



Combating an Epidemic of Prescription Opioid Abuse

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ABSTRACT The past decade has witnessed an alarming increase in the number of deaths due to prescription opioids that has paralleled the rise in the number of opioid prescriptions dispensed. Prescription drug monitoring programs, abuse-deterrent formulations and proper disposal of opioids have been promoted to help combat the opioid epidemic. We discuss changes that dentists, the third most frequent prescribers of opioids, can implement to help reduce the risk of prescription opioid abuse in their communities.

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The addiction and abuse potential of opioids is well-known, with tight regulations governing the prescribing and dispensing of these agents at the state and federal levels. In the late 1990s, however, greater focus began to be placed on the regular assessment and treatment of pain, with state medical boards loosening restrictions on the prescribing of opioids for chronic, noncancer pain. In 2001, the Joint Commission on the Accreditation of Health Care Organizations introduced new pain management standards, with recommendations to regularly assess and treat patients for pain by making “pain the fifth vital sign.”¹ Coincidentally, around 2000, reports began to surface regarding adverse cardiovascular effects associated with selective cyclooxygenase-2 inhibitors (COX-2 inhibitors), which had been developed as safer alternatives to nonselective, nonsteroidal anti-inflammatory drugs (NSAIDs). In 2005, after reports of

adverse cardiovascular effects associated with nonselective NSAIDs as well, the U.S. Food and Drug Administration (FDA) requested that warnings about adverse gastrointestinal and cardiovascular effects be added to all prescription NSAIDs. NSAIDs, along with acetaminophen and opioids, had been one of the most frequently utilized classes of drugs for the treatment of pain. Over the past decade, with fewer pharmacologic options perceived to be safe and effective for pain management, the use of opioids in the U.S. has significantly increased, with a similar increase in opioid-related overdoses and overdose-related deaths.² Easier access to prescription opioids, caused by increased prescribing, has undoubtedly contributed to the prescription opioid epidemic in the U.S. This article reviews the scope of and contributors to the current prescription opioid epidemic, and discusses various strategies that dentists can adopt to help combat the epidemic.

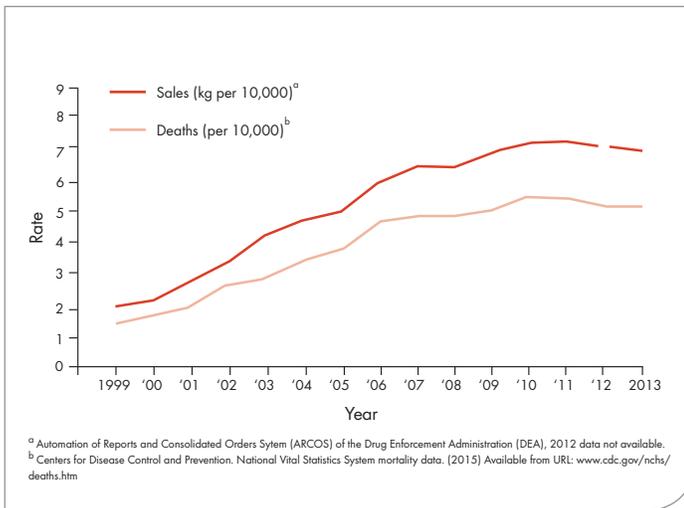


FIGURE 1. Rates of prescription opioid sales and deaths, 1999 to 2013.⁵ Adapted from injury prevention and control: prescription drug overdose. Centers for Disease Control and Prevention website, www.cdc.gov/drugoverdose/data/index.html. Accessed May 2, 2015.

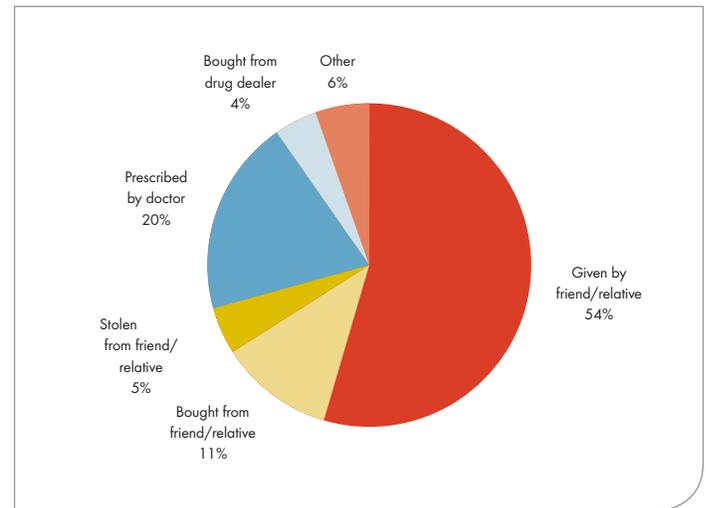


FIGURE 2. Source of prescription opioid used for nonmedical purpose.¹⁴ Adapted from Jones CM, Paulozzi LJ, Mack KA. Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United States, 2008-2011. *JAMA Intern Med* 2014;174(5):802-3.

The Opioid Epidemic

Hydrocodone-containing products are the most frequently prescribed medication in the U.S., with 136.7 million prescriptions dispensed in 2011, bypassing chronic disease state medications, such as levothyroxine and simvastatin.³ In fact, with just 4.6 percent of the world's population, the U.S. consumes 80 percent of the world's opioid supply and 99 percent of the world's hydrocodone supply.⁴ Current data on annual opioid medication sales in the U.S. are estimated to equate to a quantity sufficient to supply every adult American with a 45-day supply of hydrocodone.³ Between 1999 and 2013, the amount of prescription opioids dispensed in the U.S. and the number of deaths due to prescription opioids have both quadrupled, with more than 16,000 deaths attributed to opioids in 2013 (FIGURE 1).⁵ Although the rate of opioid prescribing appears to be gradually leveling off, a significant decline in the rate of opioid prescribing has yet to be observed.

Dentists and the Opioid Epidemic

In a 2009 nationwide study of opioid prescribing patterns, dentists prescribed 8 percent of all prescriptions for opioids, just behind primary care physicians (28.8

percent) and internists (14.6 percent), and were the main prescribers of opioids for patients aged 10 to 19 (30.8 percent).⁶ Dentists are also estimated to be frequent prescribers of immediate-release opioids, which tend to be more frequently abused than extended-release opioids.⁷ It must therefore be considered that some of the opioids prescribed by dentists will end up being used for nonmedical purposes.

Dentists are uniquely positioned health care professionals in the community as they frequently come in contact with adolescents and young adults. The rates of current use of illicit drugs is highest among young adults aged 18 to 25 (19.6 percent) than any other age group.⁴ Because adolescents and young adults may infrequently need to seek the care of other health care professionals, dentists may be the only health care professionals who will have the opportunity to screen many of the patients in this age group for potential substance abuse problems and help refer patients to available resources.

Acute Pain Versus Chronic Pain

Pain is often misleadingly classified as being either "acute" or "chronic" based on the duration of symptoms. While acute

pain is usually thought of as a symptom of underlying tissue damage and activation of nociceptors caused by trauma or surgery that typically resolves as the injury heals, chronic pain may signal some sort of underlying disease pathology, as in the case of fibromyalgia or multiple sclerosis, or result from abnormal continued activation of nociceptors long after an injury has healed.⁸ As such, pharmacologic interventions that may be useful for acute pain may have no effect in a patient with chronic pain and the management of a patient with chronic pain will usually require multiple modalities, with pharmacologic therapy playing a moderate adjunctive role.⁸

While there is evidence for the short-term use of opioids for the management of acute pain, the evidence for the long-term use of opioids for the management of chronic pain has come under scrutiny. A recent systematic review of the scientific literature found a lack of data regarding the effectiveness of long-term opioid use for chronic pain.⁹ Despite widespread use of opioids for chronic pain, no controlled studies have evaluated the use of long-term opioids greater than one year for outcomes related to pain, function or quality of life.⁹ On the other hand, evidence from

TABLE 1

Definitions to Describe Prescription Drug Misuse, Abuse and Related Events^{13,28,29}

Misuse	Any intentional therapeutic use of a drug product in an inappropriate way.
Abuse	Any intentional, nontherapeutic use of drug product or substance, even once, for the purpose of achieving a desirable psychological or physiological effect.
Addiction	Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm and craving.
Aberrant Drug-Related Behavior	A behavior outside the boundaries of the agreed-on treatment plan which is established as early as possible in the doctor-patient relationship.
Physical Dependence	A state of adaptation manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug and/or administration of an antagonist.
Tolerance	A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more drug's effects over time.

Adapted from Savage SR, Joranson DE, Covington EC, Schnoll SH, Heit HA, Gilson AM. Definitions related to the medical use of opioids: Evolution towards universal agreement. *J Pain Symptom Manage* 2003;26(1):655-67. Smith SM, Dart RC, Katz NP, Paillard F, Adams EH, Comer SD, et al. Classification and definition of misuse, abuse, and related events in clinical trials: ACTION systematic review and recommendations. *Pain* 2013;154(11):2287-96. Gourlay DL, Heit HA. Pain and addiction: managing risk through comprehensive care. *J Addict Dis* 2008;27(3):23-30.

observational studies appears to suggest that opioid therapy for chronic pain is associated with increased risk for overdose, abuse and dependence.⁹ An observational study of patients receiving opioids for chronic noncancer pain found that, compared to patients taking no more than 20 mg of oral morphine equivalents per day, patients taking 50 mg to 99 mg per day had a 3.7-fold increase in overdose risk, and patients taking 100 mg or more per day had an 8.9-fold increase in overdose risk.¹⁰ Various guidelines, therefore, recommend exercising extreme caution when prescribing greater than 90 mg to 200 mg of oral morphine equivalents per day for a patient, or consulting a pain management specialist for referral.^{11,12}

Definitions Related to the Medical and Nonmedical Use of Opioids

Confusion is common among clinicians and patients regarding the terminology used to describe different patterns of nonmedical use of opioids (TABLE 1). For example, symptoms of physical dependence or tolerance to opioids are frequently mistaken for signs of opioid addiction. Many patients taking opioids on a chronic basis,

whether for medical or nonmedical use, may exhibit symptoms of physical dependence, such as withdrawal symptoms upon abrupt discontinuation, or tolerance, such as requiring higher doses to achieve the same effects. However, these symptoms alone are not sufficient evidence of opioid addiction. A consensus definition developed by the American Pain Society, American Academy of Pain Medicine and the American Society of Addiction Medicine identifies four additional criteria for addiction: impaired control over drug use, compulsive use, continued use despite harm, or craving.¹³ While opioid addiction implies ongoing nonmedical use of opioids, opioid abuse can include ongoing nonmedical use of opioids, as well as a one-time nonmedical use of an opioid. Opioid misuse, in contrast to opioid abuse, is defined as taking a prescription opioid for pain relief, but in a way not originally prescribed. For example, taking a higher dose or taking a dose more frequently than prescribed would be considered misuse. Taking an opioid that had been prescribed for dental pain when one has back pain would also be considered misuse.

Sources of Prescription Opioids Used for Nonmedical Purposes and the Role of Health Care Providers

Where do nonmedical users of prescription opioids obtain their opioids? Based on data from the National Survey on Drug Use and Health, an estimated 70 percent of nonmedical users obtained the opioids from friends or family members and only 20 percent reported obtaining the opioid through a legitimate doctor's prescription (FIGURE 2).¹⁴ However, compared to those who reported the lowest frequency of opioid use (on to 29 days), those who reported the highest frequency of opioid use (200-365 days) were more likely to obtain opioids via prescription from a physician (17.9 percent versus 27.3 percent).¹⁴ The sobering reality is that most prescription opioids that are being used for nonmedical purposes originated from legitimate prescriptions. Thus, efforts to combat the prescription opioid epidemic must target the diversion and sharing of legitimate prescriptions for opioids, as well as increased vigilance and screening for patterns of inappropriate opioid use before prescribing. Although most health care providers are well aware

of the potential dangers of prescription opioids, providers may not be as aware of the factors contributing the opioid abuse problem in the U.S. and recent policy changes to try to address the problem.

Prescription Opioid Hoarding

Given that the vast majority of nonmedical users of prescription opioids are obtaining them from friends or family members, there is a concern that most leftover opioid prescriptions end up in the medicine cabinet rather than being discarded. But why do patients have leftover prescription opioids in the first place?

Several studies have focused on trying to determine how many tablets of opioid medications patients actually use following painful procedures, compared to how many tablets they were prescribed. A 2006 survey of oral and maxillofacial surgeons in the U.S. revealed that 85 percent of the respondents almost always prescribed an opioid after third molar extractions and the average number of opioid tablets prescribed was 20 (range eight to 40).¹⁵ However, the number of tablets patients actually consumed was not determined. To better characterize prescription opioid consumption following third molar extractions, Weiland et al. conducted a phone survey with 48 patients at 24 hours and seven days following surgery.¹⁶ The median number of opioid tablets prescribed was 20 (range 10 to 40), and patients reported consuming a median of three tablets (range 0 to 10) at 24 hours, and a median of eight tablets (range 0 to 34) by day seven. None of the patients reported discarding their unused opioid tablets (median 12 tablets), and most reported storing the unused tablets in medicine cabinets.

A survey of adults in Utah confirmed that hoarding of leftover prescription opioids was common, with 72 percent of patients who had been prescribed an opioid reporting that they had leftover medication, and 71 percent of those patients reporting that they had kept the medication.¹⁷

Utilizing nonopioid analgesics and limiting the quantity of opioid medications prescribed after painful procedures may help to reduce the abuse and diversion of leftover prescription opioids. Additionally, all health care providers should educate patients on the hazards of hoarding and sharing leftover prescription opioids and counsel on recommended methods for disposal.

Disposing Leftover Prescription Opioids

The FDA recommends disposing of most medications by mixing with an unpalatable substance, such as used coffee grounds or kitty litter, placing in a sealed plastic bag and throwing in the household trash.¹⁸ However, for certain controlled substances, such as the prescription opioids hydrocodone, oxycodone, hydromorphone, morphine and others, the FDA recommends that these controlled Schedule II medications be flushed down the toilet or sink to reduce the risk for overdose due to accidental ingestion.¹⁸

Alternatively, patients may turn in leftover prescription opioids to participating law enforcement agencies and pharmacies that are registered with the Drug Enforcement Agency to take back controlled substances.¹⁹ In many communities, police stations have locked boxes for the collection of unneeded controlled substances. A few specially registered pharmacies may be able to accept leftover controlled substances for disposal. However, these registered and participating sites may be uncommon or difficult to find in the community.

The different recommended methods for disposing of different types of medications can cause confusion among patients and health care providers. Recently, AB 623 aimed at reducing prescription opioid-related deaths by reducing opportunities for inappropriate access was introduced in the California Legislature by Assemblymember Jim Wood, DDS (D-Healdsburg). One component of the bill proposed by Dr. Wood, a practicing dentist, would mandate

that pharmacists counsel patients on the proper storage and disposal of opioids, thus helping to ensure that the majority of patients receiving prescription opioids are educated on how to safeguard the supply of prescription opioids in the community.

Abuse-Deterrent Formulations of Opioids

Abuse-deterrent formulations (ADFs) of opioids have been developed to prevent manipulation of the opioid formulations for the purpose of abuse. Some ADFs, such as hydrocodone extended-release (ER) and oxycodone ER, are formulated to resist physical alteration through chewing, crushing or dissolving, while other ADFs, such as morphine plus naltrexone and oxycodone plus naloxone, contain opioid antagonists that will block the euphoric effects of the opioid component when the formulation is manipulated through chewing, crushing or dissolving.²⁰

Although ADFs may help to reduce abuse of the particular opioid formulation, they do not appear to be associated with decreased rates of opioid abuse and opioid-related deaths overall.^{21,22} Unfortunately, as we have started to regain control over access to prescription opioids, more and more opioid abusers have begun turning to heroin as a cheap and readily accessible alternative. In one survey, although abuse of an ER formulation of oxycodone declined after it was changed to an ADF in 2010, reported use of heroin increased and 25-30 percent of respondents reported continued abuse of the oxycodone ADF.²³ Prescribers should therefore continue to exercise caution by limiting prescribing of ADFs of opioids.

Prescription Drug Monitoring Programs

Most states now have prescription drug monitoring programs (PDMPs), although the components of the programs are not all the same. It is hoped that accurately maintained PDMPs will help prescribers, pharmacists, law enforcement officials and regulatory boards to more effectively monitor and investigate

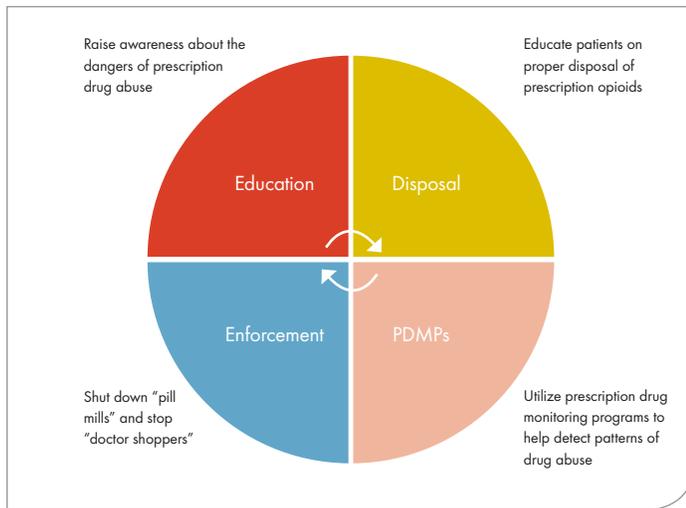


FIGURE 3. The prescription drug abuse plan.³⁰
Adapted from Executive Office of the President of the United States. Epidemic: Responding to America's prescription drug abuse crisis, 2011. www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/rx_abuse_plan.pdf.

patterns related to the prescribing, dispensing and use of controlled substances. California's PDMP is known as the Controlled Substance Utilization Review and Evaluation System (CURES) and is overseen by the California Department of Justice. Under CURES, information regarding prescriptions dispensed for Schedule II, III and IV substances must be electronically transmitted to CURES within seven days of dispensing.²⁴ While reporting of prescriptions to CURES is mandatory, checking the CURES database before prescribing or dispensing is currently not mandatory. However, health care providers involved in the prescribing or dispensing of controlled substances are encouraged to access the CURES Patient Activity Reports for patients under their direct care to assess for warning signs of inappropriate use of controlled substances, or "doctor shopping," a practice in which patients visit many different prescribers to obtain prescriptions. CURES appears to be an underutilized resource, with only an estimated 9.8 percent of the total number of licensed prescribers and pharmacists in California registered in 2014.²⁵ New legislation mandates that all California pharmacists and prescribers of controlled substances be registered with CURES by July 1, 2016, to facilitate ready access to records

and help CURES realize its full potential.²⁴

PDMPs have been implemented with the hope of helping to reduce the abuse and misuse of controlled substances, but without substantial evidence to demonstrate potential or actual benefits. Results have begun to trickle in from different states to suggest possible beneficial effects on the prescribing and dispensing of controlled substances after implementation of PDMPs. Florida's PDMP, implemented in 2011, was associated with a significant, 25 percent, decline in oxycodone-caused mortality, which was inversely related to the number of PDMP queries.²⁶ The investigators hypothesize that health care providers may have changed their prescribing habits for individual patients after querying the PDMP. Indeed, health care provider access to PDMP information has been shown to influence the prescribing habits of physicians treating patients presenting to the emergency department with painful conditions unrelated to acute injuries, with fewer or no opioids prescribed after reviewing PDMP data, compared to what was originally planned.²⁷

Conclusions

The prescription opioid abuse problem has reached epidemic proportions in the U.S. A liberalized attitude toward prescribing of

TABLE 2

Reducing the Risk of Prescription Drug Abuse: Strategies for Health Care Professionals⁷

Screen for Substance Abuse	Inquire about alcohol, tobacco and drug use prior to prescribing opioids.
Minimize the Risk of Leftover Opioids	Prescribe the minimum quantity of opioid to manage acute pain. Educate patients to dispose of and never share leftover prescription opioids.
Prevent "Doctor-Shopping"	Use PDMPs to verify drug-use history. Be suspicious of patients who ask for specific drugs or report that their medication was lost or stolen.

Adapted from Denisco RC, Kenna GA, O'Neil MG, Kulich RJ, Moore PA, Kane WT, et al. Prevention of prescription opioid abuse: The role of the dentist. *J Am Dent Assoc* 2011;142(7):800-10.

opioids that began over a decade ago has undoubtedly contributed to the problems we are experiencing now. Dentists, who are estimated to be responsible for 8 percent of all the prescriptions for opioids in the U.S. and the major prescribers of opioids among the 10-to-19-year-old age group, can play a major role in helping to combat the prescription opioid epidemic. Regaining control over access to prescription opioids will most likely require a multifaceted approach, including education, monitoring, proper disposal and enforcement, as no one intervention is likely to be successful on its own (FIGURE 3). Strategies that health care professionals should adopt to help reduce the risk for prescription drug abuse include screening patients for substance abuse prior to prescribing opioids, prescribing the minimum quantity of opioid to manage acute pain, educating patients to dispose of and never share leftover prescription opioids, and using PDMPs to verify drug-use histories and prevent "doctor shopping" (TABLE 2). However, as more programs are successfully implemented to control access to prescription opioids, health care professionals must also remain vocal advocates for their patients with legitimate needs for opioids, to ensure that the pendulum does not swing too far in the opposite direction, resulting in needless patient suffering. ■

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