A National Epidemic of Unintentional Prescription Opioid Overdose Deaths: How Physicians Can Help Control It

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Both the usage of prescription drugs such as opioid analgesics and benzodiazepines and overdoses involving them have increased dramatically in the United States since the 1990s. Patients using these drugs often have a combination of painful conditions, substance abuse, and other forms of mental illness. Psychiatrists and many primary care physicians might not be familiar with existing evidence-based guidelines for opioid prescribing or with programs designed to reduce the abuse of prescription drugs such as state prescription drug monitoring programs. Psychiatrists need to be informed regarding this problem to partner effectively with both pain specialists and primary care providers in their community.

J Clin Psychiatry 2011;72(5):589–592

Submitted: *September 7, 2010; accepted March 22, 2011.*
Online ahead of print: *April 19, 2011 (doi:10.4088/JCP.10com06560).*
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In a seminal paper in 1986, Portenoy and Foley[1] described 38 patients treated with opioids for intractable noncancer pain for more than 6 months with a median daily dose of less than 20 morphine milligram equivalents (MME) per day. The lack of clinically significant adverse events in this group led them to conclude that physicians could safely and effectively prescribe opioid medications to patients without a history of substance abuse with "relatively little risk of producing the maladaptive behaviors which define opioid abuse."[1(p184)] This paper, perhaps more than any other, began to push American physicians toward greater acceptance of the use of opioid analgesics to treat chronic noncancer pain.

In 2000, a *JAMA* article[2] noted that the prescribing of opioid medications in the United States had increased substantially between 1990 and 1996, thus documenting the dramatic shift in the attitude of physicians toward the role of opioids in managing chronic pain. No corresponding increase in emergency department visits involving opioid abuse had occurred during 1990–1996.[2] However, by the time the paper was published, the situation was not so reassuring; more recent data indicated that the number of emergency department visits involving opioid analgesic abuse was 75% higher in 2000 than in 1996.[3] Without being recognized, the epidemic of abuse of opioid analgesics had begun.

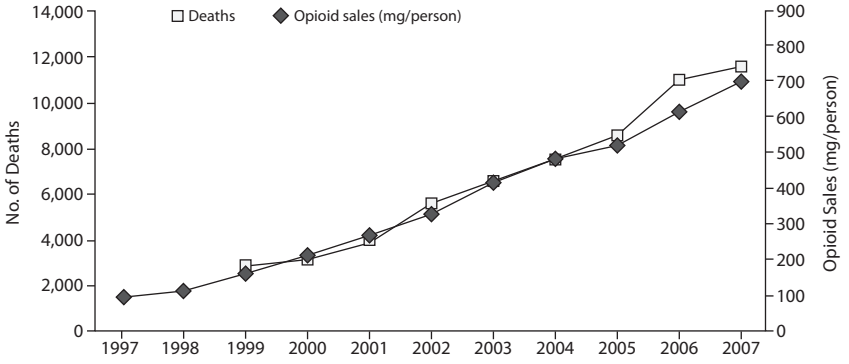
By 2005, long-term opioid therapy was being prescribed to an estimated 10 million US adults.[4] The volume of prescribed opioid analgesics was 100 MME per person in 1997; in 2007, the MME per person had increased to almost 700 MME.[5] This 7-fold increase approximately paralleled the rise in unintentional opioid analgesic overdose deaths (Figure 1).[6] By 2007, opioid analgesics were involved in at least 11,500 of the 27,500 fatal unintended drug overdoses in the United States according to death certificates, more than those overdoses involving heroin and cocaine combined (Figure 2).[6] During the same time frame, drug suicides also increased, and by 2007 opioid analgesics were involved in roughly 3,000 of the 8,400 overdose deaths in the United States that were suicides or of undetermined intent.[6] Various reports concluded that opioid analgesic abuse contributed to these deaths based on substance abuse histories, use of multiple providers for drugs, use of drugs without prescriptions, evidence that the drugs were injected or snorted, and use in concert with illicit drugs.[7,8]

Largely because of this increase in opioid-related deaths, overall drug overdose death counts have reached epidemic levels, in some places exceeding deaths from the perennial leading causes of injury mortality. In 2007, for example, nonsuicidal drug poisoning deaths exceeded either motor vehicle traffic or suicide deaths in 20 states. In some states, as can be seen in data from Ohio (Figure 3), the number of deaths from unintentional drug poisonings passed the numbers of deaths from both suicide and motor vehicle crashes.[9] More recent data indicate that emergency department visits due to opioids, sedatives, and sleep aids used nonmedically, ie, use without a prescription, taking more than prescribed, or use solely for the feeling it causes, continued to increase through 2009.[10] Rates for benzodiazepines were comparable to those for opioid analgesics.

The extent of these harmful effects was not envisioned in 1986 and was not recognized until much later. At the time, no one realized that a variety of factors would facilitate opioid abuse. First, some persons—especially those in rural communities—now had ready access to opioids for the first time in their lives. Second, pharmaceuticals, unlike illicit drugs, were not stigmatized and did not subject the user to the risk of infection or contamination. Last, the reduction in the share of the drug bill paid by consumers since 1990 made pharmaceuticals more available and less expensive, thus increasing the profit margin for the resale of prescriptions. A vial of one hundred 10- to 80-mg pills might be purchased for a $3–$50 copay and immediately sold for $1,000–$8,000.[11] Such wide profit margins have contributed to the proliferation of so-called "doctor shopping" and robberies of pharmacies.

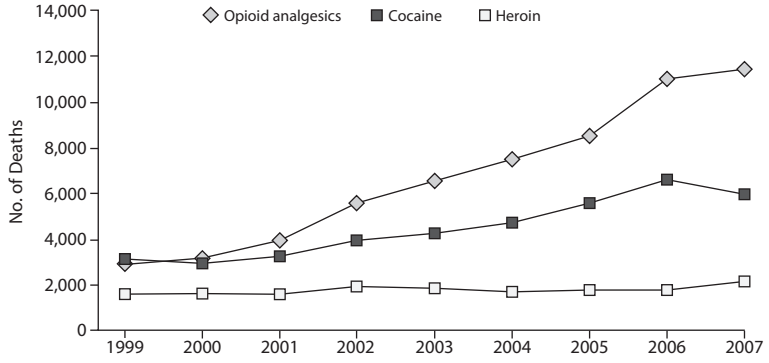
Perhaps most importantly, providers failed to anticipate the extent of the overlap of mental illness, including substance abuse, and chronic pain. Both chronic pain and mental illness are common; the National Comorbidity Survey Replication reports that 26% of Americans aged 18 years and older will suffer from a diagnosable mental disorder in any given year,[12] and lifetime prevalence rates are clearly much higher. From 15% to 30% of patients with many mental illnesses, including unipolar, bipolar, anxiety, psychotic, and attention-deficit/hyperactivity disorders, will also have substance abuse problems.[13] Similarly, people with substance abuse problems are likely to have another mental illness.[14] Nevertheless, opioids, and higher doses of them, are more likely to be prescribed for persons with depressive or anxiety disorders than for persons who have no mental illness.[15] As a result, opioids, benzodiazepines, and sleep aids are frequently prescribed in combination despite their potentially harmful additive and interactive physiologic effects. These same drug combinations are also frequently found in the toxicology of people dying of drug overdoses.[8]

Figure 1. Unintentional Overdose Deaths Involving Opioid Analgesics Parallel Per Capita Sales of Opioid Analgesics in Morphine Equivalents by Year, United States, 1997–2007[a]



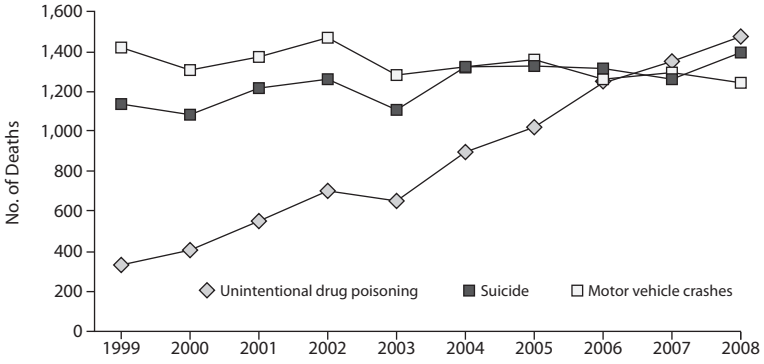
[a]Data on deaths are from Centers for Disease Control and Prevention WONDER.[6] Data on drug sales are from the Drug Enforcement Administration ARCOS system data.[5]

Figure 2. Unintentional Overdose Deaths by Major Type of Drug Involved, United States, 1999–2007[a]



[a]Data are from Centers for Disease Control and Prevention WONDER.[6]

Figure 3. Deaths From Unintentional Drug Poisoning, Suicide, and Motor Vehicle Crashes, Ohio, 1999–2008[a]



[a]Data from Ohio Department of Health.[9]

Health care providers need to shoulder some responsibility for correcting this problem. Guidelines for the clinical management of chronic noncancer pain with opioids have been available for longer than a decade,[16,17] but more recent guidelines are more cautious and evidence-based.[18] Most guideline authors now agree in principle with the assertion that "long-term opioid therapy should only be conducted in practice settings where careful evaluation, regular follow-up, and close supervision are ensured."[19(p208)] The difficulty lies in following the guidelines in typical practice settings with constraints on the physicians' time, insurance coverage, and the ability to self-pay.

Although substance abuse and chronic pain are common problems among patients seen by psychiatrists, psychiatrists lack training in pain medicine.[20] So do many primary care providers, who are known to prescribe most of the antidepressants[21] and a large percentage of the antianxiety agents. At a minimum, providers should be familiar with the basics of careful opioid prescribing. Before prescribing opioids, the treating provider should try nonscheduled medications as well as, when possible, physical therapy, psychotherapy, exercise, and other forms of nonpharmacologic management and give such measures an adequate trial. If opioids are necessary, the next step should be screening patients for substance abuse and mental health problems, especially a history of depression.

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Before prescribing an opioid for chronic pain:

- Know the basics of safe opioid prescribing.
- Try nonscheduled medications, physical therapy, psychotherapy, exercise, and other nonpharmacologic management. Give these adequate trials.

Resources

Urine drug testing algorithm
http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf

State prescription drug monitoring programs
http://www.pmpalliance.org/node/79

If long-term opioid prescribing is necessary:

- Screen for substance abuse and mental health problems, especially depression. Use information from family members as applicable.
- Request a record of the patient's history of use of controlled substances from other treating physicians and the state's prescription drug monitoring program (PDMP).
- Perform a baseline urine drug test and then routine random urine drug testing and pill counts during treatment.
- Monitor regularly to see whether opioids are being used as directed and treatment goals are being met. Check the patient's record in the PDMP periodically.

If problems arise:

- Avoid discharging the patient. Discuss the reasons for your concern with him or her.
- Patients obtaining controlled substances from multiple providers or using them with illicit drugs can be tapered to lower doses and connected to substance abuse treatment professionals.
- Consider consultation with a pain management specialist if dosage increases significantly with no improvement in function.

Information from family members is often helpful in this regard. Finally, the physician should request a record of the patient's history of use of controlled substances from other treating physicians and the state's prescription drug monitoring program (PDMP). PDMPs have now been enacted in 44 states and are operational in 35. Almost all PDMPs now collect information on Schedule II–IV drugs, so they track both opioid analgesics and sedatives. Use of PDMP data before and during prescribing can identify warning signs in some patients and be reassuring for others.[22]

Once a decision has been made to initiate opioid therapy for chronic pain, the physician should get a baseline urine drug test. Once treatment is under way, random urine drug testing and pill counts should be employed routinely. A recent review has shown a modest reduction in opioid abuse with the use of urine drug testing combined with treatment agreements.[23] Regular evaluations are necessary to make sure patients are using opioids as directed and to determine if treatment goals are being met. Check the patient's record in the PDMP periodically. Most PDMPs require that pharmacies submit prescription data to the central registry within 2 weeks of dispensing.

If problems arise, physicians should refrain from discharging the patient from their practice. Discuss the reasons for your concern with the patient. Patients found to be obtaining controlled substances from multiple providers or using them in concert with illicit drugs can be tapered to lower doses and connected to substance abuse treatment professionals. Consider consultation with a pain management specialist if opioid dosage has increased significantly without an improvement in function.[24]

Finally, both primary care providers and psychiatrists should help their communities make the policy changes necessary to address this problem. Support initiating a PDMP if your state does not have one. Advocate improvements in data access that will make PDMP data easier to obtain, more timely, and inclusive of information from neighboring states when patients cross state lines. Support state regulatory initiatives designed to identify and discipline physicians, dentists, or pharmacists who are knowingly abetting "doctor shopping," operating "pill mills," or engaging in prescription fraud. In addition, partner with community efforts at the city or county level. Several states are home to initiatives to promote safer prescribing practices that make physicians part of a team to address the problem of prescription abuse. For example, in North Carolina, the Safer Opioid Prescribing (SOP) initiative was launched in 4 counties. SOP included a 4-pronged approach: outreach and education for physicians, community building around prescription misuse, education of patients about storage and disposal of abusable drugs, and technical assistance to physicians to implement safer prescribing practices. Preliminary data show that PDMP registration and usage by physicians increased significantly in these counties.[25]

Psychiatrists who routinely check the prescription records of their patients in their state PDMPs might find that they share many patients with community physicians who treat chronic pain. They might also find that many of the tools used in managing chronic pain with opioids such as urine testing and PDMPs can play a role in managing therapy with benzodiazepines and that many policy changes can help prevent the abuse of scheduled psychotherapeutic drugs as well as opioid analgesics. Mental health providers are therefore natural partners with primary care providers and pain specialists in managing the growing problem of prescription drug abuse.

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Potential conflicts of interest: **Dr Weisler** is or in his career has been a consultant to Abbott, AstraZeneca, Biovail, Bristol-Myers Squibb, Cephalon, Corcept, Eli Lilly, Forest, GlaxoSmithKline, Johnson & Johnson, Organon, Otsuka America, Pfizer, Pharmacia, ProPhase, Sanofi, Sanofi-Synthelabo, Shire, Solvay, Sunovion, Takeda, Transtech, Validus, and Wyeth; is or has been on the speakers bureaus of Abbott, AstraZeneca, Biovail, Bristol-Myers Squibb, Burroughs Wellcome, Cephalon, Ciba Geigy, Eli Lilly, Forest, GlaxoSmithKline, Janssen, Johnson & Johnson, Novartis, Organon, Pfizer, Sanofi, Sanofi-Synthelabo, Schering Plough, Shire, Solvay, Validus, and Wyeth; has received research support from Abbott, AstraZeneca, Biovail, Bristol-Myers Squibb, Burroughs Wellcome, CeNeRx, Cephalon, Ciba Geigy, CoMentis, Dainippon Sumitomo Pharma America, Eisai, Eli Lilly, Forest, GlaxoSmithKline, Janssen, Johnson & Johnson, Lundbeck, McNeil, Medicinova, Merck, National Institute of Mental Health, Neurochem, New River, Novartis, Organon, Pfizer, Pharmacia, Repligen, Saegis, Sandoz, Sanofi, Sanofi-Synthelabo, Schwabe/Ingenix, Sepracor, Shire, Sunovion, Synaptic, Takeda, TAP, Transcept, UCB, Vela, and Wyeth; and has held or holds stock in Bristol-Myers Squibb, Cortex, Merck, and Pfizer. **Dr Patkar** has had relationships with AstraZeneca, Bristol-Myers Squibb, Forest, GlaxoSmithKline, Janssen, McNeil Consumer and Specialty, Organon, Orphan Medical, Titan, Pfizer, Reckitt Benckiser, Cephalon, Jazz, and Lundbeck. **Dr Paulozzi** reports no potential conflicts of interest.

Funding/support: None reported.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

REFERENCES

1. Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. *Pain*. 1986;25(2):171–186.
2. Joranson DE, Ryan KM, Gilson AM, et al. Trends in medical use and abuse of opioid analgesics. *JAMA*. 2000;283(13):1710–1714.
3. Substance Abuse and Mental Health Services Administration. Trends in drug-related emergency department visits, 1994–2002 at a glance. http://dawninfo.samhsa.gov/old_dawn/pubs_94_02/shortreports/files/DAWN_EDvisits_glance.pdf. Accessed March 24, 2011.
4. 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(12):1166–1175.
5. US Department of Justice (USDOJ) DEA. ARCOS: Automation of Reports and Consolidated Orders System. www.deadiversion.usdoj.gov/arcos/index.html. Accessed August 27, 2010.
6. Centers for Disease Control and Prevention. WONDER [online database]. 2010. http://wonder.cdc.gov. Accessed October 12, 2010.
7. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA*. 2008;300(22):2613–2620.
8. Toblin RL, Paulozzi LJ, Logan JE, et al. Mental illness and psychotropic drug use among prescription drug overdose deaths: a medical examiner chart review. *J Clin Psychiatry*. 2010;71(4):491–496.
9. Ohio Department of Health. Epidemic of prescription drug overdose in Ohio. 2010. http://www.healthyohioprogram.org/diseaseprevention/dpoison/drugdata.aspx. Accessed September 1, 2010.
10. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. The DAWN Report: Highlights of the 2009 Drug Abuse Warning Network (DAWN) findings on drug-related emergency department visits. http://www.oas.samhsa.gov/2k10/DAWN034/EDHighlights.cfm. Updated December 28, 2010. Accessed March 25, 2011.
11. Drug Enforcement Administration. Oxycodone. http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/summary.htm. Accessibility verified April 6, 2011.
12. Kessler RC, Chiu WT, Demler O, et al. Prevalence, severity, and comorbidity of 12-month *DSM-IV* disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry.* 2005;62(6):617–627.
13. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry.* 2004;61(8):807–816.
14. Sullivan MD, Edlund MJ, Steffick D, et al. Regular use of prescribed opioids: association with common psychiatric disorders. *Pain*. 2005;119(1–3):95–103.
15. Braden JB, Sullivan MD, Ray GT, et al. Trends in long-term opioid therapy for noncancer pain among persons with a history of depression. *Gen Hosp Psychiatry*. 2009;31(6):564–570.
16. American Academy of Pain Medicine and American Pain Society. 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. *Clin J Pain*. 1997;13(1):6–8.
17. Federation of State Medical Boards of the United States I. Model policy for the use of controlled substances for the treatment of pain. http://www.fsmb.org/pdf/2004_grpol_Controlled_Substances.pdf. Accessed June 21, 2007.
18. Chou R, Fanciullo GJ, Fine PG, et al; American Pain Society–American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113–130.
19. Von Korff M, Deyo RA. Potent opioids for chronic musculoskeletal pain: flying blind? *Pain*. 2004;109(3):207–209.
20. Elman I, Zubieta JK, Borsook D. The missing *P* in psychiatric training: why it is important to teach pain to psychiatrists. *Arch Gen Psychiatry*. 2011;68(1):12–20.
21. Stagnitti MN. Antidepressants prescribed by medical doctors in office based and outpatient settings by specialty for the US civilian noninstitutionalized population, 2002 and 2005. Statistical Brief #206. Rockville, MD: Agency for Healthcare Research and Quality; 2008. http://www.meps.ahrq.gov/mepsweb/data_files/publications/st206/stat206.pdf.
22. Baehren DF, Marco CA, Droz DE, et al. A statewide prescription monitoring program affects emergency department prescribing behaviors. *Ann Emerg Med*. 2009;
23. Starrels JL, Becker WC, Alford DP, et al. Systematic review: treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. *Ann Intern Med*. 2010;152(11):712–720.
24. Washington State Agency Medical Directors' Group. Interagency guidelines on opioid dosing for chronic non-cancer pain. http://www.agencymeddirectors.wa.gov. Accessed March 5, 2011.
25. Governor's Institute on Alcohol and Substance Abuse [North Carolina]. Safer Opioid Prescribing Summary Sheet. http://www.sa4docs.org/sop-kbr. Accessed March 31, 2011.

To learn more about the prescription drug overdose epidemic, see "Prescription Drug Overdoses: An American Epidemic," a CDC Grand Rounds presentation. http://www.cdc.gov/about/grand-rounds

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