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Opioid Dosing Trends and Mortality in Washington State Workers' Compensation, 1996–2002

Gary M. Franklin, MD, MPH,[1]* Jaymie Mai, PharmD,[2] Thomas Wickizer, PhD,[3] Judith A. Turner, PhD,[4,5] Deborah Fulton-Kehoe, PhD, MPH,[1] and Linda Grant, BSN, MBA[2]

Background *The use of opioids for chronic non-cancer pain has increased in the United States since state laws were relaxed in the late 1990s. These policy changes occurred despite scanty scientific evidence that chronic use of opioids was safe and effective.*
Methods *We examined opiate prescriptions and dosing patterns (from computerized databases, 1996 to 2002), and accidental poisoning deaths attributable to opioid use (from death certificates, 1995 to 2002), in the Washington State workers' compensation system.*
Results *Opioid prescriptions increased only modestly between 1996 and 2002. However, prescriptions for the most potent opioids (Schedule II), as a percentage of all scheduled opioid prescriptions (II, III, and IV), increased from 19.3% in 1996 to 37.2% in 2002. Among long-acting opioids, the average daily morphine equivalent dose increased by 50%, to 132 mg/day. Thirty-two deaths were definitely or probably related to accidental overdose of opioids. The majority of deaths involved men (84%) and smokers (69%).*
Conclusions *The reasons for escalating doses of the most potent opioids are unknown, but it is possible that tolerance or opioid-induced abnormal pain sensitivity may be occurring in some workers who use opioids for chronic pain. Opioid-related deaths in this population may be preventable through use of prudent guidelines regarding opioid use for chronic pain.* Am. J. Ind. Med. 48:91–99, 2005. *© 2005 Wiley-Liss, Inc.*

KEY WORDS: chronic pain; mortality; opioids; workers' compensation

[1]Department of Occupational and Environmental Health Sciences, Occupational Epidemiology and Health Outcomes Program, University of Washington School of Public Health and Community Medicine, Seattle, Washington
[2]Washington State Department of Labor and Industries, Olympia, Washington
[3]Department of Health Services, University of Washington School of Public Health and Community Medicine, Seattle, Washington
[4]Department of Psychiatry and Behavioral Services, University of Washington School of Medicine, Seattle, Washington
[5]Department of Rehabilitation Medicine, University of Washington School of Medicine, Seattle, Washington

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*Correspondence to: Gary M. Franklin, Research Professor, Department of Environmental and Occupational Health Sciences, University of Washington, 1914 N. 34th Street, no. 101, Seattle, WA 98103. E-mail: meddir@u.washington.edu

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INTRODUCTION

By the end of the last decade, many state medical boards implemented dramatic liberalization of regulations regarding use of opioids for the treatment of chronic, non-cancer pain (chronic pain) [Federation of State Medical Boards of the US, 1998]. In Washington State, preliminary guidelines were published in April 1996 and final regulations, having the weight of law, were implemented in October 1999 [Washington Administrative Code, 1999]. These policies represented a 180-degree change from the nearly complete prohibition of regular opioid use for chronic pain, particularly in the ambulatory care setting, prior to that time. This policy shift was consistent with strong opinions by advocates that persons with chronic pain had been previously

undertreated [Hill, 1996], and with consensus statements from professional organizations representing pain management specialists [American Academy of Pain Medicine, 1997]. The scientific basis for this policy reversal was from limited studies suggesting that true addiction in clinical settings may be relatively rare [Portenoy, 1996], and from small, short-term controlled trials demonstrating efficacy for pain relief [Moulin et al., 1996]. The fundamental assumption here is that with prudent clinical guidelines, potentially serious problems such as tolerance, dependence, addiction, and diversion could be avoided while patients with chronic pain gained relief from pain and improved quality of life.

The effect of these policies, following rapid diffusion among treating physicians, is only now coming into focus. Between 1980 and 2000 in the United States, rates of office visit prescriptions for opioids for chronic musculoskeletal pain doubled and rates of more potent opioid prescriptions increased 4.5-fold [Caudill-Slosberg et al., 2004]. These increased prevalence rates could reflect appropriate use. However, a 2000–2001 national survey of medical examiners' reports of deaths attributable to prescription oxycodone use [US Department of Justice, 2002] and a report from Utah [Caravati et al., 2005] documenting a dramatic recent increase in accidental poisoning deaths, largely from prescription drugs, especially prescription opiates, are worrisome.

Since 1998, we have observed increased deaths associated with prescription opioid use in the Washington State workers' compensation system. Therefore, we used the Washington State workers' compensation database to examine opioid prescription patterns for injured workers between 1996 and 2002. Our objectives were to: examine the prevalence of opioid prescriptions, determine whether there was a shift towards greater use of more potent opioids during this period (from Schedule III/IV to Schedule II), determine whether the average daily dose of potent Schedule II opioids increased over this period, and describe deaths among workers attributable to use of prescription opioids.

METHODS

Setting and Data Acquisition

The Washington State Department of Labor and Industries (DLI) is the sole regulator of workers' compensation coverage in Washington State and is the direct insurer for two-thirds of the non-Federal workforce in the state, covering approximately 1.2 million eligible workers. The remaining one-third of the eligible workforce is covered by approximately 400 larger self-insured companies. The DLI receives approximately 170,000 claims for work-related injuries and illnesses annually.

We examined data obtained from the DLI administrative database, the Medical Information Payment System (MIPS), which tracks all health care services for which payment is requested. For outpatient prescriptions, MIPS point-of-sale records information includes data such as, but not limited to, national drug code (NDC), drug class, quantity, day's supply, drug strength, prescribing practitioner, and schedules of controlled substances (II, III, IV, or V).

Opioids are scheduled by the Drug Enforcement Administration (DEA) according to their potential for abuse and dependence. Schedule II opioids have the greatest potential for abuse and dependence; this category includes formulations of fentanyl, methadone, morphine, and oxycodone. Methadone has a long half-life; fentanyl, morphine and oxycodone have shorter half-lives but are formulated in slow-release form. Typical Schedule III opioids include formulations of hydrocodone and codeine, and typical Schedule IV opioids include formulations of propoxyphene.

Temporal Trend of Opioid Prescription Use

To investigate the temporal trend of opiate use statewide in the workers' compensation system, we examined the total number of prescriptions for all opioids paid annually during 1996–2002. In addition, we investigated changes in prescription of Schedule II opioids compared to prescription of Schedules III and IV opioids.

Schedule II Dosing Trends

To examine the change in average daily dosages of Schedule II drugs, we used published equi-analgesic conversions for transdermal fentanyl (25 mcg/hr), oral levorphanol (4 mg), oral methadone (15 mg), oral morphine (45 mg), and oral oxycodone (30 mg). If the published equi-analgesic conversion was a range, we used the mid-point of that range [American Pain Society, 1999; Wolters Kluwer Health, 2004]. The daily dose for each Schedule II opioid prescription was calculated as (total quantity ÷ days supply) × (drug strength). These doses were then converted to morphine equivalent doses (mg/day).

Identification of Opiate-Related Deaths

The DLI is notified of all deaths for persons who are receiving benefits for a work-related injury claim. We requested death certificates for all such workers who had a compensable claim (i.e., a claim where wage replacement benefits were paid); died between January 1995 and December 2002; and had at least one of the following characteristics: (a) a prescription for a Schedule II or Schedule III opioid within 3 months of death, (b) at least 20 Schedule II or Schedule III opioid prescriptions for their work-related injury over the course of their claim, or (c) reported to the DLI provider review unit as an opioid-related death.

Two hundred sixty-six death certificates met these screening criteria. Of these, 60 listed cause of death as ''overdose'' or ''intoxication'' from opiates. These 60 cases were reviewed by two authors (G.M.F., J.M.) independently. Of these 60 cases, 5 were listed as suicide and 55 were listed as accidental death on the death certificate. For each of these 55 accidental deaths, the two authors obtained information on each of the following six factors from death certificates and supplementary autopsy reports (factors 1, 2, 3, 5, and 6), and from the computerized database (factor 4), in order to classify the deaths as to whether they were definitely, probably, or possibly related to prescription opiate use. Greater weight was given to information directly obtainable from the death records because as medical examiner cases, all of these cases received autopsies and most had documented toxicology. Factors 2 and 3 were added to increase the certainty that the death was related only to prescription drug use, and not to mixed prescription and non-prescription substance use.

1. Cause of death listed as ''toxic overdose,'' ''acute intoxication,'' ''overdose,'' or ''intoxication'' AND drugs listed included opioids
2. Other drugs (e.g., antidepressants) mentioned on the death certificate likely to be prescribed medications
3. Terms ''medication'' or ''prescription'' appear in the description of the underlying cause, nature, or associated cause
4. DLI records indicate worker received schedule II, III, or IV opioids within 3 months of death
5. Presence or mention of illicit drug use (e.g., methamphetamine, cocaine, heroin)
6. Presence or mention of alcohol use

We considered the death to be definitely due to prescription opiate use if the following criteria were met: both 1 and 2 or 3 were present and both 5 and 6 were absent. We considered the death to be probably due to prescription opiate use if the following criteria were met: both 1 and 4 were present and both 5 and 6 were absent. We considered the death to be possibly due to prescription opiate use if the following criteria were met: met criteria for definite or probable and either 5 or 6 was present. No disagreement between the two reviewers for definite/probable versus possible cases occurred.

Finally, we abstracted from specific fields on the death certificates information related to gender, age at death, and smoking status.

RESULTS

The total number of paid prescriptions for Schedule II–IV opioids increased only modestly during 1996–2002, from approximately 120,000 prescriptions annually in 1996 to approximately 150,000 annually in 2002 (Fig. 1). Overall, it appears that prescriptions for Schedule III opioids increased very slightly, while prescriptions for Schedule IV opioids decreased modestly. By contrast, prescriptions for Schedule II opioids increased 2.5 times, from approximately 23,000 annually in 1996 to approximately 57,000 annually in 2002. As a percent of all scheduled opioids (II–IV), Schedule II prescriptions increased from 19.3% in 1996 to 37.2% in 2002.

Oxycodone HCl controlled-release (OxyContin) accounted for nearly 30% of the Schedule II opioid prescriptions during 1996–2002 (Fig. 2). For the long-acting opioids, the mean (SD) daily morphine equivalent dose

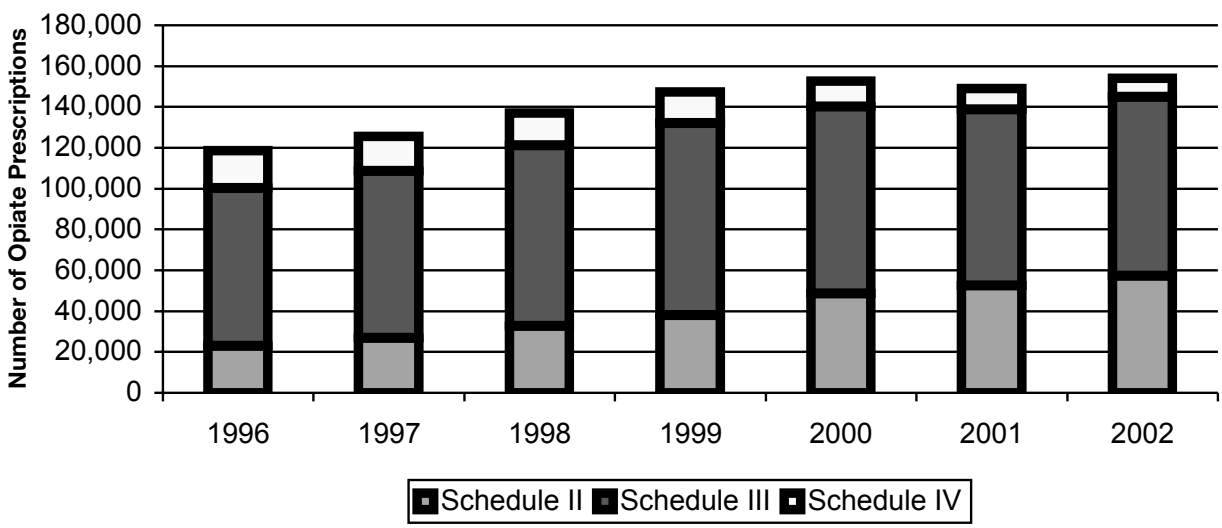

FIGURE 1. Yearly trend of scheduled opioids, Washington State, 1996–2002.

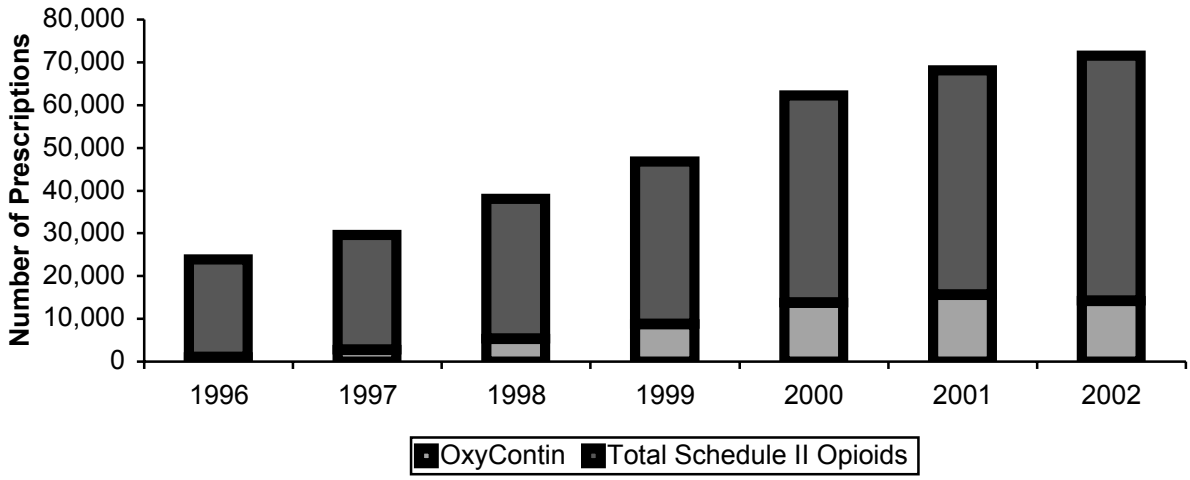

FIGURE 2. Yearly trend of schedule II opioid prescriptions, Washington State, 1996–2002.

increased from 88 (10) mg/day in the first quarter of 1996 to 132 (6) mg/day in the fourth quarter of 2002 (Fig. 3). This represents a 50% increase in average daily dose.

Of the 55 deaths potentially related to accidental prescription opioid overdose, 32 met our criteria for definitely or probably, and 12 met our criteria for possibly, related to accidental prescription opioid overdose. The total number of definite, probable, or possible deaths increased after 1997, reaching a peak in 2000 (Fig. 4). The 44 definite, probable and possible cases are enumerated in Table I in regard to year of death, age at death, smoking status, and which criteria were met regarding the case definition. Among these cases, the mean age at death was 40 years, 84% were male, and 69% were smokers; these proportions were the same for definite/probable and possible cases.

Among the definite/probable (N = 32) cases, oxycodone was mentioned in 15 cases, and methadone was mentioned in 23 cases (some of these were overlapping). The most common treated conditions were low back pain (62.5%, 20/32) and carpal tunnel syndrome (9.4%, 2/32). Only 6.3% (2/32) of the cases would be considered catastrophic injuries (1 spinal cord injury, 1 crush injury). For the 32 definite/probable cases, 9/32 had other co-morbid conditions listed on the death certificate as possibly contributing to death, but not resulting in the underlying cause of death (accidental opioid overdose): 6 with cardiovascular disease, 2 with

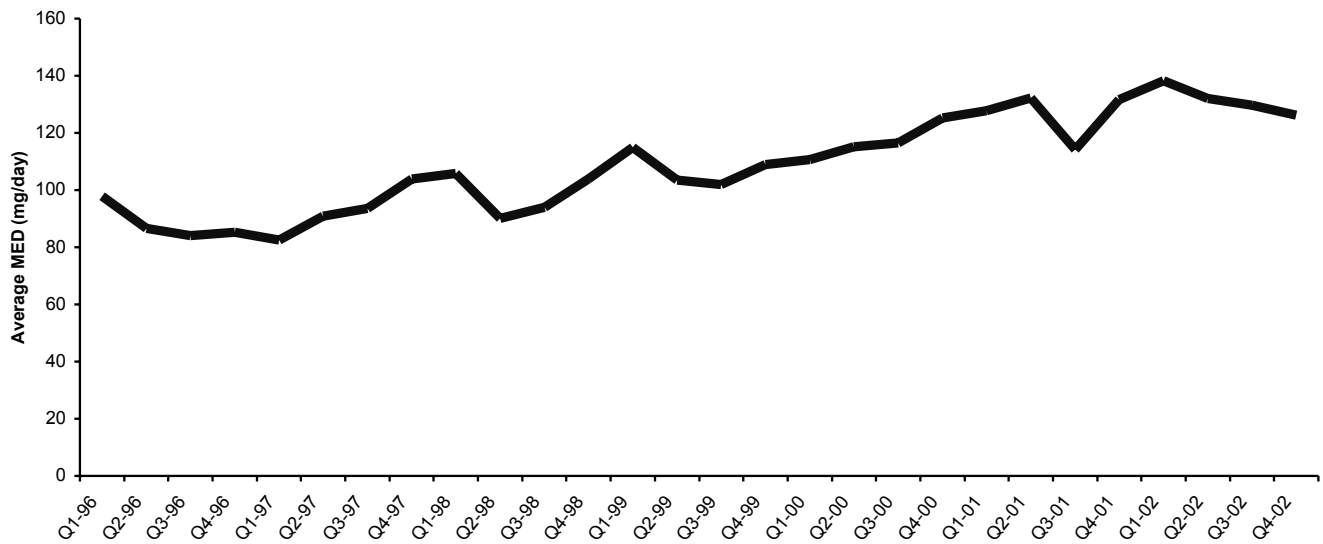

FIGURE 3. Trend of schedule II opioids, Morphine equivalent dosages, Washington State, 1996–2002.

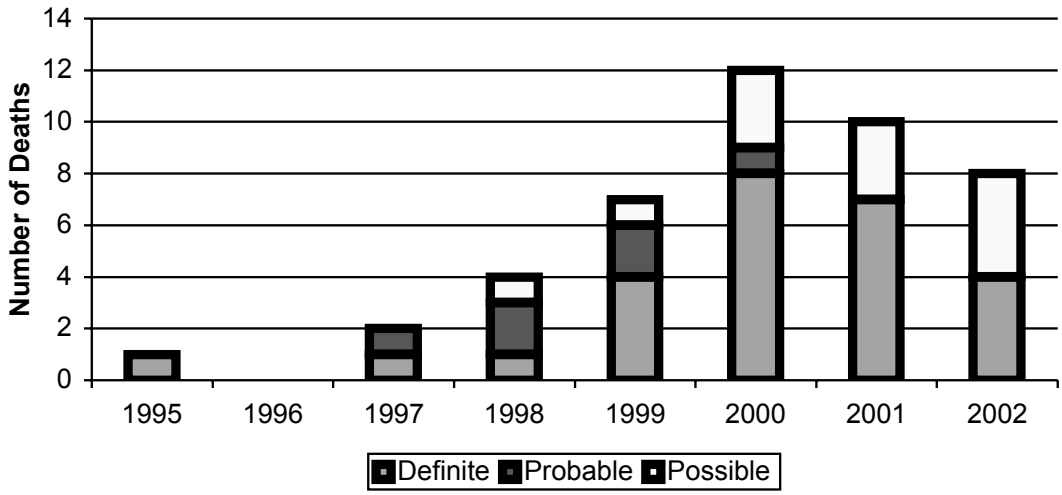

FIGURE 4. Washington workers' compensation opioid-related deaths, 1995–2002.

COPD, and 1 with early liver cirrhosis. None of these cases had known terminal illness such as cancer. Finally, the most common listed drugs on the death certificates (N = 32) in addition to opioids were 11 occurrences with antidepressants, 6 occurrences with benzodiazepines, and 2 occurrences with sedative-hypnotics (some of these cases were overlapping).

DISCUSSION

The dramatic shift in public policy allowing much more liberal use of opioids for chronic pain in Washington State, starting in 1996 and finalized in 1999, appears to have been associated with a number of changing patterns of opiate use among injured workers: a modest overall increase in opioid prescriptions; a dramatic shift from use of Schedule III/IV opioids to use of more potent Schedule II opioids; and among the long acting opioid prescriptions, a 50% increase in average daily morphine equivalent dose. Concomitant with these changes in opioid use, we also observed an increase in worker deaths attributable to accidental overdose of prescription opiates.

A shift to increased prescribing of potent, longer-acting opioids for chronic pain has been reported nationally [Caudill-Slosberg et al., 2004] and internationally [del Pozo, 1999], however, the clinical evidence justifying such a shift is sparse. Chou et al. [2003] in a recent systematic review, found insufficient evidence to conclude that long-acting opioids as a class are more effective or safer than short-acting opioids for chronic pain. In addition, there is no available evidence from clinical trials to demonstrate that severe adverse events, including addiction, differ for long versus short-acting opioids [Chou et al., 2003].

The slow but steady rise in dosage of Schedule II drugs has been previously reported from Australia [Bell, 1997]. In our setting, the shift from approximately 88 mg/day morphine equivalents in 1996 to 132 mg/day morphine equivalents in 2002 for Schedule II long acting opioid prescriptions is of concern and suggests the possibility of substantial tolerance developing among patients with chronic pain who use opioid medications chronically. DLI opioid use guidelines developed in collaboration with the State medical society [Washington State Department of Labor and Industries, 2000] recommend that physicians obtain a pain management specialty consultation when daily morphine equivalent doses exceed 120 mg. In other words, the average daily dose of potent opioids prescribed for Washington State injured workers has now exceeded this ''red flag'' dose.

The reasons for the Schedule II opioid dosage escalation in this population of injured workers with chronic pain are not clear. However, possible explanations include pharmacologic tolerance and opioid-induced abnormal pain sensitivity resulting in the need for higher doses to achieve the same pain relief [Ballantyne and Mao, 2003]. Another unresolved question regarding chronic opioid use in the injured worker population relates to whether opioid efficacy in pain reduction also extends to improvement in function. This is a key point, since a crucial goal of the workers' compensation system is to contribute to restoration of function so that a worker may ultimately return to productivity. No direct evidence for a beneficial effect on function in the injured worker population has been published, and results regarding function in studies of other populations have been mixed [Ballantyne and Mao, 2003].

The most alarming observation is the substantial increase in accidental poisoning deaths attributable to opioids. The pattern in these death cases is not dissimilar to those reported by the DEA in a 2-year study of medical examiner death cases related to oxycodone [US Department of Justice, 2002]. In that study, 464 cases were reported to be specifically attributable to oxycodone use. Similar to our cases, the

TABLE I. Prescription Opioid-Related Deaths, Washington State Workers' Compensation, 1995–2002

Injured worker	Year of death	Age	Criteria[a]						Result	Smoking history
			1	2	3	4	5	6		
1	1995	36	X	X		X			Definite	Y
2	1997	25	X		X	X			Definite	N
3	1997	42	X			X			Probable	Y
4	1998	45	X		X	X			Definite	N
5	1998	35	X			X			Probable	Y
6	1998	34	X			X			Probable	Y
7	1998	39	X			X		X	Possible	N
8	1999	43	X			X			Probable	Y
9	1999	41	X		X	X			Definite	Y
10	1999	39	X		X	X			Definite	Y
11	1999	37	X	X			X		Possible	Y
12	1999	28	X		X	X			Definite	N
13	1999	41	X			X			Probable	Y
14	1999	55	X		X	X			Definite	Y
15	2000	44	X		X	X			Definite	Y
16	2000	49	X			X			Probable	Y
17	2000	33	X			X		X	Possible	N
18	2000	40	X	X	X				Definite	Y
19	2000	49	X	X		X			Definite	Y
20	2000	31	X	X	X	X			Definite	Y
21	2000	48	X		X				Definite	N
22	2000	32	X	X		X		X	Possible	N
23	2000	33	X	X		X			Definite	N
24	2000	40	X		X		X		Possible	Y
25	2000	36	X	X		X			Definite	Y
26	2000	45	X	X	X	X			Definite	N
27	2001	58	X	X		X			Definite	Y
28	2001	47	X	X	X	X			Definite	Y
29	2001	36	X	X		X			Definite	N
30	2001	47	X	X		X			Definite	Y
31	2001	44	X	X	X	X			Definite	Y
32	2001	37	X	X			X		Possible	N
33	2001	27	X	X					Definite	Y
34	2001	41	X	X		X	X		Possible	Y
35	2001	31	X	X		X		X	Possible	Y
36	2001	41	X	X					Definite	N
37	2002	45	X	X		X			Definite	N
38	2002	25	X	X			X		Possible	N
39	2002	38	X	X			X		Possible	Y
40	2002	48	X	X		X			Definite	Y
41	2002	50	X			X	X	X	Possible	N
42	2002	40	X	X					Definite	Y

(*Continued*)

TABLE I. (*Continued*)

Injured worker	Year of death	Age	Criteria[a] 1	2	3	4	5	6	Result	Smoking history
43	2002	48	X	X					Definite	Y
44	2002	44	X	X		X	X		Possible	Y
Average Age		40								

[a]Criteria are as follows:

1. Cause of death listed as "toxic overdose," "acute intoxication," "overdose," or "intoxication" and drugs listed included opioids.
2. Other drugs (e.g., antidepressants) mentioned on the death certificate likely to be prescribed medications.
3. Terms "medication" or "prescription" appear in the description of the underlying cause, nature, or associated cause.
4. DLI records indicate worker received schedule II, III, or IV opioids within 3 months of death.
5. Presence or mention of illicit drug use (e.g., methamphetamine, cocaine, heroin).
6. Presence or mention of alcohol use.

DEA death cases also included: additional mention of other prescription drugs (particularly, benzodiazepines, another opiate, antidepressant medication, and muscle relaxants) or over-the-counter antihistamines or cold medications; and a minority of deaths attributable to alcohol-drug interactions (19%) or to cocaine use (15%). We conservatively classified persons who had any mention of ethanol or an illicit drug (e.g., cocaine, methamphetamine) as only ''possible'' cases, even if they met other criteria for inclusion as accidental poisoning related to prescription opioids. In our case series, oxycodone (N = 15) and methadone (N = 23) were the most common opioids mentioned on death certificates (some of these cases were overlapping).

A possible causal link between high doses of potent opioids and death from accidental overdose relates to respiratory depression. Tolerance to respiratory depression from opioids is less than complete and may be slower than tolerance to euphoric and other effects [White and Irvine, 1999]. Concomitant use of other drugs, including benzodiazepines, can markedly increase the chance of death due to potentiation of respiratory depression effects [Wolff, 2002]. In addition, these long-acting opioids may have severe adverse consequences in a delayed fashion, hours after ingestion [Wolff, 2002].

It is possible that the risk associated with respiratory depression effects of long-acting opioids may be greatest at night, when recognition of respiratory depression may be reduced. Patients in a methadone-maintenance program on stable doses of methadone were more likely than healthy controls to have substantial sleep-disordered breathing, including central sleep apnea and periodic breathing [Teichtahl et al., 2001]. Other investigators have reported observations of unique sleep-disordered breathing abnormalities during non-rapid eye movement sleep of patients on sustained-release opioids for chronic pain [Farney et al., 2003]. These abnormalities included ataxic breathing, central apnea, and sustained hypoxemia. Further research is needed to more fully understand the respiratory depression and sleep-disordered breathing effects of various opioids when used long-term for chronic pain, and patient risk factors for respiratory depression.

Another possibility to explore in future research is whether delayed metabolism might be a contributing factor in some deaths in long-lasting opioid users. Some individuals with variant alleles of cytochrome P450 have delayed metabolism of oxycodone [Jannetto et al., 2002]. Delayed metabolism could be a factor in cases of oxycodone-associated deaths in which higher than expected (relative to therapeutic dose) blood opioid levels are found post-mortem [Drummer et al., 1994].

Among the 44 definite, probable, or possible deaths related to prescription opioid use, 84% were men and 69% were smokers. To our knowledge, no studies have directly addressed gender or smoking as risk factors related to morbidity or mortality associated with opioid use in chronic pain. Smoking as a possible risk factor is intriguing. One study found that smokers deprived of nicotine after coronary artery bypass graft required as much as one-third more opioid for postoperative analgesia than non-smokers [Creekmore et al., 2004]. Another study found smoking to be associated significantly with opioid analgesic use after open cholecystectomy [Glasson et al., 2002]. The reasons for this association are unknown; possible reasons include opiate use to avoid nicotine withdrawal symptoms, a pharmacokinetic interaction between smoking and opiates (e.g., smoking-related metabolism of opiates), and tolerance to opiates in smokers [Creekmore et al., 2004]. It is also possible that smokers might require higher doses for pain relief, and these higher doses might contribute to death by accidental overdose.

These descriptive observations from the Washington State workers' compensation system regarding opioid use can only be considered preliminary; however, the findings are

alarming and led us to send an ''Opiate Warning Letter'' to all prescribing providers in our system in 2004 (Appendix). The letter asks providers to more closely follow published guidelines related to opioid use for chronic pain. These guidelines include assessing pain and function at every visit, and co-signing an opioid information form after educating the patient [Washington State Department of Labor and Industries, 2000].

We were not able to report death rates relative to person-months of exposure to opioids. However, during the time frame of this study, similar to national claim trends, annual worker claims for lost time fell by approximately 15% in Washington State. Thus, it is likely that the increased deaths reported here are a conservative marker of a true increasing trend. Consistent with our observations, a recent dramatic increase in deaths since 1999 related to non-illicit opioid drug use has been reported from Utah. [Caravati et al., 2005]. Comparing two periods (1991–1998 vs. 1999–2003), deaths attributable to methadone increased from 2 to 33 per year, and deaths attributable to oxycodone and other opioids increased from 10 to 48 per year.

In their recent review, Ballantyne and Mao [Ballantyne and Mao, 2003] concluded that ''. . .very large doses of opioids are prescribed for patients with chronic pain that is not associated with terminal disease, often in the absence of any real improvement in the patient's pain or level of functioning. Whereas it was previously thought that unlimited dose escalation was at least safe, evidence now suggests that prolonged, high-dose opioid therapy may be neither safe nor effective'' (page 1951). We recommend that providers be cautious about dose escalation, and consider discontinuing opioids and pursuing other management strategies if treatment goals (reduced pain, improved function) are not met. Ideally, for injured workers, opioid use should decrease pain and improve function under conditions of stable dosage. Detailed guidelines reflecting such appropriate use in workers' compensation were disseminated statewide in 2000 and included tools for tracking pain and function [Washington State Department of Labor and Industries, 2000]. At this time, however, there is evidence that function may not improve with chronic opioid use [Moulin et al., 1996]; that substantial dose escalation of potent, Schedule II opioids has occurred over recent years; and that preventable deaths attributable to use of potent opioids have increased. We recommend that consultation with a pain management specialist be obtained if average daily morphine equivalent doses reach 120 mg. In addition, we recommend surveillance of all deaths potentially related to prescription opioid use in workers' compensation and other health systems in order to better inform public policy and to implement prevention strategies aimed at what are almost certainly preventable deaths. Finally, longer term, prospective studies are needed to more rigorously address the important issues raised from these observations.

Two other important issues should be investigated in future studies. First, we were not able to determine the relative contributions of inappropriate prescribing versus patient misuse of opioids in the deaths reported here. Methods to accurately identify persons at risk for opioid misuse are only in development [Chabal et al., 1997; Adams et al., 2004]. Second, while we believe the trends reported here reflect more general trends [Caravati et al., 2005], it may be that persons in the workers' compensation system and in other disability engendering systems are at even higher risk for dose escalation without functional improvement or for misuse [Chabal et al., 1997; Adams et al., 2004]. Methods to more clearly identify patients with chronic pain who may remain on effective stable doses of opioids with functional improvement from those who may die is clearly a critical research question.

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REFERENCES

Adams LL, Gatchel RJ, Robinson RC, Polatin P, Gajraj N, Deschner M, Noe C. 2004. Development of a self-report screening instrument for assessing potential opioid medication misuse in chronic pain patients. J Pain Symptom Manage 27:440–459.

American Academy of Pain Medicine. 1997. The use of opioids for the treatment of chronic pain: A consensus statement from the American Academy of Pain Medicine and the American Pain Society, Glenview, IL.

American Pain Society. 1999. Principles of analgesic use in the treatment of acute pain and cancer pain, 4th edn. Skokie, IL: American Pain Society.

Ballantyne JC, Mao J. 2003. Opioid therapy for chronic pain. N Engl J Med 349:1943–1953.

Bell JR. 1997. Australian trends in opioid prescribing for chronic non-cancer pain, 1986–1996. Med J Aust 167:9–10.

Caravati EM, Grey T, Nangle B, Rolfs RT, Peterson-Porucznik CA. 2005. Increase in poisoning deaths caused by non-illicit drugs–Utah, 1991–2003. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5402a1.htm. Accessed January 21, 2005.

Caudill-Slosberg MA, Schwartz LM, Woloshin S. 2004. Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs. 2000. Pain 109:514–519.

Chabal C, Erjavec MK, Jacobson L, Mariano A, Chaney E. 1997. Prescription opiate abuse in chronic pain patients: Clinical crieteria, incidence, and predictors. Clin J Pain 13:150–155.

Chou R, Clark E, Helfand M. 2003. Comparative efficacy and safety of long-acting oral opioids for chronic non-cancer pain: A systematic review. J Pain Symptom Manage 26:1026–1048.

Creekmore FM, Lugo RA, Weiland KJ. 2004. Postoperative opiate analgesia requirements of smokers and nonsmokers. Ann Pharmacother 38:949–953.

del Pozo G. 1999. Opioid consumption in Spain—the significance of a regulatory measure. Eur J Clin Pharmacol 55:681–683.

Drummer OH, Syrjanen ML, Phelan M, Cordner SM. 1994. A study of deaths involving oxycodone. J Forens Sci 39:1069–1075.

Farney RJ, Walker JM, Cloward TV, Rhondeau S. 2003. Sleep-disordered breathing associated with long-term opioid therapy. Chest 123:632–639.

Federation of State Medical Boards of the US. 1998. Model guidelines for the use of controlled substances for the treatment of pain: A policy document of the Federation of State Medical Boards of the United States, Inc., Dallas, TX.

Glasson JC, Sawyer WT, Lindley CM, Ginsberg B. 2002. Patient-specific factors affecting patient-controlled analgesia dosing. J Pain Palliat Care Pharmacother 16:5–21.

Hill CS, Jr. 1996. Government regulatory influences on opioid prescribing and their impact on the treatment of pain of nonmalignant origin. J Pain Symptom Manage 11:287–298.

Jannetto PJ, Wong SH, Gock SB, Laleli-Sahin E, Schur BC, Jentzen JM. 2002. Pharmacogenomics as molecular autopsy for postmortem forensic toxicology: Genotyping cytochrome P450 2D6 for oxycodone cases. J Anal Toxicol 26:438–447.

Moulin DE, Iezzi A, Amireh R, Sharpe WK, Boyd D, Mersky H. 1996. Randomised trial of oral morphine for chronic non-cancer pain. Lancet 347:143–147.

Portenoy RK. 1996. Opioid therapy for chronic, non-malignant pain: A review of the critical issues. J Pain Symptom Manage 11: 203–217.

Teichtahl H, Prodromidis A, Miller B, Cherry G, Kronborg I. 2001. Sleep-disordered breathing in stable methadone programme patients: A pilot study. Addiction 96:395–403.

US Department of Justice. 2002. Drug Enforcement Agency. Summary of Medical Examiner Reports on Oxycodone-Related Deaths, May 16. http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/oxycodone.htm.

Washington Administrative Code. 1999. WAC 246-919-800-830.

Washington State Department of Labor and Industries. 2000. http://www.lni.wa.gov/migration/ClaimsInsurance/Files/Providers/ProvBulletins/PbFiles/PB0004.pdf.

White JM, Irvine RJ. 1999. Mechanisms of fatal opioid overdose. Addiction 94:961–972.

Wolff K. 2002. Characterization of methadone overdose: Clinical considerations and the scientific evidence. Ther Drug Monit 24:457–470.

Wolters Kluwer Health. 2004. Drug facts and comparisons.

Appendix

IMPORTANT WARNING—PRESCRIPTION OPIATES

February 2004

Dear Attending Physician:

Please read this letter and think carefully about the content.

Scientific evidence does not yet provide clear guidance on which patients with chronic, non-cancer pain can safely use opiate-based pain relievers, in what dose, or for how long. The enclosed article, reprinted with permission from The New York Times, provides in layman's terms the current medical challenges in determining the most appropriate use of these powerful drugs. A review of opioid therapy in chronic pain recently published in the New England Journal of Medicine (2003; 349: 1943–1953) concluded that ''. . .very large doses of opioids are prescribed for patients with chronic pain that is not associated with terminal disease, often in the absence of any real improvement in the patient's pain or level of functioning. Whereas it was previously thought that unlimited dose escalation was at least safe, evidence now suggests that prolonged, high dose opioid therapy may be neither safe nor effective.''

The following information is relevant to potentially serious problems that may arise from use of opioids for chronic pain:

- The Drug Enforcement Agency (DEA) has reported 464 deaths as OxyContin-verified (N = 146) or OxyContin-likely (N = 318) from a national survey of medical examiners in 2000–2001 (www.deadiversion.usdoj.govand access Drugs & Chemicals of Concern–oxycodone).
- The Department of Labor and Industries has also identified deaths between 1995 and 2002, associated with overdose of prescription opioids, particularly oxycodone and methadone. The majority of these deaths have occurred since 1999.
- The department has verified two patterns that may be related to these deaths:
  - A dramatic (~40%) shift from Schedule III to Schedule II opioids.
  - A dramatic increase in average daily (morphine equivalent) dose of long-acting opioids from approximately 80 mg/day in 1997 to over 130 mg/day in 2001.
- In addition to opiates, both DEA-reported and DLI opioid-related deaths also have had evidence of multiple prescription drug use, including use of benzodiazepines, tricyclic anti-depressants, and muscle relaxants.

We have included the department's opioid guideline, developed in collaboration with the Washington State Medical Association. Please use this guideline before prescribing opioids for chronic, non-cancer pain, and attend to the principles outlined in that document.

Sincerely,

Robert J. Malooly
Assistant Director for Insurance Services

Gary Franklin, MD, MPH
Medical Director