

Cost of Pain Medication to Treat Adult Patients with Nonmalignant Chronic Pain in the United States

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ABSTRACT

BACKGROUND: Nonmalignant chronic pain (NMCP) is a public health concern. Among primary care appointments, 22% focus on pain management. The American Academy of Pain Medicine guidelines for NMCP recommend combination medication therapy (including analgesics, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, antidepressants, and anticonvulsants) as a key component to effective treatment for many chronic pain diagnoses. However, there has been little evidence outlining the costs of pain medications in adult patients with NMCP in the United States, an area that necessitates further consideration as the nation moves toward value-based benefit design.

OBJECTIVES: To estimate the cost of pain medication attributable to treating adult patients with NMCP in the United States and to analyze the trend of outpatient pain visits.

METHODS: This cross-sectional study used the National Ambulatory Medical Care Survey (NAMCS) data from 2000-2007. The Division of Health Care Statistics, National Center for Health Statistics, and the Centers for Disease Control and Prevention conducted the survey. The study included patients aged ≥ 18 years with chronic pain diagnoses (identified by the ICD-9-CM codes: primary, secondary, and tertiary). Patients prescribed at least 1 pain medication were included in the cost analysis. Pain-related prescription medications prescribed during ambulatory care visits were retrieved by using NAMCS drug codes/National Drug Code numbers. National pain prescription frequencies (weighted) were obtained from NAMCS data, using the statistical software STATA. We created pain therapy categories (drug classes) for cost analysis based on national pain guidelines. Drug classes used in this analysis were opioids/opioid-like agents, analgesics/NSAIDs, tricyclic antidepressants, selective serotonin reuptake inhibitors, antirheumatics/immunologics, muscle relaxants, topical products, and corticosteroids. We calculated average prices based on the 3 lowest average wholesale prices reported in the *Red Book 2009* for maximum recommended daily dose. Total pain medication costs were calculated in 2009 and 2013 dollar values. The study analyzed NMCP-related outpatient visit trends and used time series analysis to forecast visits using U.S. population data and statistics.

RESULTS: The total costs of prescription medications prescribed for pain were \$17.8 billion annually in the United States. Cost estimates were captured based on a total of 690,205,290 (~690 million) weighted outpatient visits made for chronic pain from 2000 to 2007 in the United States. Of those patients, 99% received a medication that could be used for NMCP. Among the patients, 29% reported taking ≥ 5 medications. A linear trend of pain visits is visible, reporting change (from 11% to 14%) from 2000 to 2007 in the United States. All agents except opioids/opioid-like agents and analgesics/NSAIDs were further categorized as adjuvant therapy to create 3 major drug class categories. The largest 3 categories of pain therapy for

the United States (annually) were analgesics/NSAIDs (\$1.9 billion), opioids (\$3.6 billion), and adjuvants (\$12.3 billion). Despite having the highest prescription frequency nationally, analgesics/NSAIDs accounted for about 11% of the overall pain medication costs. This study found that adjuvant therapy accounted for 69% of the total pain medication costs. Among adjuvants, 33.5% of the cost was contributed by antirheumatics/immunologics. Other adjuvants included muscle relaxants (4.4%), topical products (8.6%), and corticosteroids (9.4%).

CONCLUSIONS: This study demonstrated national prescribing costs and use within various drug categories of pain medications in a large outpatient population over an 8-year period in the United States. Policymakers, stakeholders, and health plan decision makers may consider this cost analysis, since they need to know how drug costs are being allocated. Moreover, information about costs and use of pain medications is valuable for the practitioner making individual patient care decisions, as well as for those who make population based decisions. This study reported an increasing trend of outpatient pain visits in the United States. Therefore, policymakers and health plan decision makers may expect a growing number of pain-related outpatient visits in coming years and allocate resources accordingly to meet the need.

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What is already known about this subject

- Chronic pain is a condition that affects approximately 100 million adults in the United States annually.
- Nonmalignant chronic pain is a public health concern. Among primary care appointments, 22% focus on pain management.
- The Institute of Medicine estimated direct care expenditure and loss of productivity for pain to be \$560-\$635 billion annually.

What this study adds

- Total costs of prescribed pain medication are \$17.8 billion annually in the United States.
- The largest 3 categories for pain therapy costs were \$1.9 billion for analgesics/nonsteroidal anti-inflammatory drugs (NSAIDs), \$3.6 billion for opioids, and \$12.3 billion for adjuvants.
- Analgesics/NSAIDs accounted for about 11% for the overall pain medication costs. Adjuvant therapy accounted for 69% of the total pain medication costs. Among adjuvants, 33.5% of the cost was contributed by antirheumatics/immunologics.

What this study adds (*continued*)

- A linear trend of national pain visits is visible, reporting change (from 11% to 14%) from 2000 to 2007 in the United States and showing a substantial increasing trend of outpatient pain visits.

Chronic pain is a condition that affects approximately 100 million adults in the United States annually.^{1,2} It can be defined as “pain without the apparent biological value that has persisted beyond the normal healing time (usually 3 months).”³ Nonmalignant chronic pain (NMCP) is a public health concern, and 22% of primary care appointments focus on pain management.^{4,5} Patients who suffer from chronic pain have been found to visit their primary care physicians up to 5 times more frequently than those patients with other disease states.^{4,6} NMCP is difficult to understand and treat because it relies heavily on the subjective report of symptoms from the patient and because of the variety of treatment options. A number of NMCP guidelines, including the American Academy of Pain Medicine, the Institute for Clinical Systems Improvement, the American Society of the Interventional Pain Physicians, and the Wisconsin Medical Society Task Force on Pain Management recommend combination medication therapy (including analgesics such as nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, antidepressants, and anticonvulsants) along with non-medication therapies such as cognitive and behavior therapy and physical therapy as key components to effective treatment for many chronic pain diagnoses.⁷⁻¹³ In addition to addressing chronic pain, emotional and cognitive effects can play an underlying role in NMCP, which extends beyond physical pain.¹ Many studies and sources have identified the undertreatment of chronic pain as a serious health issue and have related it to a number of causes, including (a) the complexity of treating many disease states and comorbidities that contribute to causing chronic pain, (b) the lack of patient and provider relationships and understanding of chronic pain, (c) society’s view or attitude towards pain, (d) legitimate concerns and exaggerated stigmas surrounding pain medication addiction, and (e) health care professionals’ lack of training in the treatment of chronic pain.^{1,5,13-17} These shortcomings in the treatment of NMCP can lead to increased health care utilization, including additional emergency department (ED) and physician visits, increased treatment cost when using inadequate or ineffective treatment, and increased indirect costs, such as lost work.^{1,3,8,9}

In the United States, the incremental cost of health care related to chronic pain is estimated to be \$261-\$300 billion.^{1,2} However, it is not known how much of this amount are direct medication costs for treatment of patients with NMCP. In addition, according to an Institute of Medicine (IOM) report, loss of productivity due to chronic pain is estimated to be \$297-\$336

billion.^{1,2} Estimates have reported that the costs to treat this condition exceed the treatment costs of patients with coronary artery disease, cancer, and acquired immunodeficiency syndrome combined.³ Large portions of society are affected by NMCP, contributing a significant portion of resources to the U.S. health care system. Further investigation on rising costs related to prescribing patterns of pain medications has been highlighted.⁹ It is of great public interest to determine and understand the cost of NMCP drug therapy, so that more focus can be placed on the use of cost-effective treatments to reduce overall U.S. health care costs.⁸

The IOM report “Relieving Pain in America” calls for better data to address the public health challenges of pain.¹ Gaining more insight into the estimated medication cost of chronic pain medication treatment will provide valuable information to clinicians, policymakers, and stakeholders in the U.S. health care system as the nation moves towards value-based pharmacy benefit design. The financial burden specific to NMCP medications has not been estimated. Therefore, the purpose of this study was to estimate medication costs attributable to the treatment of chronic pain patients by using data from a large national prescribing database from U.S. outpatient settings. The study also calculated costs based on different types of pain medication categories used for common chronic pain conditions. Further, we analyzed the trend of outpatient chronic pain visits in the United States.

Methods

Study Design and Patient Population

The cross-sectional data were collected from the National Ambulatory Medical Care Survey (NAMCS). The study used data from years 2000 to 2007 for patients aged ≥ 18 years with NMCP. This national probability sample survey was conducted by the Division of Health Care Statistics, National Center for Health Statistics, and the Centers for Disease Control and Prevention.⁵

Data Collection

NAMCS collected data from the physician or physician staff in outpatient settings in the United States. This NAMCS basic sampling unit was the physician-patient office visit. This study sampled only office visits of nonfederally employed physicians primarily engaged in direct patient care (exceptions included anesthesiology, pathology, and radiology). NAMCS used a multistage sampling procedure. Each physician was randomly selected for a 1-week reporting period to gather patients’ reason for visit; medical diagnosis made (primary, secondary, and tertiary); medications prescribed; screening tests ordered; and follow-up plan, in addition to various other kinds of information about the practice site, such as use of electronic medical records. For the purposes of this analysis, the relevant NAMCS variables that were collected included patient demographics, reason for visit, diagnoses, and medications prescribed.

TABLE 1 Study Categories for Pain Medication Drug Class

Drug Class	Medications Included	
Opioids, opioid-like agents, and combination opioid/analgesics	Codeine and acetaminophen, ^a codeine and aspirin, fentanyl patch, hydrocodone/acetaminophen, hydrocodone/ibuprofen, hydromorphone, levorphanol, meperidine, methadone, morphine, ^a oxycodone, ^a oxycodone and acetaminophen, oxycodone and aspirin, oxycodone and ibuprofen, oxymorphone propoxyphene, propoxyphene and acetaminophen, tramadol, tramadol and acetaminophen	
Analgesics/NSAIDs (nonselective and selective)	Acetaminophen, aspirin, celecoxib, ^a choline magnesium trisalicylate, diflunisal, magnesium salicylate, salsalate, sodium salicylate, sulindac, diclofenac potassium, etodolac, fenoprofen calcium, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate sodium, mefenamic acid, meloxicam, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, sulindac, tolmetin	
ADJUVANT THERAPIES	Tricyclic antidepressants	Amitriptyline, desipramine, doxepin, imipramine, nortriptyline
	SSRIs	Citalopram, escitalopram, ^a fluoxetine, fluvoxamine, paroxetine, sertraline
	Other antidepressants	Bupropion, duloxetine, ^a venlafaxine ^a
	Anticonvulsants	Carbamazepine, divalproex sodium, gabapentin, lamotrigine, oxcarbazepine, phenytoin, pregabalin, ^a tiagabine, topiramate, ^a valproic acid, zonisamide
	Antirheumatics/immunologics	Abatacept, ^a adalimumab, ^a anakinra, ^a etanercept, ^a hydroxychloroquine, infliximab, ^a leflunomide, methotrexate, rituximab, ^a sulfasalazine
	Muscle relaxants	Baclofen, carisoprodol, chlorphenesin, chlorzoxazone, cyclobenzaprine, metaxalone, methocarbamol, tizanidine, orphenadrine, carisoprodol with aspirin, carisoprodol with aspirin and codeine, methocarbamol with aspirin, orphenadrine with aspirin and caffeine
	Topical products	Capsaicin, lidocaine patches ^a
Corticosteroids (tablets, solutions, and injections)	Betamethasone acetate, betamethasone sodium phosphate, dexamethasone acetate, dexamethasone sodium phosphate, hydrocortisone acetate, hydrocortisone sodium succinate, methylprednisolone acetate, prednisone, prednisolone sodium phosphate, prednisolone tebuate, triamcinolone acetonide, triamcinolone diacetate triamcinolone hexacetonide	

^aGeneric products were not available or had limited availability during the study period; therefore, brand name formulations, including extended-release formulations, were included in the cost estimation.

NSAID = nonsteroidal anti-inflammatory drug; SSRI = selective serotonin reuptake inhibitor.

The study included visits with “chronic problem–routine” and “chronic problem–flare” as a major reason for visit in the NAMCS database. These were selected as part of the inclusion criteria in order to eliminate visits related to acute pain diagnosis.^{5,18} We included patients aged ≥ 18 years with chronic pain diagnoses (identified by *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes).¹⁹ We created pain therapy categories for cost analysis based on pain medication using NAMCS Drug Codes/National Drug Code numbers and national pain guidelines.^{7,12,14,18,20} Publicly available online documents provide further details on the NAMCS sampling and weighting methods.⁵ For the purposes of this study, we evaluated prescribing frequencies for common pain therapies to manage chronic pain in U.S. outpatient settings.^{5,18} Pain medication drug classes (Table 1) were the following: opioids/opioid-like agents, analgesics/NSAIDs, tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), other antidepressants, anticonvulsants, antirheumatics/immunologics, muscle relaxants, topical products, and corticosteroids. All agents except for opioids/opioid-like agents and analgesics/NSAIDs were further categorized as adjuvant therapy to create 3 major drug class categories: opioids/opioid-like agents, analgesics/NSAIDs, and adjuvants.²¹ Because the NAMCS database does not include the dosage or frequency for medications prescribed and fails to indicate whether therapy was the immediate-release or extended-release formulation, 2 pharma-

cotherapy sources (Lexi-Comp online and *Pharmacotherapy* by Joseph Dipiro^{14,20}) were consulted to select the maximum daily recommended dose and calculate the 30-day supply prices from *Red Book 2009*. When generic products were not available, brand name formulations, including extended-release, were included in the cost estimation and are noted in Table 1. The common units sold (e.g., quantity of 20, 30, 45, 60, 100, 120) were selected for each drug based on availability and the standard quantities. To be consistent with pricing, doses prescribed (medication strength) were based on the 2 pharmacotherapy sources named above.^{14,20} The costs from various manufacturers and distributors were averaged to obtain the 3 lowest prices a patient in the United States would expect to pay for that particular drug and the average price for a 30-day supply. For all pain therapies, the maximum recommended dose was used to determine the 30-day supply prices from *Red Book 2009*.⁴

Data Analysis

The study estimated the total expenditure of common pain medications (i.e., opioids, analgesics, NSAIDs, antidepressants, anticonvulsants) prescribed for common nonmalignant pain diagnoses (identified by ICD-9-CM codes: primary, secondary, and tertiary). Weighted prescription frequencies were obtained from NAMCS data (2000-2007) using statistical software STATA, version 12 (StataCorp, College Station, TX).

TABLE 2 Costs of Pain Medication by Therapy Category in the United States, 2000-2007^a

Drug Class	Average Costs for Patient (\$)	Weighted Frequency	Total Costs 2000-2007 (\$)	Total Annual Costs for United States (\$)	Rounded Annual Figure (\$ Billions)	Total Drug Costs (%)
Opioids/opioid-like	251.14	113,855,349	28,593,632,348	3,574,204,043	3.57	20.08
Analgesics/NSAIDs ^b	104.93	143,343,104	15,040,991,903	1,880,123,988	1.88	10.56
Tricyclic antidepressants	22.70	19,085,819	433,248,091	54,156,011	0.05	0.30
SSRIs	75.39	96,334,224	7,262,637,147	907,829,643	0.91	5.10
Other antidepressants	154.29	47,043,097	7,258,279,436	907,284,930	0.91	5.10
Anticonvulsants	86.55	48,645,826	4,210,296,240	526,287,030	0.53	2.96
Antirheumatics/immunologics	1,959.18	24,330,603	47,668,030,786	5,958,503,848	5.96	33.47
Muscle relaxants	155.49	40,058,998	6,228,773,599	778,596,700	0.78	4.37
Topical products	874.57	14,071,705	12,306,691,042	1,538,336,380	1.53	8.64
Corticosteroids ^c	273.13	49,120,138	13,416,183,292	1,677,022,912	1.68	9.42
Total		595,888,863	142,418,763,884	17,802,345,486	17.8^d	100.00

^aDrug prices are based on 30-day supply at the maximum daily recommended dose, using 3 lowest manufacturer prices listed in Red Book 2009 to reflect market pricing.³ Expenditure for a specific pain medication was calculated by multiplying the volume of medications prescribed between 2000 and 2007 (referred to as “frequency” by NAMCS) with average price for 30-day supply at the maximum daily dose (calculated from Red Book) of the specific pain medication.

^bNonselective and COX-2 selective inhibitors.

^cTablets, solutions, and injections.

^dInflation adjusted (as per Consumer Price Index).²³ The 2013 total annual cost for pain medication therapy in the United States was \$18.33 billion.

NSAID = nonsteroidal anti-inflammatory drug; SSRI = selective serotonin reuptake inhibitor.

TABLE 3 Demographic Information About Study Participants^a

Variable	Estimated Percentage
Age (mean, years)	53.27
Gender	
Female	62.84
Race	
Caucasian	87.26
African American	9.27
Hispanic	7.63
Other	3.45
Polypharmacy	
Having > 5 medications	29.20

^aN = 690,205,290 weighted outpatient visits.^{2,5}

Pain medication frequency analyses were statistically weighted using the NAMCS sampling weights to make national estimates for all pain therapy categories. All statistics provided in the NAMCS are office visit data. The average prices of medications were calculated from Red Book 2009. Medication costs were calculated from the average of the 3 lowest average wholesale prices (AWP) from the Red Book for the most common packaged quantity sold in the United States.⁴ The average prices were calculated based on the 3 lowest prices reported in the Red Book for maximum recommended daily dose.

Prices of the pain medication were collected using Microsoft Excel (Microsoft Corporation, Redmond, WA). Expenditure for a specific pain medication was calculated by multiplying the volume of medications prescribed between 2000 and 2007 (referred

to as “frequency” by NAMCS) with average price for 30-day supply at the maximum daily dose (calculated from Red Book) of the specific pain medication (Table 2). Table 2 provides total pain medication costs calculated in 2009 dollar value. We also showed inflation-adjusted cost estimates in 2013 dollars using the U.S. Bureau of Labor Statistics Consumer Price Index.^{22,23} Additionally, this study conducted a visit-trend analysis and used time series analysis to forecast visits using U.S. population data and statistics. First, we evaluated national chronic pain (noncancer) visit trends by using NAMCS outpatient data from 2000 to 2007. These multilevel weighted data were used to gather nationally representative samples for NMCP visits in the United States, where the unit of analysis was the individual patient visit.⁵ NAMCS reported patients’ reason for visit, and medical diagnosis (primary, secondary, and tertiary) made during the outpatient visits was included for this analysis. We used time series analysis to extrapolate pain visit frequencies for coming years using U.S. population data and statistics found at census.gov.²³

Results

The average price for each pain medication by category for NMCP is presented in Table 2, for approximately 690 million weighted outpatient visits taking place between 2000 and 2007 in the United States. Almost all (99%) of patients received a NMCP medication during the visit. Among those patients, 29% reported receiving ≥ 5 medications (polypharmacy; Table 3). National prescription percentages for each pain therapy category are presented in Table 2. Nationally, about 113.8 million prescriptions were made for opioids/opioid-like medications to treat NMCP between the years 2000 to 2007. Therefore, the

FIGURE 1 Pain Medication Costs by Major Drug Classes

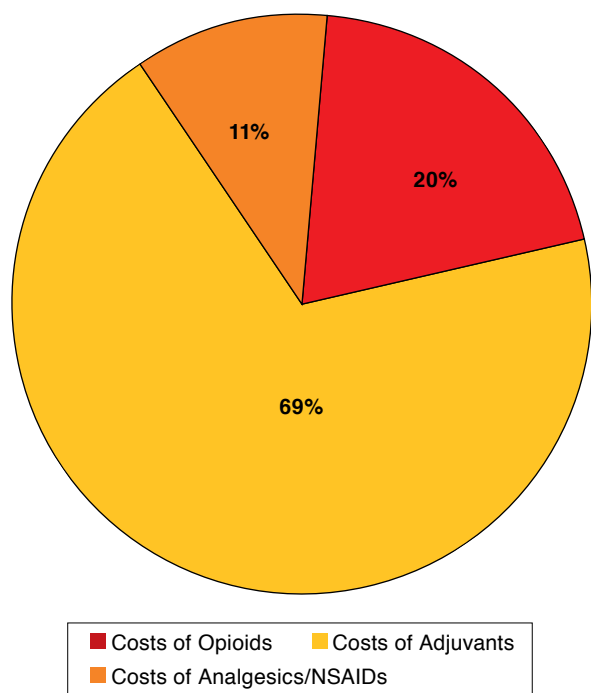
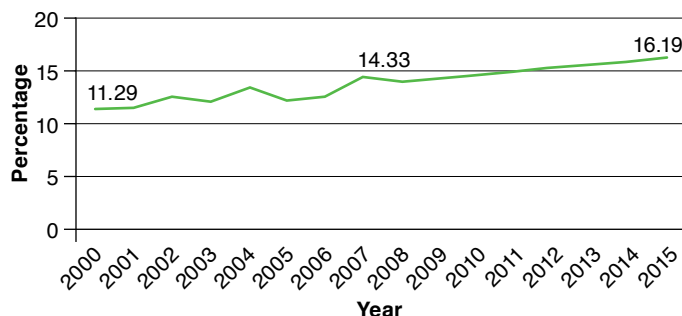


FIGURE 2 Estimated Percentage of Pain Outpatient Visits by Year, 2000-2007, and Extrapolated Figures up to 2015



Note: The graph shows the linear trend in pain visits over study period (2000-2007). Using time series analysis, extrapolated pain visit % for 2015 is 16.19%.²⁴ Number of yearly pain-related visits: 2000 = 77,924,177; 2001 = 79,787,732; 2002 = 86,206,641; 2003 = 83,652,881; 2004 = 92,487,509; 2005 = 84,412,107; 2006 = 86,896,846; 2007 = 98,906,418.

NSAID = nonsteroidal anti-inflammatory drug.

annual expenditure for opioids/opioid-like medications prescribed for NMCP in the United States was estimated to be \$3.6 billion annually (Table 2). The opioids/opioid-like medication category contributed 20.08% of the total pain medication costs (Table 2, Figure 1). Analgesics/NSAIDs were prescribed 143.3 million times in the 8-year study period. Analgesics/NSAIDs accounted for 11% of overall pain medication costs (Table 2, Figure 1). Based on this analysis, the total cost of all pain medications prescribed for the 8-year duration was approximately \$142.4 billion (\$17.8 billion annually).

This study also analyzed national NMCP outpatient visits. We reported weighted patient visits and found that in 2000 there were 77,924 visits, similar to national figures for other years—2001: 79,787; 2002: 86,206; 2003: 92,487; 2005: 84,412; 2006: 86,896; and 2007: 98,906 (Figure 2). This study found a linear trend in national pain visits, reporting an upward trend in NMCP visits (from 11% to 14%) from 2000 to 2007 in the United States. Figure 1 illustrates the large difference in pricing for analgesics/NSAIDs compared with opioids and adjuvants. Analgesics/NSAIDs, opioids, and adjuvant therapy accounted for 11%, 20%, and 69% of total costs respectively (Figure 1). Adjuvant therapy was commonly used to treat NMCP in conjunction with other pain medications. These

included the drug classes antirheumatics and immunologics, muscle relaxants, topical products, corticosteroids, SSRIs, tricyclic antidepressants, other antidepressants, and anticonvulsants (Table 2, Figure 1). In this study period, adjuvant therapy cost \$98.7 billion in 8 years. Among adjuvants, antirheumatics/immunologics costs were \$47.6 billion per year and contributed to 32.8% of the total pain medication costs (Table 2). Other adjuvant costs included muscle relaxants (4.4%), topical products (8.6%), and corticosteroids (9.4%; Table 2, Figure 1). The 3 major drug categories for pain therapy costs for the United States annually were analgesics/NSAIDs (\$1.9 billion), opioids (\$3.6 billion), and adjuvants (\$12.3 billion).

The use of NSAIDs resulted in an annual cost of approximately \$1.9 billion. Celecoxib was one of the costly medications prescribed over the 8-year period, accounting for approximately 29.7 million weighted prescriptions, according to the NAMCS frequency. The opiate class incurred costs of \$28.6 billion for the United States from 2000 to 2007 (\$3.6 billion annually). The most prescribed opiate was hydrocodone/acetaminophen, with 39 million weighted prescriptions written from 2000 to 2007, contributing to the pain medications expenditures of \$4.3 billion.

Discussion

Our study estimated that the total cost of NMCP medications in the United States was approximately \$142.4 billion (\$17.8 billion annually) between the years 2000 and 2007. A study conducted by the IOM estimated direct medical costs and loss of productivity for pain to be \$560-\$635 billion annually, where both cancer and noncancer chronic pain were considered.^{1,2} The incremental costs of health care related to pain were estimated to be \$261-\$300 billion, and loss in productivity for pain was

estimated to be between \$297-\$336 billion for 2008.^{1,2} In contrast, our study specifically evaluated the direct costs of medications only for the treatment of NMCP and elucidated costs by drug categories of pain medications (Table 2), providing new information specifically for those interested in potential costs for chronic pain medications as defined by medication category. Further, we provided a breakdown of the use of the various drug categories used to treat chronic pain.

Over the 8-year study period, we identified a notable change in pain visits (from 11% to 14%) in the United States (Figure 2). This percentage could be different from previously reported studies, as there are wide variations in literature, based on how pain is defined and which population is studied.^{24,25} With the continuing increase in the aging population who experience more NMCP conditions and increasing awareness of the undertreatment of chronic pain, outpatient chronic pain visits may continue to increase in the coming years. Therefore, policymakers and decision makers should consider allocating resources accordingly to meet the potential growing need. In addition, anticipating the growing demand for managing chronic pain mandates a need for the assessment of educational training to better prepare clinicians to manage NMCP. A recent study identified the underutilization of guideline-recommended chronic pain therapies, including pharmacotherapy, nonpharmacotherapy, and combination therapies, suggesting the need for enhanced knowledge and training.¹⁸ However, the dangers of opioids and NMCP medication should not be ignored. While beyond the scope of this study, which focused on medication costs and NMCP visits, further evaluation, analysis, research, and training in NMCP management should include balancing the increased recognition and awareness of the undertreatment of NMCP with the increased risk of abuse, misuse, overdose, potential polypharmacy, and drug interactions that come with the use of opioids and combination pain medication therapy.^{7-9,12,15-17,20,26}

This study emphasized the breakdown of the use of the various types of pain-related drug categories. Despite having the highest in weighted frequency for prescriptions nationally, analgesics/NSAIDs accounted for about 11% for the overall costs of NMCP medications for those years in the United States (Table 2). Opioids accounted for 20% of the overall pain medication-related costs.

In our study, the direct costs of medications were calculated using national survey data for prescription frequencies and medication prices published in the *Red Book 2009*, reporting AWP. We believe these are conservative cost estimates, since the average prices were calculated based on the 3 lowest prices reported in the *Red Book 2009* for maximum recommended daily dose for a 30-day supply. In addition, while this study captured pharmacotherapy treatments prescribed in a large outpatient office visit population, it did not include chronic pain populations managed in hospital outpatient and ED set-

tings. Areas that warrant future research include measuring the costs of the pain medication for patients treated in the hospital outpatient and ED settings, as well as investigating better sources to measure the use of nonpharmacotherapy and complementary and alternative medicine treatments.

This study considered several categories of antidepressants, including SSRIs, tricyclic antidepressants, and other antidepressants. The other antidepressants category included 3 medications: bupropion, duloxetine, and venlafaxine (Table 1). This category of other antidepressants accounts for about 5.1% of the total pharmacotherapy costs for those years. The greater cost of this drug class may be attributed to the brand name-only status in a small class of medications during the 2000-2007 time frame. Two additional medications (desvenlafaxine [Pristiq] and milnacipran [Savella]) added into this drug class in the United States after 2007 were not included in this study. Of the antidepressants, Cymbalta and Savella have U.S. Food and Drug Administration-labeled indications for chronic pain conditions.¹⁴ Other antidepressants may be used as unlabeled indications for chronic pain conditions or may be used for depression, which is often closely associated with chronic pain as part of what is known as the syndrome of chronic pain.²⁰

Tricyclic antidepressants (average monthly cost of therapy \$22.70) resulted in the least expensive option compared with all antidepressant categories, according to *Red Book 2009* (Table 2). Tricyclic antidepressants are more cost-effective because of generic options available.^{14,20} Moreover, tricyclic antidepressants, although used as an unlabeled indication, have demonstrated efficacy comparable to or better than other classes of antidepressants for certain types of chronic pain.^{11,13,21} However, this study reports underutilization of tricyclic antidepressants (0.3%). Similarly, a previous study reported the underutilization of tricyclic antidepressants (2%) out of all NMCP treatment options.^{18,21} This low rate of use could be due to the fact that tricyclic antidepressants have higher side effect profiles, and they are not always well tolerated. However, from these data, our study cannot establish this conclusion.

According to *Red Book 2009* (Table 2), the antirheumatic/immunologic category is shown to be the highest in average price (\$1,959.18 per 30-day supply). The antirheumatic/immunologic category accounts for about 33.5% of the total cost for all pain medications, although this figure represents a relatively small patient population.

This study provides new insight into the costs attributable to treat adult patients with NMCP in the United States based on pain medication categories. Although the costs of the therapy may not be the sole consideration by a clinician when prescribing, clinicians' treatment plans are increasingly influenced by drug insurance plan formularies. Therefore, not only decision makers, but also clinicians increasingly expect to consider costs of the medication, as health plans sometimes "provide financial inducements for enrollees to select the least expensive drugs

while avoiding the restrictions of entirely closed formulary systems.²⁷ Unfortunately, most times these therapy costs and prices are not shared publicly; therefore, we hope that these national estimates may guide policymakers to illustrate costs and use of pain-related health care resources, and that these estimates will guide clinicians based on evidence-based guidelines and health technology assessments that include cost considerations.

Limitations

Though not without limitations, the results are appealing, since this study shows a measure to capture money spent on pain medications in the United States. There are several limitations to this study. First, information collected from the NAMCS database did not provide pain assessment information, so that whether the pain was effectively treated is not known, nor is whether additional therapy was needed at extra cost to these patients later. Second, the NAMCS database does not include the dosage or frequency for medications prescribed, and it fails to designate whether therapy was the immediate-release or extended-release formulation. Third, the NAMCS database was based on the number of patient visits at each office, not on individual patients. Another limitation of our study is that it reflects only cost estimations rather than actual costs incurred for each patient. The NAMCS dataset provides data on the medication ordered, supplied, administered, or continued during the visit, not capturing the prescription-filled data. Therefore, we do not know whether these prescribed medications were actually filled by the patients or their caregivers. For the purposes of this study, medications ordered, supplied, administered, or continued during the office visits were included in cost analysis, not capturing prescription-filled data or claims. Hence, this study reflects the “treatment plan” and used this plan to base the study’s cost estimation. Also, the NAMCS dataset covers only outpatient office visits and is based on voluntary survey reporting data provided by the physicians/staff; the data do not consider pain management handled in hospital outpatient setting and in the ED setting. Finally, this study did not consider the cost of nonpharmacological therapy such as physical therapy and or complementary alternative therapy (i.e., massage, nutritional supplementation, physical therapy).²⁰ Further research including nonpharmacological costs would strengthen this cost analysis for NMCP treatment.

Conclusions

This study describes the cost of pain medications prescribed to a large outpatient population over an 8-year period in the United States. Policymakers, stakeholders, and health plan decision makers may consider this cost analysis as they need to know how drug costs are being allocated. Moreover, information about costs and use of pain medications is valuable for the practitioner making individual patient care decisions, as well as for those who make population-based decisions. Pharmacists

can educate other health care professionals regarding different treatment options with cost analysis or even with comparative effectiveness research as the nation moves toward value-based benefit design. The increased trend in pain visits was highlighted, so that health care providers and health plan decision makers can consider allocating scarce resources efficiently. In addition, these results can assist others in providing a baseline resource to further evaluate the costs and effectiveness of various therapies for pain management to assist in the development of effective pain management algorithms to diminish the public health burden of chronic pain.

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DISCLOSURES

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Study concept and design were contributed by Rasu and Knell. Vouthy had primary responsibility for data collection, with assistance from Rasu. Data interpretation was the work of Rasu, Knell, and Vouthy, assisted by Fikru and Agbor Bawa. The manuscript was written by Rasu, Knell, and Vouthy, assisted by Crowl and Stegeman, and was revised primarily by Rasu, aided by Vouthy, Knell, and Agbor Bawa.

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