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Evidence-Based Evaluation of Complementary Health Approaches for Pain Management in the United States

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Learning Objectives: On completion of this article, you should be able to (1) name complementary health approaches used for pain management; (2) discuss the evidence supporting the use of complementary health approaches for pain management; and (3) provide examples to your patients of complementary health approaches that might be considered as part of a comprehensive pain management plan.

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Abstract

Although most pain is acute and resolves within a few days or weeks, millions of Americans have persistent or recurring pain that may become chronic and debilitating. Medications may provide only partial relief from this chronic pain and can be associated with unwanted effects. As a result, many individuals turn to complementary health approaches as part of their pain management strategy. This article examines the clinical trial evidence for the efficacy and safety of several specific approaches—acupuncture, manipulation, massage therapy, relaxation techniques including meditation, selected natural product supplements (chondroitin, glucosamine, methylsulfonylmethane, *S*-adenosylmethionine), tai chi, and yoga—as used to manage chronic pain and related disability associated with back pain, fibromyalgia, osteoarthritis, neck pain, and severe headaches or migraines.

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The most recent national estimate suggests that 126 million adults experience some pain in a given year,[1] with about one-third (40 million adults) having severe pain. Pain is often associated with poor general health, health-related disability, and increased health care utilization.[2] Yet according to the Institute of Medicine,[2] pain is routinely undertreated in health care; pain care that is provided is often fragmented, without a comprehensive assessment or treatment plan, and patients may encounter difficulty obtaining the full range of potential treatments.

Back pain, joint pain, neck pain, and headaches are among the most common types of pain experienced by US adults (Table 1).[3-6] The prevalence rates for these conditions have remained relatively stable over time. Among the many pharmacological and nonpharmacological approaches that have been incorporated into pain management strategies are complementary health approaches. This broad category of care includes procedures by licensed practitioners such as acupuncturists, chiropractors, and massage therapists, as well as self-care approaches such as relaxation techniques (eg, meditation) and meditative movement-based approaches (eg, yoga and tai chi) and natural products such a glucosamine and herbal medicines. National surveys going back more than 25 years have consistently found that these complementary approaches are used by about 30% to 40% of the US public in a given year,[7-11] although use of a given approach may wax and wane over time (Table 2).

Although a substantial part of this use is for overall wellness and prevention,[12,13] painful conditions are the most common health conditions for which individuals turn to these complementary approaches.[7,8,10,11,14] In 2007, for example, about 14.3 million adults used a complementary health approach for their back pain, about 5.0 million used these approaches for their neck pain, and 3.1 million for their arthritis.[7] Far fewer individuals used complementary health approaches for other chronic diseases such as depression (1.0 million), hypertension (0.8 million), diabetes (0.7 million), or cancer (0.4 million).

TABLE 1. Age-Adjusted Percentages of Selected Health Conditions Among US Adults, NHIS 2002, 2007, 2012[a]

Health condition	2002[3]	2007[4]	2012[5,6]
Low back pain in the past 3 mo	26.4%	25.4%	27.6%
Arthritis	20.9%	20.3%	20.6%
Neck pain in the past 3 mo	13.8%	12.8%	13.9%
Severe headache or migraine in the past 3 mo	15.0%	12.3%	14.1%
Fibromyalgia during lifetime	NA	NA	1.75%

[a]NA = not available; NHIS = National Health Interview Survey.

TABLE 2. Age-Adjusted Percentages of Use for Selected Complementary Health Approaches by US Adults, 2002-2012

Complementary health approach	2002[7]	2007[8]	2012[9]
Acupuncture	1.1%	1.4%	1.5%
Manipulation	7.5%	8.6%	8.4%
Massage therapy	5.0%	8.3%	6.9%
Meditation	7.6%	9.4%	8.0%
Natural product supplements	18.9%	17.7%	17.7%
Yoga, tai chi, and qigong	5.8%	6.7%	10.1%

Based on national survey data,[14] this high use of complementary health approaches for painful conditions translated into $8.5 billion in out-of-pocket payments for these approaches to manage back pain, $3.6 billion to manage neck pain, and $2.3 billion to manage arthritis. Substantially less is spent out-of-pocket on complementary health approaches to treat other chronic health conditions such as depression ($1.1 billion), hypertension ($0.7 billion), diabetes ($0.3 billion), and cancer ($0.2 billion).

Given the high use of complementary health approaches for pain, a number of specific complementary approaches have undergone mechanistic and clinical evaluations culminating in phase 3 trials. This article examines the clinical trial evidence for the efficacy and safety of several widely used approaches—acupuncture, manipulation, massage therapy, relaxation techniques including meditation, selected natural product supplements (eg, chondroitin and glucosamine), tai chi, and yoga (defined in Supplemental Appendix 1, available online at http://www.mayoclinicproceedings.org)—as used to manage chronic pain and related disability associated with back pain, osteoarthritis (OA), neck pain, and severe headaches or migraines, conditions frequently seen and managed in the primary care setting.

Fibromyalgia was included in this review as an example of a complex pain syndrome that is often managed with a multimodal approach that may include complementary approaches. Cancer pain is certainly a major public health concern but is more likely to be addressed outside the primary care setting (eg, by oncologists, at cancer centers, as part of palliative care).

The randomized, controlled clinical trial (RCT) is considered the strongest study design for investigating the efficacy and safety of pharmacological, behavioral, and physical interventions. To identify examples of RCTs for each complementary approach, we performed searches of the MEDLINE database for articles published from January 1, 1966, through March 31, 2016, using the search strategy outlined in Supplemental Appendix 2 (available online at http://www.mayoclinicproceedings.org). In order to make this review as relevant as possible to primary care physicians in the United States, we limited this review to RCTs either proformed in the United States or that included participants from the United States. This decision was based on 2 factors. First, the unique health care system in the United States vs other countries means that the standard care or usual care control groups used in the United States and other countries may vary substantially. Thus, whether a given complementary approach performs better than usual care in another country may not reflect how the approach would perform in US trials. Another factor is that the training and licensure of acupuncturists, chiropractors, and naturopathic doctors vary substantially among countries, as does the marketing, regulation, and use of dietary supplements. For instance, in Germany, the location of some of the largest acupuncture trials, acupuncture is only practiced by medical doctors, whereas the vast majority of acupuncture treatment in the United States is provided by licensed acupuncturists. Thus, the findings from German trials may not be directly comparable to acupuncture as practiced in the United States.

Brief summaries of the reviewed RCTs are presented with details provided in online supplemental tables. The findings of these RCTs also illustrate several methodological issues that should be considered when interpreting the trial data. These issues are summarized briefly at the end of this article.

LOW BACK PAIN

Acupuncture

We found 4 RCTs (total participants, 1092)[15-18] that assessed the clinical benefit of acupuncture for treatment of low back pain (LBP) (age range, 28-60 years; most participants were white) and used primary study outcomes of self-report of pain intensity (numeric rating scale or visual analog scale [VAS]) and/or functional disability (Roland-Morris Disability Questionnaire, Oswestry Disability Index [ODI], or Disability Rating Index). Cherkin et al[15,16] reported modest improvement in pain intensity and function compared with usual care. In pregnant women using auricular acupuncture, Wang et al[17] found a significant reduction in pain intensity and improved functional status compared with no treatment. Comparison of verum to sham acupuncture had mixed results, with 2 RCTS[16,18] finding no significant difference and 1 RCT[17] finding a slight but significant difference. No significant adverse events were reported.

Massage Therapy

We identified 8 RCTs that studied the use of massage for LBP[15,19-25] (total participants, 829). Massage types included Swedish/relaxation, structural, structural integration, and muscle energy; sessions varied in duration from 15 to 90 minutes. For chronic LBP (cLBP), 2 larger studies[15,19] comparing massage with usual care reported modest improvements in pain and function at 10 weeks, but the benefit was not sustained at 52 weeks.[15] Three smaller studies compared massage to either usual outpatient rehabilitation[24] or relaxation[22,23] and did not observe significant between-group differences for pain and/or function. For acute or subacute LBP, 2 smaller studies found significant, albeit modest, improvements in pain compared with no treatment (−1.5 points on a numeric rating scale)[21] or function (−18% on the ODI)[25] compared with a putative placebo. No RCTs reported significant adverse events.

Osteopathic Manipulative Therapy

Six RCTs of osteopathic manipulative therapy (OMT) for LBP were identified (total participants, 1308).[26-31] Two RCTs examined OMT compared with sham OMT for cLBP[30,31] using

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similar intervention paradigms and reported mixed results, with 1 finding no significant difference and 1 reporting a 9-mm reduction in pain intensity on a VAS. Two RCTs compared OMT with usual care for acute or subacute LBP,[26,27] and both reported no significant improvement for function/disability but mixed results for pain intensity for between-group differences. In pregnant women with LBP, 2 studies compared the benefit of adding OMT or placebo ultrasound treatment to usual obstetric care and reported significant modest improvements with added care but no significant between-group differences.[28,29] No RCTs reported significant adverse events.

Spinal Manipulation

We reviewed 24 RCTs[32-55] (total participants, 4503; all adults) of spinal manipulation (SM) for LBP. Recent data suggest that for cLBP, the "dose" of SM (defined as the number of sessions) may affect outcomes,[45,46,56] and hence the dose utilized was dichotomized for this report depending on whether 6 or more sessions of SM were provided in a given study. No RCTs reported significant adverse events.

Chronic LBP. There were 9 studies of SM for cLBP (total participants, 1882),[32,35-37,40,44-46,50] 8 of which employed 6 or more sessions for treatment, and 1 of these studies included principally (more than two-thirds) adult women.[32] Among the 4 larger RCTs (each with 200 or more participants)[37,44,46,50] that compared high-velocity low-amplitude SM with an active comparison (exercise, usual care, physical therapy, light touch), 3 found significant, albeit modest, between-group differences for pain intensity and/or function. Two studies directly examined the dose of high-velocity low-amplitude SM,[45,46] and both found that higher doses (12 and 18 sessions of SM) provided larger improvement at 12 and 52 weeks, respectively. One RCT utilized a putative placebo SM[32] and found that after the first session, the results of verum SM were better than sham SM and better than no treatment, but at 2 weeks, there were no significant between-group differences. One RCT compared thrust to nonthrust SM[40] (less than 6 sessions) and reported no significant between-group differences.

Acute, Subacute, or Mixed LBP. There were 15 studies of SM for either acute, subacute, or a mixture of types of LBP (total participants, 2621).[33,34,38,39,41-43,47-49,51-55] Six of these studies were of modest to moderate size (ie, >100 participants) and utilized 6 or more sessions of SM.[38,42,49,51,53,54] The results of these studies were mixed, with some reporting modest significant benefit of SM compared with active intervention (physical therapy, education ["back school"], medication, usual care) at about 4 weeks for pain intensity and/or function,[42,49,54] but others reporting no significant between-group differences.[38,51,53] One RCT examined pregnant women with LBP[42] and found that adding SM and exercise to usual obstetric care provided modest improvement in pain and function/disability.

There were 5 studies of SM for either acute and/or subacute LBP that used less than 6 treatment sessions,[33,39,41,47,55] but only 1 of these (and the largest) was an effectiveness study: Fritz et al[41] conducted an RCT of 4 sessions over 4 weeks of SM plus exercise vs usual primary care and at 3 months found significant between-group improvement in function (−3.2 points on the ODI). The other 4 studies (sample sizes ranged from 54 to 123 patients) compared different types of SM and/or SM with an active intervention (eg, exercise). In general, these 4 studies reported that all groups had improvement in back pain, and there were very small or no significant between-group differences. However, it is unclear whether these 4 studies were sufficiently powered to definitively ascertain whether differences existed.

There were 4 studies of SM that by design addressed mixed LBP[34,48,52,53] (ie, the inclusion criteria allowed participants with acute, subacute, or chronic LBP); 3 of these studies utilized 6 or more treatment sessions. All studies had one or more active comparison groups (eg, massage, electrical stimulation, usual care, corticosteroid injection, physical therapy), and in all studies, all groups improved but there were no significant between-group differences.

Yoga

We identified 6 RCTs of yoga for cLBP[57-62] (total participants, 596; all adults, predominantly female). Three named forms of yoga were studied: hatha,[57,58] viniyoga,[59,60] and iyengar[61,62]; all were performed in group settings, with class durations from 60 to 90 minutes and the

number of sessions ranging from 12 to 24, either once or twice per week, with recommendations for home practice. Compared with usual care, 2 studies[59,60] found that yoga provided improvements in pain and function, but the results were mixed when compared with exercise/stretching. A dose-response study[57] compared once-weekly to twice-weekly classes and found that they produced equivalent improvements in pain intensity and function. Three smaller studies compared yoga with wait list[58,61] or education control[62] and reported significant modest reductions in pain intensity and function/disability. No RCTs reported significant adverse events.

Additional information on all back pain RCTs can be found in Supplemental Table 1 (available online at http://www.mayoclinicproceedings.org).

FIBROMYLGIA

All trials we reviewed for fibromyalgia used the 1990 American College of Rheumatology (ACR) classification criteria,[63] except one[64] that used an older definition.

Acupuncture

Four RCTs examined acupuncture vs sham acupuncture for pain, physical function, global well-being, sleep, fatigue, and adverse events.[65-68] Martin et al[68] found a significant improvement between electroacupuncture vs sham electroacupuncture. Differences were seen on the Fibromyalgia Impact Questionnaire (FIQ) scores for fatigue and anxiety. No other trial found significant differences between groups on any outcome. There were no serious adverse events reported in any of these studies. In one study, minor adverse events (eg, discomfort at the site of needle insertion or simulation of needles) were reported by 89% of participants.[65]

Relaxation Techniques

Two studies (93 total participants, mostly female and white) investigated biofeedback vs control groups (attention control and placebo) as a treatment for symptoms of fibromyalgia.[64,69] Buckelew et al[64] found a significant improvement in the Tender Point Index score in the biofeedback group vs an attention control group but not for any other outcome measure. Nelson et al[69] did not find any differences between biofeedback and a placebo biofeedback. A small study (90 women) found that mindfulness-based stress reduction significantly reduced perceived stress and sleep disturbance and lessened the severity of symptoms in persons with fibromyalgia vs a wait list control group.[70] Another RCT examined the effects of affective self-awareness, a technique that places primary importance on the awareness and expression of emotions underlying fibromyalgia symptoms, in 45 women with fibromyalgia and found significant pain reduction and improved physical functioning vs a wait list control group.[71] Astin et al[72] examined the effects of an intervention combining mindfulness meditation and qigong and found that the combined intervention yielded no better results than an educational/support control group for pain, depression, and physical functioning. Two studies[73,74] (112 total participants, mostly female) examined guided imagery vs usual care as a treatment for symptoms of fibromyalgia. One study[74] found a significant decrease in the FIQ score compared with the usual care control group. The second study[73] found positive effects of guided imagery on pain intensity, fatigue, and depression vs the control group. Both studies found improvements in self-efficacy for managing symptoms. Only one study[69] reported on adverse events, and none were noted.

Massage

A small study (12 women) examined Swedish massage vs myofascial release therapy for fibromyalgia symptoms.[75] No difference was seen between groups on the FIQ.

Tai Chi

A study of 98 adults with fibromyalgia (aged 40 years and older, mostly white and female) compared Yang-style tai chi (modified for fibromyalgia patients) with an educational control and found that the tai chi group had a greater decrease in the FIQ score.[76] Another study (59 adults with fibromyalgia) compared Yang-style tai chi with a control combining wellness education and stretching classes and found that the tai chi group had greater improvement in the FIQ score.[77]

Yoga

A small study (53 women) investigated yoga vs wait list for management of fibromyalgia

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symptoms and found that those practicing yoga had significant improvement in the FIQ score.[78] No adverse events were noted.

Additional information on all fibromyalgia RCTs can be found in Supplemental Table 2 (available online at http://www.mayoclinicproceedings.org).

NECK PAIN

Massage

Four randomized controlled trials examined whether massage could relieve symptoms associated with chronic neck pain.[79-82] One study did not report patient demographic characteristics, and the others studied patients aged 20 to 64 years. Primary outcomes included scores on the Neck Disability Index (NDI) (a 10-item neck pain questionnaire), the pain VAS, and range of motion. Sherman et al[81] found significant improvement of the NDI score for those randomized to 10 massage therapy session over 10 weeks vs those assigned to a self-care book on managing neck problems. In an RCT by Field et al,[80] individuals were randomized to either a wait list control or 30 minutes of massage therapy weekly for 4 weeks combined with daily self-massage. At the completion of the intervention, those assigned to massage therapy had improvements in pain and range of motion compared with the control group. Sherman et al[82] reported a dose-response relationship between the number and duration of massage sessions per week and improvement in the NDI score and neck pain intensity. The findings indicated that 60 minutes of massage 2 to 3 times per week was significantly better than either 30 or 60 minutes of massage once per week after the 4 weeks of treatment. In a follow-up to the study by Sherman et al,[82] Cook et al[79] obtained repeated consent from the participants and randomized them to one additional massage therapy session per week for 6 additional weeks. At the end of treatment, those randomized to the additional sessions had significantly improved pain and function vs those who did not receive the additional sessions; the difference between groups was no longer significant after 14 weeks of follow-up.

Spinal Manipulation

We reviewed 3 randomized trials of SM for neck pain.[83-85] One study assessed manipulation compared with mobilization with a 2×2×2 factorial design: with or without heat or with or without electrical muscle stimulation[84]; no significant differences in outcomes were seen between groups. Evans et al[83] compared SM combined with supervised exercising to supervised exercising alone and also to home exercise. After completion of the 12-week intervention, no difference was seen between SM combined with supervised exercising and supervised exercising alone; however, both these groups had significant improvement in neck pain vs only home exercise. Maiers et al[85] assessed the efficacy of 3 treatments: (1) SM plus home exercise, (2) supervised rehabilitation exercise plus home exercise, and (3) home exercise alone. Spinal manipulation with home exercise produced significantly better reduction in pain than home exercise alone. No significant difference was seen between SM and home exercise vs supervised rehabilitation exercise plus home exercise.

There was one RCT of manual cervical distraction,[86] a traction-based therapy with low, medium, and high forces assessed. The goal of the study was to identify a viable sham control. The study end points included pain VAS, NDI score, and a credibility and expectancy questionnaire. The investigators did report benefit in medium- or high-force interventions.

Additional information on all neck pain RCTs can be found in Supplemental Table 3 (available online at http://www.mayoclinicproceedings.org).

OA OF THE KNEE

Acupuncture

Four RCTs examined whether acupuncture could relieve symptoms associated with OA of the knee.[87-90] These studies used similar definitions of knee OA. Participants were predominantly female, had mean ages between 60 and 65 years, and had knee pain for an average of 9 to 11 years. All studies incorporated either the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total score or the WOMAC pain subscore as the primary outcomes. In 2 of the trials,[89,90] no difference was seen between verum acupuncture and sham acupuncture for either the primary or secondary outcome measure. The third trial,[87] which used a sham control, found significantly better

improvement in both the WOMAC pain subscale and function subscale after 14 weeks of treatment. For the 3 trials that also incorporated either an attention control[87] or standard care controls,[88,90] verum acupuncture produced significantly better improvement in primary and secondary outcomes than that observed in the control group. Across trials, adverse events associated with acupuncture were few, with the most common complaints being pain at the needling site and muscle soreness that resolved soon after the treatment session ended.

Glucosamine and Chondroitin

We reviewed 8 RCTs examining the efficacy of 2 dietary supplements, glucosamine and/or chondroitin, in individuals with knee OA.[91-98] These studies varied substantially in how knee OA was defined, as well as in the primary outcome measures used.

Three different configurations of glucosamine were used: glucosamine hydrochloride (HCl),[93-95] glucosamine sulfate,[91,92,98] and glucosamine bound to a polymer.[97] One trial did not identify the configuration of glucosamine.[96] Doses of glucosamine varied from 1000 mg/d for 6 weeks[98] to 1500 mg/d for 24 weeks.[91,95] Chondroitin sulfate was studied in 2 trials at a dose of 1200 mg/d for 6 months[91,95] and in 1 trial at the same dose but for 8 weeks.[93] All studies employed a placebo control group. Participants in 2 trials were exclusively[93] or predominantly[96] males, participants in 4 other trials were predominantly females,[91,94,95,98] and the remaining 2 trials had a close balance of men and women.[92,97] The mean age of the trial participants varied from 45 years[93] to 72 years.[95] Mixed results were found in trials comparing glucosamine vs a placebo control with pain relief or functional improvement as the primary outcomes. Three trials found glucosamine superior to placebo,[92,97,98] and 3 trials found no difference between groups.[91,94,96]

Mixed results were seen in the 3 trials studying a combination of glucosamine and chondroitin. Leffler et al[93] found that a combination of glucosamine HCl and chondroitin sulfate (and manganese acerbate) was superior to placebo for providing pain relief. In 2 other trials, the combination of glucosamine (either sulfate or HCl) and chondroitin sulfate were no better than placebo for either pain relief or function.[91,95]

Across trials, adverse events were generally mild (gastrointestinal distress being the most common) with no differences seen between those taking glucosamine or chondroitin and those taking placebo.

Massage Therapy

Two RCTs studied the efficacy of Swedish massage therapy for symptoms associated with OA of the knee.[99,100] The 2 studies were similar in that both defined knee OA using the ACR criteria,[101] required a baseline score of at least 40 on the pain VAS, and included participants who were predominantly white females. In the earlier study,[100] after completing the 8-week intervention, participants in the massage group had significant improvement vs those randomized to usual care in the WOMAC total score as well as in each of the WOMAC subscale scores (pain, function, and joint stiffness). In a dosing study,[99] individuals were randomized to 1 of 5 groups for 8 weeks: (1) usual care, (2) 240 minutes of massage over 8 weeks, (3) 360 minutes of massage, (4) 480 minutes of massage, and (5) 600 minutes of massage. Only individuals receiving at least 480 minutes of massage therapy (groups 4 and 5) had substantial improvement in the WOMAC total score and the WOMAC pain subscale score vs the usual care group. Across the 2 trials, only one adverse event, discomfort at the knee in one participant, was noted.

Methylsulfonylmethane

One RCT compared methylsulfonylmethane (MSM) (6 g/d for 12 weeks) with a placebo control.[102] Knee OA was based on ACR criteria.[101] Outcome measures were the WOMAC subscale scores for pain, function, and stiffness. Individuals randomized to MSM had significant improvement in both the WOMAC pain and functions scale scores. However, the authors cautioned that the differences between groups were small (<20%) and probably not clinical meaningful. No difference in adverse events was seen between groups.

S-Adenoylsmethionine

One RCT compared the dietary supplement *S*-adenoylsmethionine (SAMe) (1200 mg/d) with celecoxib (200 mg/d for 16 weeks) in a

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crossover design that included a 1-week washout period.[103] Knee OA was defined by ACR criteria,[102] and the study population was primarily female and white. The primary outcomes were pain VAS scores, WOMAC subscale scores for pain, function, and stiffness, and clinician assessments of OA severity. By the end of the trial, no differences were seen between the 2 treatment arms on any of the outcome measures. However, the sample size was insufficient to establish equivalency. Overall, adverse events were less common in those taking SAMe than in those taking celecoxib.

Tai Chi

We reviewed 4 RCTs that examined the efficacy of tai chi in patients with confirmed knee OA using various criteria for diagnosis.[104-107] The 4 RCTs had similar study populations, primarily white and female, with mean ages ranging from 65 to 79 years. Mean body mass index (calculated as weight in kilograms divided by height in meters squared) was also similar across the studies, ranging from 27.8 to 30.0 kg/m^2.

In the study by Hartman et al,[105] participants randomized to a Yang-style tai chi group had significant improvement on the Arthritis Self-Efficacy Scale vs those in the routine care group. The remaining trials compared tai chi to attention controls.[104,106,107] All found that the tai chi (either Yang style or Sun style) groups did better than the attention control groups on both primary and secondary outcomes. Across trials, the most common adverse event associated with tai chi was minor muscle soreness that resolved after a few days.

Yoga

Park et al[108] completed a quasi-experimental trial with participants randomized to either sitting yoga or Reiki; however, the attention control group was chosen as a convenience sample from other participants meeting the inclusion/exclusion criteria. The primary outcome measures were the WOMAC total score and the WOMAC pain, function, and stiffness subscale scores. The mean age of participants was 80 years, with 68.7% being male. Individuals randomized to yoga had substantially better reduction in the WOMAC function score than either the Reiki group or the attention control group ($P<.02$). No other differences were seen between the 3 groups. No adverse advents were reported for any of the groups in this study.

Additional information on all OA RCTs can be found in Supplemental Table 4 (available online at http://www.mayoclinicproceedings.org).

SEVERE HEADACHE AND MIGRAINE

Most of the studies we reviewed defined cervicogenic headache, migraine, and tension-type headache with criteria from the International Classification of Headache Disorders, second edition.[109,110]

Acupuncture

Coeytaux et al[111] randomized patients with chronic daily headache to management by a neurologist with or without acupuncture. The acupuncture group had significantly reduced headache impact test scores vs the control group, but there were no significant differences in pain severity.

Massage

One small study that compared myofascial trigger point massage, a sham device, and wait list found that massage reduced headache frequency but did not significantly reduce the intensity or duration of headaches.[112]

Omega-3 Fatty Acids

One study randomized adolescents with migraine to omega-3 fatty acid or placebo in a crossover study.[113] Adolescents experienced a reduction in headache frequency when taking either fish oil or placebo, but there was no significant difference between the treatments. Another study randomized patients with chronic headaches to increased omega-3 and lower omega-6 fatty acids in the diet or to lower omega-6 fatty acids in the diet.[114] The participants on high omega-3 and low omega-6 fatty acid diets had greater improvement on the Headache Impact Test and in the number of headache days.

Relaxation Techniques

Six trials that we reviewed evaluated stress management, relaxation, or biofeedback for headache disorders.[115-120] Slavin-Spenny et al[120]

TABLE 3. Summary of Evidence for Selected Complementary Health Approaches by Type of Pain (Sham or Placebo and/or Attention Controls)[a,b]

Approach	Back pain	Fibromyalgia	OA of knee	Neck pain	Severe headache/migraine
Acupuncture	1 Positive trial, 2 negative	1 Positive trial, 3 negative trials	1 Positive trial, 3 negative	NA	NA
Chondroitin	NA	NA	1 Negative trial	NA	NA
Glucosamine	NA	NA	2 Positive trials, 3 negative trials	NA	NA
Chondroitin and glucosamine	NA	NA	1 Positive trial, 2 negative trials	NA	NA
Massage therapy	1 Positive trial	NA	NA	2 Positive trials	1 Positive trial
MSM	NA	NA	1 Positive trial	NA	NA
Omega-3 fatty acids	NA	NA	NA	NA	1 Negative trial
Relaxation approaches	NA	1 Positive trial, 2 negative	NA	NA	3 Positive trials
SAMe	NA	NA	NA	NA	NA
Spinal manipulation	6 Positive trials, 3 negative	NA	NA	1 Negative trial	1 Positive trial
Osteopathic manipulation	1 Positive trial, 1 negative	NA	NA	NA	NA
Tai chi	NA	2 Positive trials	3 Positive trials	NA	NA
Yoga	1 Positive trial	NA	1 Positive trial	NA	NA

[a]MSM = methylsulfonylmethane; OA = osteoarthritis; NA = no US randomized controlled trials identified; SAMe = *S*-adenoyslmethionine.

[b]Positive trials are those in which the complementary approach provided statistically significant improvements in pain severity or pain-related disability or function compared with the control group. Negative trials are those in which no difference was seen between groups.

randomized students with chronic headache to expression training, relaxation training, or wait list. Both active treatments produced significant decreases in headache frequency vs the wait list control but did not differ among themselves. Two trials examined complementary approaches to either tension headaches or migraine.[116,117] D'Souza et al[117] randomized students to relaxation training, written emotional disclosure, or neutral writing. The relaxation group had greater reductions in headache frequency and the associated headache disability compared with the other 2 groups. Devineni and Blanchard[116] randomized participants to an Internet behavioral intervention or a wait list. Participants in the behavioral intervention had improvement in the headache index score vs those in the wait list group. A trial randomized children with migraine to hand-warming biofeedback with stress management, hand-cooling biofeedback (attention control), or wait list.[119] The warming biofeedback group had improved headache index scores compared with the other groups. Holroyd et al[118] randomized participants with chronic tension headache to tricyclic antidepressant, placebo, stress management, or stress management plus tricyclic antidepressant. Both the medication and stress management groups had improvements over placebo, but the combination produced the best outcomes. Blanchard et al[115] randomized patients with headache to biofeedback with relaxation training, biofeedback plus cognitive therapy, sham meditation, or a headache monitoring control condition. All of the treatment groups including the sham meditation group had improvements in the headache index score in comparison with the monitoring control group.

Spinal and Osteopathic Manipulation

One trial randomized patients with chronic cervicogenic headache to 2 doses of SM or light massage.[121] Based on the literature, the light massage should have little, if any, specific effects and was therefore chosen as a control for time and physical contract with the patient. Haas et al[121] found improvement over all time points favoring SM compared with light massage and a dose effect with the SM. Two RCTs were identified that assessed manipulation in individuals with tension headache.[122,123] The first trial randomized patients with chronic tension-type headache to SM or amitriptyline and found no

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TABLE 4. Summary of Evidence for Selected Complementary Health Approaches by Type of Pain (Wait List, Usual Care, or Routine Care Controls)[a,b]

Approach	Back pain	Fibromyalgia	OA of knee	Neck pain	Severe headache/migraine
Acupuncture	2 Positive trials	NA	2 Positive trials	NA	1 Positive trial
Massage therapy	3 Positive trials, 1 negative	NA	2 Positive trials	3 Positive trials	NA
Natural products supplements	NA	NA	NA	NA	NA
Relaxation approaches	NA	4 Positive trials	NA	NA	4 Positive trials
Spinal manipulation	4 Positive trials, 3 negative	NA	NA	NA	NA
Osteopathic manipulation	2 Positive trials, 2 negative	NA	NA	NA	NA
Tai chi	NA	NA	1 Positive trial	NA	NA
Yoga	4 Positive trials	1 Positive trial	NA	NA	NA

[a]No US RCTs identified; OA = osteoarthritis.

[b]Positive trials are those in which the complementary approach provided statistically significant improvements in pain severity or pain-related disability or function compared with the control group. Negative trials are those in which no difference was seen between groups.

differences between the groups[122]; however, the trial did not appear to be powered to detect noninferiority. The second study was a small trial that randomized patients to osteopathic manipulation, a palpation examination, or no treatment.[123] The authors noted an improvement in headache severity for the SM group; however, no statistical comparisons were made between groups. Nelson et al[124] randomized patients with migraine to amitriptyline, SM, or both treatments. Their study found no significant differences between the groups; however, it did not appear that the trial was powered to detect noninferiority.

Additional information on all headache RCTs can be found in Supplemental Table 5 (available online at http://www.mayoclinicproceedings.org).

OVERALL SUMMARY OF RCT DATA

Tables 3 and 4 provide concise summaries of the reviewed clinical trial data for each complementary approach stratified by painful health conditions and various control groups. In these tables, positive trials are those in which the complementary approach provided statistically significant improvements in pain severity or pain-related disability or function compared with the control group. Negative trials are those in which no difference was seen between groups. Based on a preponderance of positive trials vs negative trials, current evidence suggests that the following complementary approaches may help some patients manage their painful health conditions: acupuncture and yoga for back pain; acupuncture and tai chi for OA of the knee; massage therapy for neck pain with adequate doses and for short-term benefit; and relaxation techniques for severe headaches and migraine. Weaker evidence suggests that massage therapy, SM, and osteopathic manipulation might also be of some benefit to those with back pain, and relaxation approaches and tai chi might help those with fibromyalgia.

SAFETY

Generally, the reporting of safety data in the reviewed RCTs was minimal. For those trials that did report safety data, we have summarized this information in the text for each painful health condition. In no case did an RCT identify a serious adverse event associated with any of the complementary approaches examined. The most common adverse events (gastrointestinal distress) were noted in trials of dietary supplements (glucosamine, chondroitin, MSM, SAMe). In some trials, tai chi and yoga were associated with minor muscle or joint soreness, and acupuncture was associated with minor pain and/or bruising at the needling site.

Comparisons to Recent Systematic Reviews

Our search criteria identified a number of recent (2010 or later) systematic reviews that covered our topics of interest.[125-133] Conclusions from these systematic reviews for practitioner approaches (acupuncture, chiropractic, massage therapy)[125-131] and dietary supplements[132] were generally consistent with our findings. For instance, in a comprehensive review of both pharmacological and nonpharmacological

approaches to management of back pain, Chou et al[125] found that acupuncture and yoga appear to be effective for improving pain and/or function in patients with back pain. A Cochrane systematic review concluded that acupuncture was a viable treatment option for OA of the knee.[127] Also concurring with the present analysis, the meta-analysis by Deare et al[126] concluded that acupuncture was not an effective therapy for pain or function in individuals with fibromyalgia. In their systematic review, Posadzki and Ernst[128] found little data supporting the use of SM for headaches. Supporting our conclusions is a recent comprehensive meta-analysis of trials studying glucosamine for OA,[132] which found considerable variability in results across trials and concluded that neither glucosamine sulfate nor glucosamine HCl provides pain relief. The RCTs examined in 2 systematic reviews of yoga for arthritis[129,130] overlapped considerably with RCTs in the present review. The authors of the systematic reviews concluded that yoga appears to be a viable option for relieving pain and discomfort associated with arthritis but that larger, better designed trials were needed. A recent systematic review[131] that included international trials found that "clinically relevant effects of OMT were found for reducing pain and improving functional status" for those with back pain. Although this conclusion is stronger than ours, the authors identified deficiencies in trial methodology and called for larger, better quality RCTs to provide firm conclusions. Not all recent systematic reviews agreed with our conclusions. A recent Cochrane Collaboration meta-analysis[133] concluded that SM was no more effective than "inert" interventions for managing back pain and related disability. However, this review only included RCTs published through 2009. We reviewed 8 RCTs published since then. Of these 8 later RCTs, 2 were negative trials[27,32] and 6 were positive trials.[36,41-43,46,54] Inclusion of these trials into the meta-analysis might have lead Rubinstein et al[133] to draw a different conclusion.

Caveats

A number of methodological issues temper our conclusions. The trial samples tend to be white, female, and older, with very few, if any, minority group participants; as such, the generalizability of the findings to the breadth of patients seen by primary care physicians in the United States is still unresolved. Often, the trials reviewed were small, with fewer than 100 total participants. Small trials are prone to more variability and to false-negative results. In many of the trials in which the statistical superiority of a given complementary health approach was reported, it was not clear if the differences vs the control group were clinically relevant. For the given painful health condition, a wide number of outcome measures were often used to assess pain and function. This plethora of outcomes may partly explain the conflicting results seen across trials. For most complementary approaches, there are no standard treatment protocols or algorithms, and in the case of dietary supplements, no rigorously established dosages and products; as such, trials of a given complementary approach rarely compare the exact same intervention. Our findings that relatively few mild adverse events and no serious adverse events were associated with complementary approaches are consistent with the findings from a number of systematic reviews.[125-133] However, even large clinical trials are not powered to identify infrequent adverse events, and therefore, it is likely that this review underestimates the entire range of events associated with the complementary approaches examined. Finally, our review was intended to be an overview of data from RCTs performed in the United States. The inclusion of RCTs performed outside the United States may have resulted in a different set of recommendations.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **ACR** = American College of Rheumatology; **cLBP** = chronic low back pain; **FIQ** = Fibromyalgia Impact Questionnaire; **HCl** = hydrochloride; **LBP** = low back pain; **MSM** = methylsulfonylmethane **NDI** = Neck Disability Index; **OA** = osteoarthritis; **ODI** = Oswestry Disability Index; **OMT** = osteopathic manipulative therapy; **RCT** = randomized, controlled clinical trial; **SAMe** = *S*-adenosylmethionine; **SM** = spinal manipulation; **VAS** = visual analog scale; **WOMAC** = Western Ontario and McMaster Universities Osteoarthritis Index

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National Institutes of Health, 6707 Democracy Blvd, Ste 401, Bethesda, MD 20892-5475 (NahinR@mail.nih.gov). Individual reprints of this article and a bound reprint of the entire Symposium on Pain Medicine will be available for purchase from our website www.mayoclinicproceedings.org.

The Symposium on Pain Medicine will continue in an upcoming issue.

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