

Economic Burden of Prescription Opioid Misuse and Abuse

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ABSTRACT

BACKGROUND: Prescription opioid abuse and its associated costs are a problem in the United States, with significant epidemiologic and economic consequences. The breadth and depth of these consequences are not fully understood at present.

OBJECTIVE: To summarize published, English-language biomedical evidence pertaining to the epidemiology and costs of prescription opioid analgesic misuse and abuse and to describe efforts to reduce the burden of these problems.

METHODS: Published English-language articles on the epidemiology and economics of abuse, misuse, or diversion of prescribed opioid analgesics in the United States were identified by searching PubMed, Web of Science, the Cumulative Index to Nursing and Allied Health Literature database (CINAHL), EconLit, and PsycInfo, using (economics OR epidemiology) AND (misuse OR abuse) AND opioid as search terms or Medical Subject Heading (MeSH) terms. Article bibliographies were also searched manually for applicable papers. The search was limited to articles published from 1995 through July 2009.

RESULTS: The literature search identified 2,347 titles, of which all but 41 were excluded as not pertaining specifically to the epidemiology or economics of prescription opioid abuse or misuse in the United States. In 2006, approximately 5.2 million individuals in the United States reported using prescription analgesics nonmedically in the prior month, up from 4.7 million in 2005. The total cost of prescription opioid abuse in 2001 was estimated at \$8.6 billion, including workplace, health care, and criminal justice expenditures. One study of commercially insured beneficiaries in the United States found that mean per-capita annual direct health care costs from 1998 to 2002 were nearly \$16,000 for abusers of prescription and nonprescription opioids compared with approximately \$1,800 for nonabusers who had at least 1 prescription insurance claim.

CONCLUSIONS: The economic burden of prescription opioid misuse and abuse is large. While the existing evidence indicates that persons who abuse or misuse prescription opioids incur higher costs and health care resource use, differences in methods used to explore this question make estimating the actual societal burden imposed by this problem difficult. Efforts to establish and maintain a balance between access to these drugs for legitimate pain management while decreasing the risk of abuse and misuse are critically important and include such tools as patient and provider education, patient screening, and use of technology.

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What this review adds to what is presently known about this subject

- This review summarizes and discusses the available estimates of the epidemiology and costs associated with opioid abuse and misuse.
- White et al. (2005) estimated that the average annual all-cause health care costs per patient ranged from \$15,884 to \$18,388 among abusers and \$1,830 to \$2,210 among demographically-matched comparison groups of nonabusers (a ratio of 8.3 to 8.7). However, because abusers had much higher rates of underlying disease, results could have been affected by confounding.
- Different definitions and methods of assessing abuse-related expenditures have resulted in variable results.
- The costs associated with opioid abuse and misuse are large and represent a significant societal burden. While efforts to decrease the epidemiologic and economic burden of opioid misuse and abuse are important, pain is commonly poorly managed in the United States. Thus, it is important to ensure that efforts to reduce opioid abuse and misuse do not adversely affect appropriate access to these drugs for pain management.

Pain is an extremely common reason for individuals to seek medical care.¹ It is also commonly undertreated in a wide variety of populations.²⁻⁸ The consequences of undertreatment of pain can include decreased healing,⁹⁻¹² increased costs and resource use,¹³⁻¹⁹ slower return to functioning,²⁰ and decreased quality of life.²¹⁻²²

Prescription opioid analgesics are essential tools in the treatment of moderate to severe pain, yet these drugs are also associated with important problems, including misuse, abuse, and diversion. While appropriate use of opioid analgesics is an important dimension of quality health care, aberrant use may contribute to poorer health outcomes. Thus, an improved understanding of overall costs associated with misuse and abuse of prescription opioid analgesics is relevant for patients, clinicians, payers, employers, and law enforcement officials, all of whom have an interest in ensuring that all medications reach only the people for whom they have been legitimately prescribed. To this end, the purposes of this review were to summarize published, English-language biomedical evidence pertaining to the epidemiology and costs of prescription opioid analgesic misuse and abuse in the United States and to discuss efforts to reduce the burden of opioid abuse and misuse.

Methods

Published English-language articles on the economics and epidemiology of misuse, abuse, or diversion of prescribed opioid analgesics in the United States were identified by searching PubMed, Web of Science, the Cumulative Index to Nursing and Allied Health Literature database (CINAHL), EconLit, and PsycInfo, using Medical Subject Heading terms where possible. Search terms used initially were (economics OR epidemiology) AND (misuse OR abuse) AND opioid. Manual searches were also performed for articles, related papers, and government websites. The bibliographies of identified articles were also searched. Studies focusing on illicit rather than prescription opioids were excluded. Since the goal of this review was to consider relatively recent estimates, the search was limited to publications from 1995 to July 2009 for each dataset.

Results

The initial search identified 2,347 articles published from 1995 through July 2009 (Figure 1). Of those articles, 2,128 were published in English, and 913 were studies examining the topic in the United States. Analyses of prescription opioids accounted for 166 of the remaining studies, all of which were evaluated by examining the titles and abstracts. Forty-one articles were identified for the current analysis.

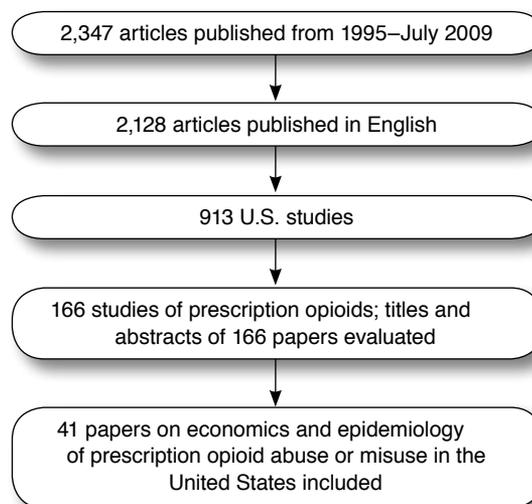
Epidemiology

Estimating the incidence, prevalence, and consequences of opioid misuse, abuse, and diversion from the biomedical literature is challenging, in part because of variable definitions and approaches to counting events. Nonetheless, there have been documented increases in the number of opioid medication prescriptions written and in some measures of misuse and abuse of these drugs²³⁻²⁹

In an analysis of drug abuse-related emergency room admissions data collected by the Drug Abuse Warning Network (DAWN) and the Automation of Reports and Consolidated Orders System (ARCOS) from 1990 to 1996, Joranson et al. (2000) concluded that increasing medical use during the period studied did not contribute to increases in the adverse health outcomes related to prescription opioid abuse.²³ During this interval, while medical use of morphine, fentanyl, oxycodone, and hydromorphone increased by 59%, 1,168%, 23%, and 19%, respectively, the number of prescription opioid abuse mentions in the DAWN data increased by only 6.6%, and the proportion of total opioid abuse mentions relative to total drug abuse mentions decreased from 5.1% to 3.8%.

In a follow-up study using data from the U.S. Drug Enforcement Agency and DAWN, Gilson et al. (2004) observed that medical and nonmedical use of fentanyl, hydromorphone, morphine, and oxycodone increased from 1997 to 2002, with the largest increases observed for oxycodone (402.9%) and fentanyl

FIGURE 1 Flow Diagram of Study Identification, Inclusion, and Exclusion



(226.7%).²⁴ The rise in opioid prescribing likely represents a response by clinicians to literature and clinical practice guidelines calling attention to the prevalence of undertreated pain.^{2-8,30,31} Mentions of fentanyl abuse increased the most (641.9%), followed by oxycodone (346.9%), hydromorphone (341.6%), and morphine (113.5%).²⁴

In 2006, data from the National Survey on Drug Use and Health indicated that approximately 5.2 million individuals reported using prescription analgesics nonmedically during the previous month—an increase, although not statistically significant, from the 4.7 million individuals recorded in the previous year.³² This estimate included 2.2 million new nonmedical users in 2006—533,000 of whom used controlled-release oxycodone. In this analysis and that of the prior year, more than half of prescription analgesics used nonmedically were obtained from friends or relatives.³³ Findings from the National Survey of American Attitudes on Substance Abuse XIII: Teens and Parents, published in 2008, address the availability of prescription opioids for abuse.³⁴ In this survey, “painkillers” were considered the most popular prescription drug class to abuse, preferred by 46% of teen respondents. Teenagers also reported that prescription medicines were generally readily available, with 31% coming from friends, 19% from parents, and 15% from the home. Additionally, for the first time in 13 years, teens reported that prescription drugs were easier to obtain than beer.

In 2006, Paulozzi et al. published 3 studies examining the link between opioid drug use and deaths from 1979 to 2002.²⁵⁻²⁷ The first study used mortality data from the National Center for Health Statistics (NCHS) to survey all deaths coded as poisoning due to legal and illegal drugs other than alcohol or tobacco.²⁵ The

death rate for unintentional, suicidal, and undetermined drug poisoning increased by 140.8% from 1990 to 2002. While specific rates were not explicitly listed, unintentional drug poisoning mortality increased by 217.6%; suicidal drug poisoning increased by 10.8%; and undetermined drug poisoning mortality increased by 193.4% over this time period. The number of deaths due to total opioid analgesic poisoning on death certificates, including events with or without heroin or cocaine, also increased by 91.2% from 1999 to 2002.²⁵ In the second analysis, Paulozzi estimated the degree to which prescription opioid analgesics were involved in deaths in U.S. urban areas from 1997 to 2002, using DAWN medical examiner and coroner surveillance system data.²⁶ The number of deaths related to all drugs increased by 27.2%, and reports of deaths attributable to prescription opioid analgesics increased by 96.6%. In the third study, Paulozzi and Ryan assessed NCHS data to determine whether variability in the rate of sale of prescription opioid analgesic use was related to the variability in rates of drug poisoning mortality in 2002.²⁷ Oxycodone and methadone were implicated most frequently as potential contributors to drug-related mortality, although these estimates do not account for drug theft prior to the prescription being filled.²⁸

In a study to address the contribution of drug crime to the availability of opioid analgesics, Joranson and Gilson (2005) estimated diversion of fentanyl, hydromorphone, meperidine, methadone, morphine, and oxycodone for nonmedical use in the United States in 22 eastern states from 2000 to 2003.²⁸ These investigators found that during the study period, nearly 28 million dosage units were diverted from 22 eastern states, mainly from pharmacies. Oxycodone accounted for the largest number of diverted dosage units (4.43 million), while the largest increase was seen with fentanyl (161.3%). The authors concluded from these data that drug theft prior to dispensing is an important contributor to the availability of opioids for nonmedical use.

Studying prescription opioid use and abuse from 233 drug treatment centers in urban, suburban and rural areas across the United States from the fourth quarter of 2003 through the end of the third quarter of 2006, Cicero et al. (2007) reported measures of patient exposure, rates of abuse per 1,000 patients filling a prescription for an opioid, and rates of abuse per 100,000 population for each drug in the zip codes monitored.²⁹ These authors found that hydrocodone and immediate-release oxycodone products were the most frequently prescribed opioid analgesics in their catchment area, followed by extended-release oxycodone, morphine, methadone, fentanyl, hydromorphone, and buprenorphine. When abuse was measured as cases per 1,000 patients, the highest rates were observed with buprenorphine, extended-release oxycodone, hydromorphone, and methadone, although specific rates were not reported. The number of abuse cases per 100,000 population was highest for extended-release oxycodone and hydrocodone.

People who abuse prescription opioids may also be at risk for more hazardous routes of administration, including intravenous use, with its increased risk for hepatitis and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS).³⁵⁻³⁷ In a 2004 retrospective chart review of patients admitted to an inpatient treatment unit for addictive disease, patients addicted to oxycodone CR (n=187) tended to progress from oral administration at first use (83%) to snorting or intravenous use by the time of hospital admission (88%), an average of 19.2 months later.³⁵ Similarly, other researchers studying patients admitted to inpatient substance abuse treatment units have reported that the route of administration tended to move from oral use (intact or chewed), to snorting, and then to intravenous use.^{36,37}

Economics

The economic burden of prescription opioid misuse and abuse is only part of the larger drug abuse problem in the United States. According to a study prepared for the Office of National Drug Control Policy, the cost of drug abuse in the United States in 2002 was estimated to be \$180.8 billion.³⁸ This estimate included resources used to address health and crime consequences and loss of productivity resulting from disability, death, and withdrawals from the workforce but does not specify the contribution of illicit use of prescription opioid analgesics to the total economic burden, as this was not feasible given the data source.

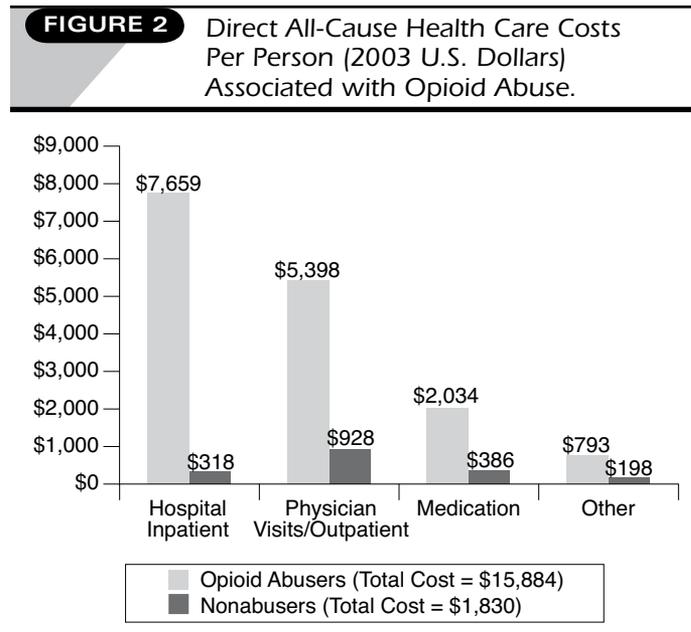
In an effort to assess the direct medical costs of prescription and nonprescription opioid abuse among insured individuals, White et al. (2005) conducted a retrospective cohort study using data from 1998 to 2002.³⁹ Opioid abusers were defined as persons aged 12-64 years, who were continuously enrolled in health care plans for at least 6 months before and after the index date (the first observed date of diagnosis of opioid abuse), and who had at least 1 claim with at least 1 of these ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) codes: 304.0 (opioid-type dependence), 304.7 (combinations of opioid abuse with any other drug dependence), 305.5 (opioid abuse), and 965.0 (poisoning by opiates and related narcotics). Poisoning by heroin (ICD-9-CM 965.01) was specifically excluded. These individuals were then randomly matched to individuals who were not diagnosed as opioid abusers, but who had at least 1 prescription claim during the analysis period. Matching was done on the basis of gender, age, employment status, and census geographic region in a 3:1 ratio.

In this analysis, abusers consumed more medical services and more prescription drugs than nonabusers. Abusers were 78 times more likely to have had an episode of nonopioid poisoning; 36 times more likely to have hepatitis A, B, or C; 43 times more likely to have other substance abuse diagnoses; 21 times more likely to have had pancreatitis; and 8.5 times more likely to have a psychiatric diagnosis compared with nonabusers. From these data, it cannot be determined whether the additional use of resources

or higher prevalence was attributable to opioid abuse. It is notable that, although the authors matched the sample of persons defined as abusers with members of the comparison group by several demographic factors, large between-group differences in rates of comorbid conditions remained, suggesting that these results may be affected by confounding. Within this analysis, mean annual direct costs in 2003 U.S. dollars were estimated to be \$15,884 per abuser and \$1,830 per nonabuser (Figure 2).³⁹

White et al. also conducted subgroup analyses to explore the potential for overlap between dependence and abuse, since dependence is neither a necessary nor sufficient characteristic of abuse or addiction.⁴⁰ In these sensitivity analyses, in which the investigators identified nonmutually exclusive subgroups of patients diagnosed either with abuse or with dependence or poisoning, persons in the abuse subgroup had total mean per-patient direct health care costs of \$18,388, compared with \$2,210 for a matched comparison group.³⁹ Per-patient costs in the dependence/poisoning group were \$16,204, and matched comparison group subjects incurred costs of \$2,179. White et al. noted that the ratios of direct all-cause health care costs of persons in the abuse or dependence/poisoning groups to those in their respective comparison groups were similar (ratios of 8.3 and 7.4, respectively) and that costs incurred by persons in the abuse subgroup were apparently higher than those in the dependent/poisoning subgroup. However, they also noted that these findings should be interpreted carefully, keeping in mind that the term “opioid abuse” is sometimes used to mean different things. Additionally, the authors noted that, based on the definitions used, the estimates they reported ranged from \$15,884 to \$18,388 per person in the abuse cohort, and \$1,830 to \$2,210 per matched control. Furthermore, when examined by category, inpatient expenditures accounted for 46% of total costs for abusers and 17% for nonabusers. Additionally, opioid abusers were 4 times as likely to visit the emergency room, had 12 times as many hospital stays, and 63 times as many outpatient visits than nonabusers. Despite the magnitude of these observed differences, it remains important to note that costs and resource use were not necessarily directly attributable to drug abuse and that substantial differences between patient groups remained, even after matching.

Birnbaum et al. (2006) conducted a broader analysis of the costs of prescription opioid abuse, separately analyzing health care, workplace, and criminal justice expenditures using data derived from the Substance Abuse and Mental Health Services Administration (SAMHSA), other governmental sources, and a proprietary claims dataset.⁴¹ In this study, the total economic burden was estimated at \$8.6 billion in 2001 dollars. Workplace costs constituted 53% of the total (\$4.6 billion) and were related to reduced wages, lower employment, and loss of productivity of workers who abused prescription opioids. Local, state, and private health care costs together accounted for 30% of the total burden identified in this study (\$2.6 billion). Of this propor-



Adapted from White et al. Direct costs of opioid abuse in an insured population in the United States (2005).³⁹

tion, 95.2% was identified as excess medical costs (defined as the average cost of medical care for a patient with a prescription opioid abuse disorder minus that for a patient without such a disorder). Although criminal justice costs accounted for 17% of the total (\$1.4 billion), costs of substance abuse treatment were not included in these analyses.⁴¹

Efforts to Reduce the Burden of Drug Misuse and Abuse

Numerous studies and clinical practice guidelines published over the last 4 decades have documented that undertreatment of pain is relatively common in the United States.²⁻⁸ Furthermore, this analgesia gap will likely increase as the U.S. population ages and as the incidence and prevalence of conditions that are either painful or for which pain is an important dimension increases. For example, survival rates for people with many types of cancer are increasing.^{42,43} A substantial proportion of these people have persistent pain as a result of their disease or its treatment and will need long-term pain management. Yet, as health care providers, payers, and policy makers, we must balance the need for adequate pain relief against the risk of diversion, misuse, and abuse.

Several approaches for reducing opioid misuse and abuse are already in practice, each with its own benefits and risks. For example, multicopy or serially numbered prescriptions can serve as a monitoring tool but add to administrative infrastructure and serve as a barrier to appropriate pain management by discouraging some practitioners from prescribing drugs that require such tools. Patient-clinician agreements can help define the expectations and responsibilities of the prescriber and patient, but

they should not be viewed as a panacea. Clinical questionnaires and screening tools are generally useful but are not foolproof in identifying individuals at risk for misusing or abusing opioid analgesics. Because no one tool is ideal in all situations, a combination of approaches will most likely be required.

On the supply side, enhanced efforts to monitor the location of controlled substances at each step from manufacturer to pharmacy, such as radio tagging each dosage unit, may be useful. As mentioned previously, information from the Drug Enforcement Administration's theft/loss database indicates that 22 states reported the loss of almost 28 million dosage units between 2000 and 2003.²⁸ Making theft of these drugs from pharmacies, wholesalers, and manufacturers more difficult is an important step toward reducing misuse and abuse.

Developing drug formulations that resist common methods of tampering is another step that may help reduce prescription opioid misuse and abuse. In 2003, the College on Problems of Drug Dependence discussed potential strategies to reduce abusability of prescription opioid analgesics.⁴⁴ These efforts include adding an antagonist, such as naloxone, or naltrexone, to reduce activity if the drug is dissolved and injected or adding a substance that can induce unpleasant side effects when the drug is taken in excess. Examples of agonist-antagonist combinations have evolved over time from Talwin NX (approved in 1982), which combines pentazocine with naloxone, to Suboxone (approved in 2002), which combines buprenorphine with naloxone.^{45,46} The rates of DAWN emergency room mentions of pentazocine per million prescriptions decreased by 70%, and medical examiner mentions by 71%, in the 2 years following the introduction of Talwin NX.⁴⁵ Similarly, a study of data from regional poison control centers reported that the average quarterly ratio of abuse cases per 1,000 prescriptions dispensed in 2003-2005 was 0.16 for buprenorphine/naloxone.⁴⁶

Other technological approaches that interfere with dosage form tampering are also being developed, including Embeda, an extended-release morphine with a sequestered naltrexone core, and Acurox, which combines immediate-release oxycodone and niacin, as well as excipients that form a viscous gel when dissolved, making extraction of the oxycodone difficult. Other efforts to resist grinding, extraction, or other manipulation of a dosage form include oxycodone formulations such as Remoxy, ReXista SR, as well as DETERx and EDACS, which are technologies designed to be resistant to mechanical manipulation and chemical challenge.⁴⁷⁻⁵⁰

Until these drugs are available and well studied, their ultimate effect on misuse and abuse will not be known, but it makes sense that the effects of the new dosage-form technologies on opioid abuse or misuse will be tied to the effectiveness of the deterrence mechanism, the availability of nonresistant formulations, how widely these drugs are prescribed, and for which patients they are prescribed, among other factors.⁵¹ In short, however, the argument for use of abuse-deterrent dosage forms depends

almost entirely on their clinical equivalence to traditional dosage forms and safety data. If the newer drugs are less efficacious, or if there is limited effect on abuse or misuse, widespread adoption will be less likely. Price will be mainly important if effectiveness and safety appear to be similar to existing products, particularly since the newer dosage forms will probably be more expensive than generics that are now available. Even if costs of the newer products are partially offset by decreases in the societal burden of misuse, abuse, and diversion, it is difficult to predict whether this reasoning will influence health care purchasers and payers to include these drugs on their formularies. It seems more likely that a combination of factors, including U.S. Food and Drug Administration policies and the evolution of technology, will be important in determining the selection of opioid formulations.

Limitations

As with all analyses, this review has limitations. Assessing the epidemiology and economics underlying opioid misuse or abuse is challenging and subject to potential confounding, selection, and information biases. Furthermore, the data are limited; the causal relations are complex; and it can be difficult to know where appropriate use of prescription opioids ends and inappropriate use begins. Despite these difficulties, the general agreement among published estimates argues against a strong effect of these potential biases. Furthermore, although epidemiologic estimates of opioid use and abuse are important, there remains a potential for these estimates to mislead. The data from the Cicero²⁹ and Paulozzi²⁵⁻²⁷ studies are logically clear, but incomplete, since the authors do not take theft into consideration in their estimates. Drug abuse can occur not only when a patient at risk for addiction is exposed to a certain drug, but also at any juncture when drugs are diverted to individuals for whom they are not medically intended.²⁸ The 2006 SAMHSA report that more than 70% of nonmedical prescription opioids that are abused come from friends or family illustrates this point.³³ Every study prompts questions for future studies to address. Among the questions prompted by these findings is the relative contribution played by the types of opioid abuse and misuse to the overall scope of the problem.

Conclusions

Prescription opioid misuse and abuse are increasingly prevalent in the United States and the economic burden these phenomena impose is substantial. As a result, it is essential to balance the treatment needs of patients with pain with efforts to decrease misuse and abuse of pain medications. To accomplish this goal, it will be important to make use of all the tools at our disposal, including careful consideration of the patient's needs; patient, provider, and payer education; screening for aberrant drug-related behaviors; and use of technology to interfere with common forms of prescription drug manipulation and disruption.

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