Economic Costs of Nonmedical Use of Prescription Opioids

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Objectives: Although the economic costs of substance misuse have been extensively examined in the published literature, information on the costs of nonmedical use of prescription opioids is much more limited, despite being a significant and rapidly growing problem in the United States.

Methods: We estimated the current economic burden of nonmedical use of prescription opioids in the United States in terms of direct substance abuse treatment, medical complications, productivity loss, and criminal justice. We distributed our broad cost estimates among the various drugs of misuse, including prescription opioids, down to the individual drug level.

Results: In 2006, the estimated total cost in the United States of nonmedical use of prescription opioids was $53.4 billion, of which $42 billion (79%) was attributable to lost productivity, $8.2 billion (15%) to criminal justice costs, $2.2 billion (4%) to drug abuse treatment, and $944 million to medical complications (2%). Five drugs—OxyContin, oxycodone, hydrocodone, propoxyphene, and methadone—accounted for two-thirds of the total economic burden.

Discussion: The economic cost of nonmedical use of prescription opioids in the United States totals more than $50 billion annually; lost productivity and crime account for the vast majority (94%) of these costs.

Key Words: prescription opioid misuse, nonmedical opioid use, abuse, opiates, oxycodone

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Although the economic costs of substance misuse have been extensively examined in the published literature, information on the costs of nonmedical use of prescription opioids is much more limited, despite the fact that it is a significant and rapidly growing problem in the United States.[1] Between the years 1999 and 2006, the number of deaths in the United States related to poisoning increased by 85% (from 20,000 to 37,000 annual deaths), with the largest increase attributable to opioid analgesics.[2] The National Survey of Drug Use and Health (NSDUH)

(formerly, the National Household Survey on Drug Abuse) estimated that, between 2001 and 2006, the number of persons using prescription pain relievers (in almost all instances opioids) for nonmedical purposes increased from 3.5 million to 5.2 million.[3] The numbers of patients seen in emergency rooms, admitted to hospital for the treatment of misuse of opioid analgesics, and dying from unintentional overdose of these agents correspondingly increased over this period.[3]

The most recent study in this area presented estimates of the cost of misuse of prescription opioid analgesics in the United States in 2001.[4] However, this study did not present cost estimates specific to individual prescription opioids. Furthermore, the data from this study are almost a decade old, and the prevalence of nonmedical use of prescription opioids and adverse outcomes related to such use has increased substantially since then.

The objective of this study was to estimate the economic burden in the United States resulting from nonmedical use of prescription opioids, using recent data from NSDUH to attribute estimates of national costs to individual drugs of misuse.

METHODS

To characterize the economic burden of the nonmedical use of prescription opioids in the United States, we used techniques of prevalence-based cost-of-illness ascertainment.[4] As is customary in such studies, economic burden was assumed to consist of both direct (medical and nonmedical) and indirect costs. Estimates of direct economic burden are intended to reflect the opportunity cost of "resources used" in the treatment of opioid misuse and its sequelae (and therefore not available for other uses). Estimates of indirect economic burden are intended to reflect the value of "lost resources" (ie, forgone productivity) as a result of opioid misuse and their sequelae. In tallying direct and indirect economic burden, both societal and healthcare systems perspectives were used.

We examined the economic burden associated with the nonmedical use of prescription opioids in terms of 4 major categories: substance abuse treatment, medical complications, productivity loss, and criminal justice. Figure 1 details our analytic approach. Within each subcategory of costs, the proportion attributable to individual prescription opioids was identified using category-specific estimates or proportions derived from NSDUH. The description that follows summarizes our efforts, however a detailed technical appendix (Supplemental Digital Content 1, http://links.lww.com/CJP/A18) is available, which presents NSDUH variables used in the analysis.

NSDUH captures data on 60,000 to 70,000 persons annually (or about 0.022% to 0.023% of the total US population). Thus, for many questions of interest, the expected number of usable responses—and hence the precision of any
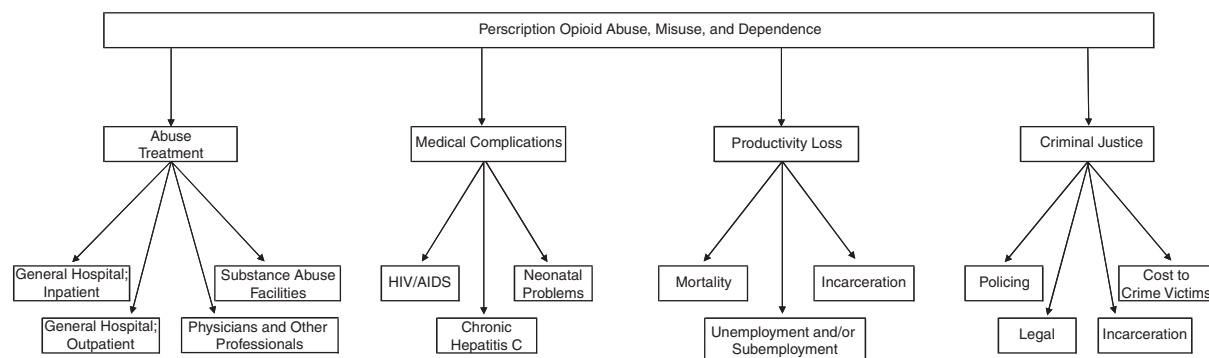
FIGURE 1. Schematic of analytic approach.

resulting estimates—is quite low. Accordingly, to increase precision, we used data from 3 years of the survey (2004 to 2006).[5–7] Response proportions for each year were weighted (using the survey year's sample size) and combined to calculate an overall proportion.

As NSDUH is a complex probability sample, analytic approaches used with data from simple random samples usually are not appropriate. Ignoring the complex design can lead to biased estimates and overstated significance levels. Sample weights and the stratification and clustering of the design must be incorporated into an analysis to obtain unbiased estimates and associated standard errors. Accordingly, to estimate sampling errors, we used the Taylor series (linearization) method within the SAS procsurvey command, using the analysis weights, stratum, and cluster design variables provided within the NSDUH dataset.

Substance Abuse Treatment

To estimate total US expenditures for treatment related to abuse of prescription opioids, we began with published estimates from a report of the Substance Abuse and Mental Health Services Administration of the US Department of Health and Human Services, entitled "National Expenditures for Mental Health Services and Substance Abuse Treatment, 1993-2003."[8] National Expenditures for Mental Health Services and Substance Abuse Treatment provided expenditure estimates for healthcare services related to the diagnosis and treatment of mental health and substance abuse disorders. Estimates for 2003 were inflated to 2006 price levels using the medical care component of the Consumer Price Index (CPI).[9] Data from the pooled 2004 to 2006 NSDUH were then used to apportion expenditure estimates into those attributable to the nonmedical use of prescription opioids versus all other drugs of misuse and, for the former, among various prescription opioids.

Medical Complications

Medical complications associated with nonmedical use of prescription opioids were assumed to consist of HIV/AIDS, chronic hepatitis C, and neonatal care. Costing of these complications is described below.

HIV/AIDS

Our estimate of the direct costs of HIV/AIDS among persons who misuse prescription opioids was based on the most recent analysis of annual direct expenditures for HIV-infected persons in the United States.[10] Bozzette's 1996 cost

estimate was adjusted to 2006 price levels, using the medical care component of the CPI.[9] As the number of persons in the United States infected with HIV has increased substantially during the past decade, the 1996 price-adjusted estimate was further adjusted upward to account for the estimated increase in the number of persons receiving care for HIV infection. This increase was assumed to be proportional to the reported increase in the population of HIV-infected persons (diagnosed and undiagnosed) between 1996 and 2003, with further adjustment for the period 2003 to 2006, assuming a constant rate of increase over the entire period 1996 to 2006.[10,11]

The indirect costs of HIV/AIDS were estimated solely on the basis of HIV/AIDS mortality. Foregone earnings for persons dying of HIV/AIDS in 2006 due to nonmedical use of prescription opioids were estimated based on the age and sex distribution of all persons dying of HIV/AIDS.[12] Discounted future earnings were calculated based on average earnings and mean life expectancy for persons with this age and sex distribution.[13]

To estimate the total percentage of HIV/AIDS cases attributable to intravenous (i.v.) drug abuse, we began with the percentages of persons living with HIV/AIDS in 2006 whose disease was attributable to injection drug use, or male-to-male sexual contact and injection drug use. To this, we added an estimate of the percentage of HIV/AIDS cases attributable to high-risk heterosexual contact with an injecting drug user. This estimate was based on the percentage of heterosexually transmitted cases in 2001 (among all cases with specified subcategory of risk) attributed to sex with an injecting drug user. We further assumed that the overall percentage of HIV/AIDS cases attributable to i.v. drug abuse reflects the proportion of the direct and indirect costs of HIV/AIDS attributable to i.v. drug abuse.

Chronic Hepatitis C

Our estimate of US total costs for chronic hepatitis C in 2006 was based on a published cost estimate reported for 1997.[14] Cost estimates were based on the data collected by the National Center for Health Statistics, the Health Care Financing Administration (now, the Centers for Medicare and Medicaid Service), the Centers for Disease Control and Prevention, the National Institute of Drug Abuse, the Agency for Healthcare Research and Quality, US Bureau of Labor Statistics, and the National Hospital Discharge Survey. The cost of chronic liver disease associated with chronic hepatitis C was considered separately from the cost

of chronic hepatitis C–associated primary liver cancer. As the number of persons with chronic hepatitis C in the United States is believed to have increased substantially between 1997 and 2006, we inflated Leigh's 1997 estimate to account for the increase in the prevalence of chronic hepatitis C.[15] We also updated Leigh's cost estimates to 2006 dollars, using the medical care component of the CPI.[8]

As is the case for HIV/AIDS, i.v. drug abuse is responsible for a large proportion of all chronic hepatitis C infections. However, in the case of chronic hepatitis C, almost all cases are attributable to direct spread through contaminated drug paraphernalia; sexual spread is unusual. The Centers for Disease Control (CDC) estimates the proportion of chronic hepatitis C infections attributable to i.v. drug abuse (any drug) to be 54.3%.[16] We assumed that this reflects the proportion of the total costs of chronic hepatitis C attributable to i.v. drug abuse. Then, to apportion the total costs of chronic hepatitis C attributable to all i.v. drug abuse into the components attributable to nonmedical i.v. use of prescription opioids versus other drugs of misuse, and among the former, among specific prescription opioids, we used the same methodology as described earlier.

Neonatal Care

Pregnant women who misuse prescription opioids on a nonmedical basis may give birth to opioid-dependent infants who require prolonged neonatal in-hospital care for opioid withdrawal syndrome. We estimated the total US cost of opioid withdrawal syndrome among newborns in 2006 using data from the Healthcare Cost and Utilization Project Kids' Inpatient Database (HCUP KID).[17] The HCUP KID database is a unique all-payer inpatient care database for children in the United States.

Using data from the 2006 HCUP KID, we estimated the total cost of hospitalization for newborns with any listed diagnosis of drug withdrawal syndrome in infants, opioid type (ICD-9-CM code 779.5). HCUP KID reports the total charges associated with hospitalizations. We assumed a cost-to-charge ratio of 66% to convert the charges reported in HCUP KID to their approximate costs. To disaggregate these expenditures into components attributable to mothers who used prescription opioids nonmedically versus heroin, we used the methodology described earlier to examine the principal opioid of misuse among problem users in NSDUH. We assumed that affirmative responses to question concerning current pregnancy are within the gestational timeframe, as NSDUH does not determine the length of the current pregnancy.

Productivity Loss

To estimate the economic burden of lost productivity associated with nonmedical use of prescription opioids, we focused attention on mortality from poisoning, unemployment and subemployment, and work loss resulting from incarceration. The economic burden represented by premature death was estimated using the discounted present value of expected future earnings of persons who died in 2005 as a result of nonmedical prescription opioid use. Productivity loss due to unemployment and subemployment was estimated based on the loss of potential productivity due to drug disorders and institutionalization/hospitalization. Finally, productivity loss due to incarceration were also estimated.[18]

Mortality From Unintentional Poisoning

The CDC National Vital Statistics System provides detailed information (including stratification by age and sex) on deaths due to poisoning by narcotics and psychodysleptics for the years 1999 to 2005, the year of the dataset that we used.[19] Paulozzi et al[20,21] have used this dataset for years before 2003 to report deaths due to prescription opioids. As death certificates occasionally list more than 1 narcotic/psychodysleptic, we calculated the percentage of all drug listings in the narcotic and psychodysleptic category that were prescription opioids and multiplied this percentage by the total number of deaths due to poisoning by narcotics and psychodysleptics in 2005 (18,347) to estimate the total number of poisoning deaths due to prescription opioids. This total number was apportioned among the 3 major categories of prescription opioids ("other opioid type," "methadone," and "other synthetic opioids") in proportion to the number of times these categories were listed.

We apportioned deaths among the individual prescription opioids in the other opioid type and other synthetic narcotic categories in a manner similar to that used to apportion the costs of misuse treatment, using the misuse treatment questions. Lost future earnings of persons who died as a result of prescription opioid poisoning in 2005 were estimated based on the age and sex distribution of those who died and the mean present value of expected future earnings among persons of the same age and sex.[13] A 3% discount rate was used to discount expected future earnings back to year of death.[21]

Unemployment and Subemployment

We based our estimates of total US costs of unemployment and subemployment in 2006 on 1998 data reported by the Office of National Drug Control Policy (ONDCP), in a document entitled "The Economic Costs of Drug Abuse in the United States, 1992 to 1998."[22] To calculate productivity losses due to unemployment and subemployment, we updated ONDCP cost estimates for drug disorders and institutionalization/hospitalization. Lost productivity due to institutionalization/hospitalization (ie, unable to work due to drug treatment) was estimated based on the number of patients using inpatient hospital or residential treatment services. Adjustment for wage inflation was based on the 2006 Bureau of Labor Statistics' Hourly Compensation Index.[23]

Apportionment of the costs of unemployment and subemployment was based on the data from NSDUH using work loss specific questions. Lost earnings were apportioned between prescription opioids and other drugs of abuse, and among the former, among specific opioid products, using an n-way tabulation of the above NSDUH question with the "ever used" question, as described earlier.

Incarceration

Estimation of productivity loss represented by the incarceration of persons for drug-related offenses used methods similar to those used in the ONDCP 2001 report. The number of persons incarcerated in local jails and in state and federal prisons was estimated using 2006 data reported by the Bureau of Justice Statistics.[24] For persons in local jails, distribution by primary offense has been reported by the Bureau of Justice Statistics, most recently for 2002.[25] For persons in federal and state prisons, distribution by offense was reported for 2006.[24] For each

type of crime, the percentage of each primary offense that is attributable to drug abuse was based on an analysis reported by Harwood et al[26] in their 1998 study (ie, 30% of burglaries are attributable to drug abuse). Lost earnings of persons incarcerated for drug-related crimes were estimated based on the age and sex distribution of those incarcerated and the average annual earnings of persons by age and sex.[13]

Criminal Justice

We estimated US total costs of police services, the legal system, and incarceration in 2006 based on a 2003 report of the Bureau of Justice Statistics.[27] Direct expenditures were tallied in terms of "direct current expenditures" (salaries, wages, fees, and commissions and purchases of supplies, materials, and contractual services) and "capital outlays" (construction and purchase of equipment, land, and existing structures). We updated 2003 cost estimates to 2006 using the CPI.[9]

Total estimated expenditures for police services, the legal system, and incarceration were stratified into expenditures for drug law violations versus all other crimes based on corresponding percentages of all arrests, as reported by the Federal Bureau of Investigation's Uniform Crime Statistics.[28,29] Expenditures for drug law violations were apportioned among various prescription opioids on the basis of their relative percentages of all drug seizures, as reported by the National Forensic Laboratory Information System.

Costs to Crime Victims

Our estimate of total US costs to crime victims was based on a published estimate of the total cost of drug-involved crimes in the United States in 1999.[30] For each type of crime, the cost to victims was estimated as the product of the number of crime victims times the percentage with drug involvement times the average cost per victim. Summation of these products across all types of crime yielded an estimate of the total cost of drug-involved crime to victims. Cost estimates were adjusted to 2006 price levels using the overall CPI.[5]

RESULTS

Substance Abuse Treatment

Expenditures for the direct treatment of all drug abuse were estimated to total $11.5 billion in 2006. Nonmedical

use of prescription opioids accounted for 19.3% of this total ($2.2 billion), apportioned as follows: (1) general hospital, inpatient—$411 million; (2) general hospital, outpatient—$325 million; (3) physician and other profession services—$363 million; and (4) substance misuse facilities—$1.12 billion. Table 1 reports the total abuse treatment costs apportioned among the opioids of interest.

Medical Complications

The estimated economic burden of medical complications stemming from all drug abuse (HIV/AIDS, chronic hepatitis C, neonatal care) was $14.7 billion in 2006. The proportion of this burden attributable to nonmedical use of prescription opioids was 6.40% ($944 million).

Mortality From Unintentional Poisoning

The estimated cost of lost productivity due to mortality from prescription opioid poisoning was $12.4 billion in 2005. On the basis of the data from the CDC National Vital Statistics System, we estimated that 11,806 persons died due to poisoning from "other opioids," "methadone," and "other synthetic narcotics." Table 2 reports estimated mortality costs for various categories of prescription opioids based on NSDUH data. Mortality costs were also apportioned on the basis of sales data for 5 prescription opioids. Calculations were based on the correlation of drug sales (in morphine equivalents) with poisoning deaths, as described in Table 3.

Unemployment and Subemployment

The total value of lost productivity due to unemployment and subemployment arising from abuse of all drugs was $30.8 billion in 2006. Costs of unemployment and subemployment related to drug disorders were $28.6 billion, and costs of institutionalization/hospitalization totaled $2.2 billion. The percentage of these costs attributable to nonmedical prescription opioid use was 47.8% ($14.7 billion).

Incarceration

The estimated cost of lost productivity due to incarceration for drug offenses was $74 billion in 2006. The total number of persons incarcerated due to drug violations was as follows: (1) federal prisons—116,534 persons; (2) state prisons—806,154 persons; and (3) local jails—367,404 persons. The percentage of these costs

TABLE 1. Abuse Treatment Costs Apportioned Among the Prescription Opioids (in $Millions)

Opioid	Percentage of all Drug Use (NSDUH) (%)	Inpatient	Outpatient	Physician and Other Professionals	Substance Abuse Facility	Total
OxyContin	3.71	$79.08	$62.57	$69.75	$215.61	$427.01
Propoxyphene	2.92	$62.22	$49.22	$54.88	$169.62	$335.94
Oxycodone	2.21	$47.12	$37.28	$41.56	$128.46	$254.41
Hydrocodone	4.59	$97.82	$77.39	$86.28	$266.69	$528.18
Codeine	1.69	$35.99	$28.47	$31.74	$98.12	$194.33
Meperidine	0.76	$16.20	$12.81	$14.29	$44.15	$87.45
Hydromorphone	0.48	$10.15	$8.03	$8.95	$27.67	$54.80
Methadone	0.86	$18.24	$14.43	$16.09	$49.74	$98.50
Morphine	0.94	$19.98	$15.81	$17.62	$54.46	$107.87
Fentanyl	0.01	$0.16	$0.13	$0.14	$0.44	$0.87
Other	1.13	$24.16	$19.12	$21.31	$65.88	$130.47
Total	19.30	$411.11	$325.26	$362.62	$1,120.83	$2,219.82

NSDUH indicates National Survey of Drug Use and Health.

TABLE 2. Mortality Costs Apportioned Among the Prescription Opioids (in $Millions) of Interest (in $Millions)

Proportion	No. Deaths (CDC/NSDUH)	Mortality
OxyContin	1553	$1,631.94
Oxycodone	925	$972.32
Hydrocodone	1921	$2,018.60
Codeine	707	$742.68
Hydromorphone	199	$209.43
Morphine	392	$412.24
Methadone	4392	$4,614.78
Propoxyphene	1359	$1,428.24
Meperidine	354	$371.79
Fentanyl	4	$3.68
Total	11806	$12,405.70

CDC/NSDUH indicates centers for disease control/National Survey of Drug Use and Health.

attributable to nonmedical prescription opioid use was 20.10% ($14.8 billion).

Criminal Justice

Total expenditures for criminal justice attributable to all drug abuse were $40.9 billion in 2006. The percentage attributable to nonmedical prescription opioid use was 21.5% ($8,775 million).

Policing/Legal/Incarceration

Total US expenditures for police services, the legal system, and incarceration related to drug abuse violations in 2006 were as follows: (1) policing—$16.9 billion; (2) legal—$8.4 billion; and (3) incarceration—$12.4 billion. Drug law violations accounted for 18.6% of all crimes. The percentage attributable to nonmedical prescription opioid use was estimated to be 20.1%, apportioned as follows: (1) policing—$3.4 billion; (2) legal $1.7 billion; and (3) incarceration—$2.5 billion.

Cost to Crime Victims

The cost to crime victims for all alcohol-involved and drug-involved crimes in the United States in 2006 totaled $23.2 billion, of which 13.3% ($3.1 billion) can be attributed to drugs only.[27] Total costs can be broken down into the following categories: (1) medical costs—$207 million; (2) work loss—$2.06 billion; and (3) property damage—$803 million. The percentage of these costs attributable to nonmedical prescription opioid use was 20.1% ($618 million).

Total Costs

The estimated total cost of nonmedical use of prescription opioids was $53.4 billion in 2006, of which $42 billion (79%) was attributable to lost productivity, $8.2 billion (15%) to criminal justice costs, $2.2 billion (4%) to misuse treatment, and $944 million to medical complications (2%). For the prescription opioids of interest, estimated associated total costs were as follows: (1) OxyContin, $7.3 billion (13.6%); (2) propoxyphene, $8.7 billion (16.3%); (3) oxycodone, $6.0 billion (11.3%); (4) hydrocodone, $12.7 billion (23.8%); (5) codeine, $4.2 billion (8.0%); (6) meperidine, $2.0 billion (3.8%); (7) hydromorphone, $1.2 billion (2.2%); (8) methadone, $6.2 billion (11.6%); (9) morphine, $2.6 billion (4.8%); (10) fentanyl, $0.03 billion (0.06%); and (11) other, $2.4 billion (4.6%). Table 4 reports the total costs of nonmedical use of prescription opioids.

DISCUSSION

We estimate that the total cost of nonmedical use of prescription opioids in 2006 was $53.4 billion, of which $42 billion (79%) was attributable to lost productivity, $8.2 billion (15%) to criminal justice costs, $2.2 billion (4%) to substance abuse treatment, and $0.9 billion to medical complications (2%). To put this estimate in the context of other diseases, obesity was estimated to annually cost $139 billion annually in 2005,[31] the burden of smoking was estimated at $193 billion in 2004,[32] and the Department of Health and Human Services estimated the total cost of Alcohol Abuse to be $184.6 billion in 1998.[33] The ONDCP estimated the total cost of all drug abuse in the United States to be $143.4 billion in 1998, with a projected increase of $8.65 billion annually to $160.7 billion in 2000.[22] The percentage attributable to lost productivity was 69%, and the percentage due to criminal justice was approximately 18%. Conservatively assuming that the ONDCP-estimated rate of increase would have continued until 2006, the ONDCP estimate for 2006 would have been $212.6 billion, of which our estimate of $53 billion for prescription opioid abuse would constitute about 25% of the total.

Although our estimates appear compatible with those of the ONDCP, they are much greater than those of the only previous study to focus exclusively on the costs of nonmedical use of prescription opioids.[4] In that study, the total cost of prescription opioid misuse in 2001 was estimated to be only $8.6 billion, despite the fact that similar items of cost were included in both that study and ours. In part, the discrepancy between the 2 estimates is attributable to inflation and the considerable increase in the prevalence of nonmedical use of prescription opioids during

TABLE 3. Mortality Costs Among "Other Opioids" Based on Sales Data (in $Millions)*

Agent	Sales (Millions of Grams)	Percentage of All Sales†	No. Deaths (CDC)	Total Costs
Codeine	2.8	3.60	206	$209.87
Oxycodone	30.6	39.60	2256	$2,309.45
Hydrocodone	25.7	33.20	1892	$1,936.20
Morphine	15	19.40	1105	$1,131.39
Hydromorphone	3.2	4.20	239	$244.94
Total	77.3	100.00	5698	$5,831.85

*Five thousand six hundred ninety-nine deaths, using ICD-10 code "other opioids" (T40.2).
†Calculations based on oral morphine equivalents.
CDC indicates centers for disease control; ICD, International Classification of Disease.

TABLE 4. Overall Costs of Opioid Abuse (in $Millions)

	OxyContin	Propoxyphene	Oxycodone	Hydrocodone	Codeine	Meperidine	Hydromorphone	Methadone	Morphine	Fentanyl	Other	Total
Abuse treatment	$427.01 (19.24%)	$335.94 (15.13%)	$254.41 (11.46%)	$528.18 (23.79%)	$194.33 (8.75%)	$87.45 (3.94%)	$54.80 (2.47%)	$98.50 (4.44%)	$107.87 (4.86%)	$0.87 (0.04%)	$130.57 (5.88%)	$2,219.82 (100%)
General hospital, inpatient	$79.08	$62.22	$47.12	$97.82	$35.99	$16.20	$10.15	$18.24	$19.98	$0.16	$24.16	$411.11
General hospital, outpatient	$62.57	$49.22	$37.28	$77.39	$28.47	$12.81	$8.03	$14.43	$15.81	$0.13	$19.12	$325.26
Physicians and other professionals	$69.75	$54.88	$41.56	$86.28	$31.74	$14.29	$8.95	$16.09	$17.62	$0.14	$21.31	$362.62
Substance abuse facilities	$215.61	$169.62	$128.46	$266.69	$98.12	$44.15	$27.67	$49.74	$54.46	$0.44	$65.88	$1,120.83
Medical complications	$166.46 (22.14%)	$0.92 (0.12%)	$26.06 (3.47%)	$1.40 (0.19%)	$0.35 (0.05%)	$54.01 (7.18%)	$197.51 (26.26%)	$30.21 (4.02%)	$273.33 (36.35%)	$1.52 (0.20%)	$0.26 (0.03%)	$752.04 (100%)
HIV/AIDS	$105.83	N/A	$16.29	N/A	N/A	$34.38	$126.04	$19.22	$174.40	$0.97	N/A	$477.14
Chronic hepatitis C	$59.98	N/A	$9.23	N/A	N/A	$19.49	$71.44	$10.90	$98.85	$0.55	N/A	$270.45
Neonatal problems	$0.65	$0.92	$0.54	$1.40	$0.35	$0.14	$0.02	$0.09	$0.08	N/A	$0.26	$4.45
Productivity loss	$5,812.23 (13.83%)	$6,689.96 (15.92%)	$4,625.47 (11.01%)	$9,811.13 (23.34%)	$3,319.65 (7.90%)	$1,541.75 (3.67%)	$750.69 (1.79%)	$5,820.45 (13.85%)	$1,790.52 (4.26%)	$20.83 (0.05%)	$1,846.57 (4.39%)	$42,029.23 (100%)
Mortality	$1,631.94	$1,428.24	$972.32	$2,018.60	$742.68	$371.79	$209.43	$4,614.78	$412.24	$3.68	N/A	$12,405.70
Unemployment/subemployment	$2,666.65	$2,241.23	$1,607.26	$3,458.50	$1,250.88	$601.58	$295.76	$789.80	$800.39	$5.77	$1,013.82	$14,731.64
Incarceration	$1,513.64	$3,020.49	$2,045.89	$4,334.03	$1,326.09	$568.38	$245.49	$415.87	$577.89	$11.37	$832.75	$14,891.89
Criminal justice	$835.43 (10.16%)	$1,667.12 (20.88%)	$1,129.21 (13.74%)	$2,392.12 (29.10%)	$731.92 (8.90%)	$313.71 (3.82%)	$135.50 (1.65%)	$229.53 (2.79%)	$318.96 (3.88%)	$6.28 (0.08%)	$459.63 (5.59%)	$8,219.41 (100%)
Policing	$346.06	$690.57	$467.75	$990.88	$303.18	$129.95	$56.13	$95.08	$132.12	$2.60	$190.39	$3,404.70
Legal	$173.03	$345.29	$233.88	$495.45	$151.59	$64.97	$28.06	$47.54	$66.06	$1.30	$95.20	$1,702.37
Incarceration	$253.46	$505.78	$342.58	$725.73	$222.05	$95.17	$41.11	$69.64	$96.77	$1.90	$139.44	$2,493.63
Cost to crime victims	$62.89	$125.49	$85.00	$180.07	$55.10	$23.61	$10.20	$17.28	$24.01	$0.47	$34.60	$618.71
Total	$7,241.13 (13.61%)	$8,693.94 (16.34%)	$6,035.15 (11.34%)	$12,732.83 (23.92%)	$4,246.25 (7.98%)	$1,996.92 (3.75%)	$1,138.49 (2.14%)	$6,178.70 (11.61%)	$2,490.67 (4.68%)	$29.49 (0.06%)	$2,436.93 (4.58%)	$53,221.50 (100%)

N/A indicates not applicable.

the period 2001 to 2006. Differences in methodology, however, also probably account for some of the discrepancy. For example, Birnbaum et al estimated prescription opioid deaths using the data from the Drug Abuse Warning Network, which is not nationally representative, but rather is based on the reports from medical examiners in selected metropolitan areas. Although Birnbaum et al did not report the actual number of prescription-opioid deaths that they estimated from Drug Abuse Warning Network, it is likely to have been much lower than the number we would have estimated using national data from the CDC Compressed Mortality Dataset. In addition, Birnbaum et al used a 6% discount rate to estimate foregone future earnings, whereas we used a more standard rate of 3%[34] (note: the present value of estimated future costs is inversely related to the discount rate). Taking into account these differences in methodology, and the two-fold increase in the number of deaths attributable to prescription opioid misuse in the period 2001 to 2006 (according to CDC Compressed Mortality Dataset), it is not surprising to find that their estimate ($865 million) is much lower than ours ($12.4 billion).

Our study has a number of significant limitations. First, we relied more on data from NSDUH, which—as its name indicates—is a household survey, and therefore does not include incarcerated persons and the homeless. Both of these omitted groups contain substantial numbers of persons who are misusing drugs. To the extent that patterns of nonmedical use of prescription opioids in these groups differ from those in NSDUH, our results may yield a biased representation of overall nonmedical use of prescription opioids in the United States.

Second, although we based our study on the best available sources, for a variety of reasons—especially the age of some of the cost estimates we used—the accuracy of many of our estimates is uncertain. For example, our estimate of the total direct costs of HIV/AIDS is from 1996, the first year in which highly active antiretroviral therapy was widely used. Although we updated this estimate to account for inflation and the increase in the prevalence of HIV/AIDS, greater use of highly active antiretroviral therapy and other expensive therapies in 2006 (vs. 1996) may impart a conservative bias to our estimates.

Third, our estimates of the proportion of costs attributable to prescription opioids versus other drugs of abuse, and our estimates of costs attributable to individual prescription opioids, assumes that costs are independent of the particular drug of abuse and that polydrug abuse does not impact these costs. In other words, i.v. abusers of heroin are assumed to have the same risk of contracting HIV/AIDS—and the same costs if they do so—as i.v. abusers of prescription opioids. No studies have yet tested this assumption, but it may be reasonably close to what is actually happening. For example, injecting use was found in over 40% of opioid-addicted youth who were using heroin and prescription opioids in 2 recent studies.[35,36] In 1 study where patients' average age was 19.1 years, average years addicted was 1.5, and slightly less than 75% were Caucasian, 18% tested positive for hepatitis C at baseline, and 4 of 83 who were negative at baseline and retested 12 weeks later became positive (thus showing a significant amount of HIV risk behavior).[35] It is clear that persons who misuse prescription opioids only by the oral route are at low risk of acquiring or spreading HIV, but some have been known to transition to injecting heroin as it often costs less. Conversely, those using heroin only by inhalation have levels of HIV risk that are comparable with those using only prescription opioids by the oral route.

Another result of this assumption of independence is that various crimes are considered to be equally likely to be committed by abusers of street drugs (eg, heroin, crack cocaine, methamphetamine) and abusers of prescription opioids. The validity of this assumption of independence is unknown. However, a recent cost-effectiveness study of opioid-addicted youth who were treated in the aforementioned study by Woody et al found that approximately 50% engaged in criminal activity for the past 30 days at the baseline assessment, and that social costs due to crime were substantial.[37] In assessing the distribution of social costs due to crimes, it is important to bear in mind that they involve costs to victims and to the criminal justice system, that use of prescription opioids without a prescription is as illegal as use of heroin, and that persons who use 1 class of opioids often use drugs from another class, depending on availability, cost, and changing preferences.

A final significant limitation concerns the method we used to apportion costs among prescription opioids. In most cases, the NSDUH questions used for apportionment could not be directly linked to cost items of interest. For example, NSDUH does not contain information on the principal drug of misuse or the drug for which treatment was received. Thus, we were limited to the number of mentions of ever having used the different prescription opioids as the principal means of apportionment of treatment costs. Whether there is a direct correlation between the frequency with which different drugs were ever used and the costs of treatment associated with abuse of these drugs is unknown. In one instance, however, we were able to compare the results of our NSDUH-based indirect apportionment with another means of apportionment. Specifically, poisoning deaths were apportioned among "other opioids" (ie, codeine, oxycodone, hydrocodone, morphine, and hydromorphone), based on both pharmaceutical sales data and NSDUH "ever used" data. The number of deaths attributed to oxycodone (oyxcodone and OxyContin combined), hydrocodone, and hydromorphone was similar with both methods of apportionment: (1) oxycodone—2478 (NSDUH) versus 2256 (sales data); (2) hydrocodone—1921 (NSDUH) versus 1892 (sales data); and (3) hydromorphone—199 (NSDUH) versus 239 (sales data). Results for codeine and morphine were substantially different using the 2 methodologies, however: (1) codeine—707 (NSDUH) versus 206 (sales) and (2) morphine—392 (NSDUH) versus 1105 (sales).

In conclusion, our study suggests that the costs of nonmedical use of prescription opioids in the United States are substantial. The great majority of these costs (94%) are accounted for by lost productivity and crime. Our estimates are consistent with prior estimates for all drug misuse reported by ONDCP, but much higher than a prior published estimate specific to prescription opioids. In our analysis of costs by specific prescription opioids, 5 drugs (OxyContin, oxycodone, hydrocodone, propoxyphene, and methadone) accounted for two-thirds of the total economic burden of the nonmedical use of prescription opioids. Given the limitations and uncertainties of our methods and sources, our results should be interpreted with caution and regarded as approximations only.

These data do not address clinical issues related to balancing the benefits of pain treatment with opioids

against the risks of nonmedical use and diversion. On the one hand, treating everyone as if they are at high risk and requiring frequent visits and urine tests can be burdensome and unnecessarily expensive; on the other, treating everyone as if they are at low risk can produce other problems. Emerging work on prescription-monitoring programs is likely to introduce new tools that can assist medical providers in identifying persons who are likely to misuse or divert prescription opioids, provided they are available to prescribers and "user friendly." However, even with the help of such programs, decisions about the risks, benefits, and specifics of pain treatment with opioids always will require clinical judgment that is informed by treatment guidelines.

REFERENCES

1. Compton W, Volkow N. Major increases in opioid analgesic abuse in the United States: concerns and strategies. *Drug Alocohol Depend.* 2006;81:103–107.
2. Warner M, Chen LH, Makuc DM. Increase in fatal poisonings involving opioid analgesics in the United States, 1999–2006. NCHS data brief, no. 22. Hyattsville, MD: National Center for Health Statistics; 2009. Available at www.cdc.gov/nchs/data/databriefs/db22.pdf. [Accessed August 5, 2010].
3. Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Results from the 2006 National Survey on Drug Use and Health. 2007. National Findings (Office of Applied Studies), NSDUH Series: H-32, DHHS Publication No. (SMA) 07-4293. Rockville, MD, 2007.
4. Birnbaum HG, White AG, Reynolds JL, et al. Estimated costs of prescription opioid analgesic abuse in the United States in 2001: a societal perspective. *Clin J Pain.* 2006;22:667–676.
5. United States Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. Office of Applied Studies. National Survey on Drug Use and Health, 2004 [Computer file]. ICPSR04373-v1. Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], 2006-05-12.
6. United States Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. Office of Applied Studies. National Survey on Drug Use and Health, 2005 [Computer file]. ICPSR04596-v2. Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], 2009-08-12.
7. United States Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. Office of Applied Studies. National Survey on Drug Use and Health, 2006 [Computer file]. ICPSR21240-v4. Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], 2009-08-12.
8. Mark TL, Levit KR, Coffey RM, et al. *National Expenditures for Mental Health Services and Substance Abuse Treatment, 1993–2003.* Rockville, MD: Substance Abuse and Mental Health Services Administration, SAMHSA Publication No. (SMA) 07-4227; 2007.
9. Department of Labor. Bureau of Labor Statistics. 2008. Available at: http://www.bls.gov. [Accessed August 5, 2010].
10. Bozzette SA, Berry SH, Duan N, et al. The care of HIV-infected adults in the United States. *New Engl J Med.* 1998;339:1897–1904.
11. Glynn M, Rhodes P. Estimated HIV prevalence in the United States at the end of 2003. National HIV Prevention Conference. 2005. Available at: http://www.aegis.com/conferences/NHIVPC/2005/T1-B1101.html. [Accessed August 5, 2010].
12. Centers for Disease Control (CDC) and Prevention. HIV/AIDS Surveillance Report, 2006. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention website. 2008. Available at: http://www.cdc.gov/hiv/topics/surveillance/resources/reports. [Accessed August 5, 2010].
13. Census Bureau. The 2008 Statistical Abstract: The National Databook. Table 120 Deaths—Life years lost and mortality costs by age, sex, and cause. 2008. Available at: http://www.census.gov/compendia/statab/cats/births_deaths_marriages_divorces.html. [Accessed August 5, 2010].
14. Leigh JP, Bowlus CL, Leistikow BN, et al. Costs of hepatitis C. *Arch Int Med.* 2001;161:2231–2237.
15. Armstrong GL, Wasley A, Simard EP, et al. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Int Med.* 2006;144:705–714.
16. Wasley A, Grytdal S, Gallagher K. Surveillance for acute viral hepatitis—United States, 2006. Centers for Disease Control (CDC) and Prevention website. 2008. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5702a1.htm. [Accessed August 5, 2010].
17. HCUP Kids' Inpatient Database (KID). Healthcare Cost and Utilization Project (HCUP). 2000 and 2003. Agency for Healthcare Research and Quality, Rockville, MD. http://www.hcup-us.ahrq.gov/kidoverview.jsp.
18. Haddix AC, Teutsch SM, Corso PS. (eds). *Prevention Effectiveness: A Guide to Decision Analysis and Economic Evaluation.* US: Oxford University Press; 2002.
19. Centers for Disease Control (CDC) and Prevention. Wonder online database: Mortality—underlying cause of death. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention website. 2005. Available at: http://wonder.cdc.gov/. [Accessed June 16, 2008].
20. Paulozzi LJ, Budnitz DS, Xi Y. Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiol Drug Safety.* 2006;15:618–627.
21. Paulozzi LJ, Ryan G. Opioid analgesics and rates of fatal drug poisoning in the United States. *Am J Prevent Med.* 2006;31:506–511.
22. Office of National Drug Control Policy. *The Economic Costs of Drug Abuse in the United States: 1992–1998.* Washington, DC: Executive Office of the President (Publication No. NCJ-190636); 2001.
23. Department of Labor. Bureau of Labor Statistics. Annual indexes of productivity, hourly compensation, unit costs, and prices. 2007. Available at: http://www.bls.gov/news.release/prod2.t14.htm. [Accessed August 5, 2010].
24. Department of Justice. Office of Justice Programs, Bureau of Justice Statistics. Prison and jail inmates at midyear 2006. 2007. Available at: http://bjs.ojp.usdoj.gov/index.cfm?ty = pb-detail&iid = 1006. [Accessed August 5, 2010].
25. Department of Justice. Office of Justice Programs, Bureau of Justice Statistics. Profile of jail inmates, 2002. 2004. Available at: http://bjs.ojp.usdoj.gov/index.cfm?ty = pbdetail&iid = 1118. [Accessed August 5, 2010].
26. Harwood H, Fountain D, Livermore G. *The Economic Costs of Alcohol and Drug Abuse in the United States 1992.* Rockville, MD: National Institutes on Drug Abuse; 1998.
27. Department of Justice. Office of Justice Programs, Bureau of Justice Statistics. Prisoners in 2006. 2007. Available at: http://bjs.ojp.usdoj.gov/index.cfm?ty = pbdetail&iid = 908. [Accessed August 5, 2010].
28. Department of Justice. Office of Justice Programs, Bureau of Justice Statistics. Justice expenditure and employment in the United States, 2003. 2006. Available at: http://bjs.ojp.usdoj.gov/index.cfm?ty = pbdetail&iid = 1017. [Accessed August 5, 2010].
29. Department of Justice. Federal Bureau of Investigation. Uniform crime statistics—Estimated number of arrests. 2006. Available at: http://www.fbi.gov/ucr/cius2006/data/table_29.html. [Accessed August 5, 2010].
30. Miller TR, Levy DT, Cohen MA, et al. Costs of alcohol and drug-involved crime. *Prev Sci.* 2006;7:333–342.
31. Cawley J. The cost-effectiveness of programs to prevent or reduce obesity the state of the literature and a future research agenda. *Arch Pediatr Adolesc Med.* 2007;161:611–614.

32. Smoking and tobacco use: MMWRs: 2002: Annual smoking-attributable mortality, years of potential life lost, and economic costs: Office on smoking and health (OSH): CDC [homepage on the Internet]. [cited 9/29/2009]. Available at: http://www.cdc.gov/tobacco/data_statistics/mmwrs/byyear/2002/mm5114a2/highlights.htm.

33. Tenth Special Report to Congress on Alcohol and Health from The Secretary of Health and Human Services. DHHS Publication. June 2000;No. 00-1583.

34. Gold MR, Siegel JE, Russell LB, et al. *Cost-effectiveness in Health and Medicine*. New York, NY: Oxford University Press; 1996.

35. Woody GE, Poole S, Subramaniam G, et al. Extended versus short-term buprenorphine-naloxone for treatment of opioid addicted youth: a randomized trial. *J Am Med Assoc*. 2008;300:2002–2011.

36. Subramaniam GA, Stitzer ML, Woody G, et al. Clinical characteristics of treatment-seeking adolescents with opioid versus cannabis/alcohol use disorders. *Drug Alcohol Depend*. 2009;99:141–149.

37. Polsky D, Glick HA, Yang J, et al. Cost-effectiveness of extended buprenorphine-naloxone treatment for opioid-addicted youth. *Data from a Randomized Trial*. 2010;105: 1616–1624.