

Massage Therapy for Osteoarthritis of the Knee

A Randomized Controlled Trial

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Background: Massage therapy is an attractive treatment option for osteoarthritis (OA), but its efficacy is uncertain. We conducted a randomized, controlled trial of massage therapy for OA of the knee.

Methods: Sixty-eight adults with radiographically confirmed OA of the knee were assigned either to treatment (twice-weekly sessions of standard Swedish massage in weeks 1-4 and once-weekly sessions in weeks 5-8) or to control (delayed intervention). Primary outcomes were changes in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and functional scores and the visual analog scale of pain assessment. The sample provided 80% statistical power to detect a 20-point difference between groups in the change from baseline on the WOMAC and visual analog scale, with a 2-tailed α of .05.

Results: The group receiving massage therapy demonstrated significant improvements in the mean (SD)

WOMAC global scores (-17.44 [23.61] mm; $P < .001$), pain (-18.36 [23.28]; $P < .001$), stiffness (-16.63 [28.82] mm; $P < .001$), and physical function domains (-17.27 [24.36] mm; $P < .001$) and in the visual analog scale of pain assessment (-19.38 [28.16] mm; $P < .001$), range of motion in degrees (3.57 [13.61]; $P = .03$), and time to walk 50 ft (15 m) in seconds (-1.77 [2.73]; $P < .01$). Findings were unchanged in multivariable models controlling for demographic factors.

Conclusions: Massage therapy seems to be efficacious in the treatment of OA of the knee. Further study of cost effectiveness and duration of treatment effect is clearly warranted.

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OSTEARTHRTIS (OA) AFFECTS as many as 21 million Americans.^{1,2} It is a dynamic process involving an imbalance in tissue homeostasis with cartilage, synovial fluid, subchondral bone, and other joint tissues and structures^{3,4} and becomes more prevalent with advancing age.⁵ By 2020, more than 50 million Americans will have OA,^{6,7} which is the most frequently reported chronic condition in the elderly population.^{5,8} The Centers for Disease Control and Prevention highlights OA as a chronic condition that causes more physical limitation than lung and heart disease and diabetes mellitus.⁹ The total cost of OA was estimated at \$60 billion in 2004.¹⁰

Osteoarthritis of the hip or knee is particularly disabling because it limits ambulation, but the affliction also strikes the hands, the spine, and the feet with the same destructive joint process.^{5,8} The end point

of the OA disease process is total loss of joint cartilage in the affected area and the need for joint replacement.

Conventional treatments for OA include pain medication (nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors), exercises, hot and cold therapy, corticosteroid injections, and, eventually, surgery to repair the joint.⁸ Despite conventional treatment, OA is often progressive and frequently leads to chronic pain and disability.¹¹ The potential toxic effects of drugs used commonly to treat OA have been especially newsworthy of late.^{12,13}

Massage therapy may diminish symptoms and improve the course of OA by increasing local circulation to the affected joint, improving the tone of supportive musculature, enhancing joint flexibility, and relieving pain.¹⁴ Massage therapy has been evaluated and found to be effective for various painful musculoskeletal con-

ditions.^{15,16} However, to our knowledge, to date, no study has specifically evaluated the effectiveness of massage therapy for OA. We performed a randomized, wait-list controlled trial of 8 weeks' duration of Swedish massage therapy for OA of the knee.

METHODS

PARTICIPANTS

Patients were recruited from January to July of 2003 from the Saint Barnabas Health Care System (the Carol and Morton Siegler Center for Integrative Medicine and the Arthritis and Rheumatic Diseases Center), Livingston, NJ. The intervention was developed in conjunction with Yale Prevention Research Center (Derby, Conn) and conducted at the Siegler Center, located in the Saint Barnabas Ambulatory Care Center in Livingston.

Eligible patients were men and women with radiographically established OA of the knee who met American College of Rheumatology criteria,¹⁷ were at least 35 years of age, and had a prerandomization score of 40 to 90 on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and visual analog scale (VAS) pain assessment scale (0 mm indicates no pain; 100 mm, worst pain ever).¹⁸ Written confirmation of OA of the knee was provided by the patient's physician. Patients with bilateral knee involvement had the more severely affected knee designated as the study knee.

Exclusion criteria were the presence of rheumatoid arthritis; fibromyalgia; recurrent or active pseudogout, cancer, or other serious medical conditions; signs or history of kidney or liver failure; asthma requiring use of corticosteroids; use of oral corticosteroids within the past 4 weeks, intra-articular knee de-pocorticosteroids within the previous 3 months, or intra-articular hyaluronate within the previous 6 months; arthroscopy of the knee within the previous year; significant injury to the knee within the previous 6 months; or a rash or open wound over the knee.

Participant recruitment involved informational letters to patients with OA at the Arthritis and Rheumatic Diseases Center at Saint Barnabas Ambulatory Care Center and institutional review board–approved fliers distributed at the Saint Barnabas Ambulatory Care Center and nearby senior living facilities and to practicing primary care physicians in the area. Volunteers were screened for eligibility over the telephone.

RANDOMIZATION AND SAMPLE SIZE

A research coordinator randomly assigned enrolled participants to receive either 8 weeks of massage therapy intervention (hereafter, the intervention group) or 8 weeks of usual care on a wait-list (hereafter, the control group) followed by the intervention using a computer-generated, blocked (blocks of 6) random allocation sequence. The control group continued with their usual care before starting the intervention.

A sample size of 66 subjects was determined to provide 80% statistical power to detect a 20-point difference between intervention and control groups at 8 weeks in the change on the WOMAC and VAS scores for walking pain, with an α of .05. The standard deviation (25.7 mm) was derived from the VAS walking pain score at 6 weeks in the acetaminophen-treated arm as reported by Geba et al.¹⁹

Each patient provided written informed consent prior to enrollment. The institutional review boards of the Saint Barnabas Medical Center; the University of Medicine and Dentistry of New Jersey, Newark; Griffin Hospital, Derby; and the Hu-

man Investigation Committee of Yale University, New Haven, Conn, approved the study.

STUDY INTERVENTIONS

Two licensed massage therapists certified by the National Certification Board for Therapeutic Massage and Bodywork provided the massage therapy. The therapists used a standard Swedish full-body therapeutic massage technique²⁰ and a standard protocol for the study intervention, which included pétrissage (compression or manipulation of soft tissue between the fingers and thumb), effleurage (gliding of hands over the skin or soft tissues), and tapotement (percussion-based massage where hands strike soft tissue in a repetitive, rhythmic fashion) techniques used at the therapists' discretion.^{21,22} Massage sessions were 1-hour long. Usual care included pain medications, exercises, or hot and cold therapy.

Initial (weeks 1-4) treatments were given with greater frequency (twice weekly) to build a loading dose of massage treatments, followed by once-weekly massage sessions for weeks 5 through 8. Participants remained supine or prone for the full hour of treatment, turning over at roughly the halfway point. To minimize practitioner variability of treatment, a standard protocol incorporating specific strokes (effleurage, pétrissage, or tapotement) was used; however, a particular sequence of strokes was not specified. Study personnel met with the massage therapists at regular intervals to assure compliance with the protocol. The control group continued to receive conventional medical care during the initial intervention period, then crossed over to receive massage (weeks 9-16) after an initial 8-week delay. Study personnel prompted subjects for all scheduled appointments to minimize attrition.

OUTCOME MEASUREMENTS

All measurements were collected at baseline and after completion of intervention (at weeks 8 and 16) in both groups. Demographic data and medical history were documented by the research coordinator. Participants were instructed to keep a daily medication usage diary.

The WOMAC is a self-administered 3-dimensional questionnaire that assesses pain, stiffness, and physical functional disability in patients with knee and hip OA using a series of 24 questions.¹⁸ A negative change in WOMAC scores from baseline indicates improvement of symptoms and limitation whereas a positive change indicates deterioration of symptoms and limitation. All 24 WOMAC items are rated on a numerical rating scale (in millimeters) ranging from 0 (no symptoms/no limitation) to 100 (maximal symptoms/maximal limitation).²³ The WOMAC scores were standardized by calculating the mean of the corresponding unweighted item scores in each dimension.²⁴ The WOMAC global score was computed as the unweighted mean of all 24 items.

Additional outcome measures assessed at each visit included the VAS for pain assessment, which is a 100-mm-long visual scale on which the participant draws a line to designate their level of pain at interview; time in seconds to walk a 50-ft (15-m) straight path; range of motion in degrees using a standard goniometric assessment as performed by a trained research assistant at the center; and adverse events (complaint, system, and severity) were recorded by the research coordinator during her routine weekly telephone call to each participant.

STATISTICAL ANALYSIS

Descriptive statistics for each relevant variable at baseline were determined to justify parametric methods. Continuous data are

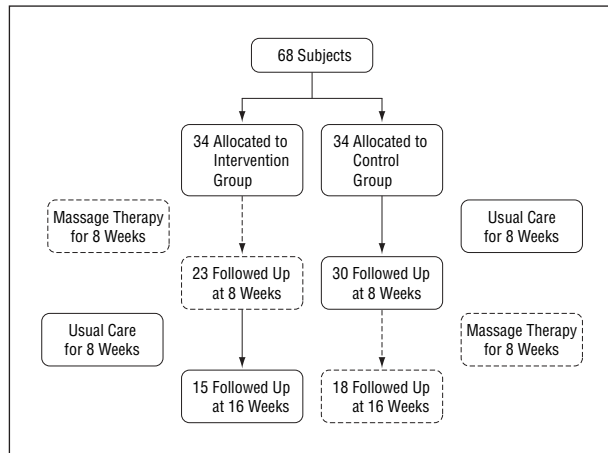


Figure. Participant flowchart.

presented as mean (SD) in the text and tables. The paired *t* test was used to examine the change in scores from baseline to follow-up examination. Changes in WOMAC and VAS scores, time to walk 50 ft (15 m), and the clinical assessment for range of motion between the treatment groups were measured using repeated measures analysis of variance. The 95% confidence intervals were determined for changes from baseline. The combined effect of independent variables (demographics, body mass index, baseline WOMAC and VAS scores, and investigators' baseline assessment for range of motion) and treatment assignment on WOMAC and VAS scores, time to walk 50 ft (15 m), and the clinical assessment for range of motion was assessed with multivariable models using analysis of variance. The WOMAC findings were validated with the VAS findings and the clinical assessment for range of motion using correlation coefficients. Analysis followed an intention to treat design (ie, the last value carried forward). Data were analyzed using SAS statistical software (version 8.2; SAS Institute, Cary, NC). Significance for the 2-tailed *t* test was set at $P < .05$.

RESULTS

PARTICIPANTS

Of 210 candidates screened, 68 subjects participated (34 subjects per group) (Figure). Approximately 82 (39%) of those screened were ineligible, and 60 (28%) were unable to complete screening or were uninterested. The study groups were comparable at baseline (Table 1); however, the mean (SD) WOMAC pain score was higher ($P = .02$) in the intervention group (52.10 [18.82] mm) vs the control group (40.69 [20.01] mm) at baseline. The stiffness, functionality, global, VAS, and range of motion scores at baseline did not differ between groups.

EFFICACY RESULTS

The mean (SD) WOMAC global score improved significantly from baseline value (-21.15 [22.46] mm; $P < .001$), as did the score in each domain (pain, stiffness, and physical functional disability) (Table 2). The greatest improvement from baseline in the intervention group was observed in pain (-23.19 [24.30] mm; $P < .001$) followed by stiffness (-21.60 [26.99] mm; $P < .001$) and

Table 1. Demographic and Baseline Characteristics by Treatment Group*

Characteristic	Intervention (n = 34)	Control (n = 34)	P Value†
Age, y	70.4 (11.3)	66.2 (11.3)	.13
BMI	28.1 (7.6)	29.0 (6.7)	.59
Sex, No. (%)			
Male	7 (20)	8 (23)	.77‡
Female	27 (79)	26 (76)	
Race, No. (%)			
White	29 (85)	29 (85)	>.99‡
Other	5 (14)	5 (14)	
WOMAC score, mm			
Pain	40.6 (20.0)	52.10 (18.8)	.02
Stiffness	52.3 (21.4)	60.34 (18.8)	.11
Functionality	49.2 (21.6)	55.1 (18.8)	.23
Global	47.6 (19.9)	54.9 (17.9)	.12
VAS pain score, mm	62.8 (18.0)	67.2 (19.3)	.40
Range of motion, degree	115.6 (13.4)	109.8 (16.7)	.11
Time to walk 50 ft (15 m), s	15.6 (8.3)	16.7 (5.6)	.50

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

*Values are presented as mean (SD) except where noted.

†*P* values were obtained from 2-tailed *t* test.

‡*P* values obtained from χ^2 test.

physical function (-20.50 [22.50] mm; $P < .001$). No significant change was observed in the control group from baseline in any of the domains. Improvements observed in the intervention group differed significantly from the control group (pain: -23.19 [24.30] mm vs -3.08 [17.58] mm, $P < .001$; stiffness: -21.60 [26.99] mm vs -4.29 [24.18] mm, $P = .007$; physical functional disability: -20.50 [22.50] mm vs -0.02 [16.37] mm, $P = .002$; and global score: -21.15 [22.46] mm vs -4.56 [15.85] mm, $P < .001$).

A similar pattern was observed in the VAS and the clinical assessment for range of motion. The change observed in VAS was highly correlated to the change in the WOMAC global score ($r = 0.84$; $P < .001$). Findings persisted after controlling for demographic and baseline clinical values.

The control group in this trial received the intervention after an initial delay of 8 weeks and thus became a second intervention group during weeks 9 to 16 (Figure). Within-group intervention effects for the entire, pooled study sample are thus available and are shown in Table 2. The mean (SD) WOMAC global scores improved significantly from baseline (-17.44 [23.61] mm; $P < .001$). Significant improvement was observed in all domains (pain: -18.36 [23.28] mm, $P < .001$; stiffness: -16.63 [28.82] mm, $P < .001$; and physical functional disability: -17.27 [24.36] mm, $P < .001$) of the WOMAC score. The VAS and range of motion scores also improved significantly from baseline (-19.38 [28.16] mm, $P < .001$; and 3.57 [13.61], $P = .03$, respectively).

At the 16-week assessment, improvements seen in the intervention group (massage intervention ceased at 8 weeks) largely persisted (Table 3). Comparing the improvements observed in the intervention group at week

Table 2. Change in Outcome Measures from Baseline at 8 and 16 Weeks*

Variable	At 8-wk Follow-up†					At 16-wk Follow-up		Pooled Analysis	
	Intervention Group (n = 34)	P Value‡	Control Group (n = 34)	P Value‡	Effect Size, d	Control Group (n = 34)	P Value‡	Total for Both Groups (n = 68)	P Value‡
WOMAC score, mm									
Pain	-23.19 (24.30) (-31.67 to -14.71)	<.001	-3.08 (17.58) (-9.21 to 3.06)	.32	0.86	-13.52 (21.49) (-21.02 to -6.02)	<.001	-18.36 (23.28) (-23.99 to -12.72)	<.001
Stiffness	-21.60 (26.99) (-31.02 to -12.19)	<.001	-4.29 (24.18) (-12.73 to 4.14)	.31	0.64	-11.66 (30.13) (-22.17 to -1.15)	.03	-16.63 (28.82) (-23.61 to -9.65)	<.001
Functionality	-20.50 (22.50) (-28.35 to -12.65)	<.001	-5.02 (16.37) (-10.73 to 0.69)	.08	0.74	-14.04 (26.02) (-23.12 to -4.97)	.003	-17.27 (24.36) (-23.17 to -11.37)	<.001
Global	-21.15 (22.46) (-28.99 to -13.32)	<.001	-4.56 (15.85) (-10.09 to 0.97)	.10	0.79	-13.73 (24.48) (-22.27 to -5.19)	.002	-17.44 (23.61) (-23.16 to -11.73)	<.001
VAS pain score, mm	-22.59 (25.97) (-31.65 to -13.5)	<.001	-1.97 (21.07) (-9.32 to 5.38)	.59	0.80	-16.18 (30.24) (-26.73 to -5.62)	.004	-19.38 (28.16) (-26.20 to -12.57)	<.001
Range of motion, degree	7.15 (11.45) (3.15 to 11.14)	.001	-1.06 (14.20) (-6.01 to 3.89)	.67	0.61	-0.01 (14.78) (-5.17 to 5.14)	.99	3.57 (13.61) (0.27 to 6.86)	.03
Time to walk 50 ft (15 m), s	-1.77 (2.73) (-2.72 to -0.82)	<.001	0.24 (4.81) (-1.44 to 1.92)	.77	0.50	0.03 (7.09) (-2.44 to 2.50)	.98	-0.87 (5.41) (-2.18 to 0.44)	.19

Abbreviations: CI, confidence interval; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

*Pooled analysis: the intervention group at the 8-week follow-up plus the control group at the 16-week follow-up. Effect size, $d = [\Delta(\text{intervention at 8 weeks}) - \Delta\text{C control at 8 weeks}] / \text{pooled SD}$ (ie, intervention plus control at 8 weeks). Data are given as mean (SD) (95% CI). The 95% CI is for the measured change from baseline to follow-up assessment.

†For $P < .05$, difference between the intervention group at the 8-week follow-up and the control group at the 8-week follow-up by repeated measures analysis of variance.

‡P values are for baseline to 8-week and 16-week measurement differences within-group paired t test.

Table 3. Comparison Between Improvements Observed in the Intervention and Control Groups*

Variable	Control Group at 8-wk Follow-up (n = 34)	Intervention Group at 16-wk Follow-up (n = 34)	P Value
WOMAC score, mm			
Pain	-3.08 (17.58) (-9.21 to 3.06)	-18.52 (22.51) (-26.37 to -10.66)	.002
Stiffness	-4.29 (24.18) (-12.73 to 4.14)	-15.51 (22.28) (-23.29 to -7.74)	.05
Functionality	-5.02 (16.37) (-10.73 to 0.69)	-17.05 (20.15) (-24.08 to -10.02)	.009
Global	-4.56 (15.85) (-10.09 to 0.97)	-17.23 (19.88) (-24.16 to -10.2)	.005
VAS pain score, mm	-1.97 (21.07) (-9.32 to 5.38)	-17.15 (21.27) (-24.57 to -9.73)	.004
Range of motion, degree	-1.06 (14.20) (-6.01 to 3.89)	3.88 (13.61) (-0.87 to 8.63)	.15
Time to walk 50 ft (15 m), s	0.24 (4.81) (-1.44 to 1.92)	-2.28 (3.96) (-3.66 to -0.90)	.02

Abbreviations: CI, confidence interval; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

*Data are given as mean (SD) (95% CI). The 95% CI is for the measured change from baseline to follow-up assessment.

16 (ie, 8 weeks after the intervention was completed) with the control group at week 8 (ie, at the end of their non-intervention period) revealed significant, residual mean (SD) differences in pain (-18.52 [22.51] mm vs -3.08 [17.58] mm; $P = .002$), function (-17.05 [20.15] vs -5.02 [16.37]; $P = .009$), WOMAC global score (-17.23 [19.88] mm vs -4.56 [15.85] mm; $P < .005$), VAS score (-17.15 [21.27] mm vs -1.97 [21.07] mm; $P = .004$), and time to

walk 50 ft (15 m) (-2.28 [3.96] seconds vs 0.24 [4.81] seconds; $P = .02$).

SAFETY

Subjects were instructed to report adverse events to the massage therapist; 1 reported increased discomfort and refused to return for the 8-week assessment.

COMMENT

This study suggests that massage therapy using the Swedish technique is safe and effective for reducing pain and improving function in patients with symptomatic OA of the knee. To our knowledge, this is the first prospective, randomized trial assessing the efficacy of massage for OA. Massage has previously shown promise for other musculoskeletal conditions such as rheumatoid arthritis and fibromyalgia.²⁵⁻²⁷ Our results are concordant with these prior findings.

In this study, the magnitude of the treatment effects (ie, effect size) at the 8-week assessment in the WOMAC scale were large, ranging from 0.64 to 0.86 (Table 2). These effects are greater than those observed by Witt et al²⁸ in a large acupuncture trial of similar design.

Using intention-to-treat analysis and carrying forward baseline values likely biased our results toward the null. The treatment effects observed were stronger when limited to only those subjects returning for follow-up. Thus, our findings are a conservative estimate of the magnitude of treatment effect. Losses to follow-up, shown in the Figure, are reflective of the real-world experience with an elderly population with impaired mobility.

We used a wait-list control design because no validated method of performing “placebo massage” has been developed. This did result in increased contact with study personnel for the intervention group during the 8-week intervention. Although Hawthorne effect^{29,30} may have been a factor in our results, both intragroup and intergroup differences were significant at 8 weeks, and the improvements in the intervention group largely persisted at the 16-week follow-up, which was 8 weeks after the subjects finished the weekly massage sessions.

We used Swedish massage because it is one of the more common and readily accessible or practiced techniques in the United States.²² There was limited precedent for selecting frequency, duration, or even type of massage. There may prove to be more—and less—effective approaches, and this will need to be elucidated in subsequent studies.

The potential importance of massage as an adjunct to or even an alternative to pharmacotherapy is self-evident. Current pharmacological treatments for OA are associated with high rates of adverse effects, such as cardiovascular, gastrointestinal, renal, and hepatotoxic effects.^{1,13,31-34} Many patients are already adding or trying massage as a therapy for OA.³⁵⁻³⁸

There are also nonconventional and nutraceutical treatments for OA. Trials regarding the efficacy of glucosamine with or without chondroitin are inconclusive. However, a recent randomized controlled clinical trial (the Glucosamine/chondroitin Arthritis Intervention Trial³⁹) suggested that the combination is effective for patients with moderate to severe OA pain. Other nutraceutical treatments, including devil’s claw and ginger,³⁵ have yet to be proven effective. Recent research has suggested that acupuncture may also be an effective option for patients with OA.⁴⁰ Establishing massage as a therapy for OA would provide an additional option to the current approaches.

Study limitations include a single intervention and homogeneous study sample. Study participants were recruited in northern New Jersey, and most of the subjects in the intervention and control groups were white women; demographic homogeneity may limit generalizability. However, in individuals older than 50 years, knee and hand OA is more prevalent in women than men.⁵ Black and white individuals have similar rates of OA, although higher body weights may contribute to a slightly higher prevalence in black persons.⁵

The study duration was only 16 weeks; OA is a chronic condition, and therefore longer studies will be needed.

Losses to follow-up were noteworthy. However, an intention-to-treat analysis was used, and therefore our findings may be conservative estimates of treatment effect.

Because participants did not keep accurate medication diaries, we cannot reliably know if change in medications in any way affected our results. It seems unlikely that the massage intervention would have caused participants to increase their medication in such a way as to lead to significant improvement in pain and function compared with the control group. Bias toward a null effect is more probable.

In conclusion, this pilot study suggests that massage therapy is efficacious in the treatment of OA of the knee, with beneficial effects persisting for weeks following treat-

ment cessation. Massage therapy seems to be well tolerated by people with painful OA of the knee. Massage also seems to decrease pain and improve function in participants who were allowed to maintain their usual treatment. Given the limitations and potential adverse effects of pharmacologic and nonpharmacologic treatments for OA, massage therapy seems to be a viable option as an adjunct to more conventional treatment modalities. Further study of massage to determine optimal treatment protocols, absolute efficacy, cost-effectiveness, and generalization to other patient groups is clearly warranted.

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REFERENCES

1. Felson DT, Lawrence RC, Hochberg MC, et al. Osteoarthritis: new insights, II: treatment approaches. *Ann Intern Med.* 2000;133:726-737.
2. Praemer A, Furner S, Rice DP. *Musculoskeletal Conditions in the United States.* Rosemont, Ill: American Academy of Orthopaedic Surgeons; 1999.
3. Baird CL. First-line treatment for osteoarthritis, I: pathophysiology, assessment, and pharmacologic interventions. *Orthop Nurs.* 2001;20:17-27.
4. Fajardo M, Di Cesare PE. Disease-modifying therapies for osteoarthritis: current status. *Drugs Aging.* 2005;22:141-161.
5. Arden N, Nevitt MC. Osteoarthritis: epidemiology. *Best Pract Res Clin Rheumatol.* 2006;20:3-25.
6. Elders MJ. The increasing impact of arthritis on public health. *J Rheumatol.* 2000; 60(suppl):6-8.
7. Lawrence RC, Helmick CG, Arnett FC, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum.* 1998;41:778-799.
8. Felson DT. An update on the pathogenesis and epidemiology of osteoarthritis. *Radiol Clin North Am.* 2004;42:1-9.
9. National Center for Health Statistics. Health, United States 2005 with chartbook on trends in the health of Americans. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/nchs/data/hs/hs05.pdf>. Accessed April 10, 2006.
10. Buckwalter JA, Saltzman C, Brown T. The impact of osteoarthritis: implications for research. *Clin Orthop.* 2004;427(suppl):S6-S15.
11. Kato T, Xiang Y, Nakamura H, Nishioka K. Neoantigens in osteoarthritic cartilage. *Curr Opin Rheumatol.* 2004;16:604-608.

12. Matchaba P, Gitton X, Krammer G, et al. Cardiovascular safety of lumiracoxib: a meta-analysis of all randomized controlled trials ≥ 1 week and up to 1 year in duration of patients with osteoarthritis and rheumatoid arthritis. *Clin Ther*. 2005; 27:1196-1214.
13. Naesdal J, Brown K. NSAID-associated adverse effects and acid control aids to prevent them: a review of current treatment options. *Drug Saf*. 2006;29:119-132.
14. Nayak S, Matheis RJ, Agostinelli S, Shiflett SC. The use of complementary and alternative therapies for chronic pain following spinal cord injury: a pilot survey. *J Spinal Cord Med*. 2001;24:54-62.
15. Ernst E. Complementary and alternative medicine for pain management in rheumatic disease. *Curr Opin Rheumatol*. 2002;14:58-62.
16. Preyde M. Effectiveness of massage therapy for subacute low-back pain: a randomized controlled trial. *CMAJ*. 2000;162:1815-1820.
17. Altman R, Asch E, Bloch D, et al; Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis Rheum*. 1986;29:1039-1049.
18. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;15:1833-1840.
19. Geba GP, Weaver AL, Polis AB, Dixon ME, Schnitzer TJ; Vioxx, Acetaminophen, Celecoxib Trial (VACT) Group. Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee: a randomized trial [published correction appears in *JAMA*. 2002;287:989]. *JAMA*. 2002;287:64-71.
20. American Massage Therapy Association. Glossary of terms. American Massage Therapy Association Web site. <http://www.amtamassage.org/about/terms.html>. Accessed April 10, 2006.
21. Taylor AG, Galper DI, Taylor P, et al. Effects of adjunctive Swedish massage and vibration therapy on short-term postoperative outcomes: a randomized, controlled trial. *J Altern Complement Med*. 2003;9:77-89.
22. Wieting JM, Cugali AP. Massage, traction and manipulation. <http://www.emedicine.com/pmr/topic200.htm>. Accessed April 10, 2006.
23. Liang MH, Larson MG, Cullen KE, Schwartz JA. Comparative measurement efficiency and sensitivity of five health status instruments for arthritis research. *Arthritis Rheum*. 1985;28:542-547.
24. Bellamy N. Outcome measurement in osteoarthritis clinical trials. *J Rheumatol Suppl*. 1995;43:49-51.
25. Brattberg G. Connective tissue massage in the treatment of fibromyalgia. *Eur J Pain*. 1999;3:235-244.
26. Field T, Hernandez-Reif M, Seligman S, et al. Juvenile rheumatoid arthritis: benefits from massage therapy. *J Pediatr Psychol*. 1997;22:607-617.
27. Sunshine W, Field TM, Quintino O, et al. Fibromyalgia benefits from massage therapy and transcutaneous electrical stimulation. *J Clin Rheumatol*. 1996; 2:18-22.
28. Witt C, Brinkhaus B, Jena S, et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet*. 2005;366:136-143.
29. Dalessio DJ. Editorial: studies on pain and the hawthorne effect. *Headache*. 1974; 14:109-110.
30. Holden JD. Hawthorne effects and research into professional practice. *J Eval Clin Pract*. 2001;7:65-70.
31. Hogenmiller MS, Lozada CJ. An update on osteoarthritis therapeutics. *Curr Opin Rheumatol*. 2006;18:256-260.
32. Hogue JH, Mersfelder TL. Pathophysiology and first-line treatment of osteoarthritis. *Ann Pharmacother*. 2002;36:679-686.
33. Malonne H, Coffiner M, Sonet B, Sereno A, Vanderbist F. Efficacy and tolerability of sustained-release tramadol in the treatment of symptomatic osteoarthritis of the hip or knee: a multicenter, randomized, double-blind, placebo-controlled study. *Clin Ther*. 2004;26:1774-1782.
34. Perneger TV, Whelton PK, Klag MJ. Risk of kidney failure associated with the use of acetaminophen, aspirin, and nonsteroidal antiinflammatory drugs. *N Engl J Med*. 1994;331:1675-1679.
35. Ernst E. Musculoskeletal conditions and complementary/alternative medicine. *Best Pract Res Clin Rheumatol*. 2004;18:539-556.
36. Nayak S, Matheis RJ, Schoenberger NE, Shiflett SC. Use of unconventional therapies by individuals with multiple sclerosis. *Clin Rehabil*. 2003;17:181-191.
37. Ramsey SD, Spencer AC, Topolski TD, et al. Use of alternative therapies by older adults with osteoarthritis. *Arthritis Rheum*. 2001;45:222-227.
38. Setty AR, Sigal LH. Herbal medications commonly used in the practice of rheumatology: mechanisms of action, efficacy, and side effects. *Semin Arthritis Rheum*. 2005;34:773-784.
39. Clegg DO, Reda DJ, Harris CL, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med*. 2006;354: 795-808.
40. Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AMK, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med*. 2004;141:901-910.