

# Trends in prescriptions for oxycodone and other commonly used opioids in the United States, 2000-2010

Kristen Kenan, Karin Mack, Leonard Paulozzi

## ABSTRACT

**Background:** Little information has been published on opioid prescribing practices in the United States as a whole for any year since 2005, despite increased use and increased overdoses. The objective of this study was to describe trends in prescribing rates and prescription sizes for commonly used opioids over the past decade.

**Methods:** We used 2 data systems. Vector One: National (VONA; data obtained for the period 2000–2009) is a service that can estimate the number of prescriptions dispensed by retail pharmacies. The Automation of Reports and Consolidated Orders System (ARCOS; data obtained for the period 2000–2010) is a mandatory reporting system that allows the US Drug Enforcement Administration to monitor certain controlled substances from the point of manufacture to the point of sale. ARCOS data represent the amount of controlled substances legitimately distributed at the retail level. We calculated crude prescription rates of various opioids from VONA data, total drug amounts distributed (as milligrams per 100 persons) from ARCOS data and morphine milligram equivalents (MME) per prescription by combining data from these 2 sources.

**Results:** The number of opioid prescriptions per 100 persons increased by 35.2%, from 61.9 to 83.7, during the period 2000–2009. The distribution of opioids to US pharmacies, in milligrams per 100 persons, increased by at least 100% for all selected opioids during the period 2000–2010. The average size of an oxycodone prescription increased by 69.7% (from 923 MME to 1566 MME) during the same period, while the average size of a hydrocodone prescription increased by 69.4% (from 170 MME to 288 MME). The increase for fentanyl was smaller (20.9%) (from 4804 MME to 5809 MME).

**Interpretation:** The rate of opioid prescribing, the amount of opioids distributed and the average prescription size all increased markedly in the United States over the past decade. Rates of death from opioid overdose also have increased steadily through 2008 and have likely continued to increase in subsequent years. Effective measures to prevent prescription drug overdoses have yet to be identified and employed.

**Kristen Kenan**, MD, MPH, is a resident with the Department of Pediatrics, University of Chicago Medical Center, Chicago, Illinois, USA. **Karin Mack**, PhD, is a behavioural scientist at the Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention, Atlanta, Georgia, USA. **Leonard Paulozzi**, MD, MPH, is a medical epidemiologist at the Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention, Atlanta, Georgia, USA.

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**Correspondence:** Karin Mack, 4770 Buford Hwy NE F62, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention, Atlanta, GA 30341 USA; [kmack@cdc.gov](mailto:kmack@cdc.gov)

➤ **THE INCREASING USE OF OPIOID ANALGESICS** for treatment of pain has been attributed in part to the liberalization of laws governing opioid prescribing for the treatment of chronic noncancer pain, the aggressive marketing efforts of the pharmaceutical industry and the introduction of new pain management standards.<sup>1,2</sup>

Before 1990, physicians in the United States took a minimalist approach to treating chronic noncancer pain with opioid analgesics; however, opioids such as oxycodone and hydrocodone are now prescribed to 1 in 25 adults for treatment of chronic pain.<sup>3–5</sup> The current extent of use of opioid analgesics in the United States is unprecedented in

the country's history and unparalleled anywhere in the world. In 1990, the world's population consumed 4 tons (3628 kg) of hydrocodone. By 2009, annual worldwide consumption had risen to 39 tons (35 380 kg), 99% of which was consumed by Americans. Similarly, 3 tons (2722 kg) of oxycodone was consumed worldwide in 1990, and 77 tons (69 853 kg) by 2009, of which Americans consumed 62 tons (56 245 kg; 81%).<sup>6</sup>

Although opioid analgesics are beneficial for the treatment of pain in carefully selected patients, their increased use in the United States has included an increase in nonmedical use. By 2000, investigative news reports revealed patients' inappropriate use of these pain-relieving drugs and their diversion to nonpatients.<sup>7</sup> Fatal and nonfatal overdoses, or poisonings, due to opioid analgesics increased markedly, and the death rate involving opioid analgesics closely tracked sales of these drugs.<sup>8,9</sup> Opioid analgesics are currently the source of more overdose deaths nationwide than heroin and cocaine combined.<sup>8</sup> By 2010 the US National Survey of Drug Use and Health showed that 4.8% of the population over the age of 12 years in the United States (i.e., 12.2 million people) reported using pain relievers nonmedically in the past year.<sup>10</sup> In addition, opioid analgesics are some of the most commonly used drugs for initiation into illicit drug abuse.<sup>10–12</sup>

In the United States, studies using medical claims data for selected populations have shown increases in the annual prescribing rates of opioid analgesics.<sup>13,14</sup> They have also shown a shift toward use of long-acting (LA) or extended-release (ER) opioids<sup>5</sup> and increasing dosages<sup>15,16</sup> through 2005. A similar trend toward increasing use and increasing dosages has been reported for Canada through 2008.<sup>17,18</sup> However, little information has been published on opioid prescribing practices in the United States as a whole for any year since 2005. The objective of this study was to describe trends in prescribing rates, proportions of LA or ER opioids prescribed and size of prescriptions for oxycodone and other commonly used opioids from 2000 through 2010 in the United States. These trends will provide a background for understanding related trends in fatal and nonfatal drug overdoses.

## Methods

**Data sources.** The following data sources were used.

*Vector One: National (VONA).* VONA is a national commercial prescription and patient measurement service that can estimate the number of prescriptions for all prescription drugs dispensed by retail pharmacies.<sup>19</sup> It collects information from 59 000 retail pharmacies, which account for nearly half of the retail prescriptions in the

United States, and uses a proprietary methodology to develop national estimates from these data. The term “retail pharmacy” includes national retail chains, mass merchandisers, pharmacy benefits managers and their data systems, and provider groups. VONA does not collect data for drugs dispensed by hospitals or long-term care pharmacies or via mail order. Prescription counts generated by VONA have been made publicly available,<sup>20</sup> and VONA data have been used in other publications.<sup>21,22</sup>

*Automation of Reports and Consolidated Orders System (ARCOS).* ARCOS is a comprehensive, automated, mandatory reporting system that enables the US Drug Enforcement Administration to monitor certain controlled substances from the point of manufacture, through commercial distribution channels, to the point of sale at the dispensing (retail) level.<sup>23</sup> ARCOS data tally the cumulative sale of licit drugs in grams and reflect the amount of controlled substances legitimately distributed to the retail level (i.e., through pharmacies, hospitals and practitioners). Manufacturers and distributors of bulk and/or dosage form-controlled substances must report inventories, acquisitions and dispositions of controlled substances in Schedules I and II (under the Controlled Substances Act), and narcotic and gamma-hydroxybutyric acid substances in Schedule III. We restricted our analyses to opioid analgesics distributed to pharmacies, to correspond to the scope of the published VONA data. We did not include methadone distributed to opioid treatment programs. We obtained study data through a special request to the Drug Enforcement Administration. Data were available for the period 2000 to 2010, although for the year 2000, data were available for only 2 opioids: oxycodone and hydrocodone.

**Study drugs.** ARCOS data was available only for fentanyl, hydrocodone, hydromorphone, methadone, morphine and oxycodone. In our analysis of VONA data on the number of prescriptions dispensed, we subdivided fentanyl, morphine and oxycodone into ER and immediate-release (IR) formulations. The “LA or ER” category included the ER formulations of these 3 drugs and oxymorphone, along with methadone. The “all others” category in the VONA analysis consisted of oxymorphone, propoxyphene, codeine, tramadol, pentazocine, dihydrocodeine, meperidine, butorphanol, levorphanol and buprenorphine.

**Statistical analysis.** We calculated crude rates of prescriptions per 100 persons from VONA data, drug amounts, in milligrams per 100 persons, from ARCOS data and morphine milligram equivalents (MME) per prescription by

combining the 2 data sources. We had no information on duration of prescriptions or daily dose. Population denominators were post-censal estimates.<sup>24</sup> We used 2 assumptions to calculate MME for the comparison of prescription size: first, that all drugs other than fentanyl are taken orally (with fentanyl being applied transdermally or transmucosally) and second, that the following doses are approximately equianalgesic: fentanyl 0.4 mg, hydrocodone 30 mg, hydromorphone 7.5 mg, methadone 10 mg, morphine 30 mg, and oxycodone 20 mg.<sup>25</sup>

**Results**

The number of prescriptions per 100 persons increased from 61.9 to 83.7 during the period 2000–2009, almost reaching a rate of one prescription per person per year (Table 1). Roughly one-third more opioid prescriptions were dispensed in 2009 than in 2000. The rate for all opioids combined increased each year through 2008. In 2009, the combined rate declined by 0.6 prescriptions per 100 persons, and the proportion of all prescriptions dispensed for LA or ER opioids declined to 8.7%.

The distribution of opioids to US pharmacies in terms of milligrams per 100 persons increased by at least 100% for fentanyl, hydromorphone, methadone and morphine between 2001 and 2010 and for hydrocodone and oxycodone between 2000 and 2010 (Fig. 1). The greatest increases were seen for oxycodone (287.3%), methadone (232.4%) and hydromorphone (227.7%). Oxycodone was consistently the drug for which the largest volume was purchased by pharmacies during the study period, and purchases of this drug accelerated after 2005. After 2005 it accounted for most of the increased distribution (in terms of milligrams per 100 persons) for these opioids. Methadone was the only opioid for which distribution declined in any year from 2007 to 2010.

The average prescription size decreased for hydromorphone, methadone and morphine and increased for other opioids during the study period (Fig. 2). The prescription size for morphine remained consistent at about 3000 MME per prescription throughout the period, with a net decline of 3% by 2009. The size of methadone prescriptions was 4160–4700 MME per prescription until 2007 and declined to 4000 MME in 2008. However, the average size of an oxycodone prescription increased by 69.7% (from 923 MME to 1566 MME) during this period, while the average size of a hydrocodone prescription increased by 69.4% (from 170 MME to 288 MME). The increase for fentanyl was smaller (20.9%) (from 4804 to 5809 MME).

**Table 1**  
**Extent of use of opioid analgesics (as number of prescriptions per 100 persons) dispensed by retail pharmacies in the United States, based on data from Vector One: National (commercial prescription and patient measurement service), 2000–2009**

Year	Fentanyl ER	Fentanyl IR	Hydrocodone	Hydromorphone	Methadone	Morphine ER	Morphine IR	Oxycodone ER	Oxycodone IR	All others	All opioids	ER or LA, % of total
2000	0.61	0.01	27.79	0.18	0.30	0.45	0.26	1.94	6.06	24.28	61.88	5.3
2001	0.82	0.02	29.41	0.20	0.42	0.53	0.27	2.30	6.63	23.57	64.17	6.3
2002	1.03	0.05	30.45	0.25	0.56	0.65	0.32	2.16	7.10	22.57	65.15	6.8
2003	1.28	0.09	31.76	0.29	0.75	0.77	0.36	2.27	7.79	21.69	67.04	7.6
2004	1.40	0.11	33.70	0.34	0.95	0.95	0.40	2.15	8.52	21.28	69.80	7.8
2005	1.45	0.12	36.00	0.41	1.16	1.09	0.40	2.17	9.49	21.15	73.44	8.0
2006	1.59	0.12	38.23	0.47	1.31	1.25	0.40	2.33	10.34	21.14	77.17	8.4
2007	1.72	0.11	40.11	0.54	1.39	1.39	0.43	2.50	11.52	21.59	81.31	8.6
2008	1.77	0.10	40.92	0.62	1.46	1.59	0.47	2.57	12.79	22.06	84.34	8.8
2009	1.64	0.08	40.10	0.71	1.44	1.68	0.42	2.52	13.62	21.49	83.70	8.7
% change from 2000 to 2009*	167.2	890.9	44.3	293.4	373.2	274.6	62.2	29.8	124.8	-11.5	35.3	NA

ER = extended-release formulation, IR = immediate-release formulation, LA = long-acting (applies only to methadone), NA = not applicable.  
\*Percent change was calculated from numbers more precise than those shown in the table.

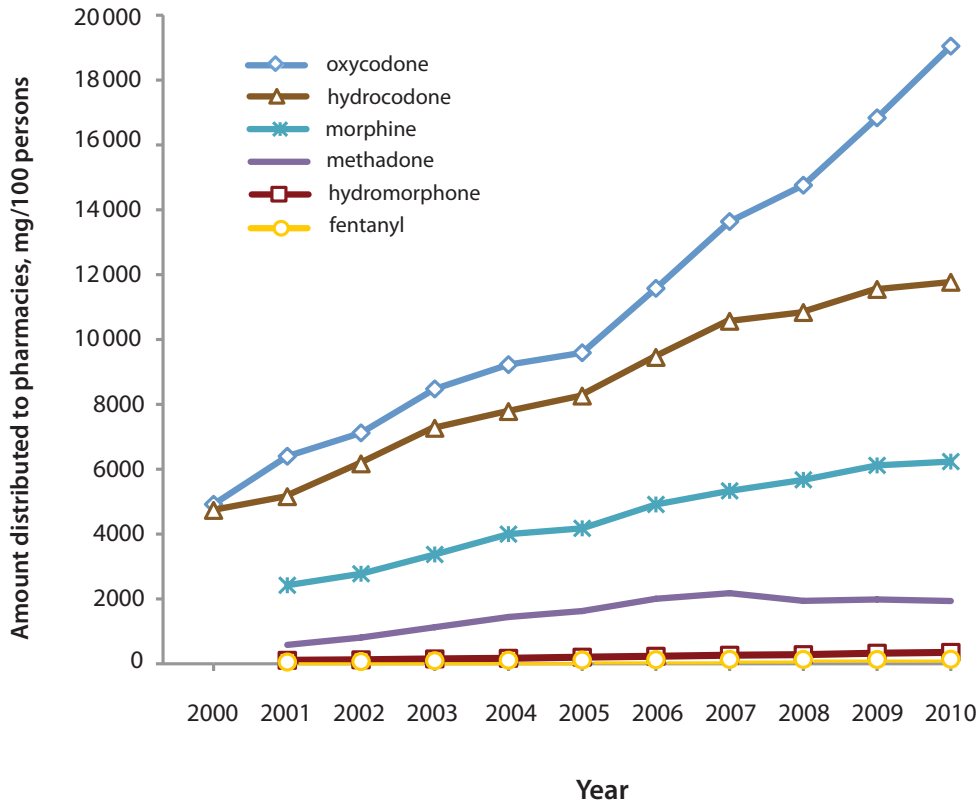


Figure 1  
Distribution of selected opioids to US pharmacies (in milligrams per 100 persons). Based on data from the Automation of Reports and Consolidated Orders System, 2000–2010.

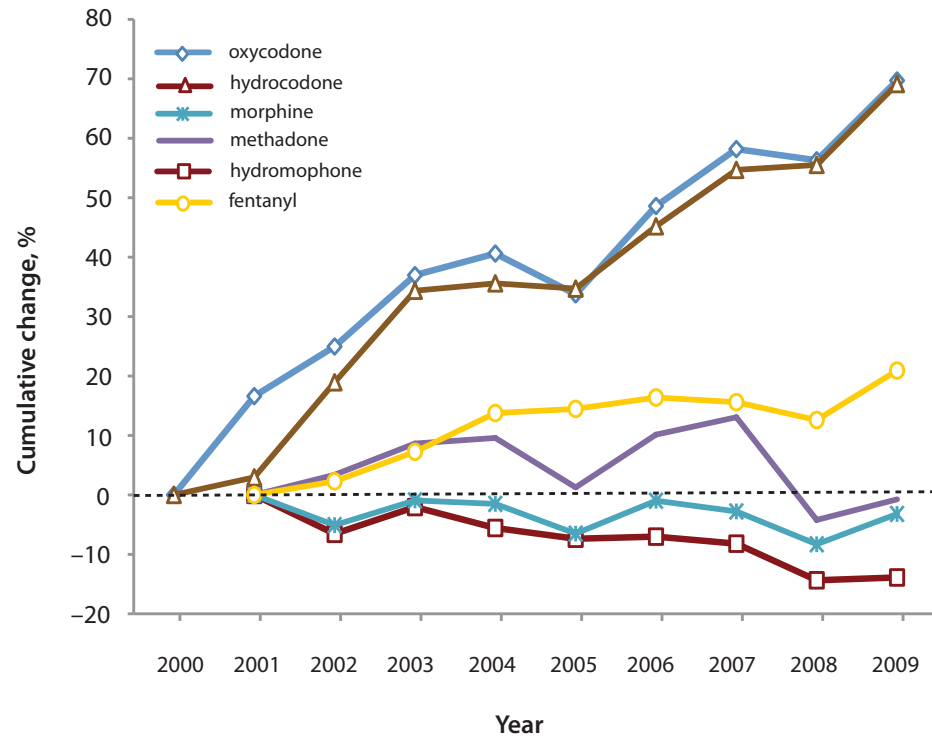


Figure 2  
Percent change in size of prescriptions (based on amounts in milligrams) for selected opioid analgesics in the United States. Based on data from Vector One: National and Automation of Reports and Consolidated Orders System, for 2000–2009.

### Interpretation

Our analyses of the VONA and ARCOS data systems expand the description of trends previously reported on the basis of more limited cohort studies,<sup>13–16</sup> which made use of medical claims data as well as previous releases of ARCOS data. The VONA data showed a steady increase in the population-based rate of prescribing of

opioid analgesics, with stabilization by 2009. However, the ARCOS data showed that the amount of opioid analgesics (in milligrams per 100 people) more than doubled through 2010. Taken together, these 2 data systems indicate an overall increase in the size of each prescription, especially for hydrocodone and oxycodone.

Our data, however, do not allow us to determine whether the increase in prescription size resulted from an increase in the number of days per prescription or an increase in the daily dosage. A shift to a higher proportion of ER formulations for a given type of opioid could increase the average number of days per prescription, since ER opioids tend to be prescribed more often for chronic pain. (The mean number of days of therapy per prescription during this decade was 8–21 for IR opioids and 23–28 for LA or ER opioids.<sup>20</sup>) The data did show a shift toward use of ER formulations of fentanyl, which might explain the increase in the size of fentanyl prescriptions. However, the proportion of oxycodone prescriptions that was for the ER formulation declined, so the increase in the average size of oxycodone prescriptions was not likely due to an increase in the number of days per prescription.

The values that we obtained for prescription size are consistent with other data sources, where comparisons are possible. For example, the average prescription size for hydrocodone in 2009 was 288 MME, which would represent a daily dosage of 14–36 MME over the range of 8 to 21 days typical for prescriptions of such IR opioids. The average oxycodone prescription in 2009 was 1566 MME. If all oxycodone had been dispensed in IR formulations the daily dosage would have ranged from 75–195 MME if the typical duration of IR opioids (8–21 days) is assumed. If all had been dispensed in ER formulations, the daily dosage would have been 56 MME if the typical duration for ER opioids (28 days) is assumed. In one large US study for the period 1997–2005, the mean daily dosage for prescribed opioids was 30–60 MME.<sup>26</sup> The increase in prescription size that we observed is also consistent with the literature. In the workers' compensation population in Washington State, the average daily dose increased from 88 to 132 MME/day over the period 1996–2002.<sup>15</sup> The mean daily dosage in the Arkansas Medicaid population declined from 54 to 50 MME from 2000 through 2005, but the median number of days supply of opioids per year increased from 25 to 38.<sup>16</sup>

The most concerning finding was the continuing trend toward greater use of opioid analgesics in general, and LA or ER opioids in particular, in the United States. Usage and prescription size have increased, despite growing awareness of the individual and social costs associated with opioid misuse and abuse. Chou and colleagues<sup>27</sup> concluded that long-term opioid therapy can be effective for patients who are carefully selected and monitored. However, these authors<sup>27</sup> and others<sup>28–30</sup> have also cautioned that opioids may be associated with potentially serious harms, including adverse effects,

abuse and overdose. The Drug Abuse Warning Network has reported steady increases in emergency department visits involving the nonmedical use of opioid analgesics, especially oxycodone, through 2009.<sup>31</sup> In 2010, the percentage of respondents to a national survey reporting past-year initiation of illicit use of pain relievers (0.8%) rivalled that for marijuana (1.0%) and was higher than that for cocaine (0.3%), heroin (0.1%) and hallucinogens (0.5%).<sup>10</sup> Nonmedical use of these drugs has deleterious effects on both health and social outcomes. For example, the economic cost of nonmedical use of prescription opioids in the United States has been estimated to total more than US\$50 billion annually.<sup>32</sup>

The rising trends in opioid use portend increasing rates of a serious health outcome, death by overdose. Measures of opioid use have been strongly correlated with the numbers of opioid-related overdoses,<sup>8,33</sup> and higher daily dosages have been recently associated with greater risk of overdose death.<sup>17,34–36</sup> The latest available data indicate an increase in opioid-related deaths in the United States through 2008,<sup>9</sup> and the results of the current study suggest that such deaths have probably continued to increase through 2010.

The only encouraging sign to date is the decline in the volume of methadone prescribed after 2007, which might have been a result of the publicity regarding overdose deaths, the revised dosage instructions and a warning placed on the drug by the US Food and Drug Administration in 2006, or the voluntary restriction, as of 1 Jan. 2008, of the highest-strength (40-mg) formulation to hospitals and facilities authorized for detoxification and maintenance treatment of opioid addiction.<sup>37,38</sup> Otherwise, these data reveal no measurable effects of educational initiatives to induce physicians and other providers to prescribe more judiciously or of regulatory efforts to reduce the nonmedical use of opioids during the 10 years since the problem first came to public attention in the United States.

The results of this study should be interpreted in light of some limitations. The VONA system is limited by its inability to capture prescriptions written and dispensed by authorized dispensing providers. Its estimation methods are proprietary and therefore cannot be validated. One limitation of the ARCOS data is an over-representation of drug consumption, because unknown quantities are used for veterinary purposes. Another limitation is that the system includes amounts re-ordered to replace drugs stolen from pharmacies or other retail-level dispensers, as well as amounts distributed to the retail level that were not actually dispensed to or consumed by patients in the same year. No evaluation of the completeness of ARCOS

data has been published. This study examined different parts of the distribution chain of the licit opioid supply (sales to pharmacies and prescriptions) and did not directly assess individual use of opioid analgesics. Previous work, however, supports the connection between sales of opioid analgesics and associated death rates.<sup>8</sup> We also do not know the precise duration of each prescription.

The ongoing problem with opioid overdoses in the United States should serve as a warning to other countries with growing consumption of opioid analgesics, such as Canada, Australia and Great Britain,<sup>6</sup> which are also experiencing increases in prescription drug abuse, overdoses and deaths.<sup>18,39,40</sup> Effective measures to address prescription drug overdoses have not been established in the United States. Helpful first steps, however, should be multifaceted and should involve a wide range of stakeholders in surveillance, improvement of clinical practice and policy changes. Continued assessment of such surveillance data will be critical both in forecasting trends in drug overdoses and in assessing the impact of prevention measures. We also need to enhance our capacity to understand the epidemic through studies of risk factors, including examining the prescription histories of people who die from prescription drug overdoses to determine the specific factors, such as high daily dosage or nonmedical use, that might contribute to overdose deaths. As regulators of health care practice, states are in a better position than federal agencies to monitor and correct inappropriate and illegal prescribing. For example, data from state prescription drug monitoring programs and insurance claims data can be used to identify and address opioid misuse and abuse by patients, as well as inappropriate prescribing by providers. State professional licensing boards can work with health care societies to develop evidence-based standards for appropriate opioid prescribing and can take action against prescribers who are practising outside of this standard of medical care. Law enforcement agencies should take action against illegal activities, such as providers prescribing large quantities of opioids solely for profit (i.e., so-called “pill mills”). In addition, the federal government can support the enhancement and adoption of best practices for state prescription drug monitoring programs and can work with individual states to identify stable funding sources for these programs. These interventions must be evaluated further, and new interventions need to be developed. The findings in this article, coupled with the increasing number of deaths involving prescription opioids, underscore the importance of a concerted, collaborative approach.

**Contributors:** Kristen Kenan compiled the data, performed the data analysis, participated in developing the study methodology and was the principal writer of the manuscript. Karin Mack oversaw the data collection and participated in developing the study methodology and in all phases of writing and editing the manuscript. Leonard Paulozzi conceived the project, oversaw the data collection and analysis, participated in finalizing the study methodology, participated in all phases of writing and editing the manuscript and is the study guarantor.

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