
ORIGINAL ARTICLE

Use and Costs of Prescription Medications and Alternative Treatments in Patients with Osteoarthritis and Chronic Low Back Pain in Community-Based Settings

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■ **Abstract:**

Objective: To evaluate the use and direct medical costs of pharmacologic and alternative treatments for patients with osteoarthritis (OA) and chronic low back pain (CLBP).

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Methods: The LifeLink™ Health Plan Claims Database was used to identify patients ≥ 18 years old, diagnosed with OA ($N = 112,951$) or CLBP ($N = 101,294$). Of these patients, 64,085 with OA and 47,386 with CLBP received pain-related treatments during CY2008 and were selected for inclusion. For patients in both cohorts, pharmacologic and alternative treatments, and direct medical costs were examined during CY2008.

Results: Opioids were the most frequently prescribed medication ($>70\%$) in both groups, followed by nonselective nonsteroidal anti-inflammatory drugs ($>50\%$). Over 30% received antidepressants, $>20\%$ received benzodiazepines, and 15% in each group received sedative hypnotics. Use of alternative treatments was as follows: chiropractor, OA 11%, CLBP 34%; physical therapy, 20% in both groups; transcutaneous electrical nerve stimulations (TENS), OA 14%, CLBP 22%; acupuncture, hydrotherapy, massage therapy, and biofeedback, $<3\%$ in both groups. Mean (SD) total healthcare costs among these patients were, OA: \$15,638 (\$22,595); CLBP: \$11,829 (\$20,035). Pharmacologic therapies accounted for approximately 20% of these costs, whereas alternative treatments accounted for only 3% to 4% of the total costs.

Conclusions: Patients with OA and CLBP used a variety of pain-related and adjunctive medications. Although,

alternative treatments are widely recommended, we found limited use of several of these in clinical practice, potentially due to the source of our data (commercial claims). Further research is needed to ascertain the extent to which such therapies contribute to the total costs of OA and CLBP management. ■

Key Words: osteoarthritis, chronic low back pain, burden, medications, alternative treatments, direct medical costs

INTRODUCTION

Osteoarthritis (OA) is a chronic condition commonly accompanied by pain and has an estimated prevalence in the United States (U.S) of 27 million individuals.¹ The economic impact of OA is evidenced by the substantial indirect costs related to work productivity losses and the incremental healthcare resource utilization compared to comparison groups without OA.²⁻⁶ A recent study reported average annual direct medical costs of OA in the United States of \$12,905 ($\pm \$21,884$) compared with \$5,099 ($\pm \$13,855$, $P < 0.0001$) in an age, gender, and region matched control group of individuals without OA.⁷

Similarly, low back pain (LBP) incurs a substantial economic burden because of its high prevalence in working adults in western countries. The reported lifetime prevalence rates of LBP in the United States, Canada, and Europe range from 49% to 70%,⁸ and in the United States alone, the estimated direct and indirect costs of LBP range from \$84.1 billion to \$624.8 billion.⁹ For patients with chronic LBP (CLBP), defined as pain lasting for ≥ 3 months,¹⁰⁻¹² average annual direct costs were calculated to be \$8,386 ($\pm \$17,507$).¹³ Although only 15% of patients with LBP develop CLBP, disability related to CLBP accounts for a substantial portion of LBP-related costs.^{1,14,15}

The direct and indirect costs of OA and CLBP have previously been explored.^{2,3,5,6,9,16} Two recent studies based on a large administrative database described comorbidities, pharmacologic treatment patterns and direct medical costs of patients with OA and CLBP in general practice setting in the United States.⁷ These studies suggested that a higher comorbidity burden and a greater likelihood of use of medications for pain and pain-related sequelae relative to control cohorts without OA or CLBP.

Treatment guidelines for the management of OA and CLBP have each recommended a multidisciplinary approach comprising pharmacologic therapies (e.g.,

acetaminophen, nonselective nonsteroidal anti-inflammatory drugs [NS-NSAIDs], cyclo-oxygenase 2 selective inhibitors [Cox-2s], opioids, tramadol, and antidepressants) and nonpharmacologic or alternative treatments (e.g., physical therapy, acupuncture, TENS, assistive devices, spinal manipulation, and supplements including chondroitin and glucosamine).¹⁷⁻²⁶ While there is an evidence base for efficacy for all of the recommended nonpharmacologic therapies, this evidence base is limited and suggests that these therapies may be of benefit only in some patients. The strongest evidence is for physical/exercise therapy; other nonpharmacologic therapies have a much lower level of evidence, and there has been a lack of rigorous evaluation of the efficacy and safety of most of the alternative and complementary therapies.

Despite OA and CLBP treatment guidelines recommending an integrated approach that includes alternative treatments, there is a dearth of objective data on the extent to which such treatments are actually prescribed in usual care, or their contribution to the total medical costs of OA and CLBP. Numerous studies have suggested that many patients with OA or CLBP have tried, are willing to try, or are using alternative therapies.²⁷⁻³⁹ However, these studies were based on patient self-report surveys and were often from either primary care settings or ex-United States; there has been a lack of studies in large US populations such as those available using claims data.

Accordingly, the purpose of this article was to describe the use and direct medical costs of alternative treatments. To provide a comprehensive assessment of OA and CLBP pain management strategies, use and costs of pharmacologic therapies were also assessed.

METHODS

Data Source

The LifeLink™ Health Plan Claims Database (IMS, Inc., Watertown, MA, USA), consisting of adjudicated medical and pharmaceutical claims data from a systematic sample of over 98 managed healthcare plans throughout the United States and representing approximately 16 million covered lives per year was used in this study. The database contains de-identified records of all paid claims for enrollees in the database. All patient identifiers have been either removed or encrypted and the database is in full compliance with HIPAA (Health Insurance Portability and Accountability

Act of 1996). Each provider or facility claim contains information on the date service was rendered, inpatient and outpatient diagnoses (ICD-9-CM format [International Classification of Diseases, Ninth Revision, Clinical Modification]), surgeries and procedures (CPT-4 [Current Procedure Terminology, 4th Edition] and HCPCS [Healthcare Common Procedural Coding System] formats), amounts charged by providers, and amounts paid by the health plans. Pharmacy records include both retail and mail order prescription, and for each prescription record the National Drug Code number, days supply, and quantity dispensed are also available. Supplemental data include patient demographic (age, gender, and region) and enrollment information (start and stop dates of health plan coverage). All records for each patient can be linked using the unique encrypted patient identifier to facilitate evaluation of each enrollees claims records over the study period.

Sample Selection

Individuals who were at least 18 years old as of January 2008, had complete data for age and gender, were enrolled in Medicare supplemental or capitated plans if they were ≥ 65 years old, were continuously enrolled during the calendar year 2008 (the study period), and had a diagnosis of OA or CLBP were selected. An OA

diagnosis was defined as ≥ 1 healthcare claim with ICD-9-CM codes 715.XX during each of CY2007 and CY2008. A diagnosis of CLBP was defined as ≥ 2 healthcare encounters with ICD-9-CM codes 720, 720.1, 720.2, 721.3, 721.42, 722.1, 722.32, 722.5, 722.73, 722.83, 722.93, 724, 724.02, 724.2, 724.3, 724.4, 724.5, 724.6, 724.7, 724.71, 724.79, 738.4, 739.3, 739.4, 756.11, 756.12, 805.4, 805.6, 846, 846.1, 846.2, 846.3, 846.8, 846.9, 847.2, 847.3, or 847.4 during each of CY2007 and CY2008, with the two claims being ≥ 90 days apart in each of the 2 years. Because acute LBP is a frequent complaint in primary care, and because CLBP by definition is LBP lasting for at least 3 months, we required that individuals have at least two claims in two consecutive years and that the two claims be at least 3 months apart, to insure that our study sample was truly reflective of CLBP as opposed to patients with episodes of acute LBP. A total of 112,951 patients with OA and 101,294 patients with CLBP were identified. From these groups, subgroups of patients with OA and CLBP who were prescribed acetaminophen, NS-NSAIDs, Cox-2s, tramadol, and opioids (the recommended first-, second-, and third-line pain medications^{17-19,21-26,40}) during 2008 were then selected, and all reported analyses were performed in these subgroups of patients. The study entry criteria are summarized in Figure 1.

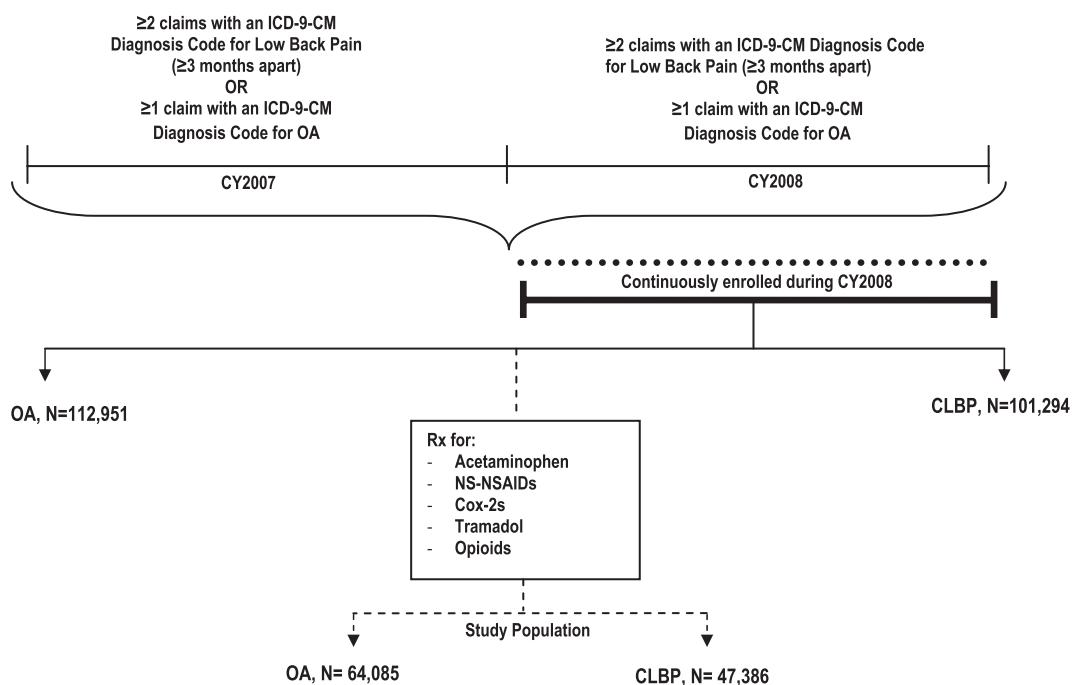


Figure 1. Study entry criteria.

Study Measures

Demographic characteristics (age and gender), and prevalence of select chronic conditions, including diseases of the cardiovascular, digestive, and musculoskeletal systems, conditions documented to occur concomitantly with chronic pain (depression, anxiety, and sleep disorders),^{41–47} and neuropathic pain conditions were examined. Presence of each comorbidity was defined as ≥1 healthcare claim with the corresponding ICD-9-CM code (Table 1) for that comorbidity during CY2008.

Use of pharmacologic and alternative treatments was assessed as the proportions of patients with OA and CLBP who had ≥1 prescription claims for pain-related or adjuvant medications (for treating pain-related anxiety, depression, and sleep impairment), or ≥1 prescription or procedure claims (CPT-4 or HCPCS codes) for the alternative therapies during CY2008. The number of prescriptions for each of the various study medications and the number of prescriptions or the number of times patients received alternative treatments (e.g., physical therapy or TENS) during CY2008 was also assessed. Direct costs of pharmacologic and alternative treatments were tabulated and included amounts reimbursed by payers and patient copays. The evaluated pain-related and adjuvant medications included acetaminophen, NS-NSAIDs, Cox-2s, tramadol, opioids, salicylates, various antidepressants (selective serotonin re-uptake inhibitors [SSRIs], serotonin-norepinephrine re-uptake inhibitors [SNRIs], tricyclic antidepressants [TCAs], tetracyclic and miscellaneous antidepressants), benzodiazepines, sedatives and hypnotics, anticonvulsants, muscle relaxants, and miscellaneous agents (e.g., nalbuphine and pentazocine).

The examined alternative treatments included acupuncture, hydrotherapy, massage therapy, physical therapy, biofeedback, TENS, cognitive behavioral therapy (CBT), heat/cold application, chiropractic care, osteopathic care, topical analgesics, assistive devices (walker [E0130 – E0159, K0458, K0459], crutches [A4635, E0110 to E0118], cane [E0100, E0105], orthotics/braces [L0100 to L0999, L1900 to L2090, L2200 to L2375, L2500 to L2550, L2650 to L2785, L2860 to L2999, L3650 to L3915, L3919 to L3978, L4000 to L4370, L4386 to L4398, L1600 to L1755, L2570 to L2640, L1800 to L1885, L2380 to L2492, L2795 to L2830, L4380], footware [L3000 to L3207, L3215 to L3649], wheelchair [E0950 to E1161, E1210 to E1298, E2201 to E2399, E2601 to E2621, K0001

to K0109, K0114, K0195, K0452, K0669, K0733 to K0737, K0800 to K0898]) vitamins, and glucosamine/chondroitin combination.

The total annual healthcare costs among the entire subgroups of patients with OA and CLBP included in these analyses during CY2008 were determined and included costs associated with physician office visits, ER visits, visits for other outpatient services including radiology and laboratory/pathology, hospitalizations, and costs of pharmacological and alternative treatments. All analyses were descriptive in nature and were performed using the SAS software system, PC version 8.0 (SAS Institute Inc., Cary, NC, U.S.A.).

RESULTS

Demographic and Clinical Characteristics

A total of 64,085 patients with OA and 47,386 patients with CLBP satisfied all the study entry criteria and were included in the analyses. The mean age of patients with OA was 56.4 ± 9.3 years, 63.1% of patients were women, whereas on average patients with CLBP were 47.7 ± 11.6 years old, 57.3% women. Clinical comorbidities of patients with OA and CLBP are presented in Table 1. Both patients with OA and CLBP had multiple pain-related and chronic comorbidities. The most prevalent comorbidities were arthritis and arthropathies other than OA (OA, 68.0%; CLBP 42.7%), hypertension (OA, 55.9%; CLBP, 35.8%), hyperlipidemia (OA 51.7%; CLBP, 36.2%), back and neck pain (OA, 22.6%; CLBP, 43.1%), and back and neck pain with neuropathic involvement (OA, 16.7%; CLBP, 39.1%). The prevalence rates for chronic pain-related sequelae were: depression (OA, 13.8%; CLBP, 16.5%), anxiety (OA, 7.2%; CLBP, 10.2%), and sleep disorders (OA, 12.9%; CLBP, 12.2%).

Use and Costs of Pharmacologic and Alternative Treatments

Exposure to, magnitude of use, and costs of pharmacologic and alternative treatments among patients with OA and CLBP during 2008 are presented in Tables 2 and 3. Opioids were the most frequently prescribed pain medications (OA, 71.7%; CLBP, 79.0%), followed by NS-NSAIDs (OA, 55.1%; CLBP, 51.5%), followed by tramadol (OA, 17.3%; CLBP, 17.5%). Additionally, patients were also prescribed “adjunctive” medications (for treating pain-related sequelae

Table 1. Clinical Comorbidities of Patients with OA and chronic LBP (CLBP)

Comorbid diagnosis	ICD-9-CM Codes	OA (N = 64,085) N (%)	CLBP (N = 47,386) N (%)
Mental disorders			
Depression	296.2X, 296.3X, 300.4, 311	8,854 (13.8)	7,822 (16.5)
Bipolar disorder	296.4X, 296.5X, 296.6X, 296.7	499 (0.8)	555 (1.2)
Anxiety	300.00, 300.5, 300.09, 300.20, 300.22, 300.23, 300.29, 300.3, 308.3	4,641 (7.2)	4,820 (10.2)
Generalized anxiety disorder	300.02	1,368 (2.1)	1,481 (3.1)
Panic disorder	300.01, 300.21	583 (0.9)	768 (1.6)
PTSD	309.81	306 (0.5)	407 (0.9)
Psychosis	296.9X, 298.X	546 (0.9)	549 (1.2)
Sleep disorders			
Insomnia/sleep disorders	780.5X, 307.4X, 347.0X, 347.1X, V69.4	8,234 (12.9)	5,772 (12.2)
Sleep apnea	780.51, 780.53, 780.57	4,485 (7.0)	2,216 (4.7)
Cardiovascular disorders			
Coronary heart disease	410.XX–414.XX	7,019 (11.0)	3,311 (7.0)
Hypertension	401.X	35,805 (55.9)	16,954 (35.8)
Hyperlipidemia	272.0, 272.1, 272.2, 272.4	33,102 (51.7)	17,139 (36.2)
Diseases of the digestive system			
Irritable bowel syndrome	564.1	1,572 (2.5)	1,248 (2.6)
Gastroesophageal reflux disease	530.11, 530.81	12,247 (19.1)	7,331 (15.5)
Gastritis	535.00–535.5X	3,696 (5.8)	2,621 (5.5)
Duodenitis	535.6X	288 (0.5)	243 (0.5)
Other	520.5–530.10, 530.19–530.7, 530.82–530.9, 536.0–537.X, 540.0–543.X, 550.00–553.XX, 555.0–558.X, 560.XX, 562.00–562.01, 562.10–562.11, 564.2–569.2, 569.41–569.81, 569.84–577.9, 579.X	14,833 (23.2)	10,622 (22.4)
Musculoskeletal pain conditions			
Lupus	710	672 (1.1)	304 (0.6)
Diffuse diseases of connective tissue	710.1, 710.2, 710.3, 710.4, 710.5, 710.8, 710.9	503 (0.8)	207 (0.4)
Arthritis and other arthropathies	711.XX, 712.XX, 713.X, 714.4X, 714.8X, 714.9X, 716.XX, 717.XX, 718.XX, 719.XX	43,548 (68.0)	20,235 (42.7)
Rheumatoid arthritis	714.0, 714.1, 714.2	3,937 (6.1)	1,088 (2.3)
Osteoarthritis	715.XX	64,085 (100.0)	9,226 (19.5)
Low back pain	720, 720.1, 720.2, 721.3, 721.42, 722.1, 722.32, 722.5, 722.73, 722.83, 722.93, 724, 724.02, 724.2, 724.3, 724.4, 724.5, 724.6, 724.7, 724.71, 724.79, 738.4, 739.3, 739.4, 756.11, 756.12, 805.4, 805.6, 846, 846.1, 846.2, 846.3, 846.8, 846.9, 847.2, 847.3, 847.4	23,219 (36.2)	47,386 (100.0)
Back and neck pain, other than low back pain	720.81, 720.89, 720.9, 721.0, 721.2, 721.5, 721.6, 721.7, 721.8, 721.90, 722.11, 722.30, 722.31, 722.39, 722.4, 722.6, 722.80, 722.81, 722.82, 722.90, 722.91, 722.92, 723.X (except 723.4), 724.01, 724.1, 724.8, 724.9, 737.10, 737.11, 737.12, 737.19, 737.20, 737.21, 737.22, 737.29, 737.30, 756.10, 756.13, 756.14, 756.15, 756.16, 756.17, 756.19, 805.8, 847.9	14,497 (22.6)	20,409 (43.1)
Other musculoskeletal pain	730.00–739.X	18,694 (29.2)	15,540 (32.8)
Neuropathic pain conditions			
Diabetic neuropathy	357.2, 250.6	502 (0.8)	238 (0.5)
Postherpetic neuralgia	053.1	122 (0.2)	84 (0.2)
Carpal tunnel syndrome	354.0	3,428 (5.4)	2,025 (4.3)
Causalgias	337.2X, 354.4, 355.71, 355.9	1,075 (1.7)	900 (1.9)
Trigeminal neuralgia	350.1	118 (0.2)	92 (0.2)
Atypical facial pain	350.2	89 (0.1)	110 (0.2)
Phantom limb pain	353.6	9 (0.0)	7 (0.0)
Autonomic neuropathies	337.1, 337.9	168 (0.3)	93 (0.2)
Other polyneuropathies	344.6, 353.0, 353.1, 353.8, 353.9, 354.1, 354.2, 354.3, 354.5, 354.8, 354.9, 355.0, 355.1, 355.2, 355.3, 355.4, 355.5, 355.6, 355.79, 355.8, 357.1, 357.3, 357.4, 357.5, 357.6, 357.7, 357.8, 357.9	2,982 (4.7)	2,222 (4.7)
Back and neck pain with neuropathic involvement	721.1, 721.41, 721.42, 721.91, 722.7X, 723.4, 724.3, 724.4	10,679 (16.7)	18,546 (39.1)

LBP, low back pain; OA, osteoarthritis.

including anxiety, depression, and sleep impairment); antidepressants (OA, 32.0%; CLBP, 34.4%), benzodiazepines (OA, 20.8%; CLBP, 26.8%), sedative and hypnotics (OA, 15.0%; CLBP, 14.9%), and muscle relaxants (CLBP, 41.5%).

One of every five patients with OA (20.2%) received physical therapy and over 20% used assistive devices (including walkers [5.5%], crutches [2.0%], canes [1.4%], orthotics/braces [13.2%], footware [3.6%], and wheelchairs [1.5%]), 11%

Table 2. Use and Costs of Pharmacologic Therapies

Medications	Percent use		No. prescriptions		Costs	
	OA (N = 64,085) N (%)	Chronic LBP (CLBP) (N = 47,386) N (%)	OA Mean (SD), Median	CLBP Mean (SD), Median	OA Mean (SD), Median	CLBP Mean (SD), Median
Opioids	45,924 (71.7)	37,435 (79.0)	5.7 (6.9), 3	6.4 (7.6), 3	287.4 (1,652.1), 27.1	364.5 (1,896.5), 29.1
NSAIDs						
Cox-2 inhibitors	9,592 (15.0)	3,440 (7.3)	3.8 (3.3), 3	3.3 (3.2), 2	690.0 (621.5), 501.2	569.7 (596.8), 298.7
NS-NSAIDs	35,339 (55.1)	24,398 (51.5)	3.6 (3.2), 2	2.7 (2.6), 2	119.3 (212.3), 41.6	67.0 (149.7), 21.6
Any NSAIDs	41,925 (65.4)	26,566 (56.1)	3.9 (3.3), 3	2.9 (2.8), 2	258.4 (431.6), 75.2	135.3 (312.6), 27.1
Salicylates	632 (1.0)	456 (1.0)	3.1 (3.8), 1.5	3.1 (3.6), 2	63.6 (160.2), 20	67.4 (140.5), 20.6
Tramadol	11,105 (17.3)	8,288 (17.5)	3.5 (3.9), 2	3.4 (4.1), 2	137.6 (327.3), 33.3	119.4 (306.2), 25.8
Acetaminophen	1,423 (2.2)	1,531 (3.2)	3.7 (4.5), 2	3.7 (5.0), 1	84.4 (207.8), 21	81.8 (237.8), 19.0
Antidepressants						
SSRIs	11,991 (18.7)	9,451 (19.9)	5.9 (3.9), 5	5.6 (3.9), 5	306.4 (414.3), 153.7	267.3 (389.6), 115.4
SNRIs	5,372 (8.4)	4,394 (9.3)	6.3 (4.3), 5	6.1 (4.4), 5	1,157.7 (924.1), 1,052.2	1,033.7 (874.4), 907.1
Tricyclic antidepressants	3,318 (5.2)	2,943 (6.2)	5.0 (4.1), 4	4.3 (3.9), 3	79.4 (362.9), 27.5	57.7 (210.1), 18.9
Tetracyclic and miscellaneous antidepressants	5,650 (8.8)	4,687 (9.9)	5.8 (4.6), 4	5.4 (4.5), 4	398.5 (596.1), 138.2	327.8 (515.5), 109.3
Any antidepressants	20,506 (32.0)	16,295 (34.4)	7.5 (5.8), 6	7.2 (5.8), 6	605.1 (812.7), 274.7	538.5 (755.9), 222.8
Benzodiazepines	13,336 (20.8)	12,679 (26.8)	5.1 (4.7), 3	5.3 (4.9), 3	80.7 (229.0), 25.4	81.1 (229.7), 25.6
Sedative and hypnotics	9,593 (15.0)	7,039 (14.9)	5.1 (4.5), 3	5.2 (4.6), 3	309.7 (462.9), 111.0	301.6 (450.7), 112.4
Miscellaneous agents	2,905 (4.5)	1,796 (3.8)	2.3 (2.9), 1	2.4 (3.0), 1	50.5 (132.2), 15.2	57.1 (138.7), 17.1
Muscle relaxants	—	19,654 (41.5)	—	3.4 (3.8), 2	—	120.4 (291.8), 27.9
Anticonvulsants	—	8,722 (18.4)	—	5.2 (4.9), 4	—	730.5 (1,165.0), 254.5

SD, standard deviation; LBP, low back pain; SNRI, serotonin-norepinephrine re-uptake inhibitor; OA, osteoarthritis.

saw chiropractors, 14.3% received TENS, 6.0% had CBT, and <2.0% received acupuncture, hydrotherapy, massage therapy, and biofeedback during 2008. Approximately, one of every three patients with CLBP (34.1%) received chiropractic care, 21.7% received TENS, 20.3% had physical therapy, 8.0% had CBT, 7.0% used some type of heat/cold therapy, 3.1% had massage therapy, and <2% had acupuncture (1.4%).

The number of prescriptions for the examined medication classes among patients with OA and CLBP during the study period were: acetaminophen (OA, 3.7 ± 4.5 ; CLBP, 3.7 ± 5.0), NS-NSAIDs (OA, 3.6 ± 3.2 ; CLBP, 2.7 ± 2.6), Cox-2s (OA, 3.8 ± 3.3 ; CLBP, 3.3 ± 3.2), tramadol (OA, 3.5 ± 3.9 ; CLBP, 3.4 ± 4.1), opioids (OA, 5.7 ± 6.9 ; CLBP, 6.4 ± 7.6), SSRIs (OA, 5.9 ± 3.9 , CLBP, 5.6 ± 3.9), SNRIs (OA, 6.3 ± 4.3 ; CLBP, 6.1 ± 4.4), TCAs (OA, 5.0 ± 4.1 ; CLBP, 4.3 ± 3.9), benzodiazepines (OA, 5.1 ± 4.7 ; CLBP, 5.3 ± 4.9), sedative/hypnotics (OA, 5.1 ± 4.5 ; 5.2 ± 4.6), and muscle relaxants (CLBP, 5.1 ± 4.9). On average, patients with OA and CLBP who received acupuncture, had 8.4 ± 8.9 and 6.4 ± 6.5 treatments during 2008, the number of physical therapy and chiropractic treatments were 11.3 ± 11.8 and 10.3 ± 11.2 and 7.2 ± 8.6 and 7.6 ± 7.0 for OA and CLBP, respectively.

Direct annual costs of pharmacological treatments among patients with OA using these medications were considerable: Acetaminophen ($\$84.4 \pm \207.8), NS-NSAIDs ($\$119.31 \pm \212.26), Cox-2 inhibitors ($\$690.0 \pm \621.5), tramadol ($\$137.6 \pm \327.3), opioids ($\$287.4 \pm \$1,652.1$), SSRIs ($\$306.4 \pm \414.3), SNRIs ($\$1,157.7 \pm \924.1), TCAs ($\$79.39 \pm \362.87), benzodiazepines ($\$80.7 \pm \229.0), and sedative/hypnotics ($\$309.7 \pm \462.9). Similarly, user-based costs of pharmacological treatments among patients with CLBP incurred were as follows: Acetaminophen ($\$81.8 \pm \237.8), NS-NSAIDs ($\$67.0 \pm \149.9), Cox-2 inhibitors ($\$569.7 \pm \596.8), tramadol ($\$119.4 \pm \306.2), opioids ($\$364.5 \pm \$1,896.5$), SSRIs ($\$267.3 \pm \389.6), SNRIs ($\$1,033.7 \pm \874.4), TCAs ($\$57.7 \pm \210.1), benzodiazepines ($\$81.1 \pm \229.7), sedative/hypnotics ($\$301.6 \pm \450.7), and muscle relaxants ($\$730.5 \pm \$1,165.0$).

Costs of alternative treatments among users of these treatments were as follows: Acupuncture (OA, $\$781.1 \pm \$1,441.2$; CLBP, $\$528.6 \pm \$1,331.5$), physical therapy (OA, $\$1,037.4 \pm \$1,507.6$; CLBP, $\$691.3 \pm \$1,045.5$), TENS (OA, $\$155.9 \pm \263.2 ; CLBP, $\$115.2 \pm \186.2), CBT (OA, $\$747.5 \pm \$1,329.3$; CLBP, $\$715.0 \pm \$1,184.3$), assistive devices (OA, $\$278.7 \pm \605.3 ; CLBP, $\$281.9 \pm \793.5), and chiropractic care (OA, $\$547.1 \pm \795.0 ; CLBP, $\$389.6 \pm \474.4).

Table 3. Use and Costs of Alternative Treatments

Alternative treatments*	Percent users		No. prescriptions		Costs	
	OA (N = 64,085) N (%)	CLBP (N = 47,386) N (%)	OA Mean (SD), Median	CLBP Mean (SD), Median	OA Mean (SD), Median	CLBP Mean (SD), Median
Acupuncture [†]	461 (0.7)	652 (1.4)	8.4 (8.9), 5	6.4 (6.5), 4	781.1 (1,441.2), 351.0	528.6 (1,331.47), 239.1
Hydrotherapy	1,213 (1.9)	630 (1.3)	9.6 (11.1), 6	7.7 (9.1), 4	590.4 (936.2), 238	442.1 (765.3), 151.4
Massage therapy	1,035 (1.6)	1,452 (3.1)	7.8 (11.8), 4	5.5 (7.4), 3	183.2 (900.3), 45.4	144.3 (289.2), 57.2
Physical therapy [†]	12,934 (20.2)	9,598 (20.3)	11.3 (11.8), 8	7.2 (8.6), 4	1,037.4 (1,507.6), 606.7	691.3 (1,045.5), 348.5
Biofeedback	18 (0.0)	21 (0.0)	4.4 (5.8), 2	2.6 (2.3), 2	318.7 (770.4), 68.4	110.5 (166.1), 57
Transcutaneous electrical nerve stimulation	9,169 (14.3)	10,294 (21.7)	9.6 (11.7), 6	6.9 (8.2), 4	155.9 (263.2), 70.8	115.2 (186.2), 55.4
Cognitive Behavioral Therapy (CBT)	3,812 (6.0)	3,763 (7.9)	9.3 (11.9), 5	8.6 (11.3), 5	747.5 (1,329.9), 381.8	715.0 (1,184.3), 384.8
Heat/cold application	4,389 (6.9)	3,325 (7.0)	10.0 (12.2), 6	7.1 (9.4), 4	121.7 (382.3), 14.1	73.3 (229.0), 8.2
Chiropractic care [†]	6,720 (10.5)	16,173 (34.1)	10.3 (11.2), 7	7.6 (7.0), 6	547.1 (795.0), 318.0	389.6 (474.4), 256.8
Osteopathic care [†]	93 (0.2)	137 (0.3)	3.9 (4.5), 2	3.6 (3.6), 2	488.3 (676.0), 258.9	430.8 (518.3), 280
Topical analgesics						
Capsaicin	4 (0.0)	1 (0.0)	1.5 (1), 1	1.0 (–), 1	3.8 (4.7), 2.9	0.0 (–), 0
Lidoderm	2,803 (4.4)	2,176 (4.6)	2.0 (1.8), 1	2.0 (1.8), 1	563.2 (720.6), 365.3	542.4 (743.6), 357.5
Diclofenac	0	–	–	–	–	–
Methyl salicylate	0	–	–	–	–	–
Any topical analgesic	2,807 (4.4)	2,177 (4.6)	2.0 (1.8), 1	1.9 (1.8), 1	562.4 (720.4), 365.3	542.1 (743.5), 357.5
Devices						
Walker	3,503 (5.5)	671 (1.4)	1.2 (0.6), 1	1.3 (0.6), 1	97.2 (49.1), 99.8	99.5 (47.9), 102.2
Crutches	1,249 (2.0)	460 (1.0)	1.2 (0.7), 1	1.2 (0.9), 1	50.7 (55.3), 40.1	52.3 (64.73), 40.11
Cane	869 (1.4)	175 (0.4)	1.0 (0.2), 1	1.0 (0.3), 1	20.7 (10.9), 17.9	20.7 (11.0), 17.9
Orthotics/braces	8,467 (13.2)	4,332 (9.1)	1.7 (1.6), 1	1.4 (1.1), 1	275.1 (426.3), 115.5	241.6 (395.1), 99.6
Footwear	2,283 (3.6)	1,280 (2.7)	1.7 (1.0), 1	1.6 (0.9), 1	185.3 (197.8), 153	186.2 (196.4), 170.8
Wheelchair	958 (1.5)	300 (0.6)	6.5 (6.6), 4	5.1 (5.2), 3	895.5 (1,745.4), 300.8	1,228.9 (2,919.7), 253.8
Any device	14,466 (22.6)	6,202 (13.1)	2.2 (2.75), 1	1.8 (2.0), 1	278.7 (605.3), 107.8	281.9 (793.5), 107.8
Vitamins	608 (1.0)	447 (1.0)	3.3 (3.1), 2	2.9 (2.7), 2	99.8 (167.8), 34.7	81.9 (139.9), 34.3
Glucosamine + chondroitin	0	–	–	–	–	–

LBP, low back pain; OA, osteoarthritis.

*Unique claims.

†Unique office visit days.

Total Healthcare Costs

Direct medical costs are presented in Table 4. The total direct medical costs among patients with OA were $\$15,637.6 \pm \$22,595.2$; costs of pharmacologic therapies were $\$3,294.3 \pm \$6,387.8$ and accounted for 21% of the total costs; whereas costs of alternative treatments were $\$450.9 \pm 1,177.9$ and accounted for 3% of the total costs. The corresponding total direct medical costs for patients with CLBP were $\$11,828.7 \pm 20,035.2$; costs of pharmacological therapies were $\$2,628.6 \pm \$5,467.0$ and accounted for 22% of the total costs; whereas costs of alternative treatments were $\$416.5 \pm \939.4 and accounted for 4% of the total costs.

DISCUSSION

This study, a subgroup analysis that characterized the healthcare resource utilization burden associated with OA and CLBP, confirms and extends two previous

burden of illness studies by reporting on subpopulations of patients prescribed pain medications.^{7,13} Because these subpopulations specifically consisted of users of pain medications, they represent potentially either sicker patients or at least treatment seekers relative to the overall OA and CLBP populations from which they were identified. These factors may account for the higher total costs observed in this study, $\$15,638$ for OA and $\$11,829$ for CLBP, relative to the $\$12,905$ and $\$8,386$ for OA and CLBP, respectively, in the overall populations.^{7,13} In particular, the costs of pharmacologic therapies and hospitalizations were higher in these subgroups relative to that previously reported for both OA and CLBP, and among patients with CLBP, the costs of total outpatient visits were also higher in the current study.

Overall, there was a high prevalence of comorbid conditions, including several that are characterized by pain and others that are often associated with pain (e.g. sleep disorders, depression/anxiety). Thus, it is not surprising that in addition to substantial use of

Table 4. Resource Utilization and Direct Medical Costs

Resource use category	Osteoarthritis N = 64,085				CLBP N = 47,386			
	Mean	SD	Median	IQR	Mean	SD	Median	IQR
Physician office visit	1,052.2	1,019.6	798.5	459.2 to 1317.5	923.0	909.3	692.5	386.7 to 1,174.5
Emergency room visits	319.7	1,245.0	0.0	0.0 to 0.0	484.8	1,783.1	0.0	0.0 to 352.4
Other outpatient visits	5,366.0	9,839.7	2,621.8	901.5 to 6,286.0	4,482.9	9,063.0	1,998.7	567.0 to 5,177.6
Total outpatient visits	6,737.9	10,409.2	3,914.4	1,714.0 to 8,042.1	5,890.7	9,778.7	3,254.5	1,322.1 to 7,025.8
Hospitalizations	5,154.5	16,175.9	0.0	0.0 to 0.0	2,893.0	13,608.0	0.0	0.0 to 0.0
Pharmacologic therapies	3,294.3	6,387.8	1,750.4	673.3 to 3,792.5	2,628.6	5,467.0	1,098.7	334.9 to 2,895.8
Alternative treatments	450.9	1,177.9	0.0	0.0 to 402.0	416.5	939.4	114.7	0.0 to 456.7
Total medical costs	15,637.6	22,595.2	8,545.7	3,990.6 to 19,497.1	11,828.7	20,035.2	6,214.5	2,812.0 to 13,025.1

pharmacologic therapy for pain, there was widespread use of adjunctive medications that are often prescribed for pain-related sequelae. The proportions of patients with OA and CLBP using pain and adjunctive medications were higher than in the previous studies^{7,13} also supporting the notion that these subpopulations may be characterized by more severe disease.

Consistent with several other studies,^{6,7,13,16} opioids were the most common class of pain medication, prescribed to 71.7% and 79.0% of patients with OA and CLBP, respectively, and were prescribed even more frequently than NSAIDs (65.4% and 56.1% of patients with OA and CLBP, respectively). Because opioids are generally recommended for patients who have severe, disabling pain that is not controlled with acetaminophen and NSAIDs, the greater prescribing of opioids may be consistent with the presence of more severe disease. Furthermore, although acetaminophen and NSAIDs are generally considered first-line for both OA and CLBP, it was not possible to determine whether the opioids were prescribed as first-line, as a result of prior treatment failure, as rescue medication, or even for one of the other comorbid pain conditions; opioids, especially short-acting opioids, are frequently prescribed as rescue pain medications or on an “as needed” basis.

Notably, the current analysis is the first claims database study that has evaluated utilization of alternative treatments in usual care. There was some use of alternative treatments, with higher use of those treatments that may most likely be covered by health insurance, such as physical therapy, TENS, walking devices, and chiropractic care. Of note, among the patients with OA, there was no utilization of glucosamine/chondroitin combination. Efficacy results using these supplements have been inconsistent,^{48–50} and specific recommendations against their use in patients with symptomatic OA of the knee have been published.⁵¹

Nevertheless, patients have previously reported that these supplements are commonly used,^{5,29,34} and it is thus possible that patients with OA in our subpopulation either used these supplements individually rather than in combination, or, more likely, may be obtaining these supplements through over-the-counter purchase.

Relative to patient self-report surveys, which have reported up to 80% of patients with OA and CLBP using one or more alternative therapies currently or within the past month,^{8,28,34,36,38} overall use of such therapies appeared to be low in the current study, even among patients with CLBP; back pain has been reported to be the most common reason for the use of complementary and alternative therapies.^{16,31} Relative to pharmacologic therapies, which accounted for approximately 20% of total costs in both OA and CLBP, the costs of alternative treatments were also low, 2.7% and 3.5% of the total costs of OA and CLBP, respectively. Several reasons for the lower use of these therapies can be proposed. First, in contrast to the other studies that surveyed a wider variety of alternative therapies, this analysis only captured those therapies that health insurers will pay for, thus likely underestimating the actual use of such therapies. Second, many acupuncture and other alternative therapy providers do not even take insurance, and thus patients may be using these therapies while paying out-of-pocket. Additionally, because these populations potentially consist of patients with greater disease severity, it is also possible that many of the patients may have previously tried alternative therapies and found them not to be of benefit. This proposal might be consistent with the uncertain benefits reported with these therapies resulting from the heterogeneity of data reported in the medical literature and the challenges of adequately assessing their effects in research and clinical settings.^{7,49,52–55}

A substantial proportion of patients had baseline comorbidities associated with or contraindicating NSAID use and used medications during the study period documented to increase the risk of NSAID-related events. While these factors could technically exacerbate the total economic burden of patient management, their contribution to the total costs could not be assessed.

It is prudent to consider the limitations associated with this analysis, including those inherent in the use of claims databases, such as errors in coding and recording, which could potentially result in misdiagnosis in a proportion of patients. Because we required claims in each of two consecutive years (at least two claims for OA and four claims for CLBP over 2 years), it is unlikely that coding errors could have substantially affected patient selection.

Another limitation associated with claims databases is an inability to link the condition of interest, OA and CLBP in the current analysis, with the prescribing of a particular medication or alternative therapy. This limitation is likely to be especially relevant considering that our populations were selected based on their utilization of pain medications, suggesting that these patients may also be sicker than the general OA or CLBP population, and characterized by multiple comorbidities, including those with neuropathic involvement for which many of the same medications are also recommended.^{8,56} The selection for inclusion of only patients using pain medications may itself be criticized, because this may limit the generalizability of the results to the overall OA and CLBP populations. However, patients who use pain medications are more likely to be the ones who are actively treating their condition and are interested in a wider range of treatment modalities, especially if prior or current therapies are providing less than optimal efficacy. Thus, this selection of patients may also be considered a strength of the study, because it enables characterization of the burden among patients whose disease is potentially severe enough to require the use of pain medications. Another limitation is the underrepresentation of individuals ≥ 65 years old in the LifeLink database (a characteristic of all United States commercial insurance databases). Although the average patient with CLBP tends to be younger and gainfully employed, OA is common in older adults. Thus, the prescription and alternative medication use documented in this study among patients with OA may not be representative of older patients with OA, and the study findings may not be generalizable to that cohort.

Claims databases have the additional limitation of not being able to ascertain to what extent patients adhere to the prescribed therapies, whether pharmacologic or complementary. Similarly, because outcomes are not captured in claims databases, it is not possible to know the basis for prescribing of any of these therapies, nor their effects on pain-related or other outcomes. A final limitation is that because this study is inherently an evaluation of costs recorded in a claims database, it does not capture the out-of-pocket expenditures of patients, whether for over-the-counter medications or alternative therapies. Thus, the data presented here not only represent a portion of the economic burden, but likely underestimate the resources that patients utilize.

CONCLUSIONS

Our results indicate that patients with OA and CLBP who were prescribed pain-related medications had a high prevalence of other chronic pain- and nonpain-related comorbidities and also used a variety of adjunctive medications. Although, alternative treatments are widely recommended, we found limited covered expenditures for them in clinical practice, particularly in patients with OA. The source of our data (commercial claims) may in part be the reason for this observed lower use because such treatments are seldom covered by health insurance plans. Future research should focus on primary data sources to more accurately estimate the extent to which such therapies contribute to the total costs of OA and CLBP management.

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REFERENCES

1. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum*. 2008;58:26–35.
2. Gabriel SE, Crowson CS, Campion ME, O’Fallon WM. Direct medical costs unique to people with arthritis. *J Rheumatol*. 1997;24:719–725.

3. Leardini G, Salaffi F, Caporali R, et al. Direct and indirect costs of osteoarthritis of the knee. *Clin Exp Rheumatol*. 2004;22:699–706.
4. Rabenda V, Manette C, Lemmens R, Mariani AM, Struvay N, Reginster JY. Direct and indirect costs attributable to osteoarthritis in active subjects. *J Rheumatol*. 2006;33:1152–1158.
5. Gupta S, Hawker GA, Laporte A, Croxford R, Coyte PC. The economic burden of disabling hip and knee osteoarthritis (OA) from the perspective of individuals living with this condition. *Rheumatology (Oxford)*. 2005;44:1531–1537.
6. Dunn JD, Pill MW. A claims-based view of health care charges and utilization for commercially insured patients with osteoarthritis. *Manag Care*. 2009;18:44–50.
7. Gore M, Sadosky A, Stacey B, Leslie D. Clinical comorbidities, treatment patterns, and healthcare costs of patients with osteoarthritis in usual care: a database analysis. *J Med Econ*. 2011;14:497–507.
8. Koes BW, van Tulder MW, Thomas S. Diagnosis and treatment of low back pain. *BMJ*. 2006;332:1430–1434.
9. Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. *Spine J*. 2008;8:8–20.
10. Coste J, Delecoeuillerie G, Cohen de Lara A, Le Parc JM, Paolaggi JB. Clinical course and prognostic factors in acute low back pain: an inception cohort study in primary care practice. *BMJ*. 1994;308:577–580.
11. Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E, Silman AJ. Outcome of low back pain in general practice: a prospective study. *BMJ*. 1998;316:1356–1359.
12. Andersson GB. Epidemiological features of chronic low-back pain. *Lancet*. 1999;354:581–585.
13. Gore M, Sadosky A, Stacey BR, Tai K-S, Leslie D. The burden of chronic low back pain: clinical comorbidities, treatment patterns, and healthcare costs in usual care settings. *Spine*. 2011; in press.
14. Frank AO, De Souza LH, McAuley JH, Sharma V, Main CJ. A cross-sectional survey of the clinical and psychological features of low back pain and consequent work handicap: use of the Quebec Task Force classification. *Int J Clin Pract*. 2000;54:639–644.
15. Ekman M, Jonhagen S, Hunsche E, Jonsson L. Burden of illness of chronic low back pain in Sweden: a cross-sectional, retrospective study in primary care setting. *Spine (Phila Pa 1976)*. 2005;30:1777–1785.
16. White AG, Birnbaum HG, Janagap CC, Buteau L, Schein J. Direct and indirect costs of pain therapy for osteoarthritis in an insured population in the United States. *J Occup Environ Med*. 2008;50:998–1005.
17. American College of Rheumatology. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheum*. 2000;43:1905–1915.
18. Simon L, Lipman A, Jacox A, et al. *Guideline for the Management of Pain in Osteoarthritis, Rheumatoid Arthritis, and Juvenile Chronic Arthritis*. APS Clinical Practice Guideline Series, No. 2. Glenview, IL: American Pain Society; 2002.
19. Jordan KM, Arden NK, Doherty M, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis*. 2003;62:1145–1155.
20. Zhang W, Doherty M, Arden N, et al. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis*. 2005;64:669–681.
21. Airaksinen O, Brox JI, Cedraschi C, et al. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. *Eur Spine J*. 2006;15(suppl 2):S192–S300.
22. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence. *Osteoarthritis Cartilage*. 2007;15:981–1000.
23. Zhang W, Doherty M, Leeb BF, et al. EULAR evidence based recommendations for the management of hand osteoarthritis: report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis*. 2007;66:377–388.
24. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. 2007;147:478–491.
25. Chou R, Huffman LH. Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Ann Intern Med*. 2007;147:505–514.
26. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage*. 2008;16:137–162.
27. Ramsey SD, Spencer AC, Topolski TD, Belza B, Patrick DL. Use of alternative therapies by older adults with osteoarthritis. *Arthritis Rheum*. 2001;45:222–227.
28. Kaboli PJ, Doebbeling BN, Saag KG, Rosenthal GE. Use of complementary and alternative medicine by older patients with arthritis: a population-based study. *Arthritis Rheum*. 2001;45:398–403.
29. Herman CJ, Allen P, Hunt WC, Prasad A, Brady TJ. Use of complementary therapies among primary care clinic patients with arthritis. *Prev Chronic Dis*. 2004;1:A12.
30. Zochling J, March L, Lapsley H, Cross M, Tribe K, Brooks P. Use of complementary medicines for osteoarthritis—a prospective study. *Ann Rheum Dis*. 2004;63:549–554.

31. Sherman KJ, Cherkin DC, Connally MT, et al. Complementary and alternative medical therapies for chronic low back pain: what treatments are patients willing to try? *BMC Complement Altern Med.* 2004;4:9.

32. Jordan KM, Sawyer S, Coakley P, Smith HE, Cooper C, Arden NK. The use of conventional and complementary treatments for knee osteoarthritis in the community. *Rheumatology (Oxford).* 2004;43:381–384.

33. Quandt SA, Chen H, Grzywacz JG, Bell RA, Lang W, Arcury TA. Use of complementary and alternative medicine by persons with arthritis: results of the National Health Interview Survey. *Arthritis Rheum.* 2005;53:748–755.

34. Dente JM, Herman CJ, Allen P, Hunt WC. Ethnic differences in the use of complementary and alternative therapies among adults with osteoarthritis. *Prev Chronic Dis.* 2006;3:A80.

35. Katz P, Lee F. Racial/ethnic differences in the use of complementary and alternative medicine in patients with arthritis. *J Clin Rheumatol.* 2007;13:3–11.

36. Chenot JF, Becker A, Leonhardt C, et al. Use of complementary alternative medicine for low back pain consulting in general practice: a cohort study. *BMC Complement Altern Med.* 2007;7:42.

37. Rosemann T, Joos S, Szecsenyi J, Laux G, Wensing M. Health service utilization patterns of primary care patients with osteoarthritis. *BMC Health Serv Res.* 2007;7:169.

38. Callahan LF, Wiley-Exley EK, Mielenz TJ, et al. Use of complementary and alternative medicine among patients with arthritis. *Prev Chronic Dis.* 2009;6:A44.

39. Marsh J, Hager C, Havey T, Sprague S, Bhandari M, Bryant D. Use of alternative medicines by patients with OA that adversely interact with commonly prescribed medications. *Clin Orthop Relat Res.* 2009;467:2705–2722.

40. Koes BW, van Tulder M, Lin CW, Macedo LG, McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. *Eur Spine J.* 2010;19:2075–2094.

41. Scopatz KA, Piva SR, Wisniewski S, Fitzgerald GK. Relationships of fear, anxiety, and depression with physical function in patients with knee osteoarthritis. *Arch Phys Med Rehabil.* 2009;90:1866–1873.

42. Allen KD, Renner JB, Devellis B, Helmick CG, Jordan JM. Osteoarthritis and sleep: the Johnston County Osteoarthritis Project. *J Rheumatol.* 2008;35:1102–1107.

43. Smith MT, Quartana PJ, Okonkwo RM, Nasir A. Mechanisms by which sleep disturbance contributes to osteoarthritis pain: a conceptual model. *Curr Pain Headache Rep.* 2009;13:447–454.

44. Schieir O, Thombs BD, Hudson M, et al. Symptoms of depression predict the trajectory of pain among patients with early inflammatory arthritis: a path analysis approach to assessing change. *J Rheumatol.* 2009;36:231–239.

45. McCracken LM, Iverson GL. Disrupted sleep patterns and daily functioning in patients with chronic pain. *Pain Res Manag.* 2002;7:75–79.

46. Smith MT, Haythornthwaite JA. How do sleep disturbance and chronic pain inter-relate? Insights from the longitudinal and cognitive-behavioral clinical trials literature. *Sleep Med Rev.* 2004;8:119–132.

47. Geisser ME, Roth RS, Theisen ME, Robinson ME, Riley JL. Negative affect, self-report of depressive symptoms, and clinical depression: relation to the experience of chronic pain. *Clin J Pain.* 2000;16:110–120.

48. Black C, Clar C, Henderson R, et al. The clinical effectiveness of glucosamine and chondroitin supplements in slowing or arresting progression of osteoarthritis of the knee: a systematic review and economic evaluation. *Health Technol Assess.* 2009;13:1–148.

49. Wandel S, Juni P, Tendal B, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ.* 2010;341:c4675.

50. Zhang W, Nuki G, Moskowitz RW, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage.* 2010;18:476–499.

51. American Academy of Orthopedic Surgeons. Treatment of osteoarthritis of the knee (non arthroplasty). Available at: http://www.aaos.org/research/guidelines/Guideline_OAKnee.asp. Accessed May 22, 2010.

52. Manheimer E, Cheng K, Linde K, et al. Acupuncture for peripheral joint osteoarthritis. *Cochrane Database Syst Rev.* 2010 Jan 20; (1): CD001977.

53. Hawker GA, Mian S, Bedinis K, Stanaitis I. Osteoarthritis year 2010 in review: non-pharmacologic therapy. *Osteoarthritis Cartilage.* 2011;19:366–374.

54. Rubinstein SM, van Middelkoop M, Kuijpers T, et al. A systematic review on the effectiveness of complementary and alternative medicine for chronic non-specific low-back pain. *Eur Spine J.* 2010;19:1213–1228.

55. van Middelkoop M, Rubinstein SM, Kuijpers T, et al. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. *Eur Spine J.* 2011;20:19–39.

56. Dworkin RH, O'Connor AB, Audette J, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc.* 2010;85:S3–S14.