opioids prescribed to persons at risk for overdose is a key component of opioid death prevention.

When managing chronic pain among patients with risk factors for prescription opioid death, providers should strongly consider non-opioid treatment options [41]. If opioids are prescribed, amounts should not exceed what is needed. Preprescription screening tools [42–44] and provider–patient treatment agreements [45] are available to help prescribers manage risk. Updating these tools to include certain risk factors identified in this study (e.g., daily smoking) is recommended.

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